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Oral Presentation Abstracts

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OAI-1

Early Detection of Hematologic Malignancies Using Machine Learning Models on Routine Complete Blood Count (CBC) Parameters

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Background and aim: early identification of hematologic malignancies remains a major challenge in clinical hematology, particularly when initial symptoms are subtle and routine laboratory results appear nonspecific. The complete blood count (CBC) is one of the most widely available and cost-effective diagnostic tests worldwide; however, interpretation of its complex multivariate patterns relies heavily on clinician expertise. Recent advances in machine learning (ML) offer the potential to automatically detect abnormal hematologic profiles and recognize early malignant signatures that may not be clinically apparent. This study aims to evaluate the capability of ML algorithms to predict hematologic malignancies using routine CBC parameters.

Methods: A retrospective dataset of anonymized CBC profiles was used, consisting of adult patients categorized into: (1) confirmed hematologic malignancy cases, and (2) non-malignant controls. Standard CBC indices—including WBC, RBC, Hb, Hct, MCV, MCH, MCHC, RDW, Platelet count, and differential leukocyte parameters—served as input features. Multiple machine-learning models were developed, including Logistic Regression, Random Forest, Support Vector Machine (SVM), and XGBoost. Data preprocessing included normalization, outlier detection, and handling of class imbalance using SMOTE. Feature importance analysis was conducted to identify the most predictive CBC variables. Model performance was assessed using cross-validation and evaluated by accuracy, sensitivity, specificity, and ROC-AUC. Normal and abnormal reference ranges were not manually encoded; the models learned discriminatory patterns directly from the dataset.

Results: Among the tested models, XGBoost demonstrated the highest predictive performance, with an accuracy of ≈92%, sensitivity ≈90%, specificity ≈93%, and an ROC-AUC of ≈0.95. RDW, WBC, platelet count, and absolute neutrophil/lymphocyte parameters ranked highest in feature importance analysis. Machine-learning algorithms successfully identified complex multivariate patterns suggestive of early malignant transformation that were not easily captured by single-parameter thresholding.

Conclusion: Machine-learning analysis of routine CBC parameters provides a promising, low-cost, and widely applicable approach for early detection of hematologic malignancies. Integrating ML-based alerts into laboratory information systems (LIS) may assist clinicians in risk stratification, prioritize high-risk CBC profiles, and support earlier diagnosis and timely referral.

keywords: Machine Learning- Hematologic Malignancies- CBC Analysis- Early Detection- XGBoost

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OAI-2

Deep Learning-Assisted Detection of NAFLD/NASH Using Blood Biomarkers with FibroScan-Aware Imputation

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Background and aim: Non-alcoholic fatty liver disease (NAFLD) and its progression to non-alcoholic steatohepatitis (NASH) affect ~25% of the global population, representing a significant health burden. Early detection is crucial, however gold-standard liver biopsy is invasive and impractical for widespread screening. While Transient Elastography (FibroScan) offers valuable liver stiffness measurements (LSM) and controlled attenuation parameter (CAP), the devices are costly and not universally available. The objective of this study is to classify healthy,_NAFL,_NASH status using routine blood biomarkers, combined with tree-based imputation of missing FibroScan values.

Methods: This study analyzed data from 4,000 participants sourced from the NAFLD section of the CDC website. Disease status (Healthy, NAFL, NASH) was labeled based on standard thresholds for (LSM) and (CAP) obtained via FibroScan. Following data preprocessing, including missing value imputation, regression models were initially developed to impute LSM and CAP values. These models used a range of demographic, anthropometric, and laboratory parameters as inputs (including Age, Sex, BMI, Waist, AST, ALT, GGT, Albumin, HbA1c, Glucose, Cholesterol, Triglyceride, HDL, Platelet, excluding LSM and CAP themselves). Subsequently, classification models (Random Forest, Neural Network, and Logistic Regression) were trained using all features, along with actual or imputed LSM and CAP values, to predict disease status. Model performance was then evaluated using standard metrics.

Results: For the imputation of LiverStiffness values, the Random Forest model was selected as the best performer among those tested, achieving a Coefficient of Determination (R^2) of approximately 0.185, although its precision was noted as limited. For CAP imputation, the Gradient Boosting model provided more acceptable performance with an R^2 of approximately 0.504. In the subsequent disease classification stage, a Neural Network model was chosen as the final predictive model, demonstrating an overall accuracy of 99% and a macro F1-score of 0.97. This model exhibited a strong ability to differentiate among Healthy, NAFL, and NASH classes, notably with error-free detection of Healthy individuals and high precision and recall for NAFL and NASH classes.

Conclusion: This study developed and evaluated models for the imputation of LiverStiffness and CAP values, as well as for the prediction of NAFLD status. The results indicated that CAP imputation using a Gradient Boosting model ($R^2 \approx 0.50$) is feasible with acceptable accuracy. However, accurate prediction of LiverStiffness (best R^2 with Random Forest ≈ 0.185) remained a significant challenge, suggesting the complexity of this variable or the need for more informative features. For final disease prediction, although the Random Forest model achieved 100% accuracy, the Neural Network model, with 99% accuracy

keywords: Non-alcoholic Fatty Liver Disease (NAFLD), Machine Learning, Data Imputation, FibroScan

OAI-3

Design and Validation of a Deep 1D Convolutional Neural Network Platform for Prediction of Carbapenem Resistance in Pseudomonas aeruginosa Using MALDI-TOF Mass Spectrometry Data

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Background and aim: Title: Deep 1D-CNN for Prediction of Carbapenem Resistance in Pseudomonas aeruginosa Using MALDI-TOF Spectra Background: Carbapenem-resistant Pseudomonas aeruginosa (CRPA) is a life-threatening pathogen with high mortality. Conventional resistance testing takes 24-48 hours. Methods: We analyzed 350 clinical isolates using MALDI-TOF mass spectrometry and developed a deep 1D convolutional neural network (1D-CNN) to predict carbapenem resistance, compared with broth microdilution as gold standard. Results: The AI model achieved 95.5% sensitivity, 97.2% specificity, and AUC 0.99, outperforming PCR (91.3%) and conventional ML methods. Turnaround time was 5 minutes. Conclusion: Deep learning transforms MALDI-TOF into a rapid, accurate resistance prediction tool for CRPA,

Methods: Methods: This cross-sectional diagnostic accuracy study included 350 clinical isolates of Pseudomonas aeruginosa collected from three teaching hospitals in Guilan province, Iran (Razi, 17 Shahrivar, and Amini hospitals) between October 2023 and December 2025. Carbapenem resistance to meropenem and imipenem was determined by broth microdilution according to CLSI M100 guidelines as the gold standard. MALDI-TOF mass spectra were acquired in the m/z range of 2000-20000 Da. A deep 1D convolutional neural network (1D-CNN) architecture with 15 layers (including convolutional, pooling, dropout, and fully connected layers) was designed for automated feature extraction and classification. Data were split into training (70%), validation (20%), and test (10%) sets. Model performance was evaluated using sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and area under the ROC curve (AUC) with 95% confidence intervals. Explainable AI (Grad-CAM) identified spectral regions contributing to resistance prediction.

Results: Results: Of 350 isolates, 132 (37.7%) were carbapenem-resistant by broth microdilution. The deep 1D-CNN platform demonstrated sensitivity 95.5% (95% CI: 88.6-98.7), specificity 97.2% (95% CI: 91.5-99.4), accuracy 96.5%, PPV 95.2%, NPV 97.1%, and AUC 0.99 (95% CI: 0.97-1.00). The AI model outperformed PCR (sensitivity 91.3%) and conventional machine learning methods (Random Forest: 88.6%; SVM: 86.1%). Notably, AI correctly identified 24 isolates (18.2%) with non-enzymatic resistance mechanisms (OprD loss + MexAB-OprM overexpression) that were undetectable by PCR. Grad-CAM analysis revealed critical m/z peaks at 3850-3950, 5700-5800, and 10400-10500 Da, corresponding to OprD porin, MexA efflux pump, and modified ribosomal proteins. Turnaround time was less than 5 minutes per isolate compared to 24-48 hours for conventional methods.

Conclusion: Discussion: Our deep 1D-CNN achieved excellent accuracy (96.5%) and AUC (0.99) for predicting carbapenem resistance in P. aeruginosa using MALDI-TOF spectra. The model detected non-enzymatic mechanisms (OprD loss, efflux pumps) that PCR misses. With 5 minute turnaround time, this AI platform addresses the critical need for rapid resistance detection in septic patients, potentially reducing inappropriate antibiotic use and mortality.

keywords: Keywords: Pseudomonas aeruginosa; Carbapenem resistance; Deep learning; MALDI-TOF; Artificial intelligence

OBa-1

Antimicrobial Resistance Profile of UTI Agents in Hospitalized Patients in The Imam Khomeini Hospital of Ardabil, Iran

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Background and aim: Antibiotics are the most effective drugs for treating urinary tract infections (UTIs). The widespread overuse and misuse of these agents has led to the emergence of antibiotic-resistant strains. Drug Resistance of Uropathogenic Bacteria led to medical, economic, and health challenges in the medical field. For this reason, this study aimed to investigate the distribution of Uropathogenic Bacteria and evaluate their antimicrobial resistance patterns among patients admitted to Imam Khomeini Hospital in Ardabil, Iran.

Methods: In this cross-sectional study, 500 urine specimens from hospitalized individuals at Imam Khomeini Hospital were collected from February to July 2025. The samples were cultured on basic media (blood agar), then in differential and selective culture media (MacConkey agar and EMB). Gram staining and standard biochemical assays were used for bacterial identification. the agar disk diffusion method was used for antibiotic susceptibility testing, in accordance with the latest Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: 404 samples (80.8%) were culture-positive. A total of seven bacterial species were identified, with Escherichia coli (50.9%) and Klebsiella pneumoniae (22.7%) being the most common uropathogens. E. coli showed the highest drug resistance to ampicillin (89%). K. pneumoniae was completely resistant to ampicillin (100%). Proteus mirabilis and Pseudomonas aeruginosa had 100% resistance to nitrofurantoin, and Enterococcus faecalis showed notable resistance to co-trimoxazole (68%). Acinetobacter baumannii had extensive resistance (60–100%) to cephalosporins and fluoroquinolones. The highest rates of multidrug resistance were observed in K. pneumoniae (86.9%), P. aeruginosa (100%), and A. baumannii (90%).

Conclusion: Our results revealed that E. coli was the most common pathogen isolated from urinary tract infections at Imam Khomeini Hospital in Ardabil. Ampicillin has lost its effectiveness against gram-negative bacteria that cause urinary tract infections. In addition, the high levels of antibiotic resistance, particularly in MDR strains, highlight the urgent need for continuous surveillance and the rational use of antibiotics.

keywords: Urinary tract infections, drug resistance, Uropathogenic, Frequency

OBa-2

Study of Cyanide Effects on Resistance of Pseudomonas aeruginosa in Intraocular Fluids

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Background and aim: Endophthalmitis due to Pseudomonas aeruginosa infection is one of the most aggressive eye infections that often leads to severe vision impairment and enucleation of the eye. The emergence of multidrug-resistant (MDR) isolates of this bacterium has proven to be a major threat to the use of antibiotics for its treatment. Besides antimicrobial resistance, the severity of the inflammation provoked by the MDR isolates plays an important role in the development of retinal complications and visual failure.

Methods: A search was performed on scientific databases PubMed, Scopus, Google Scholar, SID, and Magiran. A total of 15 studies were identified that explored the clinical presentations, in vitro inflammatory reactions, animal models, and molecular pathways of P. aeruginosa endophthalmitis. The information gathered included clinical results, antibiotic sensitivity, host inflammatory reaction, and promising methods of treatments such as nanoplatforms and anti-biofilms.

Results: The analysis of the reviewed studies showed that patients were predominantly presenting with hypopyon and high visual impairment (hand motion or worse vision), and despite early treatment, enucleation rates were high. The isolates were found to be relatively sensitive to ceftazidime and fluoroquinolones; however, severity of disease remained high. MDR strains showed enhanced and sustained inflammatory reactions within retinal cells, such as upregulation of TLRs, cytokines like IL-6, TNF-α, IL-1β, IL-8, MMP-9, and activation of NF-κB and MAPK signaling pathways. Animal studies showed rapid retinal damage, enhanced inflammatory cell infiltration, and enhanced retinal cell death. Multifunctional nanoplatforms like Ga-mSiO_2-BFN were found to effectively combat MDR infections, limit consequent inflammation, and show good results. Cyanide, along with virulence factors of bacteria, biofilm, and regulatory proteins, has emerged as an important pathogen.

Conclusion: The poor prognosis associated with endophthalmitis due to P. aeruginosa and its multi-drug-resistant form still seems to prevail. The intensified inflammatory reaction due to resistance, besides antibiotics, has been shown to contribute significantly to the permanent damage to the retina. The results not only highlight the importance of multiple modalities using antimicrobial drugs and immunomodulators but novel approaches like nanoplatforms and anti-biofilms as well.

keywords: Endophthalmitis; Pseudomonas aeruginosa; Multidrug resistance; Retinal inflammation; Antibiotic susceptibility.

OBa-3

Virtual Screening for Dual Inhibitors of Host MMP-1 and Pseudomonas aeruginosa PqsR: Adapalene as a Candidate for Diabetic Wound Therapy

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Background and aim: Chronic wounds impose a significant clinical and socioeconomic burden due to impaired healing, persistent inflammation, and susceptibility to biofilm-forming pathogens. Pseudomonas aeruginosa is the predominant pathogen in non-healing wounds, where quorum-sensing regulators such as PqsR promote virulence and biofilm formation. Concurrently, host fibroblast collagenase (MMP-1) is pathologically overexpressed, contributing to extracellular matrix degradation and delayed tissue repair. Current therapies inadequately address this combined pathogen–host dysfunction.

Methods: A structure-based drug-repurposing strategy was employed using integrated computational approaches. The DrugBank compound library was screened against two therapeutic targets: the P. aeruginosa PqsR receptor and human MMP-1. Molecular docking was performed using AutoDock Vina to identify high-affinity binders to key active-site residues. Lead compounds were further evaluated through 100 ns molecular dynamics simulations to assess binding stability, conformational behavior, and interaction energetics.

Results: Among screened compounds, Adapalene emerged as a promising dual-target candidate, exhibiting strong binding affinity and stable interactions with both PqsR and MMP-1. Molecular dynamics simulations confirmed sustained complex stability and favorable energy profiles throughout the simulation period, indicating robust target engagement.

Conclusion: This study identifies Adapalene as a potential dual-function therapeutic agent capable of attenuating P. aeruginosa virulence via quorum-sensing inhibition while concurrently limiting host collagen degradation through MMP-1 modulation. These findings support further experimental validation and suggest that Adapalene may represent a novel, mechanism-based approach for managing chronic wound infections.

keywords: Chronic wounds; Pseudomonas aeruginosa; MMP-1; Adapalene; Molecular docking; Molecular dynamics

OBa-4

Role of Gut and Vaginal Microbiome in Facilitating Synergistic Infection by Streptococcus agalactiae and Escherichia coli

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Background and aim: The female gastrointestinal tract and vaginal microbiota are complex interactive, dynamic systems that are essential for the preservation of reproductive, immune, and metabolic homeostasis. Dysbiosis, which is essentially a state of decreased Lactobacillus species, has been linked with conditions such as reproductive failure, vaginal infections, and pregnancy-related complications. It has recently been suggested that the translocation of bacteria from the gastrointestinal tract to the vagina promotes the colonization of the vagina by pathogenic bacteria such as Streptococcus agalactiae, which happens to have synergistic effects with bacteria such as Escherichia coli, thereby increasing the severity of the infection.

Methods: This review is based on analysis of literature retrieved from Google Scholar, PubMed, and SID databases published between 2018 and 2025. The reviewed studies addressed interactions between the gut and vaginal microbiome, microbial metabolism, host immune responses, bacterial adhesion mechanisms, metagenomic profiling, and pathogen colonization, with particular focus on S. agalactiae and E. coli in pregnancy-associated infections, both symptomatic and asymptomatic.

Results: Imbalance of the gut-vaginal microbiome community was significantly linked with the reduced prevalence of Lactobacillus dominance and increased colonization with Enterobacteriaceae species of origin. Among them, E. coli showed significant overgrowth in host-dysbiotic conditions within the vagina, presenting with attributes of extraintestinal pathogenic lineages. On the other hand, S. agalactiae showed increased adherence to epithelial glycans, which is supported by changes within pH and availability of glycosaminoglycans. The high affinity of pathogen glycans is different from that of commensals Lactobacillus species, resulting in efficient colonization of bacteria within the host. It appears that the presence of S. agalactiae together with E. coli induces synergistic pathogenicity, which increases host susceptibility to infections, especially in the urogenital tract, as well as increased risks of pregnancy-related adverse conditions.

Conclusion: The imbalance in intestinal and vaginal microbiota promotes the growth and cooperation of S. agalactiae with E. coli, which combines to induce the development of urogenital infections. The mechanisms of cooperation, which occur via microbial modulation, can serve as a basis for developing a targeted approach to treating urogenital infections to prevent complications resulting from infections.

keywords: Gut microbiome, Vaginal microbiome, Streptococcus agalactiae, Escherichia coli, Microbial dysbiosis

OBa-5

Crossing the roads on synbiotics in Women's Gynecologic Health: Modulating Vaginal-Gut Axis for Prevention and Treatment

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Background and aim: Among the most prevalent health conditions affecting women, gynecologic disorders—such as bacterial vaginosis, recurrent vulvovaginal candidiasis, pelvic inflammatory conditions, and other urogenital infections—have a substantial impact on clinical burden and quality of life. Recent research emphasizes how crucial the vaginal-gut axis and both sites' microbiota are for controlling pathogen resistance, mucosal immunity, vaginal pH, and reproductive health. Synbiotics are probiotic and prebiotic combinations used to improve clinical outcomes in gynecologic conditions and restore microbial balance. Synbiotics may stop pathogen overgrowth and infection recurrence stasis by boosting lactic acid production, encouraging the growth of lactobacillus species, and boosting mucosal immunity.

Methods: Following keywords were utilized for the search using databases PubMed, Scopus, Medline, and Google Scholar: "Synbiotic AND gynecology," "Vaginal microbiota AND reproductive health, and Synbiotic therapy AND vaginal infections. Recent studies focusing on the role of synbiotics in gynecologic disorders were systematically reviewed and analyzed.

Results: According to the clinical data, women who suffer from gynecologic disorders—specifically, bacterial vaginosis and recurrent fungal infections—show an increase in opportunistic pathogens and a decrease in lactobacillus species. Increasing beneficial lactobacillus species like Lactobacillus crispatus, Lactobacillus rhamnosus, and Lactobacillus plantarum and Bifidobacterium longum either alone or combination have been displayed to alleviate bacterial vaginosis. Synbiotics facilitates in lowering vaginal pH, reducing the recurrence of infections, improving mucosal inflammation, and boosting local immune responses, along with improving reproductive outcomes in some populations, revealing benefits of synbiotics administration. Additionally, publication shows that probiotic-prebiotic formulations work to restore the microbiome more effectively and sustainably than probiotics alone, underscoring the importance of the vaginal-gut axis.

Conclusion: A promising and beneficial treatment approach for women's gynecologic health is the use of synbiotics. Synbiotics greatly aid in the treatment of gynecologic disorders by improving infection rates, lowering inflammation, and restoring the natural microbial ecosystem. These results support the development of microbiome-based treatments for women's health and highlight the significance of regulating the vaginal-gut axis.

keywords: Synbiotic, Women's health, Vaginal microbiota, Lactobacillus, Bacterial vaginosis

OBa-6

Antibacterial Potential of Thymol-Chitosan Nanocomposite Against Streptococcus mutans and Actinomyces viscosus: Insights into Protein Leakage and Cytotoxicity

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Background and aim: Background: Tooth decay as the most common infectious-nutritional disease in the world. Nanotechnology, as a part of advanced technology related to the products comprising nanoparticles, can be used in a variety of industrial and pharmaceutical applications. The current work aims to investigate the antibacterial effect of thymol-loaded chitosan nanocomposite (TLCN) against Streptococcus mutans and Actinomyces viscosus as the main cariogenic bacteria.

Methods: Methods: Antibacterial activity of TLCN was assessed on S. mutans and A. viscosus through broth microdilution method based on the Clinical and Laboratory Standards Institute (CLSI) procedures. The effects on protein leakage in the tested bacteria, as well as its cytotoxicity on cancer (KB) and normal (HGF1-PI1) cell lines, were studied by Bradford's method and cell viability assay, respectively.

Results: Results: The size of the nanocomposite varied from 100 to 600 nm. The best minimum inhibitory concentration (MIC) related to nanocomposite + chlorhexidine was reported 2.66 for both bacteria. TLCN dose-dependently increased the protein leakage (P0.05). The findings exhibited that the exposure of the tested bacteria to TLCN, dose-dependently increased the protein leakage; whereas at 1/2 and 1/3 MIC markedly (P0.05) elevated the protein leakage in the tested bacteria. The 50% cytotoxic concentration (CC50) of nanocomposite against on normal (HGF1-PI1) and cancer (KB) cells were 149.6 and 68.4 µg/mL, respectively.

Conclusion: Conclusion: These results revealed that TLCN, especially in combination with chlorhexidine, displayed potent antibacterial effects against S. mutans and A. viscosus as the main cariogenic bacterial causes. However, extra examinations are mandatory to clarify the exact mechanisms and its toxicity mainly in clinical settings.

keywords: Nanomedicine, Bacteria, Oral cavity, Tooth decay, Protein leakage

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OBa-7

Frequency of Antibiotic Resistance Genes to Doxycycline, Rifampin, Streptomycin, and Cotrimoxazole in Human Brucella Isolates Using PCR and REP-PCR

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Background and aim: Brucellosis remains one of the most important zoonotic diseases worldwide and continues to pose significant public health challenges, particularly in endemic regions. The emergence of antimicrobial resistance among Brucella species has raised concerns regarding treatment efficacy and disease control. Comprehensive evaluation of phenotypic resistance patterns, resistance-associated genes, and genetic diversity is essential for optimizing therapeutic strategies and improving epidemiological surveillance of brucellosis.

Methods: In this study, 74 Brucella isolates obtained from patients with suspected brucellosis were identified using conventional biochemical tests. Antimicrobial susceptibility was assessed by disk diffusion and broth macrodilution methods to determine minimum inhibitory concentrations (MICs) for doxycycline, rifampin, streptomycin, and cotrimoxazole. Resistance-associated genes (tetB, rpoB, S12, and dfrA) were detected using polymerase chain reaction (PCR). Genetic diversity among the isolates was investigated using repetitive extragenic palindromic PCR (REP-PCR), and banding patterns were analyzed to assess genetic relatedness and clustering.

Results: The highest phenotypic resistance was observed against cotrimoxazole (18.9%), whereas doxycycline showed the lowest resistance rate (4.05%). MIC analysis demonstrated that most isolates remained within established susceptibility ranges for first-line anti-brucellosis agents. Among resistance-associated genes, dfrA was the most prevalent (24.3%), while rpoB, S12, and tetB were detected at lower frequencies. REP-PCR analysis revealed distinct genetic clustering patterns among the isolates, indicating variability in genetic relatedness. A relative concordance between phenotypic resistance profiles and genotypic findings was observed, although complete genotype–phenotype agreement was not universal.

Conclusion: The findings indicate that human Brucella spp. isolates remain largely susceptible to first-line therapeutic agents; however, notable resistance to cotrimoxazole and, to a lesser extent, rifampin highlights the need for continuous antimicrobial resistance monitoring. The combined application of phenotypic susceptibility testing, resistance gene detection, and REP-PCR provides a robust and practical framework for surveillance of antimicrobial resistance and molecular epidemiology of brucellosis in endemic regions.

keywords: Brucellosis Antimicrobial Resistance Polymerase Chain Reaction Minimum Inhibitory Concentration Brucella

OBa-8

Modulation of Alzheimer's Disease Pathology Through a Bacteroides fragilis–Butyrate Gut–Brain Axis

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Background and aim: Alzheimer's disease (AD) is a progressive neurodegenerative disorder with limited disease-modifying therapies. Increasing evidence implicates the gut microbiota in AD pathogenesis, but mechanistic links remain incompletely defined.

Methods: The mouse model of AD was used to assess gut microbiota composition, beta-amyloid (Aβ) deposition, and cognitive function. Mice were treated with Bacteroides fragilis or butyrate. Signaling through FFAR3 and downstream SIRT2 expression was evaluated. Fecal and serum samples from individuals with AD were analyzed for microbial composition and butyrate levels.

Results: AD mice displayed enrichment of Firmicutes and depletion of Bacteroidetes, correlating with increased Aβ accumulation. Administration of B. fragilis or butyrate reduced Aβ burden and improved cognitive performance. Butyrate signaling through FFAR3 downregulated SIRT2, attenuated ferroptosis, and mitigated AD pathology. Human AD samples similarly showed reduced Bacteroidetes abundance and butyrate levels.

Conclusion: A B. fragilis–butyrate–FFAR3 signaling axis modulates AD pathology by suppressing ferroptosis and amyloid accumulation. Targeting specific gut microbes or their metabolites may provide a novel adjunct approach for AD prevention and therapy.

keywords: Alzheimer's disease; gut–brain axis; Bacteroides fragilis; butyrate; FFAR3; ferroptosis; beta-amyloid.

OBa-9

Nano Formulations of clostridial Beta and Epsilon Toxins: A Novel Approach to Studying Humoral Immunity in Animal Models

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Background and aim: Clostridium perfringens is a widespread, spore-producing bacterium that causes fatal diseases in sheep, cattle, and goats. It can generate up to eighteen toxins, with beta, and epsilon toxins being the most pathogenic. The most common preventive approach is vaccination with toxoids prepared from bacterial cultures, which induce neutralizing antibodies. Nanovaccines present notable benefits compared to traditional toxoids, particularly regarding production efficiency, and are increasingly recognized as a promising solution. This article reviews the principal strategies for creating nanovaccines incorporating beta and epsilon toxins of C. perfringens and their potential application in protecting mammalian livestock.

Methods: PLGA nanoparticles loaded with toxins and red blood cell membrane–coated nanotoxins were synthesized and evaluated for safety, residual toxicity, and potency. A total of thirty rabbits were immunized under either single- or three-dose schedules with nanotoxins (NTs), red blood cell membrane-camouflaged nanotoxins (RBCNTs), as well as pentavalent clostridial toxoid vaccine and PBS controls. Anti-toxin titers were quantified over 150 days using an optimized indirect ELISA and validated by mouse neutralization tests. Protective efficacy was assessed via subcutaneous challenge with 100 MLD and statistical analyses were performed using SPSS, with significance set at p 0.05.

Results: Animals receiving three-dose regimens developed significantly higher and longer-lasting antibody titers compared to those given a single dose (p 0.05). The results of ELISA showed that PLGA significantly enhanced immunogenicity compared with the pentavalent clostridial toxoid vaccine. RBCNTs group (three-doses schedule) generated stronger immune responses than NTs group. RBCNTs group showing the highest antibody levels and complete survival following challenge. The pentavalent clostridial toxoid vaccine failed to provide protection beyond 24 hours, whereas RBCNTs group (three-doses schedule) sustained elevated titers and effective protection for up to 150 days.

Conclusion: RBC membrane–coated PLGA nanotoxoids show enhanced stability, prolonged circulation, and robust immunity against epsilon and beta toxins, outperforming traditional vaccines. These RBCNTs represent a promising nanovaccine approach for clostridial enterotoxemia, with sustained protection that could help safeguard livestock and reduce infection-related losses.

keywords: PLGA, RBC membrane-camouflaged nanotoxins, Clostridium perfringens toxins

OBa-10

Investigation of the antibacterial activity of black seed hydroalcoholic extract in healing skin wounds infected with Staphylococcus aureus in rats

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Background and aim: Bacterial infections caused by Staphylococcus aureus are one of the main factors delaying the healing of skin wounds. The use of antibacterial herbal compounds can be a safe and cost-effective solution to accelerate the wound healing process. This study aimed to evaluate the antibacterial effects of hydroalcoholic extract of black seed (Nigella sativa) on the healing process of infected skin wounds in a rat model.

Methods: In this experimental study, 18 male rats were randomly divided into positive control, negative control, and a group receiving hydroalcoholic extract of black seed. A full-thickness excisional wound was created on the back of the animals and then S. aureus ATCC 25923 was inoculated into the wounds to induce local infection. In the negative control group, a full-thickness excisional skin wound was created on the back of the rats and inoculated with S. aureus, but no treatment or dressing was applied. In the treatment group, after creating a full-thickness excisional wound and inducing infection with S. aureus, topical treatment with hydroalcoholic extract of black seed was performed for 14 days. The wound healing process was evaluated by measuring wound area and assessing macroscopic changes at different time intervals.

Results: The results of this study showed that treating wounds with hydroalcoholic extract of black seed significantly reduced the wound size compared to the control group. In addition, signs of infection, including inflammation, discharge, and redness, were significantly reduced in the group receiving the extract. These results indicate the effective antibacterial activity of black seed extract against S. aureus ATCC 25923 and its role in accelerating the wound healing process.

Conclusion: Based on the findings of this study, hydroalcoholic extract of black seed can be used as a natural agent with antibacterial and regenerative properties in the treatment of infected skin wounds. Further studies are recommended to determine the molecular mechanisms and optimize the dosage.

keywords: Staphylococcus aureus, black seed, skin wound

OBa-11

Evaluation of a Targeted Antibiofilm Combination Strategy Against Methicillin-Resistant Staphylococcus aureus from Infected Wounds

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Background and aim: Methicillin-resistant Staphylococcus aureus (MRSA) is a leading cause of infected wounds and is particularly difficult to eradicate due to its capacity to form biofilms. Biofilm-associated infections exhibit high tolerance to antimicrobial agents, underscoring the need for targeted antibiofilm strategies.

Methods: Thirty Staphylococcus aureus isolates were obtained from infected wound samples provided by a hospital microbiology laboratory and reconfirmed using standard differential and biochemical tests. Biofilm-forming capacity of all isolates was evaluated using a biofilm assay, and optical density (OD) measurements were used to compare biofilm biomass. The MRSA isolate exhibiting the highest OD value was selected as the candidate strain for further analysis. Antibacterial activity of N-acetylcysteine (NAC), recombinant lysostaphin (rLyso), and niosomal rLyso, alone and in combination, was assessed by determining minimum inhibitory and bactericidal concentrations (MIC/MBC). Antibiofilm efficacy was evaluated on mature biofilms using minimum biofilm eradication concentration (MBEC) analysis and confirmed by fluorescence microscopy and confocal laser scanning microscopy. Cytotoxicity was assessed on L929 fibroblast cells, and therapeutic efficacy was further investigated in a murine wound infection model with histopathological evaluation.

Results: Biofilm screening identified a clinical MRSA isolate with markedly higher biofilm-forming ability compared with other wound-derived isolates. The combination of NAC and niosomal rLyso demonstrated the most pronounced antibacterial and antibiofilm activity against the selected MRSA strain, resulting in reduced MIC and MBEC values compared with monotherapies. Microscopic analyses revealed substantial biofilm disruption and decreased bacterial viability. The combination treatment showed high biocompatibility at effective concentrations and achieved complete bacterial clearance, accompanied by improved wound healing in vivo.

Conclusion: Targeting a biofilm-producing MRSA isolate derived from infected wounds using a combination of NAC and niosomal recombinant lysostaphin resulted in potent antibiofilm and antibacterial effects in vitro and effective therapeutic outcomes in vivo. This targeted antibiofilm strategy may represent a promising approach for managing drug-resistant, biofilm-associated MRSA wound infections.

keywords: Methicillin-Resistant Staphylococcus aureus; Biofilms; Infected Wounds; Antimicrobial Resistance; Antibiofilm Strategy

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OBa-12

Advancing Therapeutics against Resistant Helicobacter pylori: Exploring new CagA Inhibitors using Molecular Docking Approach

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Background and aim: Helicobacter pylori is a Gram-negative bacterium that colonizes in human stomach. WHO considers it a "high priority" pathogen for more research and development of new antibiotics. This bacterium shows increasing resistance to antibiotics. CagA is an important virulence factor linked to more severe gastric diseases and a higher risk of gastric cancer. A recent meta-analysis of community-based studies estimated the overall prevalence of H. pylori in Iran to be 54% and the metronidazole resistance rate to be 64.9%. This study aimed to identify the most effective inhibitor of CagA using molecular docking analysis as a novel approach to addressing the

Methods: The 3D structure of the CagA protein (PDB ID: 4DVY) was obtained from the RCSB Protein Data Bank. ZINC153731, a CagA inhibitor (PubChem CID: 255591024), and 20 of its analogs, after checking through Lipinski rules, were retrieved from the PubChem database in SDF format. The protein and inhibitory ligands were prepared for docking using Molegro Virtual Docker version 6.0. After docking, the best interaction with the top binding affinity, which resulted in the lowest binding energy, was analyzed through Molegro Molecular Viewer v.7 software. Finally, the pharmacokinetic properties of the ligand were evaluated using the SwissADME server

Results: The best ligand was methyl 3-[4-hydroxy-3-(3-methylbut-2-enyl)phenyl]prop-2-enoate (PubchemCID:126304) with a molecular weight of 246.30 g/mol and binding energy of -108.758 kcal/mol, higher than ZINC153731 with -84.8365 kcal/mol. The ligand made one steric bond with Thr 464 and one hydrogen bond with the Thr 464 residue, and no electrostatic interaction. The ADME results showed a water solubility score (logS) of -3.66, a hydrophilic score (LogP) of 3.20, and a polarity score (TPSA) of 46.53 Å², hydrogen bond donors of 1 and hydrogen bond acceptors of 3. In addition, GI absorption is high and passes the BBB (Blood-brain barrier).

Conclusion: These results indicated that methyl 3-[4-hydroxy-3-(3-methylbut-2-enyl)phenyl]prop-2-enoate was a better inhibitor than ZINC153731, also a promising CagA inhibitor candidate. Further in vitro and in vivo studies are required to confirm its potential as a therapeutic agent.

keywords: Helicobacter pylori, CagA, Molecular Docking, ADME.

OBa-13

Determination of effective prophylactic responses of truncated pilin protein as a vaccine candidate against uropathogenic Escherichia coli

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Background and aim: Uropathogenic Escherichia coli (UPEC) is a major cause of more than 80% of urinary tract infections (UTIs), a global health problem, and the second most common infectious disease. UTIs are responsible for approximately 40% of all nosocomial infections and 50% of all bacteremia. Since an approved vaccine against UTIs is not yet approved, evaluating different antigens, injection routes, and adjuvants is necessary to access the ideal vaccines.

Methods: In this study, we constructed a fusion protein composed of a truncated form of FimH antigen, the key virulence factor of UPEC, and the FliC antigen of Salmonella typhimurium as an adjuvant. After bioinformatics analysis, the fusion protein was cloned, expressed, and immunologically evaluated in mice. The bladder challenge assay was also used to examine the level of protection in the bladder and kidneys of the immunized mice.

Results: The levels of IgG and IgA antibodies in the serum and urine of mice vaccinated with the truncated FimH.FliC (tFimH.FliC) significantly increased compared to the FliC and PBS groups. The cytokine assay showed that tFimH.FliC fusion protein induced higher levels of IFN-γ, IL-4, and IL-17 than the FimH and PBS groups. Additionally, the results of the challenge assay showed a significant decrease in the colony count of bacteria in all of the groups compared to the control group.

Conclusion: Our findings showed that the designed candidate can develop effective prophylactic responses against UTIs caused by UPEC strains and that truncated FimH, without an unwanted domain, is an ideal vaccine target

keywords: Urinary tract infection, FimH.FliC, Fusion protein, Uropathogenic Escherichia coli

OBa-14

Efficacy of ICU Surface Disinfection in Modulating Bacterial Contamination

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Background and aim: Environmental contamination in intensive care units plays a crucial role in the persistence and spread of healthcare-associated infections. Disinfectants are widely used to control microbial burden on hospital surfaces; however, their performance under routine clinical conditions requires continuous assessment.This study evaluated the effectiveness of four routinely used surface disinfectants—a quaternary ammonium–based agent, an aldehyde-containing disinfectant, an alcohol-based spray, and a rapid-action multi-purpose disinfectant—in controlling bacterial contamination on ICU surfaces in hospitals of Abadan City.

Methods: A descriptive-analytical study was conducted in the ICUs of three hospitals. Surface samples were collected from frequently touched areas before and after disinfection, resulting in a total of 600 samples. Bacterial identification was performed using standard culture-based and biochemical methods. Data analysis was carried out using paired t-tests.

Results: Microbiological assessment prior to disinfection demonstrated heterogeneous levels of contamination across ICU surfaces, indicating variable exposure to microbial reservoirs. Post-disinfection findings showed a marked alteration in the composition and density of surface-associated bacteria. Gram-negative organisms, particularly Pseudomonas aeruginosa and Klebsiella pneumoniae, were more frequently isolated than Gram-positive species, suggesting greater environmental persistence. Although all disinfectant categories reduced overall contamination, their performance varied according to surface characteristics and bacterial groups, with some organisms showing reduced sensitivity under routine conditions.

Conclusion: The study highlights that surface disinfection influences not only the quantity but also the distribution of bacterial populations in ICU environments. These findings support the implementation of targeted disinfection strategies and continuous microbiological surveillance to enhance infection control programs and reduce healthcare-associated infections.

keywords: Intensive Care Unit (ICU) Surface Disinfection Bacterial Contamination Infection Control

OBa-15

Evaluation of Virulence Profiles and Molecular Typing of ESBL-Producing Uropathogenic Escherichia coli: Dominance of ST131 and Emergence of ST421 in Iran

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Background and aim: Globally, the clonal lineages ST69, ST73, ST95, ST127, and ST131 account for more than half of Uropathogenic Escherichia coli (UPEC) infections. The present study aimed to characterize and compare antimicrobial susceptibility profiles, virulence genes, and resistance determinants between ST131 and non-ST131 isolates collected from hospitalized patients in Iran over a three-year period (2021–2024).

Methods: In this cross-sectional study, 179 confirmed E. coli isolates were examined. The susceptibility of the ESBL-producing strains was determined via the combined disk test (CDT). PCR was performed to identify each of the blaCTX-M-15 and blaCTX-M-14 genes and virulence factors. Common STs were identified via multiplex PCR and MLST, and a clonal relationship was drawn.

Results: Overall, 75.4% of the isolates were MDR and 52.5% were ESBL producers, predominantly harboring blaCTX-M-15 (52.5%). The most frequent virulence genes were sat (44.7%), kpsM II-K2 (41.3%), and iroN (40.2%). ST131 was the dominant lineage (63.1%), followed by ST69 (8.4%), ST95 (7.3%), and ST73 (3.9%); notably, ST421 was detected for the first time in Iran. ST131 isolates presented significantly greater resistance to cephalosporins and a stronger association with ESBL production and blaCTX-M-15. Virulence profiles varied across STs, with iroN enriched in ST131.

Conclusion: This study highlights the dominance of ST131 and the first detection of ST421 among UPEC strains in Iran, with blaCTX-M-15 as the principal ESBL determinant. The heterogeneous virulence landscape underscores the clinical threat of MDR clones, emphasizing the necessity of molecular surveillance and strengthened infection control strategies in hospital settings.

keywords: UPEC, ESBL, ST131, Virulance factor, Antibiotic resistant

OBa-16

Investigating the prevalence of contamination of hands of personnel in special care departments of hospitals

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Background and aim: Hospital-acquired infections are always one of the threats to patients admitted to hospitals, which mostly occur after 48 hours of hospitalization and increase the morbidity, mortality, and cost of treatment. These infections are mainly through contact and initially with The hands of employees and people who deal with patients. The purpose of this study is to investigate the prevalence of contamination Fungal and bacterial infections of the hands and jewelry of the personnel of the special care departments of Urmia hospitals

Methods: In this descriptive research, 8 internal emergency departments, pediatrics, NICU, men's surgery, women's surgery, CCU, and ICU, sampling was done using sterile wet swabs from different areas of the personnel's hands and ornaments, and then the swabs were cultured on bacterial and fungal culture media. The detection of bacterial species after 24 hours of culture in EMB Agar and blood agar culture media was investigated using differential culture media diagnostic discs and biochemical methods. Also, to identify the fungal species, Saburodextrose agar was used, which was checked for growth or non-growth for a week, and a grown sample was used to identify the genus and species using the slide culture method and lactophenol staining

Results: The results of the research are that out of 100 cultured personnel samples, 22 people did not have any contamination. 68 of the personnel had multiple bacterial and fungal infections. Coagulase-negative staphylococci were 35 cases 12 people had Aspergillus niger and 10 people had Staphylococcus aureus

Conclusion: The source of most hospital infections is bacteria and fungi that enter the body of patients during surgery or clinical procedures. It is important to wash hands and rings regularly to prevent bacteria from permanently residing in the skin. Also, the use of appropriate disposable equipment personal hygiene, and Regular trimming of nails can be useful in control and prevention.

keywords: Investigating, contamination, jewelry

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OBa-17

Development of a High-Efficiency Dual-Layer Alginate–Whey Protein Encapsulation System to Enhance Gastrointestinal and Storage Stability of Lactobacillus plantarum

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Background and aim: The industrial and therapeutic efficacy of probiotic formulations depends on maintaining high viable cell counts during processing, freeze-drying, storage, and gastrointestinal transit. Rapid viability loss under acidic gastric conditions, bile salts, and technological stresses remains a major limitation. This study aimed to design and optimize a structurally stable, electrostatically reinforced dual-layer encapsulation system to significantly improve the survival of Lactobacillus plantarum under technological and physiological stress conditions.

Methods: Encapsulation was performed using the external ionic gelation method with 0.1 M $CaCl_2$ as the crosslinking solution. Sodium alginate was prepared in 0.01 M acetate buffer at pH 4.7 as the core matrix. Whey protein isolate (90%) was applied as a secondary coating at pH 4.1 to promote electrostatic complex formation. Beads were washed in acetate buffer at pH 4.4. Zeta potential analysis was conducted to determine optimal charge interactions for bilayer stabilization. Different bacteria-to-alginate ratios (1:3, 1:4, and 1:5 w/w) and two dripping techniques were evaluated for bead uniformity and morphology. Encapsulation efficiency, viable cell counts (CFU/g), Gram staining, SEM and FE-SEM imaging (T0: free cells; T1: alginate-coated; T2: WPI-coated), FT-IR spectroscopy, resistance to simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) for 5 hours, and storage stability at 4°C for 8 weeks after freeze-drying were systematically assessed.

Results: Encapsulation efficiency reached 90.4%, indicating successful entrapment of Lactobacillus plantarum. Opposite zeta potential values for alginate (−25 to −27 mV at pH 4.7) and WPI (+10.9 to +13.4 mV at pH 4.1) confirmed electrostatically driven bilayer formation. FE-SEM revealed compact, spherical microcapsules with a continuous outer coating, while FT-IR confirmed intermolecular interactions between alginate and WPI. Under simulated gastric conditions, encapsulated cells showed only a 0.96 log CFU/g reduction in viability compared with 3.79 log CFU/g for free cells. Under simulated intestinal conditions, free cells completely lost viability, whereas encapsulated cells retained significantly higher viability. After freeze-drying, viable counts remained at 11.64 ± 0.09 log CFU/g and decreased slightly to 11.50 ± 0.07 and 10.84 ± 0.47 log CFU/g after one and two months of storage at 4°C, respectively, remaining above the recommended minimum probiotic level (6 log CFU/g).

Conclusion: The optimized alginate (pH 4.7)–WPI (pH 4.1) bilayer system, stabilized at pH 4.4 and produced by external ionic gelation, effectively improved the resilience of Lactobacillus plantarum against freeze-drying, refrigerated storage, and simulated gastrointestinal conditions. The electrostatically reinforced bilayer architecture enhanced structural stability and maintained high cell viability, highlighting its potential as a delivery system for probiotic applications in functional foods, nutraceuticals, and pharmaceuticals.

keywords: Lactobacillus plantarum ATCC 14917; Dual-Layer Encapsulation; Sodium Alginate; Whey Protein

OBa-18

The relationship between dietary patterns and Helicobacter pylori infection in patients with dyspeptic symptoms

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Background and aim: Helicobacter pylori infection is highly prevalent, yet there are many ambiguities regarding the protective or risk-related role of dietary patterns in its development. This highlights the need to investigate the association between food group intake and the infection. Therefore, this study aimed to determine this relationship in patients with dyspeptic symptoms referred to Imam Reza Hospital in Tabriz.

Methods: In this cross-sectional study, 225 participants (104 H. pylori-positive, 121 H. pylori-negative) were enrolled. The average daily intake of five food groups—bread and grains, fruits and vegetables, meat, dairy, and fats—was assessed using a food frequency questionnaire (FFQ). Data were analyzed using multivariate logistic regression with SPSS, adjusting for confounders (age, sex, education level, smoking), to examine the association between each food group intake and H. pylori infection.

Results: H. pylori infection was more common in men (55.9% vs. 36.8%; P = 0.004) and decreased with higher education (P 0.001). After adjusting for confounders, moderate intake of bread and grains (OR = 0.441, P = 0.015) and borderline protective effect of fats (OR = 0.469, P = 0.05) were observed. Dairy intake was higher in uninfected group, while fruit/vegetable intake was higher in infected group. No significant association was found for meat.

Conclusion: The relationship between food intake and H. pylori infection is complex. Moderate intake of bread, grains, and possibly fats may be protective. Male sex and low education are strong independent risk factors. These findings may guide future prevention strategies.

keywords: Helicobacter pylori, Dietary intake, Dyspepsia, Risk factors

OBa-19

Molecular Characterization and Clonal Analysis of Carbapenem-Resistant Acinetobacter baumannii: Insights Into Biofilm-Related Gene Coexistence in Clinical Isolates

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Background and aim: The emergence of multidrug-resistant Acinetobacter baumannii (MDR A. baumannii) and biofilm-producing ability have become a worldwide serious concern. This study is aimed at investigating the clonal relationships, coexistence of carbapenemase-resistant and biofilm-related genes, and biofilm biomass capacity in 57 A. baumannii isolates obtained from patients in intensive care units (ICUs).

Methods: Antibiotic resistance patterns to 11 antibiotics were determined using the disc diffusion test. The minimum inhibitory concentrations (MICs) of imipenem and colistin were evaluated by the microdilution method. All isolates were subjected to PCR for the detection of carbapenemase- and biofilm-related genes and examined for the biofilm-forming ability using crystal violet staining methods. The clonality relationship was identified by rep-PCR.

Results: Overall, 49 (86%) isolates were characterized as extensively drug-resistant (XDR) with a high MIC for imipenem. Eight isolates were resistant to colistin (MIC64 µg/mL). Additionally, 86.21% of isolates were strong biofilm formers, which correlated with the PDR phenotype. All isolates carried at least three genes related to biofilm formation. Genotypically, 100% of isolates had bla OXA-51-like, bla OXA-24-like, and bla TEM genes, followed by bla VIM (61.4%), bla OXA-23-like (24.6%), bla SHV (1.8%), and bla KPC (1.8%), whereas bla CTX-M and bla OXA-58-like genes were not found in the isolates. The rep-PCR analysis identified 10 distinct genotypes, among which GTG Type 3 showed a significant correlation with strong biofilm formation. Moreover, the greatest number of colistin-resistant isolates (MIC64 µg/mL) were located in this cluster.

Conclusion: This study highlights the emergence of PDR A. baumannii strains carrying a variety of β-lactamase and biofilm-related genes in ICUs, underscoring the urgent need for improved infection control measures and antimicrobial stewardship programs to address the spread of these formidable pathogens.

keywords: Acinetobacter baumannii; antimicrobial resistance; biofilm-related genes; carbapenemase; rep-PCR

OBa-20

Bartonella in fleas: A serious public health challenge in Iran and the One Health approach

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Background and aim: Bartonella spp. are zoonotic pathogens of global concern, transmitted by fleas from rodents to humans. This study aimed to characterize the microbiome of vector fleas in plague-endemic (Akanlu, Bukan, Sarab) and non-endemic (Tello) regions of Iran, focusing on Bartonella diversity, its association with dominant rodent host Meriones persicus and flea vector Xenopsylla buxtoni, and the public health implications for urban and rural settings. The findings support a One Health approach to surveillance and control of emerging flea-borne zoonoses in Iran.

Methods: Fleas were collected from rodents in four regions—three plague-endemic (Hamadan, West and East Azerbaijan) and one non-endemic (Tello, Tehran). DNA from 146 individual fleas and 13 pools—mainly X. buxtoni—was extracted and subjected to 16S rRNA amplicon sequencing (V3–V4 regions). Microbiome composition, Bartonella phylotypes, and variations by flea sex, species, and location were analyzed using QIIME2 and STAMP. Fisher's exact test assessed sex–abundance associations. Dominant bacterial genera (Bartonella, Sphingomonas, Wolbachia, Cardinium, Rickettsia, Ralstonia) were mapped across sites. Phylogenetic relationships of representative sequences were inferred using MEGA.

Results: Bartonella dominated flea microbiomes (52%), with nine distinct phylotypes; the most prevalent (isolate 9c98) clustered with known human/rodent pathogens and was detected in all samples. Female fleas harbored significantly more Bartonella. Geographic patterns were evident: Bartonella and Wolbachia were enriched in female fleas from Akanlu, while Bartonella and Sphingomonas (16%) predominated in male fleas from Bukan. Critically, Bartonella was detected in Tello—a non-plague area in northeastern Tehran—indicating transmission risk beyond traditional foci. Other potential pathogens (Rickettsia, Ralstonia) and biofilm-forming bacteria further confirm fleas as reservoirs of diverse zoonotic agents.

Conclusion: Fleas in Iran carry diverse, clinically relevant Bartonella strains—even in non-endemic urban areas like Tello—posing a significant public health threat, particularly for diseases such as endocarditis and cat scratch fever. These findings underscore that Bartonella risk extends beyond plague foci, necessitating enhanced surveillance in Tehran's clinical and veterinary laboratories. A robust One Health framework integrating human, animal, and environmental monitoring is essential to mitigate transmission and strengthen early-warning systems for emerging flea-borne zoonoses in Iran.

keywords: Bartonella; flea microbiome; zoonotic diseases; One Health; plague foci

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OBa-21

Investigation of intracellular master symbionts Wolbachia, Cardinium, and Rickettsia in fleas and their co-infection patterns in plague-prone regions of Iran

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Background and aim: Fleas are key vectors of zoonotic pathogens like Yersinia pestis and also harbor diverse intracellular bacteria. This study aimed to investigate the presence, diversity, and co-occurrence patterns of three master symbionts—Wolbachia, Cardinium, and Rickettsia—in fleas collected from historically plague-endemic and non-endemic regions of Iran, to assess their potential role in vector biology and biocontrol strategies.

Methods: Fleas belonging to five species (Xenopsylla buxtoni, X. nuttalli, Pulex irritans, Nosopsyllus iranus iranus, and Ctenophthalmus rettigi smiti) were collected from four regions: Akanlu, Bukan, Sarab (plague-endemic), and Tello (non-endemic). DNA was extracted from pooled specimens (n = 13), and the V3–V4 hypervariable regions of the 16S rRNA gene were amplified and sequenced using Illumina HiSeq (NGS). Bioinformatic analyses were performed using QIIME2, STAMP, and MEGA for taxonomic profiling, diversity assessment, and phylogenetic reconstruction.

Results: Six bacterial genera dominated flea microbiomes: Bartonella (52%), Sphingomonas (16%), Wolbachia (15%), Cardinium (5%), Rickettsia (3%), and Ralstonia (2%). Triple co-infections with Wolbachia, Cardinium, and Rickettsia were detected in 10 out of 13 flea pools (both sexes). Wolbachia (30%) was most abundant in P. irritans, Cardinium (70%) in female N. iranus iranus, and Rickettsia (33%) in X. buxtoni from Tello. Phylogenetic analysis revealed Wolbachia supergroups A, B, and an F; Cardinium clustered within group A; and Rickettsia sequences segregated into pathogenic and symbiotic clades.

Conclusion: With regard to the potential role of these symbionts in modulating the transmission of zoonotic pathogens such as Y. pestis, our findings could pave the way for novel preventive strategies targeting at-risk populations in plague-prone regions. This study reports, for the first time, widespread triple co-infection of fleas with three master reproductive symbionts. Their high prevalence and phylogenetic diversity suggest potential roles in flea fitness, adaptation, and pathogen interaction. These findings support exploring these symbionts in paratransgenic or symbiont-based biocontrol strategies against flea-borne zoonoses within the One Health framework.

keywords: Wolbachia; Cardinium; Rickettsia; Microbiome of fleas; Plague-endemic regions

OBa-22

Anti-biofilm Activity of ZnCo-ZIF Against Methicillin-Resistant Staphylococcus aureus (MRSA) ATCC 33591

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Background and aim: Methicillin-resistant Staphylococcus aureus (MRSA) is recognized as a major healthcare-associated pathogen and a leading cause of hospital-acquired infections worldwide. It imposes a substantial clinical and economic burden. Furthermore, the ability of MRSA to form biofilms significantly enhances its persistence and tolerance to antimicrobial treatments, making infection management particularly challenging. Therefore, the development of effective antibiofilm agents is of considerable interest. Zeolitic imidazolate frameworks (ZIFs) have recently attracted attention because of their unique physicochemical properties and potential antimicrobial applications. In this study, the anti-biofilm activity of synthesized ZnCo-ZIF was evaluated against MRSA ATCC 33591.

Methods: The anti-biofilm activity of ZnCo-ZIF was assessed using the crystal violet microtiter plate assay. Serial two-fold dilutions of ZnCo-ZIF were prepared to obtain final concentrations of 250, 125, and 62.5 µg/mL. MRSA ATCC 33591 was cultured in tryptic soy broth (TSB) supplemented with 1% glucose and incubated for 24 h. The bacterial suspension was adjusted to 0.5 McFarland standard and diluted in TSB. Equal volumes of bacterial suspension and ZnCo-ZIF solutions were added to 96-well microplates and incubated at 35 ± 2°C for 24 h. Wells containing bacteria without ZnCo-ZIF served as positive controls, while wells containing medium without bacteria served as negative controls. Following incubation, wells were washed with phosphate-buffered saline (PBS), stained with 0.1% crystal violet, and the bound dye was solubilized with 95% ethanol. Optical density was measured at 600 nm, and biofilm inhibition percentages were calculated. All experiments were performed in triplicate.

Results: ZnCo-ZIF demonstrated a concentration-dependent inhibitory effect on biofilm formation by MRSA ATCC 33591. The highest inhibition was observed at 250 µg/mL, resulting in 82.56% biofilm reduction compared with the untreated control. At concentrations of 125 µg/mL and 62.5 µg/mL, ZnCo-ZIF inhibited biofilm formation by 67.87% and 55.82%, respectively. The findings indicate that increasing concentrations of ZnCo-ZIF significantly enhanced its anti-biofilm activity. Even at the lowest tested concentration, more than 50% inhibition of biofilm formation was achieved. These results suggest that ZnCo-ZIF effectively interferes with biofilm development and may represent a promising antibiofilm agent against MRSA.

Conclusion: The synthesized ZnCo-ZIF exhibited substantial anti-biofilm activity against MRSA ATCC 33591 in a concentration-dependent manner. The highest inhibitory effect was achieved at 250 µg/mL, demonstrating over 80% reduction in biofilm formation. Given the critical role of biofilms in chronic and antibiotic-resistant infections, ZnCo-ZIF may serve as a promising candidate for the development of novel antimicrobial and antibiofilm strategies. Further studies are required to investigate its mechanism of action, biocompatibility, and effectiveness in in vivo models.

keywords: ZnCo-ZIF; MRSA; Biofilm Inhibition; Crystal Violet Assay; Methicillin-Resistant Staphylococcus aureus.

OBa-23

Nanostructured Lipid Carriers Co-loaded with Doxycycline, Gentamicin, and Thymol for Enhanced Intracellular Antibacterial Activity against Brucella melitensis

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Background and aim: Brucellosis is a zoonotic infection caused by Brucella spp., which persist within macrophages and complicate treatment. This study developed nanostructured lipid carriers (NLCs) co-loaded with doxycycline, gentamicin, and thymol to enhance intracellular delivery and antibacterial activity against Brucella melitensis.

Methods: Drug-loaded NLCs were prepared using high-shear homogenization followed by sonication. The formulations were characterized in terms of particle size, polydispersity index (PDI), zeta potential, morphology by FE-SEM, encapsulation efficiency, and in vitro drug release profile. Cytotoxicity was assessed using the MTT assay on J774A.1 macrophage. Antibacterial activity and intracellular efficacy against Brucella melitensis were evaluated using microbiological and cell-based assays.

Results: The optimized formulation showed a size of 398 ± 30 nm, PDI 0.35, and zeta potential −17.5 mV, with 97% encapsulation efficiency and stable morphology over nine months. The system exhibited sustained release up to 95% at 80 h, in contrast to rapid diffusion from free drugs. Intracellular studies showed that Gen–Dox–Thy@NLC achieved a 3.4-log reduction in bacterial load, demonstrating significantly higher efficacy (~1.6-log greater reduction) compared with free drugs (p 0.05), while maintaining macrophage viability above 85%.

Conclusion: The co-loaded NLC formulation provided controlled drug release, improved intracellular delivery, and enhanced antibacterial activity against Brucella melitensis. These findings suggest that Gen–Dox–Thy@NLC may serve as a promising candidate for brucellosis treatment and warrants further in vivo studies.

keywords: Brucella melitensis, Nanostructured Lipid Carriers, doxycycline, gentamicin, thymol

OBi-1

Genistein in combination with Chlorogenic acid ameliorates insulin resistance and oxidative stress in skeletal muscle of high-fat diet fed mice

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Background and aim: Increasing evidence has demonstrated that oxidative stress plays a significant role in the pathogenesis of muscle insulin resistance. The beneficial impacts of genistein (GEN) and chlorogenic acid (CGA) on insulin resistance have already been revealed. However, their combined effects on skeletal muscle oxidative stress and insulin resistance have not been completely understood. The aim of the present study was to determine the effect of GEN in combination with CGA on skeletal muscle insulin resistance in high-fat diet (HFD) fed C57BL/6 mice.

Methods: C57BL/6 male mice were fed an HFD for 15 weeks. The mice were then divided into five groups: standard chow diet (SCD), HFD, HFD + GEN, HFD + CGA, and HFD + GEN + CGA for 10 weeks

Results: The findings indicated that single treatment with GEN or CGA, and with a stronger effect of GEN+CGA combined treatment, decreased body weight gain and improved glucose intolerance. Moreover, following treatment with GEN and CGA alone or in combination with further effect, the level of plasma and muscle triglyceride (TG) were reduced. Furthermore, the combination therapy of GEN and CGA with greater efficacy than the single treatments, could decrease several oxidative stress markers in the skeletal muscle. Treatment with GEN and CGA alone or in combination could increase the expression of NF-E2–related factor 2 (Nrf2), heme oxygenase-1 (HO-1), and NAD(P): Quinone Oxidoreductase 1 (NQO1)

Conclusion: The data of this study suggest that the combination of GEN and CGA might ameliorate insulin resistance and reduce oxidative stress in the skeletal muscle of mice fed HFD.

keywords: Genistein, Chlorogenic Acid, Oxidative Stress, Insulin Resistance, Skeletal Muscle, Nrf2

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-2

Production and Comprehensive Biochemical Characterization of a Novel Recombinant Trypsin from Fenneropenaeus merguiensis

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Background and aim: Trypsin is a key serine protease with applications in biotechnology, diagnostics, and protein processing. Conventional extraction from marine sources is inefficient and yields enzymes with variable purity. Recombinant production offers a reliable platform for generating enzymes with improved biochemical properties. This study aimed to express, purify, and characterize a novel recombinant trypsin derived from Fenneropenaeus merguiensis.

Methods: The cDNA encoding a putative trypsin (801 bp) was isolated from the hepatopancreas of F. merguiensis and expressed in E. coli Rosetta-gami. The recombinant enzyme was purified using nickel sepharose affinity chromatography. Biochemical characterization included spectrophotometric kinetic and thermodynamic analyses, circular dichroism, and spectrofluorimetry. Molecular weight was determined by SDS-PAGE. Kinetic parameters (Km, Vmax, kcat, kcat/Km) were measured using casein as substrate.

Results: Sequence alignment revealed a high similarity (92–95%) with trypsins from F. chinensis, P. vannamei, and F. mondon. The purified recombinant enzyme exhibited a molecular weight of 23 kDa. Optimal activity was observed at pH 8 and 50 °C, with stability across pH 7–9 and retention of ~50% activity from 40–70 °C. The enzyme's half-life at pH 8 and 50 °C was 21.72 minutes. Kinetic analysis yielded Km = 130.4 µg/ml, Vmax = 0.0617 $\mu g \cdot min^{-1} \cdot ml^{-1}$, kcat = 131.8 min^{-1}, and kcat/Km = 1.01 $min^{-1} \cdot \mu g^{-1}$. The recombinant trypsin displayed favorable thermal stability and alkaline tolerance, indicating its potential for industrial and biotechnological applications.

Conclusion: A novel recombinant trypsin from F. merguiensis was successfully produced, purified, and biochemically characterized. Its thermal stability, alkaline pH tolerance, and favorable catalytic efficiency highlight its suitability as a promising alternative to traditional marine-derived trypsins for biotechnological and diagnostic applications.

keywords: Recombinant trypsin; Fenneropenaeus merguiensis; Enzyme characterization; Thermal stability; Kinetics; Biotechnology

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-3

Combining Molecular and Biochemical Markers to Develop a Multi-Biomarker Model for Early Preeclampsia Detection

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Background and aim: Preeclampsia is a complex hypertensive disorder and a leading cause of maternal-fetal complications. Its early detection is challenging, as symptoms arise after irreversible placental damage. The condition involves angiogenic imbalance, oxidative stress, and immune dysfunction, with elevated sFlt-1 and reduced VEGF levels. While traditional markers like uric acid and LDH lack specificity, integrating miR-155 may improve diagnostic accuracy through a more precise multi-biomarker approach.

Methods: This case-control study included 40 pregnant women (20 preeclamptic, 20 normotensive) between 20–32 weeks of gestation. Venous blood samples were collected and divided into serum and EDTA tubes. Serum sFlt-1 and VEGF were measured by ELISA, and uric acid and LDH by enzymatic methods. Total RNA, including miRNAs, was extracted from peripheral blood mononuclear cells, and miR-155 expression quantified by qRT-PCR using U6 as control. Relative expression was calculated by the 2^−ΔΔCt method. Data were analyzed with GraphPad Prism 8 using t-test or Mann–Whitney U test, correlations by Pearson/Spearman, and ROC and logistic regression for diagnostic evaluation.

Results: Serum sFlt-1, uric acid, and LDH levels were significantly higher in women with preeclampsia, while VEGF and miR-155 expression were markedly reduced (p 0.001). miR-155 showed a strong inverse correlation with sFlt-1 and a positive association with VEGF, indicating its role in angiogenic regulation. ROC analysis showed that individual biomarkers had good predictive accuracy. However, the combined panel of miR-155, sFlt-1, VEGF, LDH, and uric acid had the best diagnostic performance, with very high sensitivity and specificity. These findings highlight the multifactorial nature of preeclampsia, suggesting miR-155 as a regulatory link between angiogenic imbalance and biochemical markers, offering a reliable strategy for early detection and risk assessment.

Conclusion: This study suggests that combining miR-155 with angiogenic and biochemical markers offers a more effective approach for the early detection of preeclampsia. The multi-biomarker model enhances diagnostic accuracy and supports timely intervention, potentially reducing risks for both mother and baby. Incorporating this strategy into prenatal screening could improve personalized risk prediction and overall pregnancy care outcomes.

keywords: Preeclampsia, miR-155, sFlt-1 / VEGF pathway, Uric acid, LDH

OBi-4

Molecular and Clinical Significance of the miR-21/MMPs/VEGF Signaling Axis as Diagnostic and Potential Biomarkers in Gastric Cancer

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Background and aim: Gastric cancer(GC) remains a major global health burden, largely due to the lack of reliable molecular indicators for early detection. Matrix metalloproteinases(MMP-2/9), vascular endothelial growth factor(VEGF), and microRNA-21(miR-21) are known contributors to tumor invasion and angiogenesis; however, their coordinated regulation and diagnostic potential have not been comprehensively evaluated.

Methods: In this case-control study, tissue samples from 27 patients and their serum were collected. Gene expression of miR-21, MMP-2, MMP-9, and VEGF was analyzed using SYBR green qRT-PCR. For protein levels, Western blotting was used, and gelatin zymography was employed to determine the enzymatic activity of MMP-2 and MMP-9 in serum. Statistical analysis was performed using SPSS 16, Graphpad prism and Rstudio softwares, with a significance level set at P0.05.

Results: Gene expression of miR-21, MMP-9, and VEGF was significantly upregulated in tumor tissues (p0.001, p=0.0081, p=0.0036, respectively). A prominent increase in the protein levels(p0.001) and enzymatic activity(p0.001) of MMP-2 and MMP-9 was also observed in patients. Correlation analysis revealed a positive correlation between miR-21 expression and tumor size(p0.001) and histological grade(p=0.001). the area under curve(AUC) for miR21 mRNA expression was 0.907(95% CI, 0.826–0.988), (sensitivity77%; specificity96%),(P0.0001).

Conclusion: Our findings suggest that miR-21, MMPs, and VEGF plays a role in gastric cancer progression through molecular convergence. Also, this study provides the first integrative evaluation of transcriptional, translational, and functional alterations in the miR-21/MMPs/VEGF axis in gastric cancer. The findings highlight miR-21 as a promising early diagnostic biomarker and reveal MMP-9 as a key effector of tumor invasion and angiogenesis.

keywords: Gastric Cancer, miR-21, MMP-2, MMP-9, VEGF, Angiogenesis, Tumor Invasion

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-5

miR-125 Overexpression in the Ovaries of a DHEA-Induced Mouse Model of Polycystic Ovary Syndrome

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Background and aim: Polycystic ovary syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age and is associated with menstrual dysfunction, hyperandrogenism, and characteristic ovarian morphological abnormalities. Recent studies highlight the involvement of microRNAs (miRNAs) in ovarian regulation and PCOS pathogenesis. Among these, miR-125 has emerged as a potential regulator of follicular development and hormonal balance.

Methods: In this experimental study, sixteen immature female NMRI mice (21–22 days old) were randomly divided into control and PCOS groups. PCOS was induced by daily intraperitoneal administration of dehydroepiandrosterone (DHEA, 6 mg/kg) for 21 consecutive days, while control animals received sesame oil as the vehicle. Ovarian morphology was evaluated using hematoxylin and eosin (H&E) staining. Serum levels of testosterone and follicle-stimulating hormone (FSH) were measured to confirm PCOS induction. The relative expression of miR-125 in ovarian tissue was assessed by real-time PCR using U6 as an internal reference.

Results: Histological examination of ovaries from the PCOS group revealed typical PCOS-like features, including the absence of corpora lutea and an increased number of atretic follicles. Hormonal analysis showed a significant elevation in serum testosterone levels accompanied by reduced FSH concentrations in PCOS mice compared with controls. Moreover, real-time PCR analysis demonstrated a marked upregulation of miR-125 expression in ovarian tissue of the PCOS group ($P \leq 0.001$).

Conclusion: The significant overexpression of miR-125 in the ovaries of DHEA-induced PCOS mice suggests a potential role for this miRNA in the pathophysiology of PCOS. These findings indicate that miR-125 may serve as a promising biomarker or therapeutic target in future PCOS-related research.

keywords: Polycystic ovary syndrome; miR-125; Ovary; Dehydroepiandrosterone; Mouse model

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-6

Association Between Exposure to Organochlorine/Organophosphate Pesticides and Hematologic Malignancies: A Case-Control Study With Molecular and Biochemical Analysis

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Background and aim: Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) are among the hematological malignancies whose occurrence has been linked to environmental risk factors, including organochlorine and organophosphates. The present study aimed to use biological, biochemical, and molecular analyses to investigate the occurrence of hematological malignancies using Kerman province's level of pesticide exposure.

Methods: A total number of 72 patients with hematological malignancies and 72 healthy people participated in this case-control study. Gas chromatography measured the organochlorine pesticide levels; oxidative stress indices (MDA and TAC) and detoxifying enzyme activity (AChE, PON1) were investigated. We applied survival models (Kaplan-Meier, Cox) and logistic regression analysis among statistical tests.

Results: The patient group (P0.001) had notably higher levels of organochlorine and organophosphate toxins. Patients' oxidative stress was raised while AChE and PON1 enzyme activities were drastically lowered. Patients showed higher markers of CD13, CD19, and CD33; the NF-κB, JAK-STAT, and PI3K/AKT signaling pathways were also triggered. Reduced survival in patients (HR=2.8, P0.001) and hematological malignancies were found to be independently caused by agricultural toxins.

Conclusion: The findings of the present study underline the need for careful monitoring and lowering of exposure in high-risk areas and the significant part of agricultural toxins in the occurrence of biochemical, genetic, and epigenetic changes resulting in hematological malignancies.

keywords: Exposure to agricultural toxins; Hematological malignancies; Oxidative stress; Detoxification enzyme

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-7

Antidiabetic effects of Astragalus adscendens extract through controlling oxidative stress, inflammation and apoptosis in streptozotocin-induced diabetic rats

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Background and aim: Diabetes mellitus is well-known as the most prevalent endocrine illness. Along with many chemical drugs that are used to control and treat diabetes, the use of herbal drugs can have a complementary effect on these drugs or even be a suitable alternative to them with fewer side effects and lower cost. To assess the effect of oral treatment of methanolic extract of the aerial parts of Astragalus adscendens in streptozotocin-induced diabetic rats.

Methods: In order to induce diabetes, rats intraperitoneally received streptozotocin at 65 mg/kg. Sixty adult male Wistar rats were allocated into six groups (10 rats per each) including the healthy control group, the diabetic group as well as the diabetic group treated with Astragalus adscendens methanolic extract at 50, 100, and 200 mg/kg per day or glibenclamide (0.6 mg/kg/day) for 28 d. The effects of Astragalus adscendens methanolic extract on the levels of glucose, insulin, alanine aminotransferase, alkaline phosphatase, aspartate aminotransferase, bilirubin, creatinine, urea, uric acid, total protein, albumin, triglyceride, cholesterol, α-amylase, oxidant/antioxidant enzymes, and inflammatory cytokines were evaluated. Real time-PCR was also used for measuring the gene expression of caspase-3, Bcl2, and Bax.

Results: The levels of glucose, cholesterol, triglyceride, creatinine, urea, uric acid, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, bilirubin, and malondialdehyde considerably declined (P0.001) in diabetic rats after treatment with Astragalus adscendens methanolic extract especially at a dose of 200 mg/kg. In addition, treatment with Astragalus adscendens methanolic extract noticeably increased the level of insulin, total protein, and albumin as well as improved the activities of catalase, glutathione peroxidase, and superoxide dismutase, as well as the expression levels of TNF-α, IL-1β, caspase-3, Bcl2 and Bax (P0.001) compared to the diabetic control group. The extract also inhibited α-amylase in a dose-dependent manner with an IC50 value of 19.6 µg/mL.

Conclusion: Astragalus adscendens methanolic extract shows potent antidiabetic, anti-inflammatory, anti-apoptotic, and antioxidant effects in diabetic rats. However, more studies are needed to verify the underlying mechanism of the effect of this plant extract and test its efficacy in clinical trials.

keywords: Herbal medicines; Astragalus adscendens; Diabetes; Antioxidant; Antidiabetes; Streptozotocin; Antiinflammation

OBi-8

Application of Risk-Based Quality Control to Optimize Sigma Metrics and Resource Utilization in Clinical Biochemistry

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Background and aim: Effective quality control ensures reliable results in clinical laboratories. Traditional QC strategies may overuse resources without improving performance. Risk-Based Quality Control (RbQC) customizes QC frequency based on analytical risk. Sigma metrics provide a quantitative measure of assay quality. This study evaluates the impact of RbQC implementation on improving Sigma Metrics in the clinical biochemistry laboratory.

Methods: This before-and-after interventional study was conducted in the clinical biochemistry section of Salman Farsi Hospital, Bushehr. Common tests (glucose, urea, creatinine, calcium, phosphorus, liver enzymes, bilirubin, LDH, CPK, amylase, and lipase) were analyzed. In Phase 1, standard QC was applied. In Phase 2, Risk-Based Quality Control (RbQC) was implemented based on Sigma Metrics. Sigma was calculated using TEa, bias (from EQA), and CV% (from IQC). QC frequency and rules were adjusted per Sigma performance. Data were analyzed using GraphPad Prism 8. A paired t-test or Wilcoxon test assessed changes in sigma values; p0.05 was considered significant.

Results: After implementing risk-based quality control, the average sigma metrics across 14 analytes increased from 3.4 ± 0.7 to 5.2 ± 0.5 (p 0.001). The most significant improvements were observed in glucose (from 3.2 to 5.8), ALT (3.6 to 5.5), AST (3.1 to 5.2), LDH (3.5 to 5.5), CPK (3.1 to 5.9), and amylase (3.1 to 5.3). Tests with baseline Sigma 4 improved by 50–70%. Overall QC frequency decreased by 32%, leading to a 28% reduction in control material consumption. These changes were statistically significant, confirming the effectiveness of the RbQC model in enhancing analytical performance and optimizing resource use. The results suggest Sigma-based QC design is superior to fixed schedules, particularly in high-volume biochemistry settings.

Conclusion: Risk-Based Quality Control Improved Sigma Metrics and reduced QC frequency and costs. This approach enables better resource utilization, fewer errors, and higher confidence in test results. Using RbQC can improve the quality of analysis and help clinical labs work more efficiently and reliably, meeting today's quality standards.

keywords: Risk-Based Quality Control, Sigma Metrics, Clinical Biochemistry

OBi-9

Nano-Quercetin–Mediated Activation of Autophagy and Amelioration of Non-Alcoholic Steatohepatitis via Inhibition of the PI3K/AKT/mTOR Pathway in Male Wistar Rats

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Background and aim: Non-alcoholic steatohepatitis (NASH) is a progressive liver disease characterized by lipid accumulation, inflammation, and hepatocellular injury, which may progress to fibrosis and cirrhosis. Impaired autophagy and overactivation of the PI3K/AKT/mTOR pathway play a key role in NASH pathogenesis. Quercetin, a natural flavonoid with antioxidant and anti-inflammatory properties, has limited bioavailability, leading to the development of nano-quercetin to enhance cellular uptake and efficacy. This study investigated the effects of nano-quercetin on autophagy activation and improvement of NASH via inhibition of the PI3K/AKT/mTOR pathway in male Wistar rats.

Methods: Male Wistar rats were randomly divided into control, NASH, and NASH plus nano-quercetin–treated groups. NASH was induced using a high-fat diet for several weeks. Nano-quercetin was administered during the experimental period. Liver tissues were collected for histopathological assessment and molecular analyses. The expression levels of autophagy-related markers (LC3-II, Beclin-1, and p62), as well as components of the PI3K/AKT/mTOR pathway, were evaluated using RT-PCR and western blot techniques.

Results: The NASH group showed significant hepatic steatosis, inflammatory infiltration, and hepatocellular ballooning compared with the control group. These changes were accompanied by suppression of autophagy markers and activation of the PI3K/AKT/mTOR pathway. Treatment with nano-quercetin markedly improved liver histopathology and reduced inflammatory responses. Moreover, nano-quercetin significantly enhanced autophagy, as indicated by increased LC3-II and Beclin-1 levels and decreased p62 expression, while concurrently inhibiting PI3K, AKT, and mTOR activation (P 0.05).

Conclusion: The findings suggest that nano-quercetin ameliorates non-alcoholic steatohepatitis by activating autophagy and inhibiting the PI3K/AKT/mTOR signaling pathway. Nano-quercetin may represent a promising therapeutic strategy for the management of NASH, although further studies are warranted.

keywords: Nano-Quercetin, NASH, Autophagy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-10

Serum CTRP1 Levels in Candidates for Coronary Artery Bypass Graft

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Background and aim: Coronary artery disease (CAD) results from atherosclerotic plaque formation, causing reduced blood flow. Its pathophysiology involves hypercholesterolemia, inflammation, oxidative stress, and endothelial dysfunction. CTRP1, an adipokine regulating metabolism and inflammation, is elevated in CAD and correlates with disease severity. Oxidized LDL increases CTRP1 and inflammation. This study assessed CTRP1 and its association with inflammatory markers in CABG patients

Methods: This study, approved by the Ethics Committee of Kerman University of Medical Sciences and following the Declaration of Helsinki, included 30 CAD patients scheduled for CABG surgery and 30 controls without CAD. All participants had a BMI below 30 kg/m², did not consume alcohol, and met inclusion criteria. After 12 hours of fasting, 5 cc of venous blood was collected from each participant to assess lipid profile, fasting blood glucose, inflammatory markers, and CTRP1 levels. Serum CRP, hs-CRP, IL-6, TNF-α, and CTRP1 were measured using ELISA, with absorbance read at 450 nm. Anthropometric data were recorded, and standard biochemical methods were applied. Statistical analyses were performed with SPSS, using appropriate parametric or non-parametric tests and Pearson correlation to evaluate associations between variables.

Results: , there were no significant differences in age or BMI between CAD patients and controls. However, the patient group had significantly higher levels of inflammatory markers, including IL-6, TNF-α, CRP, and hs-CRP, indicating elevated systemic inflammation. Circulating CTRP1 levels were markedly higher in patients (37.12 ng/mL) compared to controls (13.34 ng/mL), with this difference being statistically significant (P 0.001). Correlation analysis demonstrated strong positive associations between CTRP1 and inflammatory markers: CRP (r = 0.461), hs-CRP (r = 0.741), IL-6 (r = 0.759), and TNF-α (r = 0.543), all with P 0.001. These findings suggest that elevated CTRP1 is closely linked to systemic inflammation in CAD patients.

Conclusion: Our data demonstrated higher circulating levels of CTRP1 in patients who were candidates for cardiac bypass surgery. Furthermore, inflammatory markers such as TNF-α, IL-6, CRP, and hs-CRP showed a positive correlation with CTRP1. However, further investigation is necessary to fully elucidate the roles of CTRP1 in coronary artery disease

keywords: IL-6; TNF-α; hs-CRP

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-11

Association of healthy eating index (HEI), alternative healthy eating index (AHEI) with antioxidant capacity of maternal breast milk and infant's urine: a cross-sectional study

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Background and aim: Maternal dietary quality may alter the nutrient content of breast milk. In this study, we aimed to investigate the relationship between the healthy eating index (HEI) and alternative healthy eating index (AHEI) of a breastfeeding mother's diet with the antioxidant profile of her breast milk and her infant's urine.

Methods: This study included 300 healthy mother-infant pairs. The participants' dietary intake was estimated using a validated semi-quantitative food frequency questionnaire. The diet quality of participants was assessed using the HEI and AHEI. The total antioxidant content of the breast milk and infant's urine was evaluated using ferric reducing antioxidant power (FRAP), 2, 2′-diphenyl-1-picrylhydrazyl (DPPH), thiobarbituric acid reactive substances (TBARs), and Thiol quantification assays.

Results: After adjusting for confounding factors, the odds of a low malondialdehyde (MDA) content of breast milk were significantly higher in the highest quartile of HEI than in the lowest quartile. The odds of low DPPH and FRAP in infant urine decreased in the highest quartile of HEI compared to the lowest quartile. No significant relationship was found between AHEI and antioxidant levels of breast milk and the infant's urine.

Conclusion: Our findings demonstrate that a high quality diet of breastfeeding mothers, identified by a higher HEI, can affect the oxidant-antioxidant balance of a mother's breast milk and her infant's urine.

keywords: HEI, AHEI, Oxidant-antioxidant balance, Breast milk, Urine, Breastfeeding mothers

OBi-12

Resveratrol improves lipid profile and recovers heart function in postoperative CABG patients

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Background and aim: Cardiovascular diseases, particularly coronary artery disease, remain a leading cause of global mortality. Although coronary artery bypass grafting is an effective treatment, postoperative complications related to cardiovascular function and oxidative stress are common. Resveratrol is a natural polyphenol with antioxidant and anti-inflammatory properties. This study aimed to evaluate the effects of resveratrol supplementation on cardiovascular indices, lipid profile, and oxidative stress markers in patients after CABG surgery

Methods: This randomized, double-blind, placebo-controlled clinical trial was conducted at Bushehr Heart Center, Iran. Sixty patients undergoing CABG were randomly assigned to receive either resveratrol capsules or placebo for 60 days. Cardiovascular parameters, lipid profile, cardiac enzymes, and oxidative stress and inflammatory markers were measured at baseline and after the intervention. Statistical comparisons were performed between the two groups to assess treatment effects

Results: Resveratrol supplementation significantly reduced systolic blood pressure, triglycerides, total cholesterol, and LDL levels, and significantly improved ejection fraction compared with placebo. Although reductions in cardiac enzymes such as CPK and LDH were observed in the resveratrol group, these changes were not statistically significant. No significant differences were found between groups in diastolic blood pressure, HDL levels, or oxidative stress markers

Conclusion: Resveratrol supplementation after CABG surgery may improve cardiovascular function and lipid profile, suggesting a potential protective role in postoperative management. However, its effects on cardiac enzymes and oxidative stress markers appear limited, warranting further studies with larger sample sizes and longer follow-up durations

keywords: Cardiovascular disease; Coronary artery bypass grafting; Resveratrol; Lipid profile

OBi-13

Correlation Between Serum Lactate Dehydrogenase Levels and Pain Severity in Vaso-Occlusive Crises Among Sickle Cell Anemia Patients

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Background and aim: Prognostic markers play a crucial role in predicting disease severity and guiding preventive and therapeutic strategies in patients with sickle cell anemia (SCA). Lactate dehydrogenase (LDH) is considered a surrogate marker of hemolysis and tissue injury. This study aimed to investigate the association between serum LDH levels and the severity of painful vaso-occlusive crises (VOC) in patients with SCA.

Methods: This cross-sectional analytical study was conducted on 89 patients with confirmed SCA who were admitted to the Emergency Hematology Department of Baghaei 2 Hospital, Ahvaz, Iran, with painful VOC in 2018. Following clinical evaluation, laboratory tests, including complete blood count (CBC), serum LDH, and C-reactive protein (CRP), were performed at admission. Pain severity was assessed using the Visual Analog Scale (VAS) by a trained nurse. Statistical analyses were performed to evaluate correlations between LDH levels and clinical outcomes.

Results: The gender distribution was balanced, with no statistically significant difference between males and females (P0.05). The mean age of participants was 15.56 ± 2.86 years (range: 4–18 years), and 83.15% were aged between 14 and 18 years. A strong and statistically significant positive correlation was observed between serum LDH levels and pain severity scores (p 0.0001). Male patients exhibited significantly higher mean LDH levels compared to females (P=0.049). Although LDH levels showed a positive correlation with the duration of hospitalization, this association was not statistically significant (P = 0.437). Six patients required intensive care unit (ICU) admission and demonstrated significantly higher LDH levels than non-ICU patients (P0.001). One ICU-admitted patient (12.1%) died; however, elevated LDH levels were not significantly associated with mortality (P=0.814).

Conclusion: Serum LDH levels are significantly associated with pain severity in SCA patients experiencing painful crises and are markedly elevated in patients requiring ICU admission, particularly among males. Although no significant relationship was observed between LDH and hospitalization duration or mortality, LDH may serve as a useful biomarker for disease severity in SCA, warranting further investigation in larger prospective studies.

keywords: Sickle Cell Anemia; Lactate Dehydrogenase; Vaso-Occlusive Crisis; Pain Severity; Prognostic

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-14

p53-Independent Apoptotic–Necroptotic Cell Death and NF-κB/STAT3 Attenuation by Nyctanthes arbor-tristis Alkaloids in Human PDAC Cells

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Background and aim: Pancreatic ductal adenocarcinoma (PDAC) is highly lethal and frequently harbours TP53 mutations, rendering classical apoptosis-targeted therapies insufficient. Non-canonical cell death pathways and inflammatory signalling hubs such as NF-κB and STAT3 are emerging as attractive targets in therapy-resistant PDAC. Nyctanthes arbor-tristis (NAT) is an underexplored ethnomedicinal plant with reported anticancer properties, including p53-independent apoptosis and necroptosis in hepatocellular carcinoma. This study aimed to investigate whether an alkaloid-enriched fraction from NAT leaves (NAT-AF) can induce p53-independent cell death and modulate NF-κB/STAT3 signalling in human PDAC cell lines, while sparing non-tumorigenic pancreatic epithelial cells.

Methods: Leaves of Nyctanthes arbor-tristis were extracted hydro-alcoholically and subjected to acid–base fractionation to obtain an alkaloid-enriched fraction (NAT-AF); total alkaloid content and major components were assessed by colorimetry and LC–MS. Human PDAC cell lines PANC-1 and MIA PaCa-2 (mutant TP53) and non-tumorigenic HPDE cells were cultured under standard conditions. Cytotoxicity and IC_{50} values were determined by resazurin viability assay and clonogenic survival. Annexin V/PI flow cytometry, cell-cycle analysis, and Western blotting for caspase-3, Bax/Bcl-2, AIF, RIPK3, MLKL and phospho-MLKL were used to characterize death pathways. NF-κB p65 and STAT3 phosphorylation, nuclear localization and transcriptional activity were evaluated by Western blot and luciferase reporter assays. Reactive oxygen species (ROS) involvement was probed using N-acetylcysteine; roles of caspases and RIPK1 were assessed using z-VAD-fmk and necrostatin-1.

Results: NAT-AF reduced viability of PANC-1 and MIA PaCa-2 cells in a concentration- and time-dependent manner with 48-h IC_{50} values of 22–35 μg/mL and ~2–3-fold selectivity over HPDE cells. Clonogenic assays confirmed marked suppression of long-term survival. Flow cytometry and immunoblotting showed a mixed apoptotic/necroptotic programme with caspase-3 activation, Bax/Bcl-2 imbalance, AIF nuclear translocation, and RIPK3/MLKL upregulation plus phospho-MLKL accumulation, while p53 and p21 levels remained largely unchanged, indicating p53-independent death. NAT-AF decreased NF-κB p65 and STAT3 phosphorylation, nuclear translocation and reporter activity by ~60–70%. ROS generation preceded cell death; N-acetylcysteine partially restored viability and apoptotic markers but did not fully reverse NF-κB/STAT3 inhibition, suggesting both ROS-dependent and independent mechanisms.

Conclusion: An alkaloid-enriched fraction from Nyctanthes arbor-tristis leaves induces p53-independent, mixed apoptotic–necroptotic cell death and attenuates NF-κB/STAT3 signalling in TP53-mutant PDAC cells with modest selectivity over non-tumorigenic pancreatic cells. NAT-AF thus represents a useful mechanistic probe for simultaneously targeting stress and inflammatory pathways in PDAC, and highlights the promise of underexplored ethnomedicinal plants as sources of multi-target anticancer leads. However, limited selectivity, incomplete pathway resolution and lack of in vivo data underscore the need for phytochemical refinement and further preclinical validation before clinical translation.

keywords: Nyctanthes arbor-tristis,Pancreatic ductal adenocarcinoma,p53-independent cell death,NF-κB,STAT3

OBi-15

Effects of Resveratrol on Inflammatory and Hematological Markers in COVID-19 Patients: A Randomized Clinical Trial

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Background and aim: Coronavirus disease 2019 (COVID-19) is characterized by excessive inflammation and immune system dysregulation, which play a key role in disease progression. Natural compounds with anti-inflammatory properties have been proposed as supportive therapeutic options. Resveratrol, a polyphenolic compound found in several plants, exhibits potent anti-inflammatory and antioxidant effects.This study aimed to evaluate the effects of resveratrol supplementation on inflammatory cytokines and laboratory parameters in patients with COVID-19.

Methods: In this double-blind randomized clinical trial, 44 patients with confirmed COVID-19 were randomly assigned to receive either resveratrol (750 mg/day, n = 24) or placebo (n = 20) for 10 days. Biochemical and hematological parameters, along with plasma levels of interleukin-1 beta (IL-1β), interleukin-6 (IL-6), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF-α), were measured at baseline and at the end of the intervention.

Results: Compared with the placebo group, resveratrol supplementation significantly reduced C-reactive protein, IL-1β, and TNF-α levels. Significant improvements were also observed in hematological parameters, including reductions in white blood cell count, neutrophils, and platelet count, accompanied by an increase in lymphocyte levels. In addition, fasting blood sugar and alkaline phosphatase levels were significantly decreased in the resveratrol group.

Conclusion: Resveratrol supplementation may reduce inflammatory cytokines and improve laboratory markers related to inflammation and immune response in patients with COVID-19, suggesting its potential. The trial was prospectively registered at IRCT.ir as IRCT20111119008129N13. Registration date: 2022–10–11.

keywords: Resveratrol COVID-19 Cytokines Inflammation

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-16

Proliferation and xenotransplantation of human spermatogonial stem cells

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Background and aim: Two-dimensional (2D) culture systems offer a valuable in vitro method for studying human spermatogonial stem cell (SSC) proliferation and differentiation, with implications for understanding spermatogenesis and managing male infertility, especially in prepubertal cancer patients. This study aimed to examine the proliferation of human SSCs co-cultured with Sertoli cells in 2D, culture system.

Methods: Testicular cells from brain-dead patients were cultured in a 2D system for 3 weeks. After culture, viable and functional SSCs were evaluated via xenotransplantation, and cell identity was confirmed using immunocytochemistry, flow cytometry, and RT-PCR. Colony number and expression of SSC and Sertoli cell markers were also assessed.

Results: Following two-step enzymatic digestion, testicular cell viability exceeded 91%. Transplanted SSCs migrated to the basement membrane of recipient mice seminiferous tubules. PLZF, α6-Integrin, and Vimentin were expressed in SSCs and Sertoli cells in 2D culture. RT-PCR analysis of human testicular cells after the second digestion revealed expression of pre-meiotic (VASA, OCT4, PLZF, α6-Integrin), meiotic (SCP3), and post-meiotic (PRM2) genes. However, after three weeks of 2D pre-culture, only pre-meiotic genes (VASA, OCT4, PLZF, and α6-Integrin) were detected; meiotic and post-meiotic genes (SCP3 and PRM2) were not expressed. SSC purification rates and enrichment during 2D culture showed that 18% of human testicular cells were PLZF-positive after the second digestion and differential plating (day 0). After 21 days of 2D culture, PLZF marker expression increased significantly compared to day 0 (73.5%, $P \leq 0.01$), demonstrating a gradual enrichment of SSCs in 2D culture over 21 days.

Conclusion: This system can enhance human SSC proliferation in prepubertal male cancer patients and azoospermic men, yielding sufficient SSCs for successful transplantation and in vitro spermatogenesis.

keywords: Two-dimensional (2D) culture system, Spermatogonial stem cell, Proliferation, Sertoli cell

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-17

Three-dimensional co-culture of human spermatogonial stem cells with Sertoli cells in soft agar culture system

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Background and aim: Mimicking the seminiferous tubule microenvironment through spatial arrangement is crucial for in vitro germ cell proliferation and differentiation. Three-dimensional (3D) culture systems offer a suitable niche, replicating the seminiferous tubule's microenvironment and spatial organization. The soft agar culture system (SACS), a 3D culture system, enhances cell-cell interactions and protects against cell damage in long-term spermatogonial stem cell (SSC) culture by creating a spatial structure for SSCs and Sertoli cells. The aim of the study was to use a 3D culture system of Sertoli cells, growth factors, and Laminin in SACS to assess SSC proliferation and colony formation.

Methods: Testicular cells from brain-dead patients were cultured in a 2D system for 3 weeks, then collected, washed with PBS, and differentially plated to reduce Sertoli cell contamination. The resulting cells were seeded in the upper layer of SACS in four different groups: 1) SACS+SSCs+Sertoli cells+DMEM/F12; 2) SACS+SSCs+Sertoli cells+DMEM/F12+10 % KSR+GDNF (20 ng/mL) + LIF (10 ng/mL); 3) SACS+SSCs+Sertoli cells+DMEM/F12+10 % KSR+GDNF+LIF+bFGF (10 ng/mL) + SCF (100 ng/mL); and 4) SACS+SSCs+Sertoli cells+DMEM/F12+10 % KSR+GDNF+LIF+bFGF+EGF (20 ng/mL) + SCF+Laminin (100 µg/mL). Human SSC colony formation, immunocytochemistry for α6-Integrin, PLZF, and c-kit, and the expression of apoptosis genes (Bax and Bcl2) were assessed by real-time PCR.

Results: After 2 weeks of co-culture, group 4 exhibited significantly more colonies than groups 1 and 2 ($P \leq 0.001$) but not group 3 ($P \geq 0.05$). Group 4 also had significantly larger colonies than all other groups ($P \leq 0.01$). At week 3, group 4 maintained significantly higher colony number and diameter ($P \leq 0.05$). Immunocytochemistry showed α6-Integrin, PLZF, c-kit, and Vimentin expression in all groups. Group 4 had higher α6-Integrin and PLZF positive cells than groups 1 and 2 ($P \leq 0.001$), but not group 3 ($P \geq 0.05$), and lower c-kit positive cells than group 1 ($P \leq 0.001$). Vimentin expression was similar across groups. α6-Integrin and PLZF expression rates were higher in group 4 than other groups ($P \leq 0.05$ and $P \leq 0.001$, respectively), while c-kit was lower than group 1 ($P \leq 0.05$). Bax gene expression was highest in group 1 ($P \leq 0.05$ vs. groups 3 & 4), and Bcl2 was higher in group 4 than groups 1 & 2 ($P \leq 0.05$).

Conclusion: This 3D co-culture system reduces apoptosis and enhances the propagation of human SSCs. Thus, it can be used to improve SSC proliferation in prepubertal male cancer patients and azoospermic men, yielding sufficient SSCs for successful auto-transplantation and in vitro spermatogenesis.

keywords: Three-dimensional co-culture, Spermatogonial stem cell, Apoptosis

17th International Congress of Lab. and Clinic
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July 20-23, 2026

OBi-18

Early Laboratory Biomarkers for Acute Kidney Injury: A Systematic Review and Meta-Analysis

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Background and aim: Acute kidney injury (AKI) is a frequent and serious complication in hospitalized patients and is associated with increased mortality, prolonged hospital stay, and long-term renal impairment. Conventional diagnosis based on serum creatinine is inherently delayed and may fail to identify kidney injury at an early and potentially reversible stage. Over the past two decades, several laboratory biomarkers have been proposed for early AKI detection; however, their diagnostic performance has been reported with considerable variability. This systematic review and meta-analysis aimed to synthesize existing evidence on the diagnostic accuracy of early laboratory biomarkers for AKI and to evaluate their potential clinical

Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science for studies published between 2005 and 2025. Original human studies evaluating early AKI biomarkers—including neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), cystatin C, interleukin-18 (IL-18), and TIMP-2•IGFBP7—were included. Study quality was assessed using the QUADAS-2 tool. Pooled diagnostic accuracy was summarized using reported area under the receiver operating characteristic curve (AUC-ROC) values, applying a random-effects model.

Results: A total of 56 studies were included in the systematic review, of which 29 provided sufficient data for meta-analysis. Urinary TIMP-2•IGFBP7 demonstrated the highest and most consistent diagnostic performance, with pooled AUC values around 0.84–0.88 across different clinical settings. NGAL showed good diagnostic accuracy, with reported AUC values ranging from 0.70 to 0.91, particularly in critically ill patients. Cystatin C exhibited moderate to good performance (AUC approximately 0.79–0.93), while KIM-1 and IL-18 showed more modest and heterogeneous results. Urinary biomarkers generally outperformed serum-based markers. Moderate heterogeneity was observed among studies.

Conclusion: Early laboratory biomarkers, particularly TIMP-2•IGFBP7 and NGAL, provide clinically meaningful diagnostic accuracy for early detection of AKI before serum creatinine elevation. Their integration into routine laboratory workflows may support earlier intervention and improve patient outcomes.

keywords: Acute kidney injury; Biomarkers; NGAL; TIMP-2•IGFBP7; D; Meta-analysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-19

Evaluation of Serum Troponin Levels in Patients Presenting to the Emergency Department of Hekmat Hospital in Sari with Chest Pain upon Admission in the First Six Months of 1404 (2025-2026)

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Background and aim: Introduction Troponin is a cardiac muscle protein that is released into the blood when myocardial cells are damaged, and it is recognized as a sensitive and specific marker for diagnosing cardiac injuries, particularly in cases of myocardial infarction. According to published data up to 2023, cardiovascular diseases are among the most common and deadly groups of diseases worldwide, accounting for 31% of all global deaths. A positive troponin test usually indicates acute damage or stress to the heart muscle and can assist in early diagnosis and better management of cardiac diseases. Additionally, examining associated factors and changes in troponin levels

Methods: Materials and Methods The present research is a retrospective case review study in which a total of 485 individuals suspected of cardiac disease presented to the emergency department of Hekmat Hospital in Sari during the first six months of 1404. One of the common methods for troponin testing is immunoassay, in which, after collecting a blood sample (usually venous), the serum and plasma are separated from the blood sample. Then, by adding it to the test kit containing specific antibodies, we wait for the immunological reaction to occur, and the result is subsequently recorded by reading the device (often using optical or chemiluminescent methods).

Results: Findings In this study, out of a total of 485 individuals suspected of cardiac disease (presenting with chest pain, shortness of breath, epigastric pain) who presented to the emergency department of Hekmat Hospital in Sari, 5 individuals (1.03%) had positive troponin levels, with an average age of 72 years. Among all suspected cardiac patients, there were 3 men with an average age of 77 years and 2 women with an average age of 64 years.

Conclusion: Conclusion It appears that the selection of patients for serum troponin level testing should be done with greater precision and sensitivity, including clinical symptoms and electrocardiographic findings, in order to avoid imposing unnecessary costs and wasting resources, time for patients, and laboratory efforts.

keywords: Troponin, Electrocardiography, Cardiac diseases, Immunoassay

OBi-20

ERMP1 Regulates GRP78 Trafficking and Surface Localization in Stressed HCT116 Cells

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Background and aim: Objective: Cell surface GRP78 (csGRP78) promotes colorectal cancer (CRC) progression by aggregating at the membrane and binding ligands to regulate proliferation, migration, invasion, stemness, and chemoresistance. In this study, we tried to investigate the role of endoplasmic reticulum metallopeptide 1 (ERMP1), an ER membrane protein, in GRP78 localization and unfolded protein response (UPR) dynamics in HCT116 CRC cells.

Methods: Methods: HCT116 cells were cultured in RPMI-1640 medium containing 10% FBS and 5% CO2 at 37˚C humidified incubator. Recombinant lentivirus vectors comprising the shRNA ERMP1 and shRNA scramble were transduced in these cells. ERMP1 downregulated cells were regarded in stressful conditions for 72 h. The expression of GRP78 proteins was evaluated by western blotting and flow cytometry assay was carried out to determine the cell surface localization of GRP78.

Results: Results: Our western blot results show that ERMP1 knockdown did not alter total GRP78 protein expression in HCT116 cells under normal conditions, suggesting no direct transcriptional regulation. However, stressors including dithiothreitol (DTT), nutrient starvation, and 5-fluorouracil (5-FU) induced substantial GRP78 upregulation in ERMP1 down regulated HCT116 cells relative to scramble controls. The flowcytometry data of csGRP78 verified that ERMP1 knock down reduced csGRP78. DTT, starvation and 5-FU further diminished csGRP78 content, suggesting that these stresses may trap GRP78 in the ER lumen to mitigate stress rather than enhancing surface translocation.

Conclusion: Conclusion: These findings reveal ERMP1 as a key regulator of GRP78 trafficking, uncoupling total expression from surface localization during UPR activation. Targeting ERMP1 may sensitize CRC cells to ER stressors by impairing adaptive GRP78-mediated survival.

keywords: Keywords: Colorectal cancer, Endoplasmic reticulum metallopeptidase 1 (ERMP1), Cell surface

17th International Congress of Lab. and Clinic
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July 20-23, 2026

OBi-21

Assessment of the triclosan-induced changes in biochemical and histopathological parameters in liver of pregnant rats

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Background and aim: Triclosan (TCS) is an extensively-used antimicrobial agent found in wide range of personal care products. Hovevere, there are concerns regarding its safety, particularly its potential to act as an endocrine disruptor, cause reproductive toxicity, and exert adverse effects on vital organ systems including liver. Considering TCS's pervasive presence and its capability to cross the placental barrier, exposure in pregnant women represents a dual risk to both the mother's health and fetal development. This study was designed to investigate the effects of TCS on the oxidative stress, inflammation, and histopathological alterations in the livers of pregnant dams during gestation period.

Methods: Eighteen female Wistar rats, confirmed to be pregnant, were randomly divided into three groups (n=6 per each group) for oral gavage administration from the 1st to the 21st day of gestation as followed: I) control: corn oil-received group (vehicle), II) low-dose TCS group: received 10 mg/kg/day of TCS, and III) high-dose TCS group: received 100 mg/kg/day of TCS. On the 21st day of gestation, maternal rats were humanely euthanized based on ethical considerations (ethical code: R.MUBABOL.AEC.1401.034), and liver tissue samples were collected for biochemical and histopathological analyses. Biochemical measurements included liver enzyme activity (ALT, AST, ALP) in serum, oxidative stress biomarkers including Malondialdehyde (MDA) levels and the activity of Catalase (CAT) and Glutathione peroxidase (GPx) enzymes as well as the level of inflammatory marker, Interleukin-6 (IL-6) in liver tissue. All biochemical parameters were measured by commercial ELISA kits.

Results: Biochemical serum analysis demonstrated a significant elevation in ALT levels in both low- and high-dose TCS-treated groups compared to the control group, strongly indicating hepatocellular injury. However, no significant changes were observed in AST or ALP levels. Regarding oxidative stress, the results revealed a significant reduction in the activity of the antioxidant enzymes CAT and GPx in the treated dams. Concurrently, MDA levels, a key biomarker of lipid peroxidation, were significantly increased. These findings strongly suggest an impaired redox balance and the induction of severe oxidative stress by TCS exposure in dose-dependent manner. Also, the measurement of inflammatory markers showed a notable elevation in IL-6 levels in the liver tissue of high-dose TCS-exposed pregnant rats. Histopathological examination corroborated the biochemical results. Hepatic sections isolated from TCS-treated dams exhibited pronounced alterations, including congestion, infiltration of inflammatory cells, cellular necrosis, and widespread vacuolar degeneration of hepatocytes, with the severity being dose-dependent.

Conclusion: Our findings demonstrate that exposure to triclosan during pregnancy induces significant maternal hepatotoxicity. The underlying mechanism involves the severe induction of oxidative stress and systemic inflammatory responses, leading to histological insult of liver. Given this evidence, the use of TCS-containing personal care products by pregnant individuals is not recommended, as it not only compromises maternal health but also carries the potential for embryotoxicity. This strongly supports the need for greater regulatory scrutiny and caution regarding TCS use during critical periods of development.

keywords: Triclosan, Pregnancy, Hepatotoxicity, Rat, Oxidative stress

17th International Congress of Lab. and Clinic
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July 20-23, 2026

OBi-22

Association of Serum Amylase, Estimated Glomerular Filtration Rate, and Serum Insulin Levels in Metabolic Syndrome and Type 1 and Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis

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Background and aim: Metabolic syndrome (MetS), type 1 diabetes mellitus (T1DM), and type 2 diabetes mellitus (T2DM) are major metabolic disorders characterized by dysglycemia, insulin dysregulation, and multi-organ involvement. Beyond endocrine dysfunction, increasing evidence suggests interplay between exocrine pancreatic activity and renal function in metabolic disease. Serum amylase has been reported to correlate inversely with obesity, insulin resistance, and T2DM, while estimated glomerular filtration rate (eGFR) remains a key marker of renal impairment and cardiometabolic risk. Altered insulin levels reflect β-cell dysfunction in T1DM and insulin resistance in T2DM and MetS.

Methods: A systematic search of PubMed, Scopus, and Web of Science was conducted for studies published between 2000 and 2025. Eligible studies included observational (cross-sectional, case–control, or cohort) designs reporting serum amylase, eGFR, and/or fasting insulin levels in adults diagnosed with MetS, T1DM, or T2DM. Two reviewers independently screened articles, extracted data, and assessed quality using the Newcastle–Ottawa Scale. Random-effects meta-analysis was performed to estimate pooled standardized mean differences (SMD) with 95% confidence intervals (CI). Heterogeneity was evaluated using the I^2 statistic. Inclusion Criteria Human studies involving adults (≥18 years). Clear diagnostic criteria for MetS, T1DM, or T2DM. Reported quantitative data for at least one of the following: serum amylase, eGFR, or fasting insulin. Presence of a healthy control or comparator group. Published in peer-reviewed English-language journals. Exclusion criteria included animal studies, pediatric populations, acute pancreatitis, advanced chronic kidney disease (stage 4–5), and incomplete biochemical data.

Results: A total of 1,248 records were identified; 32 studies (n = 8,964 participants) met inclusion criteria. Meta-analysis demonstrated significantly lower serum amylase levels in T2DM compared with controls (SMD = −0.62; 95% CI: −0.85 to −0.39; I^2 = 58%). Patients with MetS also showed modestly reduced amylase levels (SMD = −0.41; 95% CI: −0.66 to −0.16). eGFR was significantly reduced in T2DM (SMD = −0.55; 95% CI: −0.79 to −0.31), whereas early T1DM showed variable but non-significant differences. Fasting insulin levels were elevated in MetS and T2DM but markedly reduced in T1DM, reflecting differing pathophysiological mechanisms. Subgroup analyses suggested a negative correlation between serum amylase and insulin resistance indices.

Conclusion: This meta-analysis indicates that reduced serum amylase and declining eGFR are associated with metabolic dysregulation, particularly in T2DM and MetS. The integrated assessment of pancreatic exocrine function, renal filtration status, and insulin dynamics may enhance understanding of metabolic disease progression and support early risk stratification. Further longitudinal studies are warranted.

keywords: Type 1 Diabetes Mellitus, Type 2 Diabetes Mellitus, Serum Amylase

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July 20-23, 2026

OBi-23

In-vitro study of homocysteine and aspirin effects on fibrinolysis: measuring fibrinolysis parameters

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Background and aim: Some studies suggest that increased homocysteine in blood leads to alterations in coagulation and fibrinolysis; however, the precise mechanism is not clear. The aim of this study was to compare different concentrations of homocysteine and aspirin on fibrinolysis in the plasma of healthy individuals in vitro.

Methods: Different concentrations of homocysteine (200, 100, and 50 µmol/1) and aspirin (100, 10, and 1 mg/l) were added to the healthy people plasma citrate. They were incubated at 37°C for 24 h. Then, fibrinolysis parameters were analyzed by the turbidimetric procedure at 405nm. The independent-samples t-test was utilized to compare them (P0.05).

Results: Findings revealed that homocysteine at 200 µmol/l with aspirin 100 ml/g had significant changes in the lysis maximum velocity (0.150 ± 0.002), half-lysis time (218 ± 5.77), the total lysis time (446 ± 5.77), and lag time in lysis (119 ± 3.60), compared to homocysteine at 200 µmol/l lysis maximum velocity (0.110 ± 0.002), half-lysis time (278 ± 7.63), the total lysis time (515 ± 14.29), and lag time in lysis (176 ± 3.60), respectively (P0.05). Homocysteine at 200 umol/l with aspirin 1 ml/g did not significantly change in either parameter (P0.05). Homocysteine at 50 µmol/l with aspirin (100, 10, and 1 mg/1) had significant changes in all fibrinolysis parameters (P0.05), compared to homocysteine at 50 umol/l. The other concentrations were compared in the same way.

Conclusion: Aspirin (more than 1 mg/1) had more effect on higher concentrations of homocysteine. Aspirin increased velocity of clot lysis and decreased lysis time of clot in the presence of homocysteine.

keywords: homocysteine, aspirin, fibrinolysis

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July 20-23, 2026

OBi-24

MOTS-c ameliorates histopathological, biochemical, inflammatory, and oxidative stress alterations in CCl_4-induced hepatic fibrosis in mice

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Background and aim: Liver fibrosis is a progressive wound-healing response to chronic hepatic injury and is still a major cause of liver-related morbidity worldwide. The condition is characterized by excessive deposition of extracellular matrix proteins, disruption of normal hepatic architecture, and gradual deterioration of liver function. Persistent inflammation and oxidative stress contribute substantially to fibrotic progression, emphasizing the need for effective therapeutic interventions. MOTS-c, a mitochondrial-derived peptide with metabolic and protective properties, has recently attracted attention for its potential protective effects in various pathological conditions. This study aimed to investigate the therapeutic effects of MOTS-c on CCl_4-induced liver fibrosis in male C57BL/6 mice.

Methods: Liver fibrosis was induced in male C57BL/6 mice through administration of carbon tetrachloride (CCl_4). Animals were randomly allocated into three experimental groups: control, fibrosis, and fibrosis treated with MOTS-c. At the end of the study period, blood and liver tissue samples were collected for biochemical, inflammatory, oxidative stress, and histological assessments. Histological examination was performed using hematoxylin and eosin, Masson's trichrome, and Sirius Red staining to evaluate tissue architecture, collagen accumulation, and fibrosis severity. Histopathological changes were graded using the Ishak and METAVIR scoring systems. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were measured as indicators of hepatocellular injury. Hepatic malondialdehyde (MDA) levels were assessed as a marker of oxidative stress, while hepatic interleukin-6 (IL-6) concentrations were determined to evaluate inflammatory activity. Liver weight was recorded during tissue harvesting. Statistical significance was defined as p 0.05.

Results: Histological analyses revealed severe architectural disruption, extensive collagen deposition, and pronounced necroinflammatory alterations in untreated fibrotic mice. In contrast, MOTS-c-treated animals exhibited improved hepatic architecture, reduced inflammatory infiltration, and diminished collagen accumulation. These findings were further supported by lower Ishak and METAVIR fibrosis scores compared with untreated fibrotic animals. CCl_4 administration induced substantial liver injury, as demonstrated by significant elevations in serum ALT and AST activities compared with control animals. Treatment with MOTS-c significantly reduced both liver enzymes, indicating attenuation of hepatocellular damage. Similarly, MDA levels were elevated in the fibrosis group, indicating increased oxidative stress, and were significantly reduced following MOTS-c treatment. Hepatic IL-6 levels were markedly increased in fibrotic mice, reflecting an enhanced inflammatory response, whereas MOTS-c administration significantly decreased IL-6 concentrations. Liver weight was significantly higher in fibrotic animals than in controls and was partially restored by MOTS-c administration.

Conclusion: MOTS-c exerts significant antifibrotic, anti-inflammatory, and antioxidative effects in experimental liver fibrosis. Moreover, MOTS-c alleviates histopathological damage by reducing collagen deposition and preserving hepatic architecture in CCl_4-induced liver fibrosis. Its protective actions are associated with reductions in hepatocellular injury markers, attenuation of oxidative stress through lowering MDA concentrations, suppression of IL-6 levels, and improvement of fibrosis-related liver weight changes. These findings support the therapeutic potential of MOTS-c as a promising candidate for managing chronic liver disease. Further studies are required to investigate underlying molecular gene expression mechanisms.

keywords: Liver fibrosis, Mitochondrial-derived peptide,Oxidative stress, inflammatory response

OBi-25

The Antifibrotic Effect of Fisetin in CCl4-Induced Liver Fibrosis in Mice Is Mediated by the Antioxidant System

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Background and aim: Liver fibrosis represents a major global health problem characterized by excessive extracellular matrix (ECM) accumulation and the disruption of liver architecture, which may eventually progress to end-stage liver diseases such as cirrhosis and hepatocellular carcinoma. Therefore, inhibiting the progression of fibrosis may improve the treatment and recovery of these diseases. Fisetin is a naturally occurring flavonol that has garnered significant attention for its pharmacological effects, including anti-inflammatory, antioxidant, neuroprotective, and senolytic properties. This study aimed to evaluate the protective effects of fisetin against carbon tetrachloride (CCl4)-induced liver fibrosis in mice, with particular emphasis on oxidative stress-related markers.

Methods: Male C57BL/6 mice were randomly divided into five groups: control group, high-dose fisetin-alone group, CCl4-treated model group, and low and high dose (50 mg/kg and 100 mg/kg) of fisetin co-treated group. Serum ALT and AST activities were analyzed to evaluate liver function. H&E, Masson's trichrome, and Sirius Red staining were performed to assess liver morphology and the degree of liver fibrosis. Hepatic glutathione (GSH) content was determined to evaluate antioxidant status. The mRNA expression levels of NRF2 and HO-1 were measured to evaluate antioxidant-related gene expression.

Results: Fisetin administration markedly reduced serum markers of liver injury, including ALT and AST. H&E staining demonstrated improved liver histopathology, with reduced hepatocellular necrosis and inflammatory cell infiltration. Furthermore, Masson's trichrome and Sirius Red staining revealed a dose-dependent restoration of liver architecture. Fisetin increased hepatic GSH content and upregulated the mRNA expression levels of NRF2 and HO-1.

Conclusion: Our findings indicate that fisetin mitigates CCl4-induced liver fibrosis by improving hepatic antioxidant status, as evidenced by increased GSH content and enhanced NRF2 and HO-1 mRNA expression. These results suggest that fisetin may be considered a promising natural candidate for further investigation in the management of chronic liver injury.

keywords: Fisetin, Liver fibrosis, Oxidative stress, Nrf2/HO-1

OBi-26

Micronutrient Status and Oxidative Stress Biomarkers in Reproductive Health: From Laboratory Diagnostics to Clinical Fertility Outcomes

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Background and aim: Infertility affects approximately one in six individuals worldwide and represents a growing public health challenge with substantial medical, psychological, and socioeconomic consequences. Increasing evidence suggests that nutritional status influences reproductive function through interconnected metabolic, endocrine, inflammatory, and oxidative stress pathways. However, the extent to which micronutrients and dietary interventions contribute to fertility outcomes remains a subject of ongoing investigation. This review aimed to synthesize current evidence regarding the role of essential micronutrients, antioxidants, and dietary patterns in male and female fertility, while evaluating their potential clinical applications in fertility optimization and assisted reproductive technology (ART).

Methods: A narrative review of contemporary literature was conducted, focusing on studies examining the effects of vitamin D, folate, vitamin B12, iron, zinc, selenium, coenzyme Q10, antioxidant status, and dietary patterns on reproductive outcomes. Evidence from observational studies, systematic reviews, meta-analyses, and clinical trials was critically evaluated to identify mechanistic pathways, clinical benefits, limitations, and future research priorities.

Results: The available evidence indicates that nutritional factors influence fertility through three major biological axes: oxidative stress regulation, hypothalamic–pituitary–gonadal (HPG) axis function, and mitochondrial bioenergetics. Vitamin D, folate, iron, zinc, selenium, vitamin B12, and coenzyme Q10 contribute to gamete quality, hormonal regulation, implantation, and early embryonic development through distinct but interconnected mechanisms. Adherence to comprehensive dietary patterns, particularly the Mediterranean diet, appears to provide more consistent reproductive benefits than isolated micronutrient supplementation. Importantly, both nutritional deficiencies and excessive supplementation may adversely affect reproductive outcomes, highlighting the existence of an optimal physiological range for fertility-related nutritional interventions.

Conclusion: Nutrition represents a modifiable determinant of reproductive health and should be considered an integral component of preconception and infertility management. Current evidence supports individualized nutritional assessment and targeted correction of documented deficiencies rather than empirical high-dose supplementation. Future advances in precision nutrition, metabolomics, nutrigenomics, and biomarker-guided interventions may facilitate personalized fertility care and improve reproductive outcomes in both natural conception and ART settings.

keywords: Infertility Micronutrients Reproductive Health Oxidative Stress Mediterranean Diet Precision Nutrition

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-27

Experimental Evaluation of Sumatriptan Effects on Hormonal Profile, Spermatogenesis, and Oxidative Stress Parameters in Adult Male NMRI Mice

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Background and aim: Sumatriptan is a selective serotonin 5-HT1B/1D receptor agonist widely used in the treatment of migraine. While its neurological effects are well characterized, limited information is available regarding its potential impact on male reproductive function. Given the involvement of serotonergic signaling in the regulation of the hypothalamic–pituitary–gonadal axis and testicular function, investigating the reproductive effects of sumatriptan may provide insight into its potential impact beyond neurological targets.

Methods: Twenty-four adult male mice were randomly divided into four groups: sham, control, and two sumatriptan-treated groups receiving 0.1 or 0.5 mg/kg/day orally for 28 consecutive days. Serum testosterone levels were measured using enzyme-linked immunosorbent assay (ELISA). Sperm parameters, including sperm count, motility, viability, and morphology, were assessed using standard laboratory methods. Testicular oxidative stress status was evaluated by measuring malondialdehyde (MDA) levels and superoxide dismutase (SOD) activity. Histological examination of testicular tissue was performed to assess germ cell populations and somatic cell counts.

Results: Sumatriptan administration significantly increased serum testosterone levels and sperm count compared with control and sham groups. Testicular MDA levels were significantly reduced, while SOD activity was increased in sumatriptan-treated animals, indicating an improvement in antioxidant status. Histological analysis revealed increased numbers of primary spermatocytes and spermatids, particularly in the high-dose group. No significant differences were observed in sperm motility, viability, morphology, or Sertoli cell number among the experimental groups.

Conclusion: These findings suggest that sumatriptan may modulate male reproductive function in mice, potentially through endocrine regulation and attenuation of oxidative stress, without inducing adverse effects on sperm quality or testicular structure.

keywords: Sumatriptan, Serotonin, Spermatogenesis, Male fertility, Oxidative stress

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-28

Albumin-Conjugated Galbanic Acid as a Candidate Anti-Migratory and Antitumor Strategy in Colorectal Cancer Models

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Background and aim: Colorectal cancer remains a major global health challenge, and the limitations of conventional chemotherapy highlight the need for alternative therapeutic strategies with improved delivery profiles. Galbanic acid is a naturally derived sesquiterpene coumarin with reported anticancer activity; however, its poor aqueous solubility limits its experimental and pharmaceutical application. Human serum albumin may serve as a biocompatible carrier for hydrophobic compounds and may improve their biological availability. This study evaluated the anti-migratory and antitumor effects of albumin-conjugated galbanic acid in colorectal cancer models.

Methods: Galbanic acid was conjugated to human serum albumin using an EDC/NHS-mediated reaction and purified before biological evaluation. For the migration study, C26 colorectal cancer cells were cultured under serum-reduced conditions using 1% FBS to minimize proliferation-associated wound closure. Scratch wound-healing assays were performed using sub-cytotoxic GBA-equivalent concentrations corresponding to approximately ½ and ¼ of the calculated IC_{50}. Images were acquired at baseline and after 12, 36, and 60 h, and residual wound area was quantified using ImageJ-based analysis from selected microscopic fields. For in vivo assessment, a syngeneic subcutaneous C26 tumor model was established in female BALB/c mice. After tumor establishment, animals were allocated to control, vehicle, free galbanic acid, and albumin-conjugated galbanic acid groups. Treatments were administered intraperitoneally at 10 mg/kg GBA-equivalent in two doses during the study period. Tumor dimensions and body weight were monitored repeatedly, and tumor volume was calculated using standard caliper-based measurements.

Results: In the scratch assay, untreated/vehicle cells showed progressive wound closure over 60 h, while both free galbanic acid and albumin-conjugated galbanic acid delayed closure. The inhibitory effect became more evident after 36 h and was most apparent at 60 h. At matched GBA-equivalent concentrations, the albumin-conjugated formulation produced a stronger anti-migratory pattern than free galbanic acid, particularly at the lower sub-IC_{50} exposure, where the difference between formulations reached statistical significance in the final time point comparison. In the animal study, treatment was initiated when average tumor volume was in the early measurable range, approximately 25–45 mm^3 depending on the analysis set. Across the monitoring period, both free and albumin-conjugated galbanic acid altered tumor growth relative to the control/vehicle condition. No clear superiority of the albumin-conjugated formulation over free galbanic acid was observed under the tested two-dose regimen. Body-weight monitoring did not show a marked cachexia-like pattern attributable to the albumin-conjugated

Conclusion: Albumin-conjugated galbanic acid demonstrated measurable inhibition of C26 cell migration and showed antitumor activity in a syngeneic colorectal cancer model. Although the in vivo effect was not clearly superior to free galbanic acid under the tested regimen, the formulation remains a promising strategy for improving the experimental delivery of poorly water-soluble galbanic acid. Further studies with optimized dose frequency, longer follow-up, histopathology, and molecular pathway analysis are warranted.

keywords: Colorectal cancer; C26; galbanic acid; albumin conjugation; scratch assay; tumor

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-29

The effect of curcumin on NRF2/Keap1 signalling pathway in the epididymis of mouse experimental cryptorchidism

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Background and aim: Nrf2/Keap1 pathway, which prevents cellular damage against reactive oxygen species production, is disrupted in epididymis following cryptorchidism. In this study, we aimed to use curcumin (Cur) as an activator of Nrf2 to decrease the effects of disruption in this pathway caused by cryptorchidism. In this study, animals were randomly divided into following groups: control, sham-surgery, sham-vehicle, sham-Cur50, sham-Cur100, cryptorchidism, cryptorchidism-vehicle, cryptorchidism-Cur50 and cryptorchidism-Cur100. For cryptorchidism induction, the animals were anaesthetised with intraperitoneal injection of 100 mg/kg ketamine and 10 mg/kg xylazine (both from Alfasan). In the midline, the skin and muscles of the abdominal wall and peritoneum were cut to

Methods: Research and animal care protocols were approved by the Ethics Committee of Arak University of Medical Sciences. Animals were housed in a 12/12-h light/dark cycle (lights on at 7:00 AM) and climate-controlled condition with free access to water and food.

Results: According to our results, all sperm parameters including concentration, movement and viability decreased in the both cryptorchidism and crypt-vehicle groups compared to the control and sham groups ($p \leq 0.05$). The use of Cur, especially at a dose of 100 mg/kg, could improve all of these parameters compared to the cryptorchidism and crypt-vehicle groups. In order to assess the effects of Cur on Nrf2/Keap1 pathway, we evaluated the expression of some genes involved in this pathway including Nrf2, NQO1, HO1 and Keap1 in the epididymis of experimental animals. According to our results, the expression of Nrf2, NQO1 and HO1 significantly downregulated in the both cryptorchidism and crypt-vehicle groups compared to the control and sham groups ($p \leq 0.05$). The level of Keap1 also decreased following cryptorchidism induction, but it was not significant. Treatment with both doses of Cur significantly increased the level expression of Nrf2 and HO1 comp

Conclusion: Our data showed that Cur, especially at high doses, could improve sperm parameters and testis histopathology, which were damaged following cryptorchidism induction. The expression of HO1, NQO1, and Nrf2 genes, which had decreased in the cryptorchidism group, showed a significant increase after administration of Cur in a dose-dependent manner. Cur, by inducing the expression of genes involved in the Nrf2/Keap1 pathway, could reduce the adverse effects of cryptorchidism and might be used as adjuvant therapy for decreasing cryptorchidism complications before surgery.

keywords: cryptorchidism, curcumin, Nrf2/Keap1 pathway, sperm parameters, testis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-30

Development of Electrochemical Microfluidic Paper-Based Device for Determination of Ovarian Cancer Biomarker

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Background and aim: Ovarian cancer is one of the gynecologic malignancies with a high mortality rate, which is likely related to the lack of clear diagnostic signs in the early stages of the disease. CA125 is a well-established and clinically important biomarker for the early detection of ovarian cancer; however, conventional CA125 assays are generally costly, time-consuming, laboratory-dependent, and less compatible with point-of-care applications. Accordingly, the present study aimed to design and develop an electrochemical microfluidic paper-based device (µPAD) for CA125 detection as a simple, low-cost, and practical platform for use in resource-limited settings

Methods: An electrochemical µPAD was designed on chromatography paper using CorelDRAW and fabricated by pen-on-paper approach to create hydrophobic microfluidic barriers and a two-layer paper platform. The device consisted of a sample layer containing the working electrode and an auxiliary layer containing the reference and counter electrodes, forming a three-electrode electrochemical system. The working electrode was modified with a 3D-reduced graphene oxide-multiwall carbon nanotubes Au nanoparticle (3DrGO-MWCNTs-AuNP) and a thiolated aptamer, followed by bovine serum albumin blocking to reduce nonspecific adsorption. Electrochemical characterization was performed at room temperature using cyclic voltammetry with an Autolab workstation and the [Fe(CN)_6]^(3-/4-)redox probe.

Results: The permanent-marker pen-on-paper strategy successfully formed hydrophobic barriers throughout the paper thickness and produced defined hydrophilic microchannels and reaction zones. Cyclic voltammetry showed that modification of the working electrode with 3DrGO-MWCNTs-AuNP markedly increased the current response, indicating improved conductivity and electron-transfer properties of the sensing surface. After aptamer immobilization, the current intensity decreased significantly, consistent with successful aptamer attachment and increased resistance to electron transfer. A further current decrease was observed after binding of CA125 to the modified electrode, demonstrating successful target recognition by the fabricated paper-based aptasensor.

Conclusion: A low-cost electrochemical µPAD for CA125 detection was successfully prototyped under resource-limited conditions. The pen-on-paper fabrication approach provided a simple, rapid, and economical method for µPAD production, while electrochemical results confirmed successful surface modification and biomarker recognition. This platform shows promise for affordable point-of-care ovarian cancer testing.

keywords: CA125; µPAD; Aptasensor; Electrochemical Biosensor; Ovarian Cancer.

OBi-31

A systematic review and meta-analysis on efficacy of pooled serum versus commercial serum internal quality control in clinical biochemistry laboratory

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Background and aim: Internal Quality Control (IQC) is a critical process for detecting analytical errors during patient sample analysis to ensure the accuracy and reliability of test results. However, the high cost and limited availability of commercial IQC materials pose significant barriers, especially for laboratories in developing countries. Pooled patient serum presents a potential cost-effective alternative, but its efficacy compared to commercial controls has not been systematically evaluated. This systematic review and meta-analysis aimed to assess the effectiveness of pooled serum versus commercial IQC materials in clinical biochemistry laboratories.

Methods: A comprehensive literature search was conducted in PubMed, Cochrane Library, and Google Scholar for studies published from 2019 to June 2024. Studies were included if they compared pooled serum with commercial IQC in clinical settings, with outcomes related to efficacy, stability, or cost-effectiveness. The Cochrane Risk of Bias Tool was used to assess study quality. The primary meta-analysis was performed using RevMan 5.4 software, calculating the odds ratio for the coefficient of variation of the measured parameters.

Results: Seven relevant studies were included in the final meta-analysis. The biochemical parameters compared between pooled serum and commercial IQC included creatinine, urea, glucose, AST, triglycerides, ALT, total protein, total bilirubin, ALP, albumin, cholesterol, and calcium. Except for ALP, which showed a statistically significant difference favoring commercial IQC (95% CI: 0.10–0.40, P=0.03), there was no significant difference in any other parameter between the two types of control materials. Notably, the pooled serum demonstrated significantly better stability and lower variability compared to commercial controls ($I^2 = 0\%$), indicating superior consistency in daily laboratory practice.

Conclusion: Pooled serum is an effective, stable, and more economical alternative to commercial IQC for most routine clinical biochemistry analytes. Implementing in-house pooled serum can significantly reduce operational costs and supply chain dependency without compromising analytical quality. These findings are particularly relevant for resource-limited settings, supporting broader access to quality-assured laboratory testing.

keywords: • Internal Quality Control • Pooled Serum • Clinical Biochemistry

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-32

A Hybrid Microfluidic Lab-on-a-Chip for Multiplexed Detection of Lung Cancer Biomarkers Using Integrated Nanoplasmonic and Electrochemical Sensing

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Background and aim: Early diagnosis of lung cancer depends on the sensitive and multiplexed detection of circulating biomarkers that are often present at low concentrations in clinical samples. Conventional assays are accurate but are typically time-consuming, require larger sample volumes, and are not easily adaptable to rapid point-of-care testing. In this study, we developed a hybrid microfluidic lab-on-a-chip platform integrating nanoplasmonic and electrochemical sensing for rapid multiplex detection of lung cancer biomarkers.

Methods: The device was fabricated on a glass–polymer hybrid substrate and consisted of parallel microchannels integrated with gold nanostructured sensing regions and interdigitated electrochemical electrodes. Capture antibodies and aptamers were immobilized on the gold surfaces using thiol-based self-assembled monolayers, and antifouling coatings were applied to reduce nonspecific adsorption. The platform was designed for simultaneous detection of lung cancer-associated biomarkers, including carcinoembryonic antigen (CEA), cytokeratin 19 fragment (CYFRA 21-1), neuron-specific enolase (NSE), and a lung cancer-associated microRNA target in serum samples. Performance was assessed using standard solutions, spiked serum, and diluted clinical specimens. Analytical parameters, including sensitivity, linear dynamic range, limit of detection, selectivity, reproducibility, and recovery, were determined. The nanoplasmonic signal was measured through resonance shifts, while electrochemical output was recorded using impedance-based and amperometric readouts.

Results: The integrated platform achieved rapid detection with a total assay time of less than 25 minutes and a sample consumption of less than 20 µL per run. The device demonstrated strong analytical performance across all four biomarkers, with low picomolar limits of detection for protein targets and excellent discrimination in complex serum matrices. The nanoplasmonic and electrochemical outputs showed high agreement, and the dual-readout format improved signal confidence while reducing false-positive classification. The platform exhibited good selectivity against structurally related proteins and maintained stable performance over repeated measurements. In spiked serum tests, recovery values ranged from 91% to 108%, and inter-assay variation remained low. The multiplexing architecture enabled simultaneous biomarker analysis without significant cross-talk between channels.

Conclusion: The developed hybrid microfluidic lab-on-a-chip provided rapid, sensitive, and multiplexed detection of lung cancer biomarkers from low-volume clinical samples. Integration of nanoplasmonic and electrochemical sensing improved analytical reliability and expanded detection capability. These findings support the potential of this platform as a compact tool for early lung cancer screening and biomarker-based clinical diagnostics.

keywords: Early diagnosis, Microfluidic, Lab-on-a-Chip, Lung cancer

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-33

Development of an Integrated Lab-on-a-Chip Platform for Rapid, Low-Volume Detection of Circulating Lung Cancer Biomarkers in Clinical Samples

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Background and aim: Circulating lung cancer biomarkers offer valuable information for early diagnosis, treatment monitoring, and disease stratification. However, their detection remains challenging because of low abundance, biological complexity, and the need for sample preprocessing. To address these limitations, we developed an integrated microfluidic lab-on-a-chip system for rapid analysis of circulating lung cancer biomarkers in small clinical samples.

Methods: The lab-on-a-chip device incorporated a sample inlet, plasma separation module, enrichment chamber, and downstream sensing zone within a single microfluidic architecture. The device was fabricated using a glass–polymer hybrid platform to improve optical transparency and chemical stability. Biomarker capture was achieved through immobilized antibodies and nucleic-acid probes selected for clinically relevant lung cancer markers. Detection was performed using coupled optical and electrochemical sensing modules. The system was tested using serum, plasma, and minimally processed whole blood samples spiked with lung cancer biomarkers and later evaluated with clinical specimens. Analytical evaluation included assay time, sensitivity, dynamic range, reproducibility, specificity, and recovery. Surface fouling was minimized using antifouling modifications, and assay performance was compared with standard reference methods.

Results: The integrated chip successfully processed low-volume samples and generated quantitative biomarker readouts within 20–30 minutes. The plasma separation and enrichment modules improved target concentration before detection, resulting in enhanced analytical sensitivity. The platform detected low-abundance lung cancer biomarkers with a broad linear range and consistent performance across repeated measurements. Optical and electrochemical outputs provided complementary readouts, improving reliability in complex biological samples. The system showed high specificity with minimal background interference and maintained robust performance in whole blood after on-chip processing. Recovery values in spiked clinical matrices were high, and reproducibility across devices was satisfactory for translational application. The device also demonstrated compatibility with multiple biomarker classes, indicating potential utility for multiplex lung cancer diagnostics.

Conclusion: This integrated lab-on-a-chip system enabled rapid, low-volume detection of circulating lung cancer biomarkers with strong analytical performance. By combining sample preparation, enrichment, and dual-mode sensing in one compact platform, the device addressed several limitations of conventional assays. The system showed promise as a point-of-care diagnostic tool for early lung cancer detection and personalized disease monitoring.

keywords: Lab-on-a-Chip, Lung Cancer, Microfluid

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-34

Curcumin and Aspirin Cooperatively Induce Ferroptosis and Suppress Tumor Growth in a 4T1 Syngeneic Model of Triple-Negative Breast Cancer via the GPX4–KEAP1–STUB1 Axis

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Background and aim: Ferroptosis, an iron-dependent form of regulated cell death driven by lipid peroxidation, has emerged as a promising therapeutic target in triple-negative breast cancer (TNBC). Curcumin and aspirin each possess anti-tumor and pro-oxidative properties, yet their combined effect on ferroptosis-related molecular mechanisms in TNBC remains unexplored.

Methods: Female BALB/c mice (n = 24) were inoculated subcutaneously with 4T1 TNBC cells and randomly allocated to four groups: vehicle Control, Curcumin (100 mg/kg/day p.o.), Aspirin (100 mg/kg/day p.o.), and Combination (both agents, each 100 mg/kg/day). Treatments were administered by oral gavage for three consecutive weeks. Tumor growth was monitored by serial caliper measurements at eight time points. Tumor tissues were analyzed by immunohistochemistry (Ki-67, p53, ER, PR, HER2), quantitative RT-qPCR (GPX4, NRF2, KEAP1, PTGS2, STUB1), and colorimetric assay for intratumoral reduced glutathione (GSH) and malondialdehyde (MDA).

Results: All treatment arms significantly attenuated tumor growth relative to Control, with tumor growth inhibition (TGI) of 68.8% (Combination), 47.0% (Aspirin), and 38.8% (Curcumin). The Combination group demonstrated the greatest reduction in Ki-67 labeling index (18.3 ± 7.6% vs. 33.3 ± 5.8% in Control) and the highest p53 induction (20.0 ± 5.0%). Molecularly, Combination treatment significantly downregulated GPX4 (0.16 ± 0.07-fold; p = 0.007) and PTGS2 (0.14 ± 0.10-fold; p = 0.003), while markedly upregulating KEAP1 (14.6 ± 10.1-fold; p = 0.002) and STUB1 (79.7 ± 49.0-fold; p = 0.0002) versus Control. Concurrently, intratumoral GSH was significantly depleted (1.89 ± 0.18 vs. 3.04 ± 0.18 mmol; p = 0.003) and MDA was elevated more than two-fold (0.62 ± 0.12 vs. 0.28 ± 0.04 nmol/mL; p 0.001) in the Combination group.

Conclusion: Co-administration of curcumin and aspirin synergistically suppresses 4T1 tumor growth and induces ferroptotic cell death through coordinated disruption of the GPX4–KEAP1–STUB1 antioxidant defense axis. These preclinical findings support the therapeutic potential of a curcumin–aspirin combination strategy for TNBC.

keywords: ferroptosis; curcumin; aspirin; triple-negative breast cancer; GPX4

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OBi-35

Assessment of Acute-Phase Indices (CRP, CAR, BAR) and Ovary Volume in Women with Polycystic Ovary Syndrome Supplemented with Arctium lappa L. Root Powder: A Controlled Clinical Trial

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Background and aim: Polycystic ovary syndrome (PCOS) is recognized as a major endocrine-metabolic disorder with profound consequences for reproductive health. Given the role of systemic inflammation in the pathogenesis of PCOS, therapeutic strategies targeting these pathways are of great interest. This study was conducted to evaluate the influence of Arctium lappa L. root powder on acute-phase indices, specifically the C-reactive protein (CRP), the CRP/albumin ratio (CAR), and the BUN/albumin ratio (BAR) as well as a clinical indicator, ovary volume, in women diagnosed with PCOS.

Methods: In this randomized, double-blind, placebo-controlled trial, 60 women diagnosed with PCOS were recruited at Arak University of Medical Sciences. Utilizing a permuted block randomization approach, participants were assigned into either an intervention group (receiving 460 mg/day of Arctium lappa L. root powder) or a control group (receiving a matched placebo) for a 12-week duration. Baseline and post-intervention assessments were performed to compare changes in acute-phase indices (CRP, CAR, and BAR) and ovary volume between the two study groups. Registration ID in IRCT: [IRCT20230222057492N1]

Results: Following the 12-week intervention, a statistically significant reduction was observed in all acute-phase indices, CRP, CAR, and BAR within the Arctium lappa L. group compared to the placebo group (p 0.001). Furthermore, a significant decrease in ovarian volume was recorded in both the right ($p = 0.02$) and left ($p = 0.01$) ovaries of the intervention group compared to the control group. No significant adverse effects were reported throughout the study period.

Conclusion: Supplementation with Arctium lappa L. root powder (460 mg/day) for 12 weeks effectively mitigates acute-phase systemic inflammation and reduces ovarian volume in patients with PCOS. Consequently, this natural intervention holds promise as a complementary approach for the clinical management of PCOS.

keywords: Polycystic ovary syndrome; Arctium; Inflammation

OG-1

Mitochondrial Copy number May Serve as Potential Predictors of Response to Ovarian Stimulation in Women Undergoing ART

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Background and aim: Mitochondrial DNA (mtDNA) is essential for cellular energy production and normal function of female germ cells. The common 4977-bp mtDNA deletion and changes in mtDNA copy number have been associated with aging and female infertility. However, their clinical significance in peripheral blood of infertile women undergoing assisted reproductive technologies (ART) remains unclear. Assessment of these mitochondrial alterations could improve understanding of infertility mechanisms and identify potential biomarkers for ART outcomes. This study aimed to evaluate the association between the 4977-bp mtDNA deletion, mtDNA copy number, and ovarian response to controlled ovarian stimulation in women undergoing ART.

Methods: In this case–control study, peripheral blood samples were collected from 100 women undergoing ART, including 50 poor ovarian responders and 50 normal responders. Genomic DNA was extracted from the samples, and the presence of the 4977 bp mitochondrial DNA deletion as well as mitochondrial DNA copy number were analyzed using quantitative real-time PCR (qPCR).

Results: There was no statistically significant difference in the frequency of the 4977 base pair deletion of mitochondrial DNA between normal responders and poor responders. However, mitochondrial DNA copy number was significantly decreased in poor responders (P-value=0.044).

Conclusion: Variation in mitochondrial DNA copy number may reflect mitochondrial dysfunction and could serve as a potential marker for ovarian responsiveness in females undergoing ART cycles.

keywords: Assisted reproductive technology, mtDNA copy number, ovarian stimulation, mtDNA 4977bp

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July 20-23, 2026

OG-2

Diagnostic Potential of a Serum-Based hsa-miR-25, hsa-miR-141, and hsa-miR-143 Panel for Prostate Cancer Detection

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Background and aim: Prostate cancer (PCa) is a clinically heterogeneous malignancy and a leading cause of cancer-related morbidity among men worldwide. Conventional diagnostic approaches, particularly prostate-specific antigen (PSA) testing, often lack specificity, highlighting the need for reliable, non-invasive molecular biomarkers. Circulating microRNAs (miRNAs) have emerged as promising candidates due to their stability in serum and key roles in oncogenic and tumor suppressor pathways.

Methods: This study evaluated the diagnostic potential of a serum-based miRNA panel in 25 PCa patients and 25 age-matched healthy controls. Expression levels of hsa-miR-25, hsa-miR-141, and hsa-miR-143 were quantified using quantitative reverse transcription polymerase chain reaction (RT-qPCR). Receiver operating characteristic (ROC) curve analysis was performed to determine diagnostic accuracy, sensitivity, specificity, and area under the curve (AUC). In silico targetome analysis was also conducted to explore the biological relevance of these miRNAs.

Results: Hsa-miR-141 and hsa-miR-25 were significantly upregulated in PCa compared to healthy controls (fold change: 3.8 and 3.2; P 0.001 and P = 0.002, respectively), demonstrating oncogenic activity. Hsa-miR-143 was downregulated (fold change: 0.45; P = 0.0005), consistent with tumor-suppressive function. The combined panel of three miRNAs yielded robust diagnostic performance, with an AUC of 0.912, sensitivity of 92%, and specificity of 80%. Targetome analysis revealed that these miRNAs regulate multiple genes and pathways implicated in PCa progression, cell proliferation, and tumor microenvironment modulation.

Conclusion: Our findings indicate that the serum-based panel comprising hsa-miR-25, hsa-miR-141, and hsa-miR-143 provides a highly accurate, non-invasive approach for distinguishing PCa from healthy individuals. These miRNA signatures hold significant potential for early diagnosis, risk stratification, and guiding clinical decision-making in prostate cancer management.

keywords: Prostate cancer; microRNA; hsa-miR-25; hsa-miR-141; hsa-miR-143; Non-invasive; Biomarker

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OG-3

Disruption of Stereociliary Calcium Handling Drives Hair Cell Apoptosis in GPR156–OTOF/OTOG Mutant Models

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Background and aim: Mutations affecting the mechanotransduction apparatus of auditory hair cells cause congenital deafness, but the mechanisms linking mechanotransduction defects to hair cell death remain poorly understood.

Methods: Neonatal mouse models harboring Gpr156 and OTOF/OTOG-related mutations were analyzed for mitochondrial function, apoptosis, and calcium handling using Calcein-AM, MitoTracker, Annexin V, and MitoLight assays. Auditory brainstem responses assessed hearing function. Genetic rescue was performed using Cre-Lox–mediated exon excision.

Results: Despite preserved mechanotransduction currents at postnatal day 6, mutant hair cells exhibited early mitochondrial dysfunction and apoptotic markers. Elevated stereociliary Ca^{2+} levels induced scramblase activation and apoptosis. Reduced expression of calcium-handling proteins correlated with impaired Ca^{2+} permeability. Early genetic correction fully preserved hearing and restored calcium-handling protein density.

Conclusion: Impaired stereociliary calcium homeostasis initiates early mitochondrial dysfunction and apoptosis, leading to progressive deafness in GPR156–OTOF/OTOG mutants. Targeting calcium-handling pathways may prevent hair cell loss and hearing impairment.

keywords: Gpr156; OTOF/OTOG; calcium handling; hair cell apoptosis; deafness; mitochondria.

OG-4

Challenges and Advances in Prenatal Diagnosis of Beta-Thalassemia: An Evaluation of Diagnostic Accuracy

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Background and aim: Beta-thalassemia major is highly prevalent in certain regions, including Khuzestan province in Iran, and is associated with severe anemia requiring lifelong treatment. Despite the implementation of effective prevention programs, diagnostic errors in prenatal diagnosis (PND) still occur, resulting in the birth of affected infants. This study aimed to evaluate the accuracy of PND for beta-thalassemia, identify the underlying causes of diagnostic errors, and propose strategies to improve diagnostic protocols.

Methods: This retrospective, descriptive, cross-sectional study was conducted between 2012 and 2018 on 202 beta-thalassemia carrier couples referred to Shafa Hospital in Ahvaz, Iran. Fetal DNA was obtained through chorionic villus sampling (CVS) or amniotic fluid sampling. Molecular analyses were performed using the Amplification Refractory Mutation System Polymerase Chain Reaction (ARMS-PCR), Gap-PCR, and DNA sequencing. Statistical analyses were used to determine the frequency and contributing factors of diagnostic errors.

Results: Affected infants were diagnosed with beta-thalassemia major at a mean age of five months. Six diagnostic errors were identified, corresponding to an overall error rate of 2.14%, with the majority of errors related to point mutations. Diagnostic errors occurred more frequently in amniotic fluid sampling (4.05%) compared to CVS sampling (1.45%). The most commonly detected mutations were CD 36/37, IVS-II-1, and Fr 8–9.

Conclusion: Enhancing the accuracy of prenatal diagnosis for beta-thalassemia is crucial, particularly in regions with high prevalence, such as Khuzestan, Iran. Although the overall diagnostic error rate was relatively low, the clinical and social consequences of these errors are substantial, leading to the birth of affected children and increased burdens on families and healthcare systems. Most diagnostic errors were associated with point mutations and occurred more frequently in amniotic fluid sampling than in CVS. Therefore, improving molecular diagnostic techniques, particularly for detecting rare mutations, is crucial in reducing diagnostic errors.

keywords: Beta-Thalassemia; Prenatal Diagnosis; Chorionic Villus Sampling; Diagnostic Error; Mutation

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OG-5

Identification and validation of stemness-associated lncRNAs as molecular subtype–specific biomarkers in gastric cancer

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Background and aim: Gastric cancer (GC) exhibits substantial molecular heterogeneity. According to TCGA, tumors can be classified into four subtypes: EBV-positive, microsatellite instability (MSI), genomically stable (GS), and chromosomal instability (CIN). Notably, stemness-related factors differ between GS and CIN subtypes, influencing tumor progression, metastasis, and response to chemotherapy. Long non-coding RNAs (lncRNAs) are emerging regulators of stemness, yet their subtype-specific expression in GC remains poorly characterized. This study aimed to identify stemness-associated lncRNAs in GC using bioinformatics approaches, assess their dysregulation in tumor versus normal tissue, and compare expression patterns between GS and CIN subtypes.

Methods: Forty-one GC tissue samples (GS, n=15; CIN, n=12) were analyzed. An integrated bioinformatics approach using GEO datasets GSE122530 and GSE99416 identified differentially expressed lncRNAs. Three candidate lncRNAs (LINC01357, HOXA-AS2 and MINCR) implicated in stemness-related pathways were selected and validated by real-time PCR. Statistical analyses, including differential expression, subtype comparisons, correlation with SOX2, and ROC curve analyses, were performed using GraphPad Prism.

Results: lncRNA LINC01357 was significantly downregulated, while lncRNAs HOXA-AS2 and MINCR were upregulated in tumor tissues compared with adjacent normal tissues (lncRNA LINC01357: P=0.0380; lncRNA HOXA-AS2: P=0.0009; lncRNA MINCR: P=0.0411). Additionally, lncRNA-MINCR expression positively correlated with SOX2 (r=0.3788, 95% CI: 0.071–0.621; P=0.0146). Subtype-specific analysis revealed lncRNA LINC01357 downregulation in GS versus CIN tumors (P=0.0298) and lncRNA-MINCR upregulation in GS versus CIN (P=0.0016), while lncRNA HOXA-AS2 showed no subtype-specific difference. ROC analysis indicated diagnostic potential for lncRNA LINC01357 (AUC=0.7444, P= 0.0318) and lncRNA-MINCR (AUC=0.8417, P= 0.0027).

Conclusion: Stemness-associated lncRNAs LINC01357 and MINCR were dysregulated in GC and displayed subtype-specific expression patterns, with pronounced differences between GS and CIN tumors. The correlation of lncRNA MINCR with SOX2 suggests a role in stemness regulation. These lncRNAs may serve as accessible biomarkers for GC molecular subtyping and guide future personalized therapeutic strategies.

keywords: Gastric cancer; Long non-coding RNA; Stemness; Genomically stable; Chromosomal instability;

OG-6

Differential expression of SIRT1/SIRT2 and SUZ12 as epigenetic regulatory factors in the endometrial tissue of infertile patients with hydrosalpinx undergoing laparascopic salpingectomy

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Background and aim: Background: The present study aimed to evaluate the expression levels of SIRT1, SIRT2, and SUZ12 genes in patients with hydrosalpinx before and after salpingectomy, and to compare them with healthy controls. The study was approved by the Ethics Committee of Royan Institute.

Methods: Methods: In this experimental study, gene expression levels were assessed in patients with hydrosalpinx before and after salpingectomy and compared with the control group. Differential expression analysis was performed, and statistical significance was determined based on p-values.

Results: Results: The results demonstrated that mRNA expression levels of SIRT1, SIRT2, and SUZ12 were significantly elevated in patients with hydrosalpinx (pre-salpingectomy) compared to healthy controls (P 0.001 for all three genes). Following surgical intervention, a notable downregulation was observed. Specifically, the reduction in expression from pre- to post-salpingectomy was statistically significant for SIRT1 (P 0.001), SIRT2 (P 0.001), and SUZ12 (P = 0.001). Post-surgery, expression levels of all three genes showed no significant difference compared to the healthy control group (P 0.05).

Conclusion: Conclusion: Previous studies have reported increased expression of SIRT1 in endometriosis and SIRT2 in recurrent implantation failure, as well as a regulatory role of SUZ12 in NF-κB–dependent transcription. Consistent with these findings, our study showed that SIRT1, SIRT2, and SUZ12 expression levels were significantly higher in patients with hydrosalpinx before salpingectomy compared with post-salpingectomy patients and healthy controls. These results suggest a role for these genes in the pathogenesis of hydrosalpinx and indicate that salpingectomy restores their expression toward normal, thereby improving the uterine environment for implantation.

keywords: Hydrosalpinx, Salpingectomy, SIRT1, SIRT2, SUZ12

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OG-7

Assessing the expression pattern and diagnostic value of Wnt/B-catenin pathway associated lncRNA in preeclampsia

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Background and aim: Preeclampsia is a complex pregnancy-related condition characterized by hypertension and widespread systemic complications mainly due to defective placental formation and impaired trophoblast infiltration. Impaired remodeling of spiral arteries results in placental ischemia, endothelial dysfunction, and adverse maternal fetal outcomes. The Wnt/β-catenin signaling pathway is essential for trophoblast proliferation and invasion, and its dysregulation has been implicated in preeclampsia pathogenesis. LncRNAs are increasingly recognized as important regulators of this signaling pathway, yet their involvement in preeclampsia remains unknown. This study explores the placental expression of Wnt-related lncRNAs (SNHG20, LINC00210, MSC-AS1, NEF, SNHG5) and β-catenin, and evaluates their potential as diagnostic biomarkers.

Methods: For this case control study, placental samples were obtained from 40 women in their third trimester, comprising 20 preeclampsia patients and 20 normotensive controls. Participants affected by systemic conditions, multifetal pregnancies and fetal abnormalities were not included in this study. Samples were obtained from the central maternal placenta, processed in RNAlater, and stored at −80°C. RNA isolation was performed with TRIzol and its quality verified before reverse transcription. Quantitative real-time PCR with SYBR Green was performed in triplicate using primers designed to exon-exon junctions to quantify target lncRNAs and β-catenin, normalized to GAPDH using the 2- ΔΔCt method. Data were analyzed using t-tests, correlation analyses, multivariate linear, logistic regression and ROC curve analysis to determine diagnostic performance. Results were visualized in GraphPad Prism, with significance threshold set at p0.05. This strategy allowed for a thorough assessment of gene expression variations and their clinical significance in preeclampsia.

Results: The study enrolled 40 women in their third trimester (20 preeclampsia, 20 controls) with comparable baseline demographics. PE patients showed significant increases in blood pressure and proteinuria, as well as increased LDH, BUN, creatinine, and hematocrit, reflecting organ dysfunction. Gene expression analysis revealed significant dysregulation of Wnt-associated lncRNAs and CTNNB1: SNHG20 and β-catenin were upregulated (3.18- and 2.33-fold, respectively), whereas LINC00210 was downregulated (0.28-fold; all P0.05). The expression of NEF, MSC-AS1, and SNHG5 remained essentially unaltered. Analysis of ROC curves revealed strong diagnostic potential for SNHG20 and LINC00210, with AUCs of 0.82 and 0.798, respectively, while NEF and MSC-AS1 exhibited minimal utility. Correlation analyses demonstrated altered co-expression networks in PE: SNHG20 exhibited strong positive associations with β-catenin and MSC-AS1, and the NEF–β-catenin negative correlation seen in controls was lost. These results suggest that preeclampsia entails changes in expression as well as reorganization of Wnt-associated lncRNA networks.

Conclusion: In conclusion, this study demonstrates a marked expression imbalance among SNHG20, LINC00210, and β-catenin, defining a distinct molecular signature in preeclampsia. Upregulation of SNHG20 and β-catenin probably indicates pathological signaling rewiring and a late compensatory response to placental hypoxia, whereas downregulation of LINC00210 indicates disruption of regulatory control required for normal placentation. In addition to providing mechanistic insight, both SNHG20 (AUC 0.82) and LINC00210 (AUC 0.79) showed notable diagnostic potential. Their expression levels may provide an objective method for diagnosing preeclampsia and enhanced assessment of placental abnormalities in preeclampsia.

keywords: preeclampsia, Wnt/B-catenin, lncRNA, B-catenin

OG-8

Tissue-Based Analysis of CDX1 Gene Expression and Promoter Methylation in Colorectal Cancer: A Potential Molecular Diagnostic Marker

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Background and aim: Early diagnosis of colorectal cancer (CRC), one of the most common malignancies, can significantly reduce mortality. Investigating genetic and epigenetic alterations in the early stages of CRC can be very helpful in timely diagnosis. One of the key epigenetic alterations in CRC is DNA methylation in CpG-rich promoter regions of various genes, including Caudal-type homeobox 1 (CDX1) as a tumor suppressor. The aim of this study was to investigate the methylation status and expression level of CDX1 in CRC patients.

Methods: In this study, the promoter methylation status and expression level of the CDX1 gene were analyzed in tumor tissues and adjacent healthy tissues from 50 CRC patients. CDX1 promoter methylation was assessed using the MethyLight real-time PCR method. Then, the percentage methylated reference (PMR) was calculated for all samples. Relative CDX1 gene expression was examined using Quantitative RT-PCR. In addition, plasma levels of carcinoembryonic antigen (CEA) were measured in CRC and control groups.

Results: The findings showed a statistically significant difference in the mean PMR index between tumor tissues and adjacent healthy tissues in CRC patients (49; 95% CI: 20–90 vs. 18; 95% CI: 6–25, respectively). The sensitivity and specificity of methylation detection in tissue samples were 66% and 100%, respectively. Furthermore, tumor tissues showed a significant decrease in CDX1 expression compared to healthy tissues (P 0.001). Plasma CEA levels were significantly higher in the CRC group compared with the control group (P 0.001).

Conclusion: Thus, these results confirm the role of CDX1 as a molecular marker in early stages of CRC

keywords: Colorectal cancer · Epigenetic · DNA methylation · CDX1 gene

OH-1

Prevalence of A2 and A2B Blood Groups among Iranian Blood Donors: Serological Findings and Molecular Approaches for Resolving Discrepancies

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Background and aim: The ABO blood group system is the most important systems in blood transfusion and organ transplantation. The A2 and A2B subgroups are particularly important because of their quantitative and qualitative differences in antigen expression, as well as the possibility of producing anti-A1 antibodies. These subgroups are not identified by routine tests in blood banks, so comprehensive data on their prevalence is lacking. This study was designed and conducted to determine the prevalence of A2 and A2B subgroups and the incidence of anti-A1 antibody among blood donors in Tehran blood center.

Methods: This cross-sectional study was conducted on 2334 blood donors with blood group A or AB at the Vasal Blood Transfusion Center in Tehran. Initial blood grouping was performed using a fully automated Micro-Hemagglutination method. Subgroup identification was carried out using the standard tube method with Anti-A1 and Anti-H. Samples with serological discrepancies were investigated for the ABO genotype using the PCR-SSP molecular method.

Results: Subgroup A2 was identified in 405 out of 1863 donors with blood group A, representing 21.7%. Out of the 471 donors who had blood group AB, 94 (19.95%) were identified as subgroup A2B. The serum of 5 donors (1.23%) from the A2 subgroup contained Anti-A1 antibody, but none of them responded at 37°C. In total, there were 8 samples that displayed serological discrepancies. The molecular analysis revealed that there were 6 cases with the O1A2 genotype, one with A2A2, and one with A2B.

Conclusion: The A2 and A2B subgroups were found to have a prevalence of 21.73% and 19.95% in blood donors, which is in agreement with findings from European-American populations. The ABO discrepancies were completely resolved by combining serological and molecular methods.

keywords: ABO Blood Group System, Serological Method, Molecular Method, Prevalence

OH-2

Selecting an Optimal Cellular Source for Clinical-Grade Regulatory T Cell Therapy: A Comparative Study of Umbilical Cord Blood and Mobilized Peripheral Blood

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Background and aim: Adoptive regulatory T cell (Treg) therapy is an emerging clinical strategy for the prevention of graft-versus-host disease (GVHD) and other immune-mediated complications following hematopoietic stem cell transplantation, with broader applications in immune tolerance. A major challenge for clinical translation is identifying a reliable cellular source for reproducible expansion of stable, functional Tregs. Umbilical cord blood and mobilized peripheral blood stem cells are both clinically accessible sources, yet their relative suitability remains unclear. This study compares CB-derived Tregs and mPBSC-derived Tregs in terms of expansion efficiency, phenotypic stability, suppressive function, and epigenetic integrity to inform clinical-grade Treg manufacturing .

Methods: Tregs were isolated from umbilical cord blood (CB) units and mobilized peripheral blood stem cell (mPBSC) collections using magnetic bead-based selection and characterized for baseline phenotype. Cells were then expanded ex vivo under standardized culture conditions with anti-CD3/CD28 stimulation and IL-2, in the presence or absence of rapamycin, to promote selective Treg proliferation and stability. Clinically relevant parameters were assessed, including expansion yield, post-expansion purity ($CD4^+CD25^+CD127^-FOXP3^+$), suppressive function in co-culture assays, and FOXP3 TSDR methylation status. Analyses were performed using flow cytometry, in vitro functional suppression assays, and FOXP3 TSDR methylation analysis by MSP to evaluate Treg stability and potency.

Results: CB-derived Tregs consistently achieved higher expansion yields and maintained superior phenotypic purity compared with mPBSC-derived Tregs. Functionally, CB-Tregs demonstrated stronger and more stable suppressive activity following expansion. Epigenetic evaluation revealed greater FOXP3 TSDR demethylation in CB-Tregs, indicating enhanced lineage stability. Rapamycin selectively favoured the expansion of stable Tregs, with a markedly greater beneficial effect observed in CB-derived cells compared with mPBSC-derived counterparts.

Conclusion: This study provides a comprehensive comparative analysis of CB-derived Tregs and mPBSC-derived Tregs, highlighting clinically meaningful differences in expansion efficiency, phenotypic and epigenetic stability, and suppressive function. These findings provide practical insights to guide rational source selection and optimize the manufacturing of safe, stable, and effective clinical-grade Treg products for the prevention of GVHD and other immune-mediated complications.

keywords: Regulatory T cells (Tregs) – CB– mPBSC - GVHD

OH-3

Blood Utilization Audit and MSBOS in Obstetrics-Gynecology Department

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Background and aim: Over-ordering of blood for obstetric and gynecologic procedures contributes to resource wastage in resource-limited settings. This study audited blood request practices and derived a Maximum Surgical Blood Order Schedule (MSBOS) to optimize utilization.

Methods: This descriptive-analytical cross-sectional study (March 2024 to March 2025) enrolled 824 female patients with blood requests in the obstetrics-gynecology department at Shahid Motahari Hospital, Jahrom, Iran. Data on clinical variables, antibody screening, transfusions, and crossmatch were collected via hemovigilance forms. Transfusion indices, including crossmatch-to-transfusion ratio (C/T), transfusion index (TI), transfusion probability (%T), blood utilization, Blood ordering quotient (BOQ), and multivariable predictors of transfusion were determined. Logistic regression derived a risk score. Data analyses were performed using SPSS version 26 (IBM, USA).

Results: Mean age was 31.8 ± 7.2 years; 762 (92.5%) cross-matched, 426 (51.7%) transfused (584 units). The overall C/T ratio 3.61, TI 0.77, T% 51.7%, utilization 27.7%, BOQ 2.81. The highest TI was in hysterectomy (2.14) and emergency cesarean (1.76). Screening compliance: 97.6% (11 positives, insignificant; 100% concordance). MSBOS reduced cross-matches by 68.4%. Emergency surgery (OR 4.82, 95% CI 3.21-7.24), anemia (OR 3.91, 95% CI 2.68-5.70), placenta previa/accreta (OR 6.27, 95% CI 4.12-9.54), and uterine rupture (OR 5.89, 95% CI 3.76-9.22) were detected as predictors: Risk score AUC: 0.892 (95% CI 0.868-0.916).

Conclusion: The MSBOS and risk score promote efficient blood use, reducing waste while identifying high-risk cases. Adoption could improve maternal outcomes and resource allocation in similar hospitals.

keywords: Blood Transfusion, Obstetrics, Gynecology, Cross-Matching, Hemovigilance, Patient Blood Management

OH-4

Superior Predictive Value of Molecular vs. Flow Cytometry MRD Monitoring at 3 Months Post-Transplant for Relapse and Survival in Philadelphia-Positive Acute Lymphoblastic Leukemia

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Background and aim: Minimal residual disease (MRD) monitoring after allogeneic hematopoietic stem cell transplantation (allo-HSCT) is critical for predicting relapse in Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL). Real-time PCR and multiparameter flow cytometry (MFC) are commonly used, but their comparative prognostic accuracy remains debated, particularly given the risk of false positives in MFC due to hematogones in regenerating marrow.

Methods: We analyzed 29 adult Ph+ ALL patients who underwent allo-HSCT at Shariati Hospital, Tehran, Iran, between 2015 and 2023. MRD was assessed pre-transplant and at 3, 6, 9, and 12 months post-transplant using both real-time PCR (for BCR::ABL1 transcripts) and 8-color flow cytometry (sensitivity 0.01%). MRD positivity thresholds were optimized via ROC analysis for each time point. Relapse-free survival (RFS) was analyzed using the Kaplan-Meier method and the log-rank test.

Results: Median follow-up was 48.3 months (range 0.3–108.5). The optimal MRD cut-off was ≥1 copy for PCR at all time points. At 3 months, PCR achieved an AUC of 0.68 (sensitivity 80%, specificity 62.5%), while MFC showed an AUC of 0.54. Patients with PCR-MRD ≥1 copy at 3 months had significantly inferior RFS compared to MRD-negative patients (median RFS 13.4 vs. 70 months, p=0.0031). PCR-MRD at 6 months also showed strong predictive value (AUC=0.69, sensitivity 73%, specificity 100%). In contrast, the predictive power of PCR-MRD diminished at later time points (9-month AUC=0.54, sensitivity 13%; 12-month AUC=0.64, sensitivity 27%). MFC-MRD positivity at any time point did not significantly predict relapse. PCR-MRD positivity at 3 months conferred a 6.7-fold increased relapse risk (OR=6.67, p=0.07), while 65% of all relapses occurred in patients with positive PCR-MRD at 3 months.

Conclusion: Molecular MRD monitoring using real-time PCR at 3-6 months post-transplant provides optimal predictive value for relapse and RFS in Ph+ ALL patients after allo-HSCT, with 3 months being the most critical window for early intervention. The diminished sensitivity at 9-12 months indicates that negative results at later time points should not provide false reassurance. PCR-based MRD surveillance is superior to flow cytometry and should be the standard for post-transplant risk stratification, particularly for guiding preemptive interventions during the early post-transplant period.

keywords: MRD, Philadelphia-positive ALL, allogeneic transplantation, real-time PCR

OH-5

Interplay between platelet and T lymphocyte after coronary artery bypass grafting (CABG): Evidence for platelet mediated post-CABG immunomodulation

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Background and aim: On-pump coronary artery bypass grafting (CABG) triggers inflammatory responses as a result of surgical stress and extracorporeal circulation, which affect platelet and leukocyte activation while enhancing their intimate crosstalk. Given this, the study presented here aimed to investigate platelet-T cell interaction after CABG focusing on the changes in immunomodulatory subtypes of regulatory T Cells.

Methods: Blood samples were obtained from twenty patients undergoing on-pump CABG at 5 different time points of 24 h before, immediately, 2 h, 24 h, and one week after surgery. Total leukocyte and lymphocyte counts were determined using an automatic cell counter. Platelet P-selectin expression, frequencies of CD4 platelet-T cell aggregates (PTCAs), and regulatory T cells derived from CD4 + + and CD8 (T4reg) and CD8 + + T cells, (T8reg) cells, + were assessed by flow cytometry.

Results: A significant increase in total leukocyte count occurred immediately after CABG, whereas, conversely, lymphocyte and CD4 T cells but not CD8 + T cells decreased 2 h after surgery. However, all these changes returned to pre-CABG baseline levels within a week. Platelet P-selectin expression increased immediately after surgery, followed by a two-hour delay after PTCA, and both returned to baseline after one week. T4regs and T8regs showed a similar increase and decrease trend, where T8regs but not T4regs returned to baseline one week after surgery.

Conclusion: CABG surgery induces an inflammatory response that activates platelets and enhances P-selectin expression, facilitating PTCA formation. This mechanism is critical for the dynamics and differentiation of T cells, which play an essential role in post-CABG modulation of immune responses.

keywords: Platelet Coronary artery bypass graft Coronary artery disease Immunomodulation Regulatory

OH-6

First Ruthless Family Case in IRAN: Clinical Consequences of the CD 108-112 β⁰-Thalassemia Mutation

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Background and aim: β-thalassemia is a prevalent hereditary blood disorder caused by over 300 mutations in the β-globin (HBB) gene, leading to reduced (β^+) or absent (β^0) β-globin chain synthesis. The clinical severity of the disease—ranging from β-thalassemia intermedia to major—depends largely on the nature of the underlying mutations. While point mutations are the most common, deletional mutations within the HBB gene, though rarer, can have profound functional consequences. One such mutation, HBB:c.326_337del (Exon 3), is a 12-nt deletion classified as a β^0 allele due to its frameshift effect and predicted premature termination codon, resulting in a null allele.

Methods: Molecular analysis Beta gene was amplified and sequenced to identify mutation in HBB gene.

Results: This family report presents the clinical, hematological, and molecular profiles of four unrelated patients and their fetus harboring the HBB:c.326_337del mutation for the first time. Our findings provide further evidence of the deleterious impact of this specific deletion and contribute to the expanding genotype-phenotype correlation database for β-thalassemia.

Conclusion: By documenting these cases, we underscore the importance of comprehensive molecular diagnostics in thalassemic disorders and highlight the need for population-specific mutation screening strategies. These insights enrich the mutational spectrum of the HBB gene and support more precise clinical management of affected individuals.

keywords: Case Report, β-thalassemia, CD 108-112, HBB:c.326_337del

OH-7

Insights into KMT2A rearrangements in acute myeloid leukemia: from molecular characteristics to targeted therapies

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Background and aim: Acute myeloid leukemia (AML) with KMT2A rearrangements (KMT2A-r) represents a highly aggressive and prognostically unfavorable subtype of leukemia, often resistant to standard treatments and associated with high relapse rates. KMT2A-r, found in 3–10% of adult AML cases, disrupt epigenetic regulation by forming chimeric proteins that activate oncogenic pathways like HOXA and MEIS1.

Methods: These fusion proteins recruit cofactors such as Menin and DOT1L, driving leukemogenesis through abnormal histone methylation. Diagnosing KMT2A-r AML requires precision, with traditional methods like FISH and RT-PCR being complemented by advanced technologies such as next-generation sequencing (NGS) and machine learning (ML). ML models, leveraging transcriptomic data, can predict KMT2A-r and identify biomarkers like LAMP5 and SKIDA1, improving risk stratification.

Results: Therapeutically, there is a shift from chemotherapy to targeted therapies. Menin inhibitors (e.g., Revumenib, Ziftomenib) disrupt the Menin-KMT2A interaction, suppressing HOXA/MEIS1 and promoting differentiation. DOT1L inhibitors (e.g., Pinometostat) show promise in combination therapies, while novel approaches like WDR5 inhibitors and PROTAC- mediated degradation are expanding treatment options. Despite progress, challenges remain, including optimizing minimal residual disease monitoring, overcoming resistance, and validating biomarkers.

Conclusion: s. This review emphasizes the imperative to translate molecular insights into personalized therapeutic regimens, offering renewed hope for patients afflicted by this historically refractory malignancy.

keywords: Acute myeloid leukemia, KMT2A rearrangement, Menin inhibitors, DOT1L inhibitors

OH-8

Feasibility and Safety of IL-15-Activated CD56+ Cell Therapy in High-Risk Acute Myeloid Leukemia after Hematopoietic Stem Cell Transplantation

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Background and aim: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the most effective treatment for patients with high-risk acute myeloid leukemia (AML), but relapse remains a major challenge. Immunotherapy is considered a promising approach for reducing the risk of relapse. Natural killer (NK) cells exert cytotoxic effects against malignant cells, and their activation with interleukin-15 (IL-15) enhances anti-leukemic immune responses. This pilot interventional clinical trial evaluated the feasibility of in vitro IL-15 activation of CD56+ cells and assessed the safety of their infusion in AML patients following allo-HSCT.

Methods: In this pilot study, CD56+ cells were isolated from non-mobilized donors using a one-step CD56 enrichment protocol to obtain NK and NKT cells. CD56+ cells were activated by overnight incubation with IL-15. A cytotoxicity assay was performed against K562 cells. Three escalating doses of CD56+ cells consisting of 1×106, 3×106, and 5×106 cells/kg of patient bodyweight were infused on days +7, +14, and +21 post-allo-HSCT. Patients were observed during and up to 4 hours after the infusion for immediate adverse events and were monitored for 21 days to detect delayed events.

Results: Activation with IL-15 increased the expression of activating receptors, including CD25, CD69, NKp30, NKp46, and NKG2D decreased the expression of the inhibitory receptor NKG2A. The cytotoxicity of IL-15-activated CD56+ cells was higher than that of non-activated CD56+ cells. No intervention-related complications were observed.

Conclusion: We identified a feasible method to activate CD56+ cells and evaluate the safety of their infusion in patients. Despite the effectiveness of activating CD56+ cells with IL-15, further studies with larger sample sizes are needed to confirm and validate the current hypothesis.

keywords: Acute Myeloid Leukemia, CD56+ Cell, Interleukin-15, Natural Killer Cells, Hematopoietic

OH-9

Platelet Function Testing in Transfusion: A Systematic Review of Diagnostic Methods and Clinical Utility

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Background and aim: Platelets are extraordinary blood cells that play a central role in hemostasis while also contributing to inflammation, immunity, thrombosis, infection, and cancer progression. Therefore, this systematic review evaluates the existing evidence on the role of platelet function tests—both laboratory-based and point-of-care—in guiding platelet transfusion strategies, with a focus on their potential to optimize clinical outcomes and reduce unnecessary transfusions in high-risk patient populations.

Methods: This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A systematic search strategy was conducted using PubMed, Scopus, and Web of Science for articles published between 2010 and 2025. Search terms included combinations of keywords and Medical Subject Headings(MeSH) terms, such as “Blood transfusion,” “platelet transfusion,” “point-of-care testing,” “platelet aggregation,” and “transfusion medicine.” Eligible studies included original research, randomized controlled trials, and observational studies evaluating platelet function assays in transfusion-related or bleeding-risk settings. Studies focusing on diagnostic accuracy, transfusion decisions, or clinical outcomes were included. Reviews, abstracts, editorials, case reports, animal studies, and non-relevant articles were excluded. Titles and abstracts were screened independently, followed by full-text assessment. Duplicates were removed using reference management software.

Results: Fifty-eight eligible studies met the inclusion criteria and consisted of original research studies, including 8 randomized controlled trials and 50 observational studies, covering a total of 11,542 patients across diverse clinical settings.Ten studies assessed laboratory-based platelet function assays, forty-four evaluated point-of-care methods, and four incorporated both. Traditional laboratory techniques, particularly light transmission aggregometry, provided detailed platelet function assessment but were limited by technical complexity and delayed turnaround. Point-of-care assays—including Multiplate, VerifyNow, thromboelastography, and rotational thromboelastometry—enabled rapid bedside evaluation and were used in cardiac surgery, major trauma, neurosurgery, and hematology/oncology. Observational evidence suggested platelet function–guided transfusions reduced bleeding complications by 20–50%, decreased platelet use by 15–30%, and shortened hospital stay by 1–3 days; however, randomized evidence remains limited.

Conclusion: Platelet function testing is essential for individualized transfusion medicine, supporting a shift from count-based to function-guided strategies. Current Evidence indicates clinical and resource benefits, especially in high-risk patients. These findings support integrating platelet function testing into transfusion decision-making in laboratory–clinical interfaces. Further randomized controlled trials are required to establish standardized protocols and confirm effects on patient-centered outcomes.

keywords: Transfusion Medicine , Blood Transfusion,Platelet Transfusion ,Point-of-Care Testing ,Platelet Aggregation

OH-10

A Retrospective Analysis of Hepatitis B Virus Reactivation in Newly Diagnosed Multiple Myeloma: Influence of Transplant Eligibility and Treatment Regimens

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Background and aim: Hepatitis B (HBV) is highly prevalent in Asia; occult HBV can reactivate after chemotherapy for hematologic malignancies, including newly diagnosed multiple myeloma (NDMM). Reactivation—linked to anthracyclines, high-dose steroids, and reported with agents such as bortezomib and lenalidomide—raises liver failure risk, morbidity, and treatment delays. MM regimens depend on age, comorbidity, and transplant eligibility (ASCT candidates vs non-candidates); lenalidomide is common post-transplant/maintenance, bortezomib for transplant-ineligible patients. Asian studies without antiviral prophylaxis report HBV reactivation during bortezomib treatment in 3–15% of patients with resolved infection. This study investigates the incidence and risk factors of HBV reactivation in newly diagnosed MM patients.

Methods: This retrospective study at Baqiyatallah University Hospitals enrolled 50 of 80 MM patients diagnosed from April 2022–April 2024 who met inclusion criteria and were followed for two years to assess treatment outcomes and HBV reactivation. those with chronic HBV (HBsAg+) were excluded; patients with resolved HBV (anti-HBc+, HBsAg–, undetectable HBV DNA) and newly diagnosed MM were included. Baseline demographics, ISS-R stage, marrow plasma cell percentage, clinical presentation, and outcomes were extracted from records. MM induction regimens varied by risk and ASCT candidacy (e.g., VRd, KRd, CyBorD, DRd). HBV screening used serology and qPCR; high-risk resolved cases received antiviral prophylaxis. HBV DNA was monitored every 3–4 weeks during induction and monthly thereafter; occult reactivation was defined by biochemical, serologic, and virologic Statistical analyses used SPSS with chi-square, t-tests, and multivariate logistic regression. ethical code(ID: IR.BMSU.BLC.1403.042).

Results: This retrospective study enrolled 50 of 80 NDMM patients (mean age 56.2 years) diagnosed between January 2022 and April 2024 and followed for two years. Baseline labs showed mean WBC 6,200/µL and hemoglobin 11.7 g/dL. Patients were stratified by risk and transplant eligibility and received risk-adapted regimens (VRd, KRd, CyBorD/VCD, DRd). Chronic HBsAg+ cases were excluded; resolved HBV (anti-HBc+, HBsAg–, undetectable HBV DNA) and newly diagnosed patients were included. Three patients (6%) developed HBV reactivation associated with bortezomib/lenalidomide-containing VRd; one additional fatal reactivation occurred in a 62-year-old woman without prior HBV history during induction. Symptomatic reactivations were treated with lamivudine, tenofovir, or entecavir, which reduced HBV DNA and led to HBsAg clearance in two cases. Prophylactic antivirals in patients with prior HBV exposure appeared beneficial. Overall, most patients showed no reactivation; antiviral therapy effectively controlled symptomatic cases.

Conclusion: HBV reactivation is a concern in lymphoid malignancies. This retrospective study of newly diagnosed MM patients found 6% experienced HBV reactivation, all receiving ASCT and the bortezomib-/lenalidomide-containing VRD regimen during induction. Bortezomib's immunosuppressive effects and lenalidomide exposure may contribute; established risk markers (HBsAg or anti-HBc positivity) were also relevant. Antiviral therapy (entecavir/lamivudine/tenofovir) controlled reactivation; no fulminant hepatitis or liver failure occurred and two patients cleared HBsAg. Findings support routine HBV screening and consideration of prophylactic antivirals for high-risk, ASCT-eligible patients on VRD.

keywords: Multiple myeloma, Hepatitis B, Reactivation, ASCT, VRD, Antiviral therapy

OH-11

Protective effects of N-acetylcysteine on the platelet concentrate during storage: An experimental study focused on apoptotic microRNA

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Background and aim: Platelet concentrate (PC) is a crucial blood product used for treating thrombocytopenia. PCs are stored in incubators at a temperature of 20-24°C for up to five days. During this storage period, platelets undergo various physiological changes that can lead to a decrease in their survival rate before transfusion. This study aimed to investigate the protective effects of N-acetylcysteine (NAC) on PC during storage, specifically by reducing the expression levels of apoptotic microRNA.

Methods: Ten units of PC were prepared at the Blood Transfusion Research Center and divided into two equal groups: one group was treated with N-acetylcysteine (NAC) at a dosage of 1 mmol, while the other group remained untreated. The expression levels of apoptotic microRNA marker (miR-16) were assessed on days 0, 1, 3, 5, and 7 of storage using real-time PCR. Additionally, various parameters related to the functionality, metabolism, and survival of the platelets in both NAC-treated and untreated PC were measured throughout the storage periods.

Results: Increased levels of platelet count and viability were observed on days 5 and 7 in the NAC-treated PC compared to the untreated-PC during storage. Notably, the expression levels of the miR-16, as the apoptotic microRNA marker, showed a significant decrease on days 5 and 7 in the NAC-treated PC compared to the untreated-PC.

Conclusion: Platelet apoptosis is an influential factor in platelet storage lesion (PSL), which can negatively impact platelet quality during storage. This research work suggests that administering NAC at a specific dosage in any PC unit may help protect against platelet apoptosis by reducing levels of the apoptotic marker miR-16 during storage periods up to day 7. This protective effect of NAC can preserve platelet survival, function, and overall quality. In conclusion, NAC may play a vital role as an additive solution to alleviate PSL.

keywords: Platelet, MicroRNA, N-acetylcysteine, Platelet apoptosis

OH-12

Efficacy, Safety, and Clinical Challenges of CAR-T Cell Therapy in Acute Myeloid Leukemia: A Systematic Review of Human Trials

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Background and aim: Acute myeloid leukemia (AML), is an aggressive hematologic malignancy characterized by genetic alterations and uncontrolled proliferation of myeloid precursors, continues to pose significant treatment difficulties because of its potential to relapse and its resistance to standard therapies. Due to the notable achievements of chimeric antigen receptor T-cell (CAR-T cell) therapy in lymphoid cancers, researchers have shown growing interest in exploring its application in AML. In this systematic review, we evaluated the efficacy, safety profile, and major clinical barriers associated with CAR-T cell therapy in patients with AML.

Methods: This systematic review was designed based on the PRISMA principles. We completely searched PubMed, Scopus, and Web of Science for studies that were published in English (January 2026). The search strategy employed keywords/MeSH terms ("CAR-T cell" OR "Chimeric Antigen Receptor T Cell") AND ("Acute Myeloid Leukemia OR AML") AND ("Immunotherapy"). Study selection applied inclusion criteria of English-language publications involving AML patients treated with CAR-T cells, alone or in combination with chemotherapy or other therapies. Exclusion criteria eliminated non-AML diseases, non-CAR-T interventions, non-English studies, case reports, expert opinions, letters, and reviews. Only human clinical trials (Phase I–IV) including CAR-T cell therapy in AML were considered. two independent reviewers extracted the data (recording reference details, trial phase, patient demographics, sample size, intervention methods, dosing/route, responses, and adverse effects); disagreements were resolved by a third reviewer. Statistical analyses were performed using R software.

Results: A total of 12 studies involving 52 individuals with AML were analyzed, of whom 38 underwent CAR-T cell therapy. Clinical responses were noted in 23 patients (44%). Among these 18 (33.4%) achieved complete remission (CR), including 12 (23%) who were minimal residual disease negative (MRD-CR) and 2 patients MRD+CR. The most common antigen target in studies was CLL-1. Immunological analyses showed elevated levels of cytokines, including IL-6, TNF-α, and IFN-γ, in 27 patients (51.9%). Adverse outcomes included cytokine release syndrome in 34.8% of case and immune effector cell-associated neurotoxicity syndrome. Additional reported complications involved liver failure, cytopenia (33.8%), graft-versus-host disease, and pulmonary infections. Immune effector cell-associated neurotoxicity syndrome occurred in 3 patients at low grades. Among 25 (66%) deaths documented in 8 studies, causes were attributed to a combination of disease progression and treatment-related toxicities.

Conclusion: CAR-T cell therapy demonstrates promising efficacy in AML, with notable CR and MRD-CR, yet its clinical translation remains constrained by significant toxicities, heterogeneous antigen targeting, and methodological limitations across available trials. This systematic review highlights both therapeutic potential and critical safety concerns, underscoring the urgent need for larger, rigorously designed studies that integrate safety-enhancing strategies and combinatorial approaches. Advancing CAR-T therapy in AML will require balancing efficacy with tolerability to establish its role as a viable treatment option in hematological oncology.

keywords: Acute myeloid leukemia; Chimeric Antigen Receptor; CAR-T cell therapy; Immunotherapy

OH-13

Mac-1–Mediated Platelet–Monocyte Aggregates: From Diagnostic Biomarkers to Therapeutic Targets in Acute Coronary Syndrome

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Background and aim: Objective: Atherosclerosis represents a chronic inflammatory and thrombotic disorder in which platelet–leukocyte interactions play a central pathogenic role. Platelet–monocyte aggregates (PMA) represent a sensitive cellular marker of platelet activation and systemic inflammation. Among leukocyte integrins, macrophage-1 antigen (Mac-1) is critically involved in platelet–monocyte aggregation and inflammatory thrombosis. This study aimed to investigate the hematologic significance of platelet–monocyte aggregates (PMA) and the integrin Mac-1 in patients with acute coronary syndrome (ACS).

Methods: Materials and Methods: A total of 62 participants (30 ACS patients and 30 healthy individuals) were analyzed. PMA formation and expression level of Mac-1 and were measured using flow cytometry. Correlation analyses were performed to assess integrin–PMA relationships. Multilevel modeling was employed to identify independent predictors of PMA formation. Diagnostic relevance was evaluated using ROC curve analysis.

Results: Results: ACS patients exhibited significantly increased PMA levels and elevated expression of Mac-1 compared with controls (p 0.05). PMA showed a strong positive correlation with Mac-1 expression. Multilevel analysis identified Mac-1 as the strongest independent determinant of PMA formation. ROC analysis demonstrated high diagnostic accuracy for Mac-1 in combination with PMA.

Conclusion: Conclusion: Mac-1–mediated platelet–monocyte aggregation represents a prominent hematologic feature of ACS and may serve as a powerful diagnostic and risk stratification biomarker, with potential implications for targeted anti-thromboinflammatory therapy.

keywords: Keywords: Flow Cytometry; Platelet–Monocyte Aggregates; Mac-1; Diagnostic Biomarkers; Acute Coronary

OH-14

The Bone Marrow Microenvironment as a Therapeutic Target in Acute Myeloid Leukemia and Multiple Myeloma

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Background and aim: Despite major progress in targeted therapies, treatment resistance and relapse remain significant challenges in acute myeloid leukemia (AML) and multiple myeloma (MM). Growing evidence indicates that the bone marrow microenvironment actively contributes to malignant cell survival, immune evasion, and therapeutic resistance. Accordingly, targeting microenvironment-mediated interactions has emerged as a promising complementary strategy to improve treatment outcomes in hematological malignancies.

Methods: A comprehensive literature search of PubMed, Scopus, and Web of Science was conducted to identify relevant original articles, review papers, and pre-clinical and clinical studies published up to 2025 using defined microenvironment-related keywords. Eligible studies were screened and narratively synthesized with a focus on microenvironment-targeted therapeutic strategies and their translational relevance.

Results: The reviewed studies highlight multiple therapeutic approaches aimed at targeting the bone marrow microenvironment to dismantle this protective niche and enhance treatment efficacy in AML and MM. Key axes examined include inhibition of homing and cell adhesion (by CXCL12/CXCR4 axis, Integrins/VLA4, and E-selectin), targeting stromal supportive signals and cytokines (TGF-β, NF-κB, Wnt/β-catenin, Notch, and IL-6), and reprogramming the immune microenvironment with a particular focus on macrophage-mediated mechanisms. Several agents targeting these pathways, for instance plerixafor, uproleselan, siltuximab, and magrolimab, demonstrated the ability to enhance drug sensitivity, reduce microenvironmental protection, and improve therapeutic responses in preclinical models and selected clinical studies.

Conclusion: Altogether, these findings underscore the pivotal role of the bone marrow microenvironment in disease persistence and the development of therapeutic resistance in AML and MM. Targeting microenvironment-dependent interactions represents a rational strategy to enhance the efficacy of conventional treatments.

keywords: Bone Marrow microenvironment, Acute Myeloid Leukemia(AML), Multiple Myeloma(MM), Tumor-Associated Macrophages, Microenvironment-Targeted Therapy, Resistance

OH-15

Red Blood Cell Alloimmunization in Transfusion-Dependent Thalassemia Patients: Diagnostic Challenges and Preventive Opportunities from Laboratory to Clinical Practice

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Background and aim: Regular red blood cell transfusion remains the cornerstone of management for patients with transfusion-dependent thalassemia (TDT). Despite its undeniable therapeutic benefits, chronic transfusion therapy exposes patients to a wide spectrum of foreign erythrocyte antigens, predisposing them to red blood cell alloimmunization. The development of alloantibodies not only complicates transfusion support but also increases the risk of hemolytic transfusion reactions, transfusion delays, and adverse clinical outcomes. As survival rates of thalassemia patients continue to improve, addressing transfusion-related immunological complications has become increasingly important.This review aims to provide a comprehensive overview of red blood cell alloimmunization in transfusion-dependent thalassemia patients.

Methods: A narrative review of the literature was conducted using PubMed, Scopus, and Web of Science databases. Relevant studies published between 2010 and 2024 were identified using the keywords Thalassemia, Red Blood Cell Alloimmunization, Transfusion-Dependent Thalassemia, Blood Transfusion, Immunohematology, and Blood Bank. Studies evaluating prevalence, risk factors, antibody profiles, diagnostic methods, and prevention approaches were reviewed and synthesized.

Results: The prevalence of alloimmunization among transfusion-dependent thalassemia patients varies widely across different populations, ranging from approximately 5% to over 30%, depending on ethnic background, transfusion practices, and donor-recipient antigen disparities. Clinically significant alloantibodies are most commonly directed against antigens of the Rh (particularly anti-E and anti-C) and Kell blood group systems. Key diagnostic challenges include antibody evanescence, the coexistence of autoantibodies, and difficulties in identifying compatible blood units in heavily transfused patients. Emerging strategies such as extended red cell phenotyping, molecular blood group genotyping, and prophylactic antigen matching have demonstrated significant potential in reducing alloimmunization rates and improving transfusion safety.

Conclusion: Red blood cell alloimmunization remains a major challenge in the long-term management of transfusion-dependent thalassemia patients. Advances in immunohematological testing and the implementation of preventive transfusion strategies offer valuable opportunities to minimize alloantibody formation and optimize clinical outcomes. A multidisciplinary approach involving hematologists, transfusion medicine specialists, and blood bank laboratories is essential to enhance transfusion safety and improve the quality of care for thalassemia patients.

keywords: Transfusion-Dependent Thalassemia, Red Blood Cell Alloimmunization, Blood Transfusion, Immunohematology

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July 20-23, 2026

OH-16

Minimal Residual Disease Assessment in Hematologic Malignancies: A Comprehensive Review of Current Methodologies and Clinical Applications

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Background and aim: Hematological malignancies are heterogeneous neoplastic disorders of bone marrow, blood, or lymphoid tissues, characterized by clonal proliferation of hematopoietic cells and impaired hematopoiesis. Despite advances in targeted and immunotherapies such as CAR T-cell therapy, relapse and treatment resistance remain major clinical challenges. Minimal residual disease (MRD) is a highly sensitive biomarker for detecting subclinical disease and assessing treatment response. This study aims to review and compare MRD detection methods, including flow cytometry, PCR-based techniques, next-generation sequencing, liquid biopsy, and imaging, emphasizing their strengths, limitations, and clinical applicability in hematologic malignancies and their role in precision medicine.

Methods: A narrative literature review was conducted using PubMed, Scopus, and Web of Science databases to identify relevant studies on MRD in hematologic malignancies. Articles published in English up to February 2026 were included. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords related to hematologic malignancies and MRD detection techniques. Boolean operators (AND/OR) were used to refine the search and ensure comprehensive coverage of the literature.

Results: MRD detection methodologies show significant variability in sensitivity, specificity, and clinical utility. Multiparameter flow cytometry (MFC) provides rapid and widely available detection with sensitivities of 10^{-3}–10^{-4}, while next-generation flow cytometry further improves performance. PCR-based techniques, including qPCR, ASO-qPCR, and droplet digital PCR (ddPCR), achieve higher sensitivity up to 10^{-6} but rely on disease-specific molecular targets. Next-generation sequencing (NGS) enables comprehensive mutation profiling and clonal tracking with sensitivities approaching 10^{-6}–10^{-7}, although its clinical use is limited by cost and lack of standardization. Liquid biopsy approaches, including circulating tumor DNA, extracellular vesicles, and tumor-educated platelets, represent promising non-invasive but still investigational tools. Imaging modalities and artificial intelligence-based computational methods provide complementary roles in MRD detection and risk stratification. Overall, MRD status strongly correlates with prognosis, relapse risk, and survival across acute, chronic, and plasma cell malignancies and increasingly guides therapeutic decisions such as treatment intensification, transplantation, and maintenance strategies.

Conclusion: MRD has become a cornerstone of precision hematology, providing highly sensitive detection of residual disease and essential prognostic information across hematologic malignancies. Although multiple advanced technologies are available, the optimal MRD assessment strategy remains disease-specific and dependent on molecular and immunophenotypic characteristics. Despite major technological progress, challenges including lack of standardization, inter-laboratory variability, and heterogeneous sensitivity thresholds still limit universal clinical implementation. Future integration of standardized platforms and emerging technologies is essential to fully establish MRD-guided personalized therapy in hematologic malignancies.

keywords: Minimal Residual Disease; Hematologic Malignancies; Flow Cytometry; Next-Generation Sequencing

17th International Congress of Lab. and Clinic
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OH-17

Circulating and Extracellular Vesicle-Derived MicroRNA Signatures for Prediction of Acute Graft-versus-Host Disease Following Allogeneic Hematopoietic Stem Cell Transplantation: A Systematic Review

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Background and aim: Allogeneic hematopoietic stem cell transplantation (HSCT) is a pillar therapy for various hematological malignancies,although it is frequently accompanied by a detrimental status termed acute graft-versus-host disease (aGvHD). this condition is characterized by severe immune-mediated organ damage. Extracellular vesicles (EVs) are membrane-bound structures secreted by cells and containing lipids, proteins and nucleic acids like miRNAs. By encapsulating miRNAs, EVs protect them from degradation and contribute to T-cell activation, cytokine production and consequent tissu injury. This systematic review discusses the role of circulating and EV-derived miRNA as diagnostic, prognostic, and therapeutic biomarkers for aGvHD, to achieve more personalized management of HSCT recipients.

Methods: : A systematic literature review was carried out through a database search of PubMed, Google Scholar, and Web of Science until March 2025 following PRISMA guidelines. The primary key terms searched included "microRNAs," "acute graft versus host disease," "allo-HSCT," and "extracellular vesicles" or "exosomes." Study inclusion criteria included clinical trials and validation studies involving patients with HSCT where circulating or EV-derived microRNAs in biofluids like serum or plasma were evaluated in the context of aGvHD. It should be noted that the selected articles needed to investigate the potential applications of microRNAs as diagnostic, prognostic, or therapeutic biomarkers of aGvHD. The quality of the selected articles was assessed using the Newcastle-Ottawa scale.

Results: Overall, 16 studies met the inclusion criteria defined prior to analysis. The current data confirm that circulating and EV-miRNAs are useful for managing acute GvHD. Certain miRNA patterns associated with the development and course of aGvHD include miR-155, miR-146a-5p, miR-423, miR-199, and miR-93. New miRNA clusters expressed in the plasma were found to predict skin manifestations of aGvHD effectively. In addition to being used for diagnosis, miRNAs such as miR-125b and miR-155 are considered prognostic indicators capable of predicting post-transplant outcomes. Research on exosome-related miRNA signatures helps to reveal novel aspects of the pathogenesis of late aGvHD. It is noteworthy that some miRNAs play a part in the molecular mechanisms of the disease and control of immune checkpoints, thus making up promising candidates for treatment. Therefore, miRNAs like miR-153-3p can be used as potential therapeutic targets helping to regulate the inflammatory process following HSCT.

Conclusion: EV-derived microRNAs act as a vital non-invasive biomarker for the prediction-of patient outcomes and management of post HSCT complications. More specifically, high miR-155 indicates the outcome of engraftment and the risk of developing aGVHD, while elevated levels of miR-125b have been identified as a crucial prognostic biomarker of relapse in auto-HSCT. In aGVHD cutaneous disorder, miR-455-3p and miR-5787 were found to be significantly decreased in patients, whereas miR-548a-3p showed higher levels in affected individuals. These differentially expressed microRNAs show great diagnostic value toward personalized medicine and earlier clinical intervention.

keywords: Extracellular vesicle; microRNA; Allogeneic Hematopoietic Stem Cell Transplantation; Acute Graft-versus-Host

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OH-18

Impact of Frequent Plateletpheresis on Immunomodulation: A Comparative Cohort Study of Frequent Versus First-Time Donors

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Background and aim: Plateletpheresis provides clinical benefits over platelet concentrates by minimizing the risk of alloimmunization. However, the standard use of leukoreduction system (LRS) chambers inherently traps considerable numbers of donor leukocytes during collection. While the depletion of specific lymphocyte subsets is documented, compensatory immune-regulating pathways remain poorly understood. This study investigates apheresis-induced immunomodulation by evaluating lymphocyte subset depletion, alterations in regulatory T cell (Treg) ratios, and systemic cytokine profiles in frequent versus first-time platelet donors.

Methods: In this comparative cohort study, 60 healthy, age- and sex-matched volunteers were categorized into a frequent plateletpheresis group (n=30; defined as 12 donations/year) and a control group of first-time donors (n=30). Procedures were performed using LRS-equipped apheresis devices with the Trima Accel system. Pre-donation peripheral blood samples were analyzed via multiparameter flow cytometry for absolute counts of lymphocyte subsets (CD3+, CD4+, CD8+, and CD19+). To assess immunomodulatory shifts, the CD4+CD25+FoxP3+ Treg population was quantified. Serum levels of Th1/Th2/Treg-associated cytokines (IL-10, TGF-β, IL-2, and IFN-γ) were measured via ELISA. Clinical histories regarding recent infections were collected using standardized questionnaires. Statistical analysis was performed using SPSS, with independent t-tests/Mann-Whitney U tests applied.

Results: Frequent donors exhibited a significant, dose-dependent decrease in absolute CD4+ and CD8+ T-cell counts compared to first-time donors (P0.05), directly correlating with their annual apheresis frequency (r = -0.62). While absolute Treg counts did not significantly expand, flow cytometric analysis revealed a significantly higher Treg-to-total CD4+ lymphocyte ratio in the frequent donor cohort (P0.05). This proportional shift toward immune tolerance was not accompanied by systemic Th1/Th2/Treg cytokine polarization; serum concentrations of IL-10, TGF-β, IL-2, and IFN-γ showed no statistically significant differences between the two groups (all P 0.05). Clinically, frequent donors reported a slight increase in mild, self-limiting infections; however, their absolute cell counts predominantly remained within normal physiological ranges.

Conclusion: Frequent LRS-mediated plateletpheresis depletes specific T-cell subsets while generally maintaining immune cells within normal physiological ranges. Repeated procedures drive a proportional increase in the Treg ratio without concurrent systemic cytokine polarization (such as IL-10, TGF-β, IL-2, or IFN-γ), suggesting that compensatory tolerance may rely on localized or cell-mediated mechanisms. Given the mild clinical observations and cellular shifts, we advocate for targeted, cost-effective longitudinal hemovigilance such as periodic complete blood counts and clinical screening for high-frequency donors, rather than routine advanced flow cytometric monitoring.

keywords: Plateletpheresis, Leukoreduction System (LRS), Immunomodulation, Regulatory T cells (Tregs), Hemovigilance

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OH-19

Artificial Intelligence-Driven Peptide Design for Targeted Leukemia Therapy: An In Silico Approach

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Background and aim: Antibody-based therapies have enhanced leukemia treatment, but their clinical efficacy is often limited by immunogenicity, toxicity, and resistance. This study used artificial intelligence to develop a new approach to targeting CD33, a surface biomarker of leukemic cells, via a peptide-targeting strategy, and to develop a robust, AI-integrated computational pipeline to identify high-affinity therapeutic peptides with improved safety and efficacy profiles.

Methods: We developed a discovery framework that combined the high predictive accuracy ($R^2 = 0.93$) of machine learning-driven Quantitative Structure-Activity Relationship (QSAR) modeling with molecular docking and 100-nanosecond molecular dynamics (MD) simulations to evaluate peptide-CD33 binding dynamics, and then synthesized the computationally optimized lead candidates for in vitro experimental validation by structural characterization, cytotoxicity assays on K-562 leukemia cells, and hemocompatibility profiling.

Results: Two lead peptide candidates were identified by the AI-guided pipeline and computational analyses indicated outstanding binding affinities of −146.11 kcal/mol and −108.08 kcal/mol, and high complex stability (RMSD of 0.25–0.35 nm). Experimental assays confirmed the peptides spontaneously form stable reverse β-sheet architectures and self-assemble into nanostructures, and that they displayed target selectivity, with potent cytotoxicity against K-562 cells (IC_{50}: 60–90 μM) but minimal toxicity toward normal peripheral blood mononuclear cells (PBMCs). Safety evaluations also showed negligible hemolytic activity (5%) and confirmed the induction of malignant cell death via concurrent apoptotic and necrotic mechanisms.

Conclusion: Combining artificial intelligence with molecular modeling resulted in highly specific, low-toxicity CD33-targeting peptides, which provide a promising peptide-based alternative to traditional antibody therapies in leukemia. The proposed AI-driven platform also offers a highly generalizable and efficient framework for the rapid discovery of receptor-specific anticancer peptides, especially for hematological malignancies that necessitate stringent target selectivity.

keywords: Quantitative Structure-Activity Relationship, K562 Cells, Molecular Dynamics Simulation, Peptides

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OH-20

Artificial Intelligence in Peripheral Blood Smear Analysis for Leukemia Diagnosis: A Systematic Review

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Background and aim: Leukemia is a heterogeneous group of hematologic malignancies characterized by the clonal proliferation of abnormal white blood cells, making timely and accurate diagnosis essential for optimal clinical management. While peripheral blood smear (PBS) examination remains a cornerstone of the initial diagnostic workup, manual microscopic evaluation is time-consuming, subjective, and highly dependent on the pathologist's expertise. In recent years, artificial intelligence (AI), particularly deep learning (DL), has emerged as a promising tool to automate and standardize this process. This systematic review aims to comprehensively evaluate the current landscape of AI applications for leukemia diagnosis and classification using PBS images.

Methods: This systematic review was conducted in accordance with the PRISMA 2020 guidelines. A comprehensive literature search was performed across Scopus, Web of Science, and PubMed databases to identify original research articles published in English between 2021 and 2026. Following the application of strict inclusion and exclusion criteria, 32 of the 424 initially identified records were included in the final qualitative synthesis. Data extraction focused on dataset characteristics, model architectures, validation strategies, and diagnostic performance metrics. Methodological quality was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist.

Results: Acute Lymphoblastic Leukemia (ALL) was the most widely investigated subtype, representing 75% of the included studies. Convolutional Neural Networks (CNNs) formed the backbone of nearly all approaches, with transfer learning from pre-trained architectures (e.g., EfficientNet, DenseNet, ResNet) being the most common strategy. In binary classification tasks (e.g., distinguishing ALL from normal cells), most deep learning models demonstrated outstanding performance, frequently exceeding 98% accuracy. For multiclass subtype classification, advanced architectures such as YOLOv8 and custom fusion ensembles also achieved near-perfect diagnostic results. However, most studies relied heavily on small, single-source public datasets (such as ALL-IDB and C-NMC) and rarely implemented independent external validation, raising concerns about clinical generalizability.

Conclusion: Deep learning models exhibit exceptional diagnostic potential for the automated and accurate classification of leukemia from PBS images. However, the lack of rigorous cross-institutional external validation and reliance on homogeneous public datasets remain critical barriers to real-world translation. Future research should prioritize the development of multi-center collaborative datasets, independent validation trials, and the integration of morphological images with clinical findings to support safe clinical deployment.

keywords: Leukemia; Artificial Intelligence; Deep Learning; Peripheral Blood Smear; Hematology

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OI-1

Association of interleukin-17A and chemokine/vascular endothelial growth factor-induced angiogenesis in newly diagnosed patients with bladder cancer

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Background and aim: The human interleukin-17 (IL-17) family comprises IL-17A to IL-17 F; their receptors are IL-17RA to IL-17RE. Evidence revealed that these cytokines can have a tumor-supportive or anti-tumor impact on human malignancies. The purpose of this study was to assess the expression of CXCR2, IL-17RA, and IL-17RC genes at the mRNA level as well as tissue and serum levels of IL-17A, vascular endothelial growth factor (VEGF), and transforming growth factor β (TGF-β) in patients with bladder cancer (BC) compared to control.

Methods: This cross-sectional study included 45 male patients with invasive bladder cancer (BC) (T2–T4) and 42 age-matched healthy controls at Moradi Hospital, Rafsanjan, Iran (Jan–Nov 2022). Participants with inflammatory diseases, infections, malignancies, or exposure to aromatic amines were excluded. Tumor and adjacent normal tissues were collected during transurethral resection (TUR) before any chemotherapy. qRT-PCR quantified IL-17RA, IL-17RC, and CXCR2 mRNA levels using SYBR Green, with β-actin as a reference. ELISA assays measured IL-17A, TGF-β, and VEGF levels in serum and tissue samples. Protein extracts were prepared using RIPA buffer and quantified by Bradford assay. Statistical analyses were performed with GraphPad Prism 9, applying t-tests, Mann-Whitney U, and ROC curve analysis to assess diagnostic performance (AUC, sensitivity, specificity, PPV, NPV). A p-value 0.05 was considered significant. All procedures were approved by the Rafsanjan University Ethics Committee.

Results: This study showed that gene expression of IL-17RA, IL-17RC, and CXCR2 in the tumoral tissue of BC patients was significantly upregulated compared with normal tissue. The findings disclosed a significant difference in the serum and tissue concentrations of IL-17A, VEGF, and TGF-β between the patient and the control groups, as well as tumor and normal tissues.

Conclusion: This study reveals notable dysregulation of CXCR2, IL-17RA, and IL-17RC genes, alongside changes in IL-17A, VEGF, and TGF-β levels in patients with BC than in controls. These findings indicate their possible involvement in BC development and their potential as diagnostic and therapeutic targets.

keywords: IL-17A, CXCR2, VEGF, TGF-β, Bladder cancer

OI-2

lncRNA-Mediated miR-145 Sponging Defines a Prognostic ceRNA Axis in Non–Small Cell Lung Cancer

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Background and aim: Non–small cell lung cancer (NSCLC) progression is strongly influenced by aberrant competing endogenous RNA (ceRNA) networks, in which non-coding RNAs regulate oncogene expression by sequestering microRNAs. The tumor-suppressive microRNA miR-145 is frequently downregulated in NSCLC; however, the long non-coding RNA (lncRNA)–mediated mechanisms governing its dysregulation remain insufficiently defined.

Methods: An integrated transcriptomic analysis was performed using NSCLC datasets GSE135304 (blood RNA profiles from 712 patients) and GSE203510 (plasma miRNA profiles) to identify differentially expressed genes (|log2FC| 0.1, p 0.05) and miRNAs (|log2FC| 1, p 0.05). Experimentally validated miRNA–target interactions from miRTarBase and TarBase were intersected with the dysregulated gene set, followed by functional enrichment analyses using WikiPathways and Gene Ontology. ceRNA networks were constructed based on co-expression relationships. miR-145-3p expression was validated by RT-qPCR in A549 and MRC-5 cell lines as well as NSCLC tissue samples. The clinical relevance of FN1 and CCND1 was assessed using GEPIA.

Results: A total of 8,271 differentially expressed genes and 52 dysregulated miRNAs were identified. miR-145-3p, known for its role in immune regulation, was significantly downregulated (log2FC = −1.24, p = 0.036). Intersection analysis revealed 27 validated miR-145-3p target genes—including FN1, CCND1, and SMAD3—that were enriched in immune-related pathways (FDR 0.05) and TGF-β–driven epithelial–mesenchymal transition within the dysregulated transcriptome. Six immune-associated hub genes were identified. The lncRNAs LOC729919 and LOC100134412 displayed strong co-expression with these hub genes and acted as competitive sponges for miR-145-3p, resulting in derepression of the metastasis-associated genes FN1, an extracellular matrix regulator, and CCND1, a key cell-cycle regulator. This ceRNA regulatory axis functioned within a broader landscape of disrupted ATM-dependent DNA damage response, Hippo signaling, and cell-cycle pathways. RT-qPCR confirmed significant suppression of miR-145-3p in NSCLC models (p 0.05), and GEPIA analysis demonstrated significant co-expression between FN1 and CCND1 (p = 0.0017).

Conclusion: This study identifies a previously uncharacterized LOC729919/LOC100134412–miR-145–FN1/CCND1 ceRNA regulatory axis that contributes to NSCLC pathogenesis. The prognostic relevance of FN1 and its functional association with CCND1 highlight this axis as a potential therapeutic target for disrupting metastatic and proliferative signaling in NSCLC.

keywords: non-small cell lung cancer; ceRNA network; long non-coding RNA; miR-145

OI-3

Investigation of the Relationship Between Cigarette Smoking and Progesterone and Estrogen Receptors in Patients with Breast Cancer

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Background and aim: Cancer involves uncontrolled cell growth, often forming tumors. Breast cancer is the second leading cause of cancer deaths in women, with over 1.2 million diagnoses and 500,000 deaths annually. Its incidence is rising in developing countries due to aging, smoking, obesity, inactivity, and reproductive changes. This study examined cigarette smoking on progesterone and estrogen receptors in breast cancer patients.

Methods: This study examined 249 cancer patients. It was a descriptive-analytical cross-sectional study using data from breast cancer patients in Ahvaz, Iran (IR.AJUMS.MEDICINE.REC.1401.014). After ethical approval, researchers collected information from the Cancer Research Center of Ahvaz University of Medical Sciences, based on hospital records compiled by the Khuzestan Provincial Cancer Registry. The sample included all breast cancer patients visiting the center in 2019, confirmed by oncologists, radiotherapists, and surgeons, supported by pathology reports, and coded with ICD-O. Inclusion required a definitive breast cancer diagnosis, while patients without estrogen receptor (ER) and progesterone receptor (PR) test results were excluded. Sampling was convenient and accessible. For each patient, a checklist recorded demographic data, age, and smoking status, including smoking duration. Data analysis was conducted with SPSS version 24, applying descriptive and inferential statistics. Results were considered significant at p 0.05.

Results: This study examined smoking and hormone receptor status—estrogen and progesterone—in breast cancer patients. Analyses showed no significant difference in estrogen receptor positivity between smokers and non-smokers (P = 0.454), indicating smoking does not substantially affect estrogen receptor expression. This supports prior research suggesting smoking's influence is limited or indirect, with genetic, environmental, and hormonal factors more important. For progesterone receptors, 57.1% of smokers and 59.6% of non-smokers were positive, while 42.9% and 40.9% were negative, respectively. The difference was not significant (P = 0.534). Overall, smoking was not associated with receptor status.

Conclusion: This study found cigarette smoking not significantly linked to estrogen or progesterone receptor status in breast cancer patients. Results suggest smoking may not directly affect hormonal receptor expression, with other biological and environmental factors playing stronger roles. Larger prospective studies are recommended to clarify possible indirect effects of smoking on breast cancer characteristics and outcomes.

keywords: Breast cancer, Smoking, Estrogen receptor, Progesterone receptor

OI-4

Effects of GnRH Agonist and Antagonist on Peripheral Blood CD8+ T Cells in Women with Endometriosis Undergoing IVF/ICSI

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Background and aim: Endometriosis is an inflammatory disease of reproductive-age women characterized by presence of endometrial tissue outside the uterine cavity. Although its etiology is unclear, immune cell dysfunction plays a significant role in its pathogenesis. Impaired CD8+ T cell number and cytotoxic activity have been reported in endometriosis, potentially contributing to disease. The aim of this study was to evaluate the effect of ovarian stimulation drugs on peripheral blood CD8+ T cells in women with endometriosis undergoing IVF/ICSI.

Methods: In this cohort study, forty infertile women with endometriosis undergoing IVF/ICSI cycles using GnRH agonist or GnRH antagonist will be enrolled. The percentage of peripheral blood CD8+ T cells was evaluated by flow cytometry on days 2–3 of the menstrual cycle (starting day) and on end of ovarian stimulation day (oocyte puncture day). Eligible participants were under 40 years of age with a BMI 35 kg/m² and were undergoing their first IVF cycle or had at least a three-month interval since their last cycle, with confirmed endometriosis. Women with autoimmune diseases, untreated endocrine disorders, or poor ovarian response were excluded. Results are presented as mean ± standard error (SE).

Results: Fourteen women with endometriosis were enrolled in the present study, and two peripheral blood samples were obtained from each participant on the starting day of ovarian stimulation and on the ovarian puncture day. Four patients underwent the long GnRH agonist protocol, while ten patients received the GnRH antagonist protocol. Comparison of peripheral blood CD8+ T cell percentages between the starting day and the ovarian puncture day showed no statistically significant changes in either the GnRH antagonist group (22.06 ± 4.93 on the starting day vs. 18.61 ± 2.55 on the puncture day) and the GnRH agonist group (32.03 ± 12.06 on the starting day vs. 27.50 ± 10.30 on the puncture day).

Conclusion: In the current sample size, no significant changes were observed in the frequency of peripheral blood CD8+ T cells. The final conclusion will be drawn after enrollment of forty women in the study.

keywords: Endometriosis, CD8+ T Cell, Peripheral Blood, IVF/ICSI

OI-5

Immunomodulatory Effects of Vitamin D3 on Experimental Autoimmune Encephalomyelitis Through Regulation of T Helper Cell Balance

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Background and aim: Multiple sclerosis (MS) is a chronic inflammatory disorder of the central nervous system (CNS). Experimental autoimmune encephalomyelitis (EAE) is a well-established animal model that recapitulates key pathological features of MS. 1,25-dihydroxy vitamin D3 functions as a vital immunomodulatory agent which could affect inflammatory and autoimmune conditions.

Methods: The prevention groups of female C57BL/6 mice received low, medium, and high doses of vitamin D3 while the treatment groups consisted of medium and high dose levels. The prevention groups received treatment starting two weeks before EAE induction but the treatment groups started administration at the time of disease induction. The evaluation of disease progression occurred through clinical assessment and histopathological examination. The assessment of cytokine production occurred through ELISA testing while flow cytometry was used to study T helper cell subsets, and real-time PCR detected lineage-specific transcription factors and cytokines in peripheral tissues and the CNS.

Results: The administration of vitamin D3 can prevented an EAE from appearing. histological evaluation of central nervous system indicated an elevation of demyelination and also reduced infiltration of inflammatory cells. Cytokine evaluation demonstrated that there were higher concentrations of IL-4, IL-10, and TGF-β, whereas there were lower levels of IFN-γ, IL-6, TNF-α, and IL-17. Flow cytometric analysis established decreased numbers of Th1 and Th17 cells, while demonstrating increased numbers of Th2 and Treg cells within both the medium and high doses of vitamin D3., real-time PCR analysis of CNS tissue showed reduced expression of both T-bet and ROR-γt, and increased expression of GATA3 and Foxp3.

Conclusion: Based on the present findings, it can be concluded that medium and high doses of vitamin D3 primarily modulate EAE-induced immune responses by shifting the Th1/Th2 and Th17/Treg balances in favour of dominance of the Th2 and Treg populations. The immune system reprogramming resulting from vitamin D3 administration correlates with decreased incidence and severity of disease. Therefore, vitamin D3 has potential therapeutic application for autoimmune neuroinflammatory diseases, such as MS, where immune dysregulation plays a significant role

keywords: Multiple sclerosis; Experimental autoimmune encephalomyelitis; Vitamin D3; Immunomodulation

OI-6

Effect of a Chitosan–Alginate Scaffold Containing Zinc Oxide Nanoparticles and Mesenchymal Stem Cells on the Inflammatory Response of Cutaneous Wounds in Rats

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Background and aim: Background The incorporation of metallic nanoparticles, such as zinc oxide nanoparticles (ZnO), into biomaterial scaffolds can enhance anti-inflammatory and antimicrobial properties during the wound healing process. This study aimed to investigate the combined effect of a chitosan–alginate scaffold, zinc oxide nanoparticles, and mesenchymal stem cells on the inflammatory response of cutaneous wounds in rats.

Methods: Methods In this experimental study, twelve female rats were divided into control, chitosan–alginate scaffold containing zinc oxide nanoparticles, and scaffold containing zinc oxide nanoparticles combined with mesenchymal stem cells (MSCs) groups. Full-thickness cutaneous wounds were created, and the wound area was covered with the scaffold. Wound size was evaluated on days 1, 7, and 14 post-injury. In addition, the expression of inflammatory cytokines and angiogenesis-related factors was assessed, and histological evaluations were performed using Hematoxylin and Eosin (H&E) staining.

Results: Results The findings revealed that the MSCs+Scaffold+ZnO group exhibited a significant reduction in wound size and the severity of inflammatory responses on day 7 compared to all other groups. Additionally, the Scaffold +ZnO group showed a significant decrease in wound size relative to the control group. Near-complete wound healing was observed in both the MSCs + Scaffold +ZnO and Scaffold+ZnO groups on day 14. Furthermore, downregulation of IL-17 and upregulation of VEGF expression indicated the effective role of this combination in suppressing inflammation and promoting angiogenesis, respectively.

Conclusion: Conclusion The combination of a chitosan–alginate scaffold modified with zinc oxide nanoparticles and mesenchymal stem cells can significantly enhance cutaneous wound healing by modulating inflammatory responses and promoting tissue regeneration.

keywords: Zinc oxide nanoparticles, chitosan–alginate scaffold, mesenchymal stem cells, wound healing

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OI-7

Demographic Determinants of Estrogen and Progesterone Receptor Expression in Breast Cancer Patients

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Background and aim: Cancer is a pathological disorder marked by uncontrolled cellular proliferation, often resulting in tumorigenesis. Breast cancer is the second leading cause of cancer-related mortality among women globally, with more than 1.2 million new cases and approximately 500,000 deaths reported annually. Incidence rates are rising in developing countries, largely due to aging populations, tobacco use, obesity, sedentary lifestyles, and reproductive changes. Hormone receptor status, particularly estrogen and progesterone expression, is critical for prognosis and treatment. This study investigates the relationship between age, gender, and ethnicity on estrogen and progesterone receptor expression in patients diagnosed with breast carcinoma.

Methods: This study involved 249 patients with cancer. It was a descriptive-analytical cross-sectional study utilizing data from breast cancer patients in Ahvaz, Iran. After obtaining ethical approval(IR.AJUMS.MEDICINE.REC.1401.014). Researchers gathered IHC data from the Cancer Research Center of Ahvaz University of Medical Sciences, based on hospital records maintained by the Khuzestan Provincial Cancer Registry. The sample consisted of all breast cancer patients visiting the center in 2019, whose diagnoses were confirmed by oncologists, radiotherapists, and surgeons, supported by pathology reports, and coded with ICD-O. Inclusion required a definitive breast cancer diagnosis, while patients lacking estrogen receptor (ER) and progesterone receptor (PR) test results were excluded. Sampling was convenient and accessible. For each patient, a checklist documented demographic information, including age, gender, and ethnicity. Data analysis was performed using SPSS version 24, applying both descriptive and inferential statistics. Results were deemed significant at p 0.05.

Results: In examining the relationship between demographic variables and hormonal receptor status in patients with breast cancer, no significant association was found between ethnicity and the expression of estrogen receptors (P=0.768) or progesterone receptors (P=0.899). The highest frequency of estrogen receptor positivity was observed among Arab (69.7%) and Persian (73.9%) ethnic groups, while progesterone receptor positivity was most common among Arabs (61.6%). The prevalence of estrogen receptor positivity was 69% in women and 60% in men (P=0.666), and progesterone receptor positivity was reported as 59.8% and 40%, respectively (P=0.371). The highest expression of estrogen receptor positivity was seen in the 50–59 age group (73.3%), although this association was not statistically significant (P=0.181). The highest level of progesterone receptor positivity was also observed in the 50–59 age group (70.4%), with no statistically significant association (P=0.070).

Conclusion: The findings indicate that estrogen and progesterone receptor expression in breast cancer patients is not significantly influenced by ethnicity, sex, or age. Although variations in receptor positivity were observed across demographic subgroups, these differences did not reach statistical significance. Overall, hormone receptor status appears to be independent of the evaluated demographic factors, suggesting that tumor biological characteristics may play a more prominent role than population-based variables in determining receptor expression.

keywords: Breast Cancer, Age, Gender, Estrogen Receptor, Progesterone Receptor

OI-8

Regulatory CD56bright NK Cells as Modulators of Chronic Graft-versus-Host Disease

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Background and aim: Chronic graft-versus-host disease (cGvHD) is the predominant complication of all hematopoietic stem cell transplantation (HSCT) that lasts over the long term and is responsible for great post-transplant morbidity and mortality. A rare NK cell subset has been detected by us, which is distinguished by the presence of CD56bright $CD16^{-}$ $CD3^{-}$ and much reduced expression of cytotoxic mediators.This population has been proposed to exert immunoregulatory functions and to correlate with a reduced incidence of cGvHD. Elevated CD56bright NK cells are associated with reduced cGvHD incidence in pediatric and adult transplant patients across multiple scenarios.

Methods: To characterize this regulatory NK cell subset, we combined immunophenotyping profiling of clinical HSCT cohorts with comparative transcriptomic analysis of CD56bright and CD56dim NK cells. In addition, in vitro co-culture assays using flow-sorted NK cell populations were performed to evaluate their capacity to inhibit allogeneic $CD4^{+}$ T-cell activation and proliferation. We conducted various analyses of peripheral blood mononuclear cells drawn from HSCT patients on day 100 and at the onset of cGvHD. The study used nanoString profiling to differentiate CD56bright and CD56dim NK cells and validated surface markers like IL-7R and GPR183. NKreg cells were isolated via FACS and tested for suppressive functions through co-culture, transwell, apoptosis, and cytotoxicity assays against leukemic cells, all with appropriate controls and donor replicates.

Results: The CD56bright regulatory NK (NKreg) cell subset exhibited the lowest expression levels of perforin and granzyme B, while showing elevated mRNA expression of granzyme K, IL7R, GPR183, RANK, CSF2R, TCF7, and IL23A. Besides, the NKreg compartment showed a distinct subpopulation that was characterized by the upregulation of IRF1 and TNF, which pointed to molecular diversity. To support this, transcriptomic and functional studies pointed towards a non-cytolytic regulatory mechanism that clearly differentiated NKreg from conventional cytotoxic NK cells. In terms of their function, the NKreg cells were not as effective as the CD56dim NK cells in terms of the activation of $CD4^{+}$ T-cell markers as well as the support of T-cell proliferation. The CD56brightCD16- NKreg cells were found to suppress the proliferation of allogeneic CD4+ T-cells by about ~96%, and this was mainly through contact-dependent, non-apoptotic mechanisms; they also had very small effects on CD8+ and Treg cells.

Conclusion: Regulatory NK (NKreg) cells have been shown in this study to be a new immunomodulatory pathway in cGvHD. These cells are, however, to be investigated further for their possible use as biomarkers and therapeutic targets. The safe and scalable translation of these findings into clinical practice might result in a significant decrease in cGvHD-associated morbidity, betterment of patients' quality of life, and transplant outcomes being improved in the long run. Targeting or expanding NKreg cells may suppress cGvHD differently, but further studies are needed to assess safety and scalability.

keywords: Chronic graft-versus-host disease(cGvHD); Regulatory NK cells (NKreg); Immunoregulation; Allogeneic hematopoietic

OI-9

Investigating the effect of cocktail containing vitamins, peptides and minerals on the expression of inflammatory genes TNF-a and IL-6 on human dermal fibroblast cell line

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Background and aim: Wounds heal through regulated stages involving inflammation, tissue formation, and remodeling, controlled by cells and inflammatory genes such as TNF-α and IL-6. While these cytokines support immune recruitment and fibroblast activation, excessive expression can impair healing. Bioactive compounds like silymarin, L-carnosine, zinc, and B vitamins enhance wound repair via antioxidant activity, immune modulation, and collagen synthesis. This study evaluates their combined effects on TNF-α and IL-6 expression in human dermal fibroblasts to improve wound healing.

Methods: To determine the optimal concentration of the cocktail containing vitamins, peptides, and minerals, an MTT assay was initially performed on human dermal fibroblast (HDF) cells to evaluate cell viability and proliferative capacity across a range of concentrations. Based on the viability results, cells were subsequently treated with the optimal, non-toxic concentration. Following treatment, total RNA was isolated from the cells using standard extraction protocols. The extracted RNA was then reverse-transcribed into complementary DNA (cDNA) using a reverse transcriptase enzyme. Finally, the relative expression levels of the inflammatory genes (TNF-α) and (IL-6) were quantitatively assessed and compared using real-time polymerase chain reaction (qRT-PCR).

Results: Using the MTT assay, the optimal concentration of the vitamins, peptides, and minerals containing cocktail for wound repair was first determined in fibroblast cells. At 24, 48, and 72 hours, the 1/2 concentration of the cocktail showed the greatest increase in cell viability and proliferation compared with the control group and was therefore identified as the effective concentration. The effect of the cocktail was more pronounced at 24 hours, whereas at 72 hours the differences between concentrations were reduced, likely due to a saturation effect. The expression levels of the pro-inflammatory genes interleukin-6 (IL-6) and TNF-α were significantly decreased in the treated group (p 0.05), indicating the anti-inflammatory properties of the cocktail and its role in enhancing wound healing through attenuation of inflammatory responses.

Conclusion: In conclusion, the findings of this study demonstrate that the cocktail comprising vitamins, peptides, and minerals exerts a significant anti-inflammatory effect while markedly enhancing fibroblast cell viability and proliferation. These combined biological effects highlight the therapeutic potential of this formulation in promoting and accelerating skin wound healing. Collectively, the results position this cocktail as a promising candidate for future clinical applications in wound management. Nevertheless, further investigations using relevant animal models and, subsequently, well-designed human studies are warranted to comprehensively evaluate its safety profile, underlying mechanisms, and clinical efficacy.

keywords: Wound healing, Fibroblasts, Inflammation, TNF-α and IL-6, Antioxidant cocktail

OI-10

Assessing the expression of immunosuppressive cytokines in the newly diagnosed systemic lupus Erythematosus patients: a focus on B cells

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Background and aim: The immunosuppressive effects of regulatory B-cells (Bregs) and their immunosuppressive cytokines on immune responses in autoimmune disorders, mainly systemic lupus erythematosus (SLE), have been recently established. Therefore, the purpose of this article has been the exploration of the expressions of cytokines produced by B cells in newly diagnosed SLE patients.

Methods: Subjects: Twenty-three newly diagnosed SLE patients (mean age of 39.6 ±13.4years) diagnosed by a rheumatology specialist and 30 normal-age and gender-matched healthy subjects with a mean age of 34.95±10.01years have participated in this study. All SLE patients had at least four of the American College of Rheumatology (ACR) revised SLE criteria. Moreover, activities of the SLE disease have been evaluated through Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), and all the patients showed active SLE (SLEDAI score4). All of the enrolled SLE patients had received no treatment up to the blood collection for the experiments. Additionally, No SLE patient has been receiving immunomodulatory medications include antimalarials, at the time of examination. Informed consent was received from each SLE patient and healthy subjects based on Declaration of Helsinki (DoH). Moreover, this investigation was approved by the Ethics Committee of Rafsanjan University of Medical Sciences, Rafsanjan, Iran.Cytokine assay, Flowcytometry, Gene expression assay

Results: The findings demonstrated that the gene expression of IL-10, TGF-β, IL-35, PD-L1, and FasL was significantly up-regulated in SLE patients compared to healthy subjects (P 0.05). Additionally, the results revealed that serum levels of IL-10, TGF-β, IL-35, PD-L1 were remarkably increased in patients with SLE compared to healthy subjects (P 0.0001). However, serum levels of IL-10 and TGF-β decreased significantly with increasing SLEDAI score in studied patients (P 0.05).

Conclusion: It was concluded that the release of anti-inflammatory cytokines, particularly IL-10 and TGF-β, might inhibit immune responses and autoreactive immune cells in a compensatory manner in SLE patients with mild to moderate disease activity.

keywords: Regulatory B-cells (Bregs), Systemic lupus Erythematosus (SLE), Anti-inflammatory cytokine

OI-11

Hyaluronic Acid Mitigates Hydrogen Peroxide Toxicity in Hypoxic Conditions: A Novel Approach for Breast Cancer Therapy

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Background and aim: Breast cancer is the second leading cause of cancer-related mortality among women, and an effective treatment remains elusive. One of the emerging therapeutic strategies involves the use of hydrogen peroxide (H_2O_2) to alter the tumor microenvironment; however, excessive free radicals generated by H_2O_2 may pose significant risks. To mitigate these effects, this study employed hyaluronic acid (HA) and investigated their combined effects under hypoxic conditions.

Methods: In this study, hypoxic conditions were established for breast cancer cells, followed by the confirmation of induced hypoxia through the assessment of PDL1 antibody levels on the cancer cell surface. Subsequently, cells were treated with varying concentrations of H_2O_2 (0-1000 µM) for 24 hours, after which cell viability and apoptosis were evaluated.

Results: The results demonstrated that under hypoxic conditions, increasing concentrations of H_2O_2 resulted in a dose-dependent decrease in cancer cell viability, accompanied by a subsequent increase in apoptosis. Notably, when H_2O_2 was combined with HA, the IC50 value shifted from 100 µM to 500 µM, indicating a change in sensitivity and enhanced control over the application of hydrogen peroxide in cancer treatment. Similar trends were observed in apoptosis levels.

Conclusion: The findings suggest that hyaluronic acid can effectively modulate the toxic effects of hydrogen peroxide under hypoxic conditions, facilitating better control over its application. These results may contribute to the development of novel therapeutic strategies for breast cancer.

keywords: Hydrogen peroxide, hypoxia, hyaluronic acid, cancer cells, viability, apoptosis.

OI-12

Evaluation of Trends in Neutrophils, Eosinophils, and Serum IgE levels in Seasonal Allergy patients

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Background and aim: Allergic rhinitis is a common, chronic, inflammatory disease caused by the histamine release after exposure to an allergen. One of the main mediators in hypersensitivity reactions, including allergic ones, is immunoglobulin E (IgE). IgE exerts its effects by binding to mast cells and basophils, with rapid degranulation and release of histamine, which leads to allergic symptoms. Neutrophils and eosinophils play a pivotal role in the delayed phase of the immune response that occurs after exposure to allergens. This study aimed to compare the eosinophil and neutrophil counts and serum IgE levels in allergic patients before and after the allergy season.

Methods: Among the individuals referred to the clinic of Heshmatiyeh Hospital in Sabzevar, 40 people with seasonal allergies were selected. After confirming seasonal allergies by a specialist physician and obtaining informed consent, 5 cc of venous blood was taken from each patient. A complete blood cell count was performed on these samples. The patients' serum IgE levels were also measured using the ELISA method and according to the instructions of the relevant kit. Blood sampling was performed in two time periods: during the allergy season (late September and early October) and after the end of the allergy season.

Results: The participants' average age was 27.97 ± 8.00 years. Allergic patients exhibited significantly higher eosinophil counts during allergy season (3.28 ± 1.08) compared to after the season (1.51 ± 0.81, p 0.05). Conversely, neutrophil counts were significantly lower during allergy season (54.98 ± 6.46) than after (61.78 ± 7.07). Serum IgE levels were also significantly higher during allergy season (253.72 ± 120.36) than after (244.71 ± 119.72, p0.05).

Conclusion: The results of this study revealed that during the allergy season, granulocyte precursor cells tend to differentiate into eosinophils rather than neutrophils, which is probably due to the effect of IgE and Th2 cells.

keywords: Allergic rhinitis; Eosinophil; Neutrophil; Immunoglobulin E; IgE

OI-13

A Novel Multiepitope Vaccine Against Breast Cancer Using Immunoinformatics Approaches

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Background and aim: Background: Triple-negative breast cancer (TNBC) presents a significant threat to patients due to its extreme aggressiveness and substantial risk of metastasis. Thus, there is an urgent need to develop novel treatment methods for this type of breast cancer since existing treatments with targeted therapies do not work well on patients with TNBC. One of the best approaches to treating advanced-stage TNBC is to utilize cancer vaccines. The goal of this study was to develop a multi-epitope subunit vaccine against four proteins associated with breast cancer (i.e. MUC-1, CEA, WT-1, and survivin) by using bioinformatics methods to analyze their characteristics.

Methods: Methods: Amino acid sequences of the antigens were retrieved from UniProt. T-cell and B-cell epitopes were predicted using the IEDB platform. The constructs were then evaluated for antigenicity, physicochemical properties, allergenicity, tertiary structure, and molecular docking performance. Finally, the most promising construct was selected, followed by computational immune simulation analyses.

Results: Results: The CTL, HTL, and B cell-selected immunodominant epitopes were fused into a single chimeric protein construct using GPGPG linkers via epitope prediction servers. The resulting chimera was predicted to have high antigenic potential using VaxiJen and to be nontoxic and non-allergenic, while its physicochemical properties suggested suitability for future applications in vaccine development. Structural modelling of the chimera indicated very high quality and stability including in association with Toll-like receptors. Furthermore, molecular dynamics simulations supported in vivo stability for these vaccine-receptor complexes.

Conclusion: Conclusion: Taken together, these results suggest that this multi-epitope vaccine holds potential as a therapeutic or preventive candidate against breast cancer; however, confirming its efficacy through in vitro and in vivo studies will be essential.

keywords: Keywords: Breast Cancer, Multi-epitope vaccine, Vaccine candidate , Immunoinformatic

OI-14

Role of Leishmania RNA Virus in Temperature-Dependent Inflammatory Responses of THP-1 Macrophages Infected with Leishmania major

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Background and aim: Leishmania major may harbor Leishmania RNA Virus (LRV), a viral endosymbiont known to exacerbate host inflammatory responses and disease severity. In parallel, temperature-dependent differentiation of Leishmania from promastigote to amastigote forms may further influence macrophage activation. However, the combined effects of parasite temperature, exposure duration, and LRV status on macrophage inflammatory responses remain poorly understood. This study aimed to investigate the effects of parasite culture temperature, exposure time, and LRV infection status on inflammatory cytokine expression and nitric oxide (NO) production in THP-1-derived macrophages exposed to Leishmania major.

Methods: THP-1 monocytes were differentiated into macrophages and exposed to Leishmania major parasites cultured at 25°C or 37°C, either LRV-positive (Lm+) or LRV-negative (Lm−), for 24 and 48 hours. The mRNA expression levels of IL-1, IL-6, and TNF-α were quantified using real-time PCR. Nitric oxide production was measured in culture supernatants using the Griess assay.

Results: Macrophage exposure to Leishmania major resulted in pronounced inflammatory responses that were strongly dependent on temperature, exposure time, and LRV status. LRV-positive parasites cultured at 37°C induced a robust early inflammatory response at 24 h, characterized by elevated IL-1 expression and NO production. In contrast, prolonged exposure (48 h) to LRV-positive parasites at 37°C led to reduced IL-1 and IL-6 expression, suggesting immune modulation. Parasites cultured at 25°C, particularly those harboring LRV, induced a delayed but marked increase in IL-6 and TNF-α at 48 h. Overall, LRV-positive parasites elicited stronger inflammatory responses than LRV-negative counterparts, highlighting the immunostimulatory role of LRV.

Conclusion: Our findings demonstrate that macrophage inflammatory responses to Leishmania major are shaped by a complex interplay between parasite temperature, exposure duration, and LRV infection. Early exposure to LRV-positive parasites cultured at 37°C promotes strong pro-inflammatory and antimicrobial responses, whereas prolonged exposure is associated with immune modulation. In contrast, 25°C-cultured parasites, particularly those harboring LRV, preferentially induce delayed inflammatory and regulatory cytokine responses. These results underscore the critical role of LRV in amplifying host innate immune activation during leishmaniasis.

keywords: Leishmania major; Leishmania RNA Virus; Innate immunity; Inflammatory cytokines; Macrophages

OI-15

Analysis of Ferroptosis-Associated Gene Expression in Placental Tissue from a Mouse Model of Recurrent Spontaneous Abortion

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Background and aim: Recurrent spontaneous abortion (RSA) is a complex condition influenced by multiple factors, including immune dysregulation and oxidative stress. Ferroptosis, a regulated form of cell death driven by iron accumulation and lipid peroxidation, has recently been linked to placental abnormalities and adverse pregnancy outcomes. Despite this, the in vivo expression profile of ferroptosis-related genes in RSA has not been well characterized. This study aimed to examine the expression patterns of selected ferroptosis-related genes in placental tissues from a murine RSA model and to evaluate the potential regulatory effect of leukemia inhibitory factor (LIF).

Methods: Placental samples were obtained on gestational day 14 from three groups: normal pregnancies (CBA/J × BALB/c), abortion-prone pregnancies (CBA/J × DBA/2J), and abortion-prone pregnancies treated with LIF. The mRNA levels of eight ferroptosis-associated genes (GPX4, TFRC, MYC, PTGS2, DPP4, HIF1A, ATG7, and MAPK8) were measured using quantitative PCR. Data were analyzed using non-parametric statistical methods.

Results: While no statistically significant differences were detected among groups, consistent expression trends were observed. Placental tissues from abortion-prone mice exhibited lower expression of GPX4 and MYC, alongside increased levels of DPP4, HIF1A, PTGS2, and MAPK8, indicating elevated ferroptotic susceptibility and inflammatory stress. Treatment with LIF partially normalized these alterations, particularly affecting GPX4, DPP4, HIF1A, and MAPK8 expression, suggesting a protective modulatory effect.

Conclusion: Although constrained by a limited sample size, the results support a potential involvement of ferroptosis-related pathways in the development of RSA and indicate that LIF may influence their regulation. Future investigations with larger sample populations and protein-level analyses are needed to better define the role of ferroptosis in RSA and assess its viability as a therapeutic target.

keywords: leukemia inhibitory factor(LIF), ferroptosis, placenta, Gene Expression, recurrent spontaneous abortion

OI-16

Elucidating the PD-1/PD-L1 Axis-Mediated T Cell Exhaustion in Chronic Brucella melitensis Infection: A Preclinical Study with Therapeutic Implications

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Background and aim: Brucella melitensis is an intracellular zoonotic bacterium responsible for chronic brucellosis, characterized by persistent infection and profound immune evasion. Although T cell exhaustion is a known feature of chronic bacterial infections, the precise contribution of the PD-1/PD-L1 checkpoint pathway in brucellosis remains unexplored. This study aimed to characterize this mechanism and evaluate its therapeutic potential.

Methods: Female C57BL/6 mice (n=12/group) were intraperitoneally infected with 10^5 CFU of virulent B. melitensis 16M. Splenocytes were harvested at weeks 2, 4, and 8 post-infection for multi-color flow cytometry analysis of PD-1, TIM-3, and LAG-3 expression on $CD4^+$ and $CD8^+$ T cells. Antigen-specific recall responses were assessed using heat-killed Brucella antigens with or without anti-PD-1 blocking antibody. Bacterial burden was quantified by CFU plating in spleen and liver. In the therapeutic cohort, anti-PD-1 mAb (200 µg i.p., biweekly) was administered starting week 4.

Results: PD-1 expression significantly increased on both $CD4^+$ (42.7 ± 3.8%) and $CD8^+$ T cells (51.3 ± 4.2%) during chronic phase (p 0.0001 vs. controls), correlating with diminished IFN-γ and IL-2 production. In vitro PD-1 blockade restored cytokine secretion (IFN-γ ↑ 3.4-fold, p 0.001). In vivo checkpoint inhibition reduced splenic bacterial load by 1.9 $\log_{10}$ CFU (p 0.001), enhanced Th1 polarization, and showed no exacerbation of histopathology.

Conclusion: B. melitensis actively exploits the PD-1/PD-L1 axis to drive T cell exhaustion, facilitating chronic persistence. Targeted PD-1 blockade represents a promising host-directed immunotherapy for refractory brucellosis. This original preclinical study opens new avenues in bacterial infectious immunology.

keywords: Brucella melitensis, PD-1/PD-L1, T cell exhaustion, immune evasion

OM-1

Molecular Identification and Antifungal Susceptibility Testing of Fungal Strain Isolated from Sinusitis Infections

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Background and aim: Background: Fungal sinusitis is a sinus infection that results from filamentous and yeast-like fungi. Fungal sinusitis infections range from chronic to acute, all causing similar symptoms such as nasal congestion and sinus pain. This study aimed to evaluate the drug susceptibility of fungal isolates collected from sinus infections.

Methods: A total of 61 fungal strains with fungal sinusitis origin, including 50 isolates of Aspergillus spp and 11 isolates of Rhizopus spp were identified using DNA sequencing with beta-tubulin and ITS genes. Antifungal susceptibility to eight drugs(including amphotericin B, itraconazole, voriconazole, posaconazole, isavuconazole, caspofungin, luliconazole, and lanoconazole) was evaluated using CLSI-M38-A2 method.

Results: Out of 61 isolates including 21 isolates of Aspergillus fumigatus, 16 isolates of Aspergillus flavus, 13 isolates of Aspergillus niger, and 11 isolates of Rhizopus arrhizus were identified by DNA sequencing. Luliconazole (MIC range: 0.032 - 0.125 and MIC50: 0.032 µg/mL) was the most active drug In vitro against Aspergillus spp., followed by lanoconazole (MIC range: 0.032 - 0.25 and MIC50: 0.064 µg/mL), posaconazole (MIC range: 0.25 - 0.5 and MIC50: 0.125 µg/mL), itraconazole (MIC range: 0.125 - 1 and MIC50: 0.25 µg/mL), caspofungin (MEC range: 0.125 - 1 and MEC50: 0.5 µg/mL), voriconazole (MIC range: 0.032 - 1 and MIC50: 0.5 µg/mL) , isavuconazole (MIC range: 0.5 - 4 and MIC50: 1 µg/mL) and amphotericin B (MIC range: 0.125 - 8 and MIC50: 1 mg/mL), in order of decreasing activity. The caspofungin, and voriconazole demonstrated poor In vitro activity against R. arrhizus isolates evaluated, followed by isavuconazole.

Conclusion: In vitro antifungal susceptibility showed that luliconazole, lanoconazole, and posaconazole had good In vitro antifungal activity against all isolates. The azole agents exhibited better activity than polyene and echinocandin against Aspergillus spp and R. arrhizus. The correct diagnosis of the fungal causative agents along with antifungal susceptibility testing(AFST) is an effective in the management of patients with fungal sinusitis.

keywords: Fungal Sinusitis, DNA Sequencing, Antifungal Susceptibility Testing

OM-2

Gastrointestinal encountered yeasts as the new emerging causes of Chronic Hives

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Background and aim: Urticaria is a reaction pattern that represents cutaneous mast cell degranulation, with the condition being defined as chronic if lesions recur for longer than 6 weeks. Considering the high incidence of chronic urticaria among the patients with colonization of yeasts in gastro-intestinal tract, we investigated all fungal colonization and invasion in the gastro-intestinal tract of cases involved hives. Our main aim was identification of all isolates in the level of species.

Methods: Our subjects included 200 cases with long time superficial lesions as Urticaria. Fresh stool sample from the cases with clinical symptoms were collected. A direct microscopic investigation performed for the detection of fungal growth in gastro-intestinal tract. The basic culture on sabouraud glucose agar used for confirming of the fungal detection. The Molecular methods and proteomics based MALDI-TOF system were used for the identification of all yeast isolates

Results: The highest age range of our cases was 40-50 and included 25% of all. Women and men similarly involved (12 cases each). Our findings of microscopic investigation included yeast budding cells in 13(54.2%) cases, blastospores 6(25%), arthrospores 3(12.5%) and pseudohypha 2(8.3%). Total of 24 yeast isolates, 7 (29.2%) cases of Geotrichum silvicola, 7 (29.2%) Candida albicans and 6(25%) Candida glabrata were the most frequent identified by MALDI-TOF system. Other yeasts included C. Africana, C. tropicalis and C. glabrata one each. Only one unknown case by MALDI-TOF system recorded.

Conclusion: A variable species of yeast fungi which are commensally live in human gastro-intestinal tract are potentially candidate of Urticaria causing agents.

keywords: Hives, Candida, Geotrichm, GI system

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OM-3

RT-qPCR analysis of SQLE expression in terbinafine-susceptible and -resistant Trichophyton indotineae isolates

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Background and aim: Dermatophytosis remains one of the most common superficial fungal infections worldwide, and reduced susceptibility to terbinafine is increasingly reported in clinical studies. Terbinafine targets squalene epoxidase, encoded by the SQLE gene, and changes in SQLE regulation may contribute to resistance. This study evaluated SQLE transcript levels in Trichophyton indotineae and compared expression between terbinafine-susceptible and terbinafine-resistant isolates.

Methods: Twelve isolates were retrieved from the Pasteur Institute biobank and confirmed as T. indotineae by ITS sequencing. The collection included one terbinafine-susceptible reference strain (PFCC5809) used as the calibrator (relative expression set to 1), three clinically terbinafine-susceptible isolates, and eight terbinafine-resistant isolates (resistance defined as MIC 0.25 µg/mL). Isolates were grown on Sabouraud Dextrose Agar, and total RNA was extracted from mycelia, quality-checked, and reverse-transcribed to cDNA. SQLE expression was quantified by RT-qPCR using β-tubulin for normalization. Reactions were run in duplicate, relative expression was calculated using the $2^{-}\Delta\Delta Ct$ method, and group differences were assessed statistically on ΔCt values.

Results: Compared with the reference strain, SQLE expression showed a clear increase in terbinafine-resistant isolates. The mean relative expression was 6.1-fold in resistant isolates, versus 1.2-fold in terbinafine-susceptible isolates, corresponding to an approximately five-fold higher expression in the resistant group. This difference was statistically significant (p 0.05).

Conclusion: In this set of ITS-confirmed T. indotineae isolates, terbinafine resistance (MIC 0.25 µg/mL) was associated with significantly higher SQLE transcript levels. These findings support SQLE expression profiling as a useful complementary approach for investigating terbinafine resistance in dermatophytes, while highlighting the need for validation in larger, well-characterized isolate collections.

keywords: Dermatophytosis; Trichophyton indotineae; terbinafine resistance; SQLE; RT-qPCR; gene expression

OM-4

Clinical Characteristics of Patients with Hematologic Malignancies andInvasiveAspergillosis: A Cross-sectional Clinical Report from Iran

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Background and aim: Invasive aspergillosis (IA) poses a significant threat to hematology departments, primarily affecting patients with hematologic malignancies (HM) who have under gone chemotherapy and are in a neutropenic status. Among HM patients, IA manifests primarily in the lungs and stands as the most severe form of aspergillosis. A prior study conducted in Iran reported an incidence rate of 23.33% for IA in HM patients. Hematopoietic stem-cell transplantation (HSCT), acute leukemia, myelodysplastic syndrome (MDS), and prolonged neutropenia were identified as the primary predisposing factors for IA The mortality rate associated with IA in acute leukemia patients ranges from70%

Methods: In this retrospective study, we used the hospital information system (HIS) database to extract clinical and paraclinical characteristics of patients with various HMs who received a diagnosis of probable or proven IA during their hospitalization at Imam Khomeini Hospital Complex in Tehran, Iran, between March 2018 and March2022

Results: After evaluating 350 patients with HM, 51 patients with IA (14.6%) were identified, of whom 40 cases (78.4%) were probable and11 (21.6%) were proven. Among these, 34 individuals (66.7%) were male. The most common symptoms were fever(n=23, 62.7%), cough (n = 20, 39.2%), and fever that did not respond to antibiotic therapy (n = 16, 31.4%). The most prevalent malignancies were AML(n=28,54.9%), ALL (n = 16, 31.4%), and lymphoma (n = 7, 13.7%). Out of the 51 patients with HM and IA, 48 (94.1%) had abnormal findings on chest CT scans, with the majority(n=31,72.1%) showing a nodule with a halo sign. Aspergillus flavus(n=19/24,79.2%)was the most commonly isolated species. Initially, patients received liposomal amphotericin B or caspofungin as empiric antifungal therapy, which was then switched to voriconazole once the diagnosis of IA was probable or proven. Eight patients(15.6%)died.

Conclusion: Patients with HM presenting with fever and cough should undergo close monitoring for IA. A higher incidence of IA is observed in AML patients, and voriconazole could be considered as antifungal prophylaxis in HM patients. A. flavus is likely the most frequent cause of IA in Iranian patients with HM.

keywords: Invasive Aspergillosis, Hematologic Malignancy, Invasive Fungal Infection

OM-5

Whole genome sequencing and antifungal susceptibility of a multidrug resistant Candida auris isolate from a patient with acute myeloid leukemia in an intensive care unit

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Background and aim: Candida auris is an emerging multidrug-resistant fungal pathogen that is rapidly spreading in healthcare settings. This pathogen is capable of asymptomatic colonization of patients, especially immunocompromised individuals, and can cause nosocomial outbreaks with high mortality. In this article, we report the sixth case of C. auris isolation from a patient with asymptomatic acute myeloid leukemia in an intensive care unit in Iran.

Methods: A 51-year-old male patient with acute myeloid leukemia undergoing chemotherapy was admitted to the intensive care unit due to severe weakness and fever. Skin swab sampling was performed and cultured on specific fungal media. Initial identification was based on colony morphology and growth at 42°C and then confirmed by molecular methods (PCR and ITS sequencing and whole genome sequencing).

Results: The isolated strain was placed in clade V (Iranian) based on ITS region sequencing. Antifungal susceptibility testing showed very high resistance to fluconazole (≥64 µg/mL) and resistance to several other azoles, but was sensitive to amphotericin B and voriconazole. Whole genome sequencing analysis revealed the presence of a Y132F mutation in the ERG11 gene (associated with fluconazole resistance) in this isolate.

Conclusion: This report confirms the presence of a C. auris clade V isolate with significant multidrug resistance and carrying the Y132F mutation in an immunosuppressed patient in Iran. The findings emphasize the need for active screening of high risk patients, antifungal susceptibility testing, and enhanced genomic surveillance to promptly identify and contain this emerging threat to the country's healthcare system.

keywords: Candida auris, Acute myeloid leukemia, Antifungal resistance, ERG11 gene

OM-6

Epidemiology and Molecular Identification of Tinea Capitis with Predominant Trichophyton tonsurans

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Background and aim: Tinea capitis is the most common superficial fungal infection in children and is rare in adults, accounting for 4–10% of dermatophytosis cases. It occurs worldwide, particularly in tropical and subtropical regions. The disease affects hair follicles and surrounding scalp skin, often leading to hair loss. Because of its high contagiousness, it commonly spreads within families and schools. Monitoring changes in epidemiology and causative species is essential for proper treatment and prevention. This study aims to evaluate patient demographics and molecularly identify fungal agents isolated from tinea capitis cases in Tehran.

Methods: Sampling was carried out at the Mycology Laboratory of Razi Hospital in Tehran from May to October 2024, during which patients also completed questionnaires. The collected samples were first examined by direct microscopy using 10–20% KOH and then cultured on Mycosel agar. The grown colonies were analyzed based on macroscopic and microscopic examination, including the slide culture method. For molecular identification, DNA was extracted according to the protocol described by Luo et al., and then PCR amplification was performed using the universal fungal primers ITS1 and ITS4. Sequencing of the PCR products was then conducted to accurately determine the fungal species.

Results: In this study, 43 of the 138 patients who were evaluated had positive microscopic and culture results. Microscopic examination identified 38 endothrix and 5 ectothrix infections. The disease was predominantly observed in males (95.3%), with a female-to-male ratio of 1:20. Most patients were children and adolescents, with a mean age of 11.4 years. The most frequent risk factor was participation in wrestling (33 cases), and 10 patients had a family history of dermatophytosis within the previous year. A total of 22 patients had a history of using antifungal medications, mainly ketoconazole and clotrimazole. Lesions were most frequently observed in the temporal scalp region (72.1%), and 15 patients also had dermatophytosis lesions on other body sites. Hair loss was the most common clinical sign (93%), followed by scaling and black dots. Overall, 38 anthropophilic and 5 zoophilic dermatophytes were identified, including Trichophyton tonsurans (88.4%), Microsporum ferrugineum (7%), and Microsporum canis (4.6%).

Conclusion: According to recent research, the anthropophilic dermatophyte Trichophyton tonsurans is the most frequent cause of tinea capitis, accounting for most endothrix cases. Tinea capitis is more prevalent in school-age and prepubescent boys, and its incidence is directly related to wrestling.

keywords: Tinea Capitis, Dermatophytes, Trichophyton tonsurans

OM-7

Using Galactomannan Test in Diagnosing of invasive pulmonary aspergillosis

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Background and aim: COVID–19–associated pulmonary aspergillosis (CAPA) is a complication of COVID-19. Galactomannan (GM) is a non-invasive test used to diagnose invasive aspergillosis.

Methods: We collected the existing studies on the diagnostic value of GM to determine a GM level for predicting CAPA. All articles on the value of GM in CAPA diagnosis published until November 2023 were reviewed. The main databases were searched using the following keywords: “aspergillus”, “aspergillosis”, “SARS-CoV-2”, “COVID”, “2019 ncovnCOV”, “novel coronavirus”, “COVID-19”, “galactomannan”, and “CAPA”. Studies with reported levels of serum or BAL GM were included. Patients were classified into two groups: non-confirmed and proven aspergillosis. Finally, the receiver operating characteristic (ROC) curve analysis was used to determine a GM level to predict the likelihood of CAPA.

Results: A total of 26 articles were selected, of which 239 patients were included. A count of 123 patients (50%) were in the non-confirmed group and 124 (50%) patients were proven. The median serum GM was 0.51 in the non-confirmed group and 0.47 in the proven group (p= 0.73). The level of GM in BAL fluid was 0.10 in the non-confirmed and 2.80 in the proven group, which was statistically different (p0.001). With 81.3 % sensitivity and 79.5% specificity, the BAL GM cut-off was 1.01 ODI.

Conclusion: The results showed that BAL GM ≥1.01 can be used to predict CAPA. Serum GM did not show any predictive value in diagnosing CAPA. However, BAL GM level can be a reliable diagnostic test in patients with CAPA.

keywords: Galactomannan, Aspergillosis, SARS-CoV-2, COVID-19, Bronchoalveolar lavage, Fungi, Viral Diseases, Invasive

OM-8

Endogenous Candida parapsilosis Endophthalmitis Following Laparoscopic:A Rare Case Report

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Background and aim: Endogenous fungal endophthalmitis is a rare but vision-threatening condition caused by hematogenous spread of fungal organisms from distant sites of infection. Candida parapsilosis, though traditionally considered less virulent than C. albicans, has emerged as a significant nosocomial pathogen associated with invasive medical procedures and prosthetic devices. Herein, we present a rare case of C. parapsilosis endogenous endophthalmitis that occurred following laparoscopic cholecystectomy in an immunocompetent patient, emphasizing the critical importance of early recognition and prompt antifungal management.

Methods: A 53-year-old woman developed progressive blurred vision and ocular pain five months after laparoscopic cholecystectomy. Comprehensive ophthalmologic examination, including slit-lamp biomicroscopy, fluorescein angiography (FA), and optical coherence tomography (OCT), was performed. Due to bilateral panuveitis and vitritis, pars plana vitrectomy (PPV) was undertaken, and vitreous samples were analyzed by direct microscopy, culture, and PCR for fungal identification. Antifungal susceptibility testing followed CLSI standards. The patient received intravitreal and systemic voriconazole with gradual corticosteroid tapering.

Results: Microscopic and molecular tests confirmed Candida parapsilosis (GenBank accession PX446517) as the causative organism. The isolate showed susceptibility to voriconazole and amphotericin B but resistance to fluconazole and itraconazole. At presentation, best-corrected visual acuity (BCVA) was 20/200 in the right eye and 20/30 in the left, with 3+ vitritis and chorioretinitis bilaterally. Following vitrectomy and combined antifungal therapy, marked improvement occurred within three months: BCVA reached 20/20 (OD) and 20/25 (OS). OCT and FA demonstrated complete resolution of cystoid macular edema, retinal vascular leakage, and inflammatory infiltrates. No recurrence or complications were observed during four months of follow-up.

Conclusion: This rare case illustrates endogenous C. parapsilosis endophthalmitis following non-ocular surgery in an immunocompetent patient. The outcome emphasizes the importance of early suspicion, molecular confirmation, and prompt antifungal therapy guided by susceptibility testing. Combining PPV with intravitreal and systemic voriconazole proved highly effective, resulting in full visual recovery. Clinicians should consider fungal etiologies in postoperative ocular inflammation, even after minimally invasive procedures, and apply rapid molecular diagnostics to ensure timely and targeted management.

keywords: Candida Parapsilosis, endophthalmiti.

OM-9

Anti-biofilm activity of carvacrol-thymoquinone nanocarriers on vulvovaginal candidiasis isolates

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Background and aim: Vaginal candidiasis represents one of the most prevalent infections affecting the female genital tract, frequently encountered in clinical settings. It is estimated that approximately 75% of women will experience vulvovaginal candidiasis (VVC) at least once in their lifetime. Given the recurrent nature of vulvovaginal candidiasis (VVC), the restricted availability of effective antifungal agents, and the recent rise in drug resistance, this study sought to assess the antifungal efficacy of carvacrol-thymoquinone delivered via a nanocarrier on Candida isolates obtained from patients with VVC.

Methods: This cross-sectional study was conducted on women with suspected VVC at Sayad Shirazi Hospital in Golestan Province during 2022-23. Vaginal swabs were collected from 108 patients presenting with symptoms of vaginal pruritus and a cheesy discharge originating from the posterior fornix of the vagina. Candida isolates were identified by the KOH test, chlamydoconidia production in cornmeal agar, germ tube production, and using CHROMagar Candida medium. Multiplex PCR method was used to identify different Candida species. Nanocarriers were synthesized using the thin-film hydration method. The morphology and size of the carvacrol-thymoquinone nanocarrier were determined using transmission electron microscopy (TEM) and dynamic light scattering (DLS). The antifungal activity of carvacrol-thymoquinone was evaluated using the broth microdilution method (CLSIM27-A3). The impact of nanocarriers on the biofilm formation capabilities of Candida isolates was assessed using the MTT assay. Data were analyzed using the Mann-Whitney U test.

Results: Based on the phenotypic and genotypic tests, 71 C. albicans (85.5%) and 12 C. glabrata (14.5%) isolates were identified. According to the results from TEM and DLS, the nanocarriers were spherical and had a diameter of approximately 50 nm. The nano-formulated drug combination could inhibit biofilm formation in C. albicans at half the minimum inhibitory concentration and in C. glabrata at the minimum inhibitory concentration. Carvacrol and thymoquinone have synergistic effects in inhibiting Candida isolates.

Conclusion: The carvacrol-thymoquinone nanocarrier combination could be an effective antifungal agent for inhibiting biofilm formation in Candida species. Therefore, further research is needed to assess the in vivo antifungal efficacy of this nanocarrier along with other antifungal drugs as an alternative treatment for VVC.

keywords: Vulvovaginal candidiasis, Carvacrol, Thymoquinone

OM-10

Diversity of Aspergillus species causing chronic pulmonary aspergillosis in cystic fibrosis patients and their antifungal susceptibility pattern

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Background and aim: Chronic pulmonary aspergillosis (CPA) is considered as one of the most significant diseases in people with cystic fibrosis (pwCF). Aspergillus fumigatus is the major species causing CPA worldwide, however in some part of the world including Middle East A. flavus was commonly reported from different clinical form of aspergillosis. On the other hand, different species of Aspergillus show different antifungal susceptibility pattern (AFSP) against antifungal agents. Therefore, in this study we aimed the prevalence of CPA in CF patients and diversity of isolated species of Aspergillus and their AFSP against different antifungal.

Methods: : In a two-year multicenter prospective cohort study, pwCF who had been referred to six centers of the Iranian CF Foundation were enrolled. Sputum samples were collected in more than two times in all included patients. Specimens were inoculated onto Sabouraud Dextrose Agar (SDA). Aspergillus species were identified by PCR-Sequencing of β-tubulin and calmodulin genes. In-vitro antifungal susceptibility testing was performed according to the Clinical & Laboratory Standards Institute (CLSI) M38-A3 guidelines. CPA were diagnosed based on the ESCMID/ERS definitions for CPA in resource-limited settings.

Results: Out of 235 CF patients, CPA diagnosis were reported in 32 (13.6%), of which (56.2%) were male, and the mean age was 18.3±9.7. A total of 304 Aspergillus isolates were molecularly identified, of which A. flavus (94, 30.9%) was the most prevalent. However, In CPA patients, Aspergillus fumigatus (36.4%) was the most prevalent followed by A. flavus (27.3%), A. niger (26.0%) and other Aspergillus species (10.4%). Across all Aspergillus species (n=77), MIC values ranged from 0.03–32 µg/mL for itraconazole, 0.06–2 µg/mL for voriconazole, 0.03–0.5 µg/mL for posaconazole, and 0.03–2 µg/mL for amphotericin B; MEC for anidulafungin ranged from 0.004–0.03 µg/mL. Species-specific analysis revealed that A. fumigatus isolates were largely susceptible to all agents tested, with elevated MICs observed only in two isolates (against isavuconazole and voriconazole, respectively). A. flavus isolates showed uniformly low MICs to conventional antifungals. Notably, 7/22 isolates(31.8%) A. niger/tubingensis isolates (4 A. tubingensis and 3 A.niger)exhibited

Conclusion: : Our results showed that CPA should be considered as one of the significant complications in patients with CF. Our finding also showed that Aspergillus fumigatus is the most prevalent species in CPA group in Iranian pwCF. Our study revealed that different species of Aspergillus show different AFSP against main antifungals in treatment of CPA. This shows the importance of performance of antifungal susceptibility testing for an appropriate treatment.

keywords: Cystic fibrosis, Chronic pulmonary aspergillosis, Aspergillus, antifungal susceptibility testing

OM-11

Detection of occult acute amyloid leukemia during the diagnosis of rhinocerebral mucormycosis

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Background and aim: Rhinocerebral mucormycosis is an invasive and rapidly progressive fungal infection that is commonly seen in uncontrolled or immunosuppressed diabetic patients. Its association with acute myeloid leukemia (AML) is of great importance, and the simultaneous diagnosis of these two life-threatening diseases represents a significant clinical challenge. This report describes a case of simultaneous diagnosis of Rhinocerebral mucormycosis caused by Rhizopus arrhizus and AML in a diabetic patient, which resulted in a successful outcome with timely treatment.

Methods: The patient was a 63-year-old man with a history of type 2 diabetes who presented to the physician with a long-standing headache and recurrent epistaxis. Blood tests and a sinus radiograph were requested. Radiological images showed a suspicious mass in the sinus, prompting referral to the Ayatollah Rouhani Hospital, Babol. On examination, swelling of the sinus mucosa with colored (bloody and purulent) discharge was observed. A rhinocerebral discharge sample was requested for direct microscopic examination, fungal culture, and pathology.

Results: The initial blood test results showed an increase in peripheral blasts and cytopenia. After additional testing (immunophenotyping), the diagnosis of acute myeloid leukemia (AML) was confirmed. Direct microscopic examination of the sinus discharge revealed wide, septate-free hyphae with right-angle branching (characteristic of mucormycosis). Culture and pathology confirmed invasive mucormycosis. Molecular sequencing identified Rhizopus arrhizus as the etiological agent. Antifungal therapy with liposomal amphotericin B was started immediately. Subsequently, an oral solution of iodine (SSKI) was added to the treatment regimen at the physician's discretion. The patient's diabetes was fully controlled with intravenous insulin. Clinical symptoms, including headache and epistaxis, gradually resolved and eventually resolved completely. A second sinus discharge sample sent for follow-up was reported to be negative by direct microscopy, fungal culture, and pathology. The patient was discharged with a favorable clinical status and no neurological complications for induction chemotherapy for AML.

Conclusion: In diabetic patients with refractory headache and epistaxis, even in the absence of obvious immunodeficiency, an invasive disease, rhinocerebral mucormycosis, should be suspected. Early diagnosis with interdisciplinary collaboration (infectious disease, hematology, radiology, pathology, and mycology), appropriate antifungal therapy, metabolic control, and then timely referral for chemotherapy can lead to an excellent outcome and long-term survival even in the setting of the coexistence of these two fatal diseases.

keywords: Rhinocerebral mucormycosis, acute myeloid leukemia (AML), Rhizopus arrhizus, antifungal therapy

OM-12

Synthesis and In Vitro Evaluation of the Antifungal Efficacy of a Silver–Curcumin Nanocomposite Against Candida albicans

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Background and aim: Candida albicans is one of the most common opportunistic fungal pathogens in humans. The increasing resistance to conventional antifungal agents has highlighted the need for novel therapeutic compounds with enhanced efficacy and reduced adverse effects. Curcumin, a natural bioactive compound, possesses well-documented antimicrobial properties; however, its poor aqueous solubility limits its clinical application. Nanotechnology-based formulations of natural compounds may provide a promising strategy to overcome these limitations. This study aimed to evaluate the antifungal activity of a silver–curcumin nanocomposite against Candida albicans.

Methods: In this study, a silver–curcumin nanocomposite was synthesized.The antifungal activity of the nanocomposite against Candida albicans strains was assessed using the broth microdilution method according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. The minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) were determined.

Results: The findings demonstrated that the silver–curcumin nanocomposite exhibited significant antifungal activity against Candida albicans. The nanocomposite effectively inhibited fungal growth and proliferation and showed considerable fungicidal activity. Compared with free curcumin, the nanocomposite displayed superior antifungal efficacy, indicating enhanced bioactivity through nanoformulation.

Conclusion: The results of this study indicate that the silver–curcumin nanocomposite possesses potent antifungal activity against Candida albicans under in vitro conditions. This nanoformulation may represent a novel and promising approach for the development of effective antifungal agents with improved therapeutic potential.

keywords: Candida albicans, curcumin, Silver–Curcumin Nanocomposite

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OM-13

Antifungal Efficacy of a Synthetic Indole Hydrazonothiazolidinone Derivative Relative to Nystatin Against Common Candida Pathogens

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Background and aim: The increasing resistance of Candida species to azole antifungals necessitates the discovery of novel, effective compounds. One such candidate is the indole hydrazonothiazolidinone derivative 2-[(2Z)-4-oxo-2-[(2Z)-(2-oxo-1,2-dihydro-3H-indol-3-ylidene)hydrazono]-1,3-thiazolidin-5-yl]acetamide. This study aimed to evaluate the antifungal susceptibility of this derivative against clinical isolates of Candida.

Methods: A total of 100 clinical Candida isolates (53 Candida albicans, 22 Candida tropicalis, 17 Candida parapsilosis, and 8 Candida glabrata) were tested for susceptibility to the indole hydrazonothiazolidinone derivative and to nystatin using the broth microdilution method according to CLSI M27 S4 guidelines. The tested concentration range for both compounds was 0.016–16 µg/mL. The minimum inhibitory concentration (MIC) was defined as the lowest concentration causing at least 50% growth inhibition relative to the positive control (this definition applied equally to both agents). Statistical analysis was performed using SPSS version 20, with significance set at p 0.05.

Results: The mean MIC of the indole hydrazonothiazolidinone derivative was 2.47 µg/mL for C. albicans, 5.63 µg/mL for C. tropicalis, and 4 µg/mL for C. parapsilosis. The mean MIC of nystatin was 1.03 µg/mL for C. albicans, 0.96 µg/mL for C. tropicalis, and 0.96 µg/mL for C. parapsilosis. For C. albicans, C. tropicalis, and C. parapsilosis, the MIC values of the derivative were significantly higher than those of nystatin (p 0.05), indicating a weaker antifungal effect. No significant difference in MIC was observed between the derivative and nystatin against C. glabrata (p 0.05).

Conclusion: The tested indole hydrazonothiazolidinone derivative exhibited lower efficacy than nystatin against C. albicans, C. tropicalis, and C. parapsilosis, whereas its efficacy against C. glabrata was comparable to that of nystatin. Following cytotoxicity and side effect evaluations and further investigations, this derivative may contribute to the development of novel antifungal therapies.

keywords: Candida albicans, Candida tropicalis, Candida parapsilosis, Candida glabrata, nystatin, 2-[(2Z)-4-oxo-2-[(2Z)-(2-oxo-1,2-dihydro-3H-indol-3-ylidene)hydrazono]-1,3-thiazolidin-5-yl]acetamide

OM-14

In Vitro Antifungal Activity of a Novel Spirocyclopropane Oxindole Derivative Against Clinical Aspergillus Isolates

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Background and aim: The increasing prevalence of azole resistance among Aspergillus species underscores the need for novel compounds with effective in vitro activity. One promising candidate is the spirocyclopropane oxindole derivative 2-benzoyl-1-([1-(4-bromobenzoyl)-1,2,3-triazol-4-yl]methyl)-3-(4-fluorobenzoyl)spiro[cyclopropane-1,3-indole]-2(1H)-one. This study aimed to evaluate the antifungal susceptibility of this derivative against clinical isolates of Aspergillus isolates.

Methods: The antifungal susceptibility of 50 clinical Aspergillus isolates [A. fumigatus (n=15), A. flavus (n=15), Aspergillus niger (n=15), and A. terreus (n=5)] to the test compound and itraconazole was assessed using the broth microdilution method following the CLSI M38-A2 guidelines. Both compounds were tested over a concentration range of 0.016–16 µg/mL. The minimum inhibitory concentration (MIC) was defined as the lowest concentration that completely inhibited (100%) fungal growth relative to the positive control. Statistical analyses were performed using SPSS version 20, with a significance level of P 0.05.

Results: The MIC50 values of the spirocyclopropane oxindole derivative were 32 µg/mL for A. fumigatus and 64 µg/mL for both A. flavus and A. niger. In contrast, the MIC50 of itraconazole was 0.25 µg/mL for all Aspergillus species tested. Statistical analysis revealed a significant difference between the MIC values of the test compound and those of itraconazole (P 0.001), indicating that the derivative exhibited substantially weaker antifungal activity than itraconazole.

Conclusion: The spirocyclopropane oxindole derivative demonstrated significantly lower antifungal efficacy against Aspergillus species compared to itraconazole. Therefore, structural optimization of this compound may be necessary to enhance its antifungal potency.

keywords: Aspergillus; Itraconazole; 2-benzoyl-1-([1-(4-bromobenzoyl)-1,2,3-triazol-4-yl]methyl)-3-(4-fluorobenzoyl)spiro[cyclopropane-1,3-indol]-2(1H)-one.

OM-15

Miltefosine Demonstrates Potent Inhibitory Effects Against Scedosporium species: An Alternative to Amphotericin B and Azoles?

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Background and aim: Scedosporium species are emerging opportunistic fungal pathogens associated with high mortality rates and intrinsic resistance to many conventional antifungals. Miltefosine, an alkylphosphocholine drug with broad-spectrum antimicrobial activity, has recently gained attention for its antifungal potential. However, data on its activity against Scedosporium species remain limited. The aim of this study is to evaluate the in vitro susceptibility of clinically relevant Scedosporium species to miltefosine in comparison with a panel of conventional antifungal agents, given the limited existing data and the high intrinsic resistance of these pathogens to standard therapies.

Methods: The in vitro susceptibility of 45 environmental isolates of Scedosporium species (21 S. apiospermum, 14 S. dehoogii, and 10 S. boydii) to miltefosine and a panel of 12 conventional antifungal agents-namely amphotericin B, itraconazole, voriconazole, posaconazole, isavuconazole, luliconazole, miconazole, ketoconazole, anidulafungin, micafungin, tolnaftate, and terbinafine- was assessed. Minimal inhibitory concentrations (MICs) were established using standard broth microdilution techniques. Data were analyzed both per species and across the entire isolate collection, with calculations of MIC ranges, modes, geometric means (GM), as well as MIC50 and MIC90 values.

Results: Miltefosine demonstrated consistent inhibitory activity across all Scedosporium species, with MIC ranges of 1–4 µg/mL, a mode of 2 µg/mL, and overall GM of 2.262 µg/mL. The MIC50 and MIC90 for total isolates were 2 µg/mL and 4 µg/mL, respectively. Notably, miltefosine showed superior activity compared to several conventional drugs: amphotericin B (GM 2.228, MIC90 16 µg/mL), itraconazole (GM 15.755, MIC90 16 µg/mL), and terbinafine (GM 15.277, MIC90 16 µg/mL). Luliconazole exhibited the lowest MIC values (GM 0.017 µg/mL), while voriconazole showed moderate activity (MIC90 4 µg/mL, range 0.032–8 µg/mL). Echinocandins (anidulafungin, micafungin) demonstrated low MICs against a subset of isolates but with limited species-specific consistency.

Conclusion: Miltefosine exhibits potent and broad in vitro inhibitory activity against clinically relevant Scedosporium species, including S. apiospermum, S. dehoogii, and S. boydii, with MIC profiles comparable or superior to several conventional antifungal agents. These findings support further investigation of miltefosine as a potential therapeutic option for Scedosporium infections, particularly in the context of multidrug-resistant isolates.

keywords: Miltefosine; Scedosporium; Antifungal susceptibility; Scedosporium apiospermum; In vitro activity

OM-16

Global evaluation of tuberculosis and cryptococcosis Co-infection: A systematic review

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Background and aim: Co-infection of tuberculosis (TB) and cryptococcosis as a consequence of impaired cell-mediated immune responses is accompanied by high mortality and morbidity rates. This study aimed to provide valuable insights into risk factors, diagnostic tests, and treatment methods used for infected patients to facilitate rapid diagnosis, prevention, and treatment.

Methods: A comprehensive and systematic search was performed in electronic databases including Google Scholar, Scopus, PubMed, and Web of Science to find all articles relevant to the scope of this research, published in English from January 2000 to December 2023. PRISMA (preferred reporting items for systematic reviews and meta-analyses) search strategy was used to validate the search process and present the eligible research data.

Results: A total of 1418 studies were recognized in the databases, among them 47 articles meeting the current research inclusion criteria were included in the study, comprising a total of 68 cryptococcosis/TB co-infected patients. India was the country with the largest number of co-infected patients (n = 26, 38.23 %). HIV infection was documented as the most prevalent underlying condition (n = 22, 31.35 %). Also, combination therapy with amphotericin B and fluconazole (63.23 %) was the most common antifungal treatment used for cryptococcal infections, and most patients (38.23 %) received rifampicin as an anti-TB therapy.

Conclusion: Comprehensive epidemiological information could be useful in early diagnosis and prompt treatment to reduce the clinical course and seriousness of infection and ameliorate overall outcomes.

keywords: Cryptococcosis, Tuberculosis, Co-infection

OM-17

Study of skin and nail Candida species as a normal flora based on age groups in healthy persons in Tehran-Iran

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Background and aim: The skin is the body's largest organ that hosts heterogeneous inhabitants. Until now, the diversity of the cutaneous microbiome was mainly investigated for bacteria and there is a little information about the skin fungal flora. Also, among skin fungal flora, Candida is found as a main member whose distribution is affected by sex, age, climate.

Methods: In this study, differences in Candida community structure associated with 9 different skin sites of 238 healthy people during 10 months from July to March 2019, are described. These subjects were divided by age into 4 groups: infants, children, adults and geriatrics. The collected samples were examined by culture on Sabouraud Chloramphenicol Agar and CHROM-agar Candida. For precise identification of species ITS1-5. 8S-ITS2 rDNA regions were sequenced where needed.

Results: The frequency of Candida species was significantly different between age groups. The most Candida isolations were related to the elderly age group and the fewest in the infants. C. parapsilosis virtually, was the predominant isolated species in all age groups. This study showed no statistically significant effect of the subject's sex on Candida population resident on human skin surface.

Conclusion: The present study createed new information about the type and percentage of Candida population in each site of the human skin, attempting to determine what influences the individual's age and sex have on the composition and percentage of cutaneous Candida community in Iranian people.

keywords: Candida species, normal flora, skin

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OM-18

Epidemiology, laboratory diagnosis and clinical aspects of fungal pulmonary infections in 384 patients hospitalized in pulmonary units in Guilan province, Iran

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Background and aim: The respiratory tract is the most common site for developing fungal infections. People who have a weakened immune system are more susceptible to respiratory system involvement with fungi. Fungal infections of the respiratory tract are largely unrecognized and their true burden is elusive. Therefore, the aim of the current study was to evaluate the clinical spectrum, demographic characteristics, risk factors, and etiology of fungal respiratory infections in 384 patients hospitalized in pulmonary units of Razi hospital, Guilan province, Iran.

Methods: A total of 384 lung specimens (192 Bronchoalveolar lavages (BAL) and 192 sputa) were obtained from patients who met the inclusion criteria. All samples were analyzed by direct microscopy and culture. Fungal identification was accomplished by internal transcribed spacer (ITS) and beta-tubulin sequencing. Also, in patients suspected to invasive pulmonary aspergillosis BAL specimens were tested for galactomannan (GM) antigen. According to the host factors (clinical symptoms, radiology findings and predisposing factors which were defined as inclusion criteria), and the positive results in direct examination, culture and serology (GM for aspergillosis) the infection was confirmed.

Results: Fungal respiratory infection was confirmed in 137 cases (35.67%) including 86 (62.77%) males and 51 (37.23%) females and the highest prevalence of infection was found in the age group of 46–72 years (n=75, 54.74%). Cough (n=129, 94.16%), dyspnea (n=111, 81.02%), purulent sputum (n=85, 62.04%) and weight loss (n=77, 56.2%) were the predominant symptoms. Tuberculosis (n=34, 24.81%), taking chemotherapy regimen (n=30, 21.89%) and diabetes mellitus (n=27, 19.70%) were the predominant underlying conditions. Candida albicans (37.22%) and Candida tropicalis (21.89%) represent the two most commonly isolated species in the current study. Furthermore, according to revised EORTC/MSG (2008) definitions for invasive fungal infections, from 5 cases of pulmonary aspergillosis, 2 (40%) cases of probable invasive pulmonary aspergillosis (IPA) and 3 (60%) cases of possible IPA were diagnosed.

Conclusion: The prevalence of pulmonary fungal infections in Guilan province was 35.67%. Tuberculosis, receiving chemotherapy within the last 3 months before admission in order to treat solid tumors and diabetes mellitus were important risk factors, and Candida albicans was the most common fungal species responsible for pulmonary fungal infection. The highest prevalence of pulmonary fungal infections was found in the age group of 46–72 years and in male patients. Many physicians missed fungal pulmonary infection because it does not show specific clinical manifestations. Given that some of uncommon causal agents of

keywords: Candidiasis, Fungal respiratory infections, Invasive pulmonary aspergillosis

OM-19

Aspergillus sydowii Fungal Sinusitis Mimicking Mucormycosis in a Patient with Sarcoidosis– A Diagnostic Challenge

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Background and aim: Fungal sinusitis is a serious infection, particularly in immunocompromised patients. Aspergillus sydowii is a rare opportunistic pathogen, and its direct microscopic appearance in tissue can occasionally mimic mucormycosis, leading to diagnostic challenges. We report a case of fungal sinusitis caused by A. sydowii in a patient with underlying sarcoidosis on chronic corticosteroid therapy.

Methods: A 42-year-old woman with sarcoidosis (on prednisolone 5 mg/day and hydroxychloroquine 20 mg/day) presented with left-sided facial swelling and numbness, four days after dental root canal treatment. She failed multiple antibiotic courses (azithromycin, ceftriaxone, clindamycin, ceftazidime) and functional endoscopic sinus surgery (FESS).

Results: Direct microscopic examination of sinus tissue revealed broad, ribbon-like, pauciseptate hyphae with right-angle and acute-angle branching – strongly suggestive of mucormycosis. However, culture remained negative. PCR amplification of the ITS region and sequencing identified A. sydowii as the causative agent. The patient finally improved after treatment with intravenous amphotericin B.

Conclusion: This case highlights that A. sydowii can produce hyphal morphology resembling mucormycosis on direct examination, potentially leading to misdiagnosis. In immunocompromised patients with suspected fungal sinusitis and negative cultures, molecular techniques such as ITS sequencing are essential for accurate identification and appropriate antifungal therapy.

keywords: Aspergillus sydowii, fungal sinusitis, sarcoidosis, mucormycosis mimic, ITS sequencing, case

OM-20

Repurposing the NSAID Sulindac as a Novel Antifungal Candidate for Difficult-to-Treat Scedosporium species

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Background and aim: Scedosporium species are emerging opportunistic molds that cause severe and often fatal infections in immunocompromised and near-drowning victims. Treatment is notoriously difficult due to the intrinsic resistance of these fungi to many standard antifungals, particularly amphotericin B and fluconazole. Voriconazole remains the primary therapeutic option, yet treatment failure and drug-related toxicities persist. Drug repurposing represents a cost-effective strategy to identify novel antifungal candidates. This study aimed to evaluate the in vitro antifungal activity of the non-steroidal anti-inflammatory drug (NSAID) Sulindac against Scedosporium isolates in comparison to established antifungal agents.

Methods: The in vitro susceptibility of 45 environmental relevant Scedosporium isolates to Sulindac and a panel of 4 conventional antifungal agents, Amphotericin B, Itraconazole, Voriconazole, and Posaconazole, was evaluated via the broth microdilution methodology, in strict conformance with the standardized CLSI guidelines. Upon completion of the designated incubation periods, the minimum inhibitory concentration (MIC) ranges, modal values, geometric means (GM), MIC50, and MIC90 were derived for each compound under investigation.

Results: Sulindac demonstrated remarkably potent and superior antifungal activity against the tested Scedosporium isolates. The MIC50 and MIC90 values for Sulindac were 0.25 µg/mL and 1 µg/mL, respectively, with a geometric mean of 0.211 µg/mL. Notably, this activity significantly outperformed all conventional antifungals tested. For comparison, Voriconazole (the current drug of choice) exhibited an MIC50 of 2 µg/mL, an MIC90 of 8 µg/mL, and a GM of 0.928 µg/mL. Posaconazole, Amphotericin B, and Itraconazole showed substantially higher values, with MIC50s of 1, 4, and 16 µg/mL, and MIC90s of 16, 16, and 16 µg/mL, respectively. Sulindac also displayed the lowest modal MIC (0.25 µg/mL) compared to the other agents (modes ranging from 4 to 16 µg/mL).

Conclusion: Our findings reveal that Sulindac possesses exceptional in vitro antifungal efficacy against Scedosporium, exhibiting substantially lower MIC values than voriconazole and other standard antifungal therapies. These results strongly suggest that Sulindac could be a highly promising repurposed candidate for the treatment of scedosporiosis. Further in vivo pharmacokinetic, pharmacodynamic, and toxicological investigations are urgently warranted to translate these findings into potential clinical applications.

keywords: Sulindac; Scedosporium; Antifungal susceptibility; Drug repurposing; Scedosporiosis

OP-1

Design and Efficacy Evaluation of a Recombinant DNA Vaccine Targeting EG95 Antigen for Prophylaxis Against Cystic Echinococcosis in BALB/c Mice

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Background and aim: Cystic echinococcosis, caused by the larval stage of Echinococcus granulosus, remains a significant public health challenge globally, with Iran recognized as an endemic area where the disease burden is substantial. Prophylactic vaccination represents a promising control strategy, and the EG95 antigen has emerged as a prime candidate for DNA vaccine development against this parasitic infection. This study aimed to construct a recombinant DNA vaccine by cloning the EG95-encoding gene into the pcDNA3 mammalian expression vector, followed by immunization of BALB/c mice with the resulting construct to assess its immunogenic potential and protective efficacy.

Methods: Total RNA extracted from E. granulosus protoscoleces was reverse-transcribed and subjected to RT-PCR amplification of the EG95 gene. The resulting 492 bp PCR product was cloned into pTZ57R/T and sequence-verified as the authentic EG95 gene. Following subcloning into the pcDNA3 expression vector, protein expression was confirmed in transfected CHO cells using SDS-PAGE and Western blot analyses. Immunogenicity assessment was conducted in ninety female BALB/c mice receiving three immunizations with the pcDNA3-EG95 construct at three-week intervals to characterize humoral and cellular immune responses.

Results: Our findings revealed that humoral immune responses, assessed through total IgG levels as well as IgG2a and IgG1 isotype measurements, demonstrated no statistically significant differences between experimental and control groups ($P \geq 0.05$). Cytokine profiling indicated elevated IFN-γ concentrations alongside reduced IL-4 levels. Notably, parasitological assessment of cyst burden in murine models demonstrated that animals immunized with recombinant pcEG95 vaccine in combination with pcIL-12 and MMT adjuvants exhibited markedly reduced cyst numbers and diminished cyst dimensions compared to other experimental cohorts.

Conclusion: Based on our experimental data, the EG95 gene-based DNA vaccine demonstrated incomplete protective efficacy against hydatid cyst development. Furthermore, our investigation revealed that co-administration of pcIL-12 and MMT adjuvants with the EG95-encoding DNA vaccine elicited substantial modulation of cell-mediated immune responses.

keywords: Echinococcus granulosus, EG95, protoscolex, DNA vaccine

OP-2

Comparison of parasitological methods, native and molecular sandwich ELISA in the diagnosis of Giardia lamblia.

مرضیه کریمی [1] © Ⓟ

[1] دانشجو

Background and aim: Giardia lamblia is a protozoan parasitic infection in humans, especially children. The common method of diagnosis of this parasite is stool examination and observation of the cysts under a microscope. Given the limitations of conventional microscopic methods for the diagnosis of Giardia lamblia, in this study, a homemade ELISA method was first developed to detect the infection, and then the efficiency of microscopic methods, the developed sandwich ELISA, and molecular methods in the diagnosis of this infection was compared

Methods: Materials and Methods: In this descriptive-analytical study based on microscopic examination and observation of Giardia parasite, 30 positive and 30 negative human stool samples were collected. In the second stage a homemade sandwich ELISA test for diagnosis of Giardia infection was developed. All the samples were then tested with molecular method (PCR) and the developed ELISA test. compared with the standard microscopic method. Finally the results of the above tests were compared with the results of microscopic method as gold standard to estimate sensitivity and specificity of the tests.

Results: 100% sensitivity and 96.6% specificity were obtained for the homemade sandwich ELISA test compared to the microscopic method as gold standard. Also, considering the microscopic method as the standard, the PCR method had a sensitivity of 86.7% and a specificity of 100%.

Conclusion: The developed homemade ELISA is is recommended as a reliable method for routine detection of Giardia lamblia in diagnostic laboratories

keywords: Giardia lamblia, Sandwich ELISA, PCR, Detection

OP-3

Toxoplasma gondii Antigen Induces Apoptosis in Colorectal Cancer Cell Lines Through Regulation of BAX/BCL2 and PI3K/AKT Pathways

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Background and aim: Colorectal cancer [CRC] remains one of the most common malignancies worldwide, and despite advances in chemotherapy and radiotherapy, treatment-related toxicity and drug resistance continue to limit therapeutic success. In recent years, biological molecules especially parasite-derived antigens have attracted attention as new anticancer candidates. Toxoplasma gondii is known for eliciting strong host immune responses that can suppress tumor growth.

Methods: This study examined the cytotoxic and pro- apoptotic effects of T. gondii lysate antigen [TLA] on CRC cell lines and explored the molecular pathways involved. Two human CRC cell lines [SW48 and SW948] and a normal cell line [HEK293] were treated with various concentrations of TLA. Cell viability and IC50 values were determined by MTT assay. Apoptosis induction was measured using Annexin V-FITC/PI flow cytometry. Expression of apoptosis-related genes [BAX, BCL2] and PI3K/AKT pathway components was evaluated via quantitative real-time

Results: PCR.TLA treatment significantly decreased the viability of CRC cells in a dose- dependent pattern, with IC50 values of 8.5 µM for SW948 and 14.8 µM for SW48, compared with 15.2 µM for HEK293, indicating selective toxicity. Flow cytometry confirmed a marked increase in apoptotic cells following TLA exposure. Gene expression analysis showed upregulation of the pro-apoptotic gene BAX and downregulation of the anti-apoptotic gene BCL2. PI3K and AKT transcripts were also elevated, suggesting involvement of the PI3K/AKT signaling axis.

Conclusion: .T. gondii lysate antigen demonstrates selective anti-proliferative and pro-apoptotic effects in colorectal cancer cells, mediated by the BAX/BCL2 balance and modulation of PI3K/AKT signaling. These findings support further investigation of T. gondii antigens as potential novel therapeutic agents for CRC.

keywords: Toxoplasma gondii, colorectal cancer, apoptosis, BAX, BCL2, PI3K/AKT, cancer therapy

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OP-4

Development and Analytical Validation of a High-Performance TES-Based Indirect ELISA Kit for Serological Diagnosis of Human Toxocariasis

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Background and aim: Human toxocariasis is a neglected zoonotic disease with a considerable seroprevalence in Iran, particularly in endemic regions. The lack of affordable and standardized serological diagnostic tools limits accurate clinical diagnosis and large-scale epidemiological surveillance. This study aimed to develop and clinically validate an indigenous indirect ELISA kit based on in-house Toxocara canis excretory–secretory (TES) antigen, manufactured under GMP and ISO 13485 standards.

Methods: TES antigen was produced from T. canis L2 larvae cultured in serum-free medium and purified by ammonium sulfate precipitation. Antigen integrity and immunoreactivity were confirmed using SDS-PAGE and Western blotting. High-binding 96-well microplates were coated with an optimized TES concentration. The diagnostic cut-off value was statistically defined as mean optical density (OD) + 3 standard deviations of 20 Toxocara-negative healthy sera. Analytical validation included precision, reproducibility, and stability testing. Clinical performance was assessed using 100 archived human serum samples, including 50 confirmed toxocariasis cases (eosinophilia and positive commercial ELISA results) and 50 confirmed negative controls. Results were compared with a commercial reference ELISA kit.

Results: The calculated cut-off value was 0.700, based on a mean OD of 0.312 ± 0.129 in negative sera. The assay demonstrated excellent analytical reliability, with intra-assay coefficients of variation (CVs) ≤ 7.2% and inter-assay CVs ≤ 9.8%. Clinical evaluation showed a sensitivity of 95.0% and a specificity of 96.0%, with positive and negative predictive values of 95.0% and 96.0%, respectively. The overall diagnostic efficiency of the assay was approximately 95%. No significant cross-reactivity was observed with sera from patients infected with other helminths, including echinococcosis. Stability studies confirmed a shelf life of at least 18 months at 2–8 °C, with preserved diagnostic performance under both real-time and accelerated aging conditions.

Conclusion: The indigenous TES-based indirect ELISA kit demonstrated high diagnostic accuracy, robust analytical performance, and long-term stability. Its performance was comparable to or superior to international reference kits while offering significant cost advantages. This assay represents a reliable and standardized tool for routine clinical diagnosis and large-scale seroepidemiological studies of human toxocariasis in endemic regions.

keywords: Toxocara canis, Toxocariasis, TES antigen, ELISA kit development, Serodiagnosis, IgG

OP-5

A molecular parasitologic study of ocular toxoplasmosis in patients referring to some ophthalmology centers in Tehran

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Background and aim: The parasite reaches to the eye and its retina through circulation. The parasite goes to the choroid and affects its neuronal layers. Toxoplasmosis is known as the most common causes of chorioretinitis. Attacks to the eye could be chronic and sometimes infection relapses. The damaged tissue associated with the eye neural layers would not repair. Emergence of clinical symptoms is related to age, the injured site and cyst size. An injury can remain active about four months and often the site of injury is in the posterior pole or proximal to it. The posterior pole scares can persist a serious

Methods: The buffy coat of the samples was employed for DNA extraction and molecular PCR test. For performing the PCR, primer of the gene was checked. The tissue, BAG1, the needed material and Amplicon Master Mix were used. Results: With the molecular method (PCR), from the 63 blood samples of the patients suspicious to ocular toxoplasmosis; 23 patients (36%) had positive form of the disease.

Results: With the molecular method (PCR), from the 63 blood samples of the patients suspicious to ocular toxoplasmosis; 23 patients (36%) had positive form of the disease.

Conclusion: Conclusion: According to the clinical diagnosis, ophthalmoscope observation and evaluation of active and passive scares as well as clinical symptoms, complementary, and PCR methods are of great importance in the two clinical diagnoses of the disease, while sensitivity and characteristic of PCR is somewhat higher.

keywords: Keywords: Ocular Toxoplasmosis, Chorioretinal Scar, Retinochoroiditis, Uveitis, PCR

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OP-6

Prevalence of Strongyloides stercoralis infection by serological and parasitological methods in patients referred to health centers in Shushtar county during 2023-2024

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Background and aim: Strongyloides stercoralis is a neglected parasitic infection endemic to tropical and subtropical regions. In immunocompromised individuals, strongyloidiasis can lead to hyperinfection and disseminated disease with potentially fatal outcomes. Although this nematode is endemic in northern and southern Iran, its prevalence in Shushtar County, Khuzestan Province, southwestern Iran, has not yet been investigated. Therefore, this study aimed to detect S. stercoralis using serological and parasitological methods among patients referred to health centers in Shushtar County.

Methods: In this cross-sectional study (October 2023–July 2024), blood (3 mL) and single stool samples were collected from patients attending health centers in Shushtar County after informed consent. Stool samples were examined using direct smear, formalin–ethyl acetate concentration, and agar plate culture. Serum samples were analyzed by indirect ELISA (NovaLisa® Strongyloides antibody kit). Data were analyzed using SPSS v26, with P 0.05 considered statistically significant.

Results: A total of 277 patients were enrolled, with a mean age of 33.4 ± 11.33 years; 81.2% (n = 225) were female and 18.8% (n = 52) were male. Serological testing showed that 6.9% (n = 19) were positive for S. stercoralis antibodies. The prevalence of S. stercoralis detected by direct smear, formalin–ethyl acetate concentration, and agar plate culture was 1.44%, 1.44%, and 3.24%, respectively. Seroprevalence was significantly associated with gender, educational level, occupation, type of residence, and soil contact (P 0.05). No significant association was observed with animal contact (P = 0.06), whereas significant associations were found with gastrointestinal and respiratory symptoms (P ≤ 0.001).

Conclusion: Parasitological methods for diagnosing strongyloidiasis have limitations, including low parasite excretion and the need for repeated sampling and skilled technicians. In contrast, indirect ELISA shows higher sensitivity for detecting S. stercoralis. Therefore, serological screening is recommended in endemic areas, particularly for individuals undergoing immunosuppressive therapy, to enable early diagnosis and prevent severe complications such as hyperinfection and disseminated strongyloidiasis

keywords: Strongyloides stercoralis, ELISA, Parasitological, Shushtar, Iran

OP-7

Molecular Detection of Cystoisospora belli and Cyclospora cayetanensis in HIV-Positive Individuals in Mazandaran Province

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Background and aim: Cystoisospora belli and Cyclospora cayetanensis cause significant morbidity in immunocompromised individuals, with HIV/AIDS patients experiencing the most severe manifestations, typically when $CD4^+$ T-cell counts fall below 200 cells/µl. To assess the burden of these pathogens, we conducted a molecular detection study in an HIV-positive population in northern Iran.

Methods: In this cross-sectional study, 50 stool samples were collected from HIV-positive individuals attending behavioral disease counseling centers in Mazandaran Province, after obtaining informed consent. The study protocol was reviewed and approved by the Research Ethics Committee of Isfahan University of Medical Sciences (Approval Code: IR.MAZUMS.REC.1402.17364). All samples were subsequently analyzed for the presence of Cyclospora cayetanensis and Cystoisospora belli using polymerase chain reaction (PCR). Data analysis was performed using Excel 2019 and IBM SPSS Statistics 26.0. The relationship between parasitic prevalence and demographic factors was assessed, with a p-value of 0.05 considered statistically significant.

Results: Among 50 patients, The prevalence of C. belli infection was 8% (n=4; 95% CI: 0.48–15.52), and prevalence of C. cayetanensis, which was 4% (n=2; 95% CI: 0.00–9.43). The majority of participants (66%) reported residing in rural villages. Among them, gastrointestinal symptoms were common, with 52% reporting issues, primarily diarrhea and abdominal cramps.

Conclusion: These findings confirm that C. belli and C. cayetanensis remain endemic threats, disproportionately affecting rural areas. The significant link between C. belli and gastrointestinal morbidity calls for increased clinical suspicion and prompt diagnostic testing. To mitigate this burden, public health efforts must prioritize focused screening and the implementation of prevention programs.

keywords: Cystoisospora belli, Cyclospora cayetanensis, HIV

OP-8

Prevalence of Acanthamoeba sp. Genotypes Isolated from Dental Unit Waterlines in Selected Dental Centers, Tehran, Iran

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Background and aim: Free-living amoebae (FLA), which usually live in various environments such as water, soil, and air, are capable of opportunistically infecting humans under certain circumstances. These protozoan parasites have been reported in various water sources. In the field of dental unit water, limited studies have been down. The aim of this study was to identify the morphological and molecular characteristics of FLA isolates from dental unit waterlines.

Methods: A total of 96 water samples were collected from selected dental units. Samples were filtered and cultured on non-nutrient agar (NNA). Polymerase chain reaction (PCR) assays and sequencing were performed using both genus/species-specific primers and a set of universal primers on positive samples. Phylogenetic relationships of positive isolates were analyzed using MEGA software.

Results: Microscopic examination revealed 22 positive samples (25%) for FLA, while molecular assays with universal primers confirmed 20 positive samples (20.8%). Based on PCR with genus/species-specific primers, 3 isolates (3.1%) were identified as Acanthamoeba genotype T4 and 1 isolate (1%) as Acanthamoeba genotype T3. Additionally, 11 isolates (11.54%) were identified as Vermamoeba vermiformis and 5 isolates (5.2%) as members of the family Vahlkampfiidae.

Conclusion: The findings of present study, highlight the need to improve filtration systems in dental units and to implement periodic screening for free-living amoebae in dental unit waterlines.

keywords: Free-living amoebae, dental unit waterlines, dental centers.

OP-9

Antitumor activity of Plasmodium berghei on intestinal cancer suppression in mice

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Background and aim: Colon cancer is one of the most common diseases of the digestive system. Plasmodium, one of the most important parasites, can be considered for the treatment of cancer, and good studies have been done in this regard in the past. Our goal in this study is to investigate the effect of Plasmodium berghei in suppressing intestinal cancer in mice

Methods: Ten Balb/c mice were inoculated subcutaneously with 0.1 ml of CT26.WT cell suspension. (106 x 5/ml) for each mouse's right forelimb axilla. On the day of tumor formation (on the sixth day After tumor cell injection), 10 mice were randomly selected They were divided into two groups (5 animals in each group). in CT26.WT+P.y group, as Plasmodium berghei infected group, 1x106 was injected intraperitoneally into each mouse with Red blood cells infected with Plasmodium berghei. Control group mice (CT26.WT) were injected intraperitoneally. Apoptosis was assessed by dUTP deoxynucleotidyl transferase (TdT) staining and the expression of apoptosis-related proteins including Bax, Bcl-2, caspase-9, and cleaved caspase-3 by western blotting. Blot and immunohistochemistry respectively. A transmission electron microscope (TEM) was used to observe the ultrastructural changes in Colon cancer cells and the expression of central protein related to mitochondrial biogenesis, PGC-1α, and mitophagy. The relevant important proteins, PINK1/Parkin, were detected by western blotting

Results: We found that Plasmodium infection decreased the weight and size of tumors and decreased the expression of Ki67 in colon cancer-bearing mice. Furthermore, Plasmodium infection promotes mitochondrial-mediated apoptosis in colon cancer cells, as up-regulated by increasing the proportion of TUNEL-positive cells. Bax, caspase-9, and cleaved caspase-3 proteins and low expression of Bcl-2 protein. In colon cancer cells, we found degraded cell nuclei, swollen mitochondria, missing cristae, and a reduced number of autolyzed outcomes. In addition, Plasmodium infection impaired mitochondrial biogenesis and mitophagy. Expression of PGC-1α, PINK1, and Parkin proteins in colon cancer cells

Conclusion: Because of the high incidence and mortality associated with colon cancer, researchers to reduce Mortality and improve the quality of life of patients are continuously looking for new treatments to inhibit the growth of colon cancer, so we investigated this issue in this study

keywords: Plasmodium berghei, intestinal cancer, suppression, BALB/c mice

OP-10

Sequencing and histopathological identification of Cutaneous leishmaniasis with molecular methods

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Background and aim: Cutaneous leishmaniasis(CL) is the most common form of skin disease caused by a single-celled parasite that is transmitted by the bite of a phlebotomine sandfly. bloodshed transmitted from infected animals rodents, dogs or humans to healthy humans can cause contamination. Symptoms usually appear three months to a year after the bite. Leishmaniasis affects almost 12 million people worldwide and it is one of the diseases that special attention should be paid to control and prevent it.

Methods: This study was conducted from 2021 to 2022 in 100 cases that have travelled to the native area of the region. In the laboratory, the wounds are prepared from the patients and the interstitial fluid of the wounds using a smear scalpel blade. Also, for further examination and a more definitive diagnosis of the patient's samples, a biopsy was performed. In addition, serous fluid from the patient's skin lesion was cultured in Schneider's Drosophila medium (Sigma, Germany), supplemented with 5% heat-inactivated fetal bovine serum (Sigma, Germany). The nested PCR method was performed using clinical samples and it was repeated twice for each batch of samples. All PCR products of the ITS-rDNA gene were sequenced and analyzed using the Taq1 enzyme with finite-length fragment polymorphism (RFLP). Collected data were analyzed using SPSS-21 and Spearman and Kendall tests.

Results: In this study, 35 positive cases were detected About 47% of the total cases of CL were in Kermanshah province in western Iran and Qasr Shirin region. 28% of the positive cases had a history of travelling to Ilam province and another 25% had a history of travelling to Fars, Hormozgan and Isfahan provinces. The prevalence of CL in men and women was 75% and 25%, respectively. The highest incidence of CL among men was observed in truck drivers and the age group of 20 to 35 years. In addition, most cases of the disease were observed during these years in summer and autumn. PCR products of the ITS-rDNA gene were sequenced. Sequence analysis showed that 30 of the 35 positive samples were Leishmania major.

Conclusion: Our case report was done in Iran and the city of Urmia, and considering that the city of Urmia is located in western Iran, you are not a native region. Therefore, our studies have been conducted on non-natives and those who have a history of travelling to human areas. With proper information and training during the trip, such cases can be prevented.

keywords: Sequencing; histopathological; Cutaneous leishmaniasis;

OP-11

Impacts of Global Climate Change on Parasite Ecology and Host-Parasite Dynamics

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Background and aim: Global climate change, characterized by rising temperatures, altered precipitation, and extreme weather events, is reshaping parasite ecology and host-parasite dynamics. These environmental shifts influence parasite distribution, life cycle dynamics, and transmission patterns, posing significant risks to human, animal, and ecosystem health. Warmer temperatures expand the geographic range of vector-borne parasites like Plasmodium and Leishmania, while altered precipitation affects vector breeding and parasite development. Host susceptibility is exacerbated by climate-induced stressors, such as habitat loss and malnutrition, amplifying disease impacts. This mini-review synthesizes recent research on how climate change drives parasite range shifts, accelerates life cycles, and alters host-parasite interactions. Case

Methods: Climate change affects parasites through multiple pathways. Rising temperatures expand the geographic range of vectors like mosquitoes and ticks, enabling parasites to invade new regions. Altered precipitation creates or eliminates vector breeding sites, while extreme weather events disrupt host-parasite dynamics. Additionally, environmental stressors weaken host immunity, increasing susceptibility to infection. For example, malaria transmission has extended to higher altitudes in East Africa due to warming climates (Caminade et al., 2014). Similarly, zoonotic parasites like Leishmania are emerging in non-endemic areas as vectors adapt to new habitats (Medlock et al., 2014). These shifts threaten human health, livestock production, and wildlife conservation, particularly in resource-limited regions. Understanding these dynamics is critical for predicting disease emergence and developing mitigation strategies. This mini-review synthesizes recent findings on how climate change reshapes parasite ecology, focusing on geographic range shifts, altered life cycles, host susceptibility, and public health implications. By examining case studies and mitigation approaches,

Results: Climate change significantly alters the geographic distribution of parasites, particularly those reliant on vectors. Rising temperatures expand the habitable range of vectors like Anopheles mosquitoes, which transmit Plasmodium species causing malaria. A study by Ryan et al. (2019) predicts that by 2050, climate-driven range shifts could expose an additional 700 million people to malaria, particularly in highland areas of Africa and South America. Warmer temperatures accelerate vector reproduction and shorten the extrinsic incubation period of parasites, increasing transmission efficiency. For instance, Plasmodium falciparum requires temperatures between 20–30°C for optimal sporogonic development, conditions increasingly met in previously cooler regions (Mordecai et al., 2020). Likewise, sandflies (Phlebotomus spp.) transmitting Leishmania are expanding into southern Europe due to warmer winters and extended transmission seasons (Medlock et al., 2014). In North America, ticks (Ixodes scapularis) carrying Babesia microti are moving northward as winter temperatures rise, increasing babesiosis cases in Canada (Ogden et al., 2017).

Conclusion: Global climate change is reshaping parasite ecology, driving range expansions, altering life cycles, and increasing host susceptibility. These changes amplify the burden of parasitic diseases, threatening human health, agriculture, and biodiversity. Case studies, such as malaria's spread to highland regions and Leishmania's emergence in Europe, underscore the urgency of addressing these dynamics. While predictive models and mitigation strategies offer promise, gaps remain in understanding long-term impacts, particularly for understudied parasites like soil-transmitted helminths. Future research should prioritize interdisciplinary approaches, integrating climate science, parasitology, and epidemiology.

keywords: Climate Change, Parasite, Ecology, Host-Parasite Dynamics

OP-12

The Potential Association Between Latent Toxoplasma gondii Infection and Opioid Abuse: A Registry-Based Sero-Molecular Case-Control Study

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Background and aim: Toxoplasma gondii is a ubiquitous parasitic protozoan that can cause neurological and psychiatric disorders, potentially impacting human emotional behavior. This study aimed to explore serological and molecular evidence of T. gondii infection in opioid abusers in northern Iran.

Methods: In this case-control study, opioid abusers who were referred to substance abuse rehabilitation centers in Mazandaran Province, northern Iran, were enrolled. Blood samples were collected from the participants to perform a serological assay to detect T. gondii IgG and IgM antibodies. A polymerase chain reaction (PCR) test was also conducted on buffy coats of the blood samples.

Results: The study comprised a total of 474 participants, with 239 individuals being opioid abusers and 235 healthy individuals serving as the control group. The results indicated that 163 opioid abusers (68.2%) were positive for T. gondii IgG, whereas 76 (31.8%) were negative. Among the control group, 63 individuals (26.8%) tested positive for T. gondii IgG, whereas 172 (73.2%) tested negative. This difference was statistically significant according to p = 0.01, odds ratio (OR) = 2.67, and 95% confidence interval (CI) = 1.03-4.15. In addition, 7.1% (17/239) of the case and 2.1% (5/235) of the control groups were PCR positive for Toxoplasma DNA. This difference was statistically significant (p = 0.01; OR = 2.96; 95%; CI = 0.94-7.01). In contrast, all of the participants were negative for T. gondii IgM antibodies.

Conclusion: Our findings demonstrated that the sero-molecular prevalence of latent T. gondii infection in opioid abusers is significantly higher than that in healthy individuals. This suggests a potential correlation between T. gondii IgG antibody positivity and PCR results with opioid abuse.

keywords: Toxoplasma gondii; opioid abuser; polymerase chain reaction; serological assay.

OP-13

Systematic Analysis of Aptamer Applications in Parasite Detection: Effectiveness, Efficiency, and Technological Advancements

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Background and aim: Neglected tropical parasitic diseases cause substantial global morbidity, demanding rapid, accurate diagnostics. Conventional laboratory techniques are hindered by lengthy procedures and infrastructure needs. Aptamers—synthetic oligonucleotides selected via SELEX—offer superior thermal stability, facile modification, and cost-effective production over antibodies. This systematic review critically evaluates aptamer-based biosensors for detecting major human parasites (Plasmodium, Leishmania, Trypanosoma, Toxoplasma, Giardia, Trichomonas, Cryptosporidium, Schistosoma, Echinococcus, and Cyclospora), assessing their diagnostic effectiveness, analytical efficiency, and technological readiness for clinical and field deployment.

Methods: A systematic search of Web of Science, PubMed, Scopus, and Embase (August 2003–August 2025) used MeSH terms: aptamer, diagnosis, detection, parasites, and protozoa. Three independent reviewers screened records, with verification by a fourth. Inclusion criteria: original English articles on aptamer-based sensors for human-infecting parasites. Extracted data encompassed parasite species, targets, aptamer sequences, SELEX rounds, dissociation constants (Kd), detection limits (LODs), linear ranges, and analytical methods.

Results: Forty-four studies met inclusion. Aptamers exhibited high affinity (Kd: pM–nM) across parasites. Electrochemical biosensors achieved exceptional sensitivity (e.g., Plasmodium PfLDH at 1.80 fM; PfGDH at 0.77 pM). Optical/colorimetric assays offered portable alternatives (Cryptosporidium: 5 oocysts/mL; Leishmania: 94 cells/mL). AnDREW workflow improved RDT sensitivity 9–11-fold. Despite strong buffer/serum performance, challenges persist: cross-reactivity, stage-specific targeting, and limited whole-blood or clinical validation.

Conclusion: Aptamer-based biosensors represent a major diagnostic advance for parasitic diseases, offering exceptional sensitivity, specificity, and stability suited for point-of-care use in resource-limited regions. However, cross-reactivity and insufficient real-world clinical validation remain critical barriers. Future work must prioritize multiplexed detection, user-friendly device integration, and extensive clinical trials. Overcoming these hurdles will establish aptamers as superior tools for early diagnosis and surveillance, ultimately supporting global control of neglected tropical diseases.

keywords: Aptamers; Biosensors; Parasite Detection; SELEX; Neglected Tropical Diseases; Point-of-Care Diagnostics

OV-1

Routine screening for occult hepatitis C infection (OCI) is not a standard procedure in medical laboratories, which has resulted in an increased incidence of OCI among high-risk groups and the general population. The objective of this study was to investi

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Background and aim: Routine screening for occult hepatitis C infection (OCI) is not a standard procedure in medical laboratories, which has resulted in an increased incidence of OCI among high-risk groups and the general population. The objective of this study was to investigate the molecular epidemiology of OCIs in Iranian injecting drug users (IDUs).

Methods: : A prospective cross-sectional study was conducted between February and December 2022 to detect hepatitis C virus (HCV) among 103 consecutive individuals who inject drugs (IDUs) in Iran. Viral RNA was extracted from plasma and peripheral blood mononuclear cell (PBMC) samples. HCV RNA was detected using reverse transcription nested polymerase chain reaction (RT-nested PCR) amplification of the 5' untranslated region (5'UTR), and a core phylogenetic tree was constructed to determine the HCV genotypes.

Results: In this particular study, 40 out of 103 individuals who inject drugs (IDUs) tested positive for the hepatitis C virus (HCV) infection. Of the 103 individuals tested, 12 (11.7%) were positive for anti-HCV and HCV RNA in plasma. Furthermore, five individuals (4.9%) were seropositive for OCI (four males and one female), while 23 individuals (22.3%) (20 males and three females) were seronegative for OCI. The age of the individuals ranged from 21 to 72 years, with a mean age of 44.58 ± 13.9 years. A high prevalence of HCV genotype 1a was observed among IDUs, with genotype 3a also being prevalent.

Conclusion: In conclusion, a high prevalence of HCV infection (38.8%) was observed among IDUs, underscoring the pressing necessity for the implementation of an efficacious strategy to eradicate HCV transmission in this high-risk population.

keywords: Hepatitis C; Drug Users; Leukocytes, Mononuclear; Reverse Transcriptase Polymerase Chain

OV-2

Enhancing Colorectal Cancer Treatment: Stem Cell-Mediated Delivery of Reovirus Combined with Adenovirus Encoding Carcinoembryonic Antigen in a Mouse Model

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Background and aim: Background: The combination of virotherapy and immunotherapy is a promising approach to cancer treatment, leveraging the unique advantages of both methods. Oncolytic viruses not only directly target cancer cells but also stimulate the immune system, enhancing the effectiveness of immunotherapy. Colorectal cancer is a leading cause of cancer-related mortality worldwide, necessitating novel therapeutic strategies. This study investigates the combined effects of virotherapy and immunotherapy on colorectal cancer using a tumoric Balb/C mouse model expressing the carcinoembryonic antigen.

Methods: Methods: An adenoviral vector encoding carcinoembryonic antigen alone or fused to DEC205 for dendritic cell targeting was administered alongside Reovirus (type 3 Dearing strain) delivered via mesenchymal stem cells. These cells serve as carriers to improve the targeting and efficacy of oncolytic Reovirus in the tumor microenvironment. Nine groups of five mice were inoculated with different schedules of combined or single treatment regimens. Tumor size was daily monitored, and immunological and immunohistochemical analyses were performed after the treatment period (19 days after tumor formation).

Results: Results: Results demonstrated that the combination therapy significantly reduced tumor size compared to single treatments and controls. Markers such as CD8/FoxP3 and Caspase-3/Ki-67 ratios proved enhanced immune activation and apoptosis.

Conclusion: Conclusion: The data demonstrated that the application of mesenchymal stem cells may limit direct viral oncolysis but improve immune-mediated treatment. This study highlights the potential of mesenchymal stem cell-mediated virotherapy combined with immunotherapy for improved colorectal cancer treatment outcomes.

keywords: Keywords: Carrier Stem Cells, Combined treatment, DEC205, Immunotherapy, Oncolytic Virotherapy

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OV-3

Enhanced Immune Response through Combinatorial Immunotherapy with CEA-Targeted Adenoviral Vector and Reovirus Reduces Postoperative Recurrence in a Murine Colorectal Cancer Model

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Background and aim: Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer- related deaths worldwide. Preventing disease recurrence remains a significant medical challenge. Current CRC treatments primarily rely on conventional methods including surgery, radiotherapy, and chemotherapy. However, these approaches have limitations and often yield unsatisfactory outcomes. Therefore, it is crucial to explore combination therapies and more effective treatments. One of the prominent therapeutic strategies is immuno/virotherapy, which represents promising results and induces long-term immune memory against tumor antigens and promotes tumor lysis. This study investigated the antitumor effects of immunotherapy and virotherapy in reducing postoperative recurrence

Methods: A mouse CRC model was established using CT26 cells expressing the carcinoembryonic antigen (CEA). For immunotherapy, an adenoviral vector expressing CEA was purified and amplified and in two doses one week apart ..subcutaneously. Reovirus was then injected intra-tumoral in three doses. Surgical resection was then performed, leaving a residual tumor layer to simulate recurrence. Post-surgery, three booster doses of the adenoviral vector were administered. Treatment efficacy on tumor recurrence was assessed by monitoring tumor size, histological changes in tumor and liver tissues, and immunological responses.

Results: Immunotherapy with adenovioral vector expressing CEA and the combination of CEA-expressing adenoviral vector immunotherapy and reovirus virotherapy significantly suppressed tumor growth and recurrence compared to the untreated group. The immuno/virotherapy group exhibited no increase in tumor size and demonstrated a stronger antitumor effect in preventing postoperative recurrence. Histological analysis revealed enhanced antitumor immune responses, particularly in the immuno/virotherapy group. Additionally, no tumor metastasis was detected in liver tissues.

Conclusion: Pre-tumor resection immunotherapy using a CEA-expressing adenoviral vector combined with reovirus effectively inhibits tumor growth. Strikingly, this immuno/virotherapy regimen induces robust antitumor immune responses and reduces recurrence rates compared to untreated controls in post-tumor resection phase, highlighting its potential as a therapeutic strategy for CRC.

keywords: colorectal cancer, oncolytic virotherapy, reovirus, immunotherapy, adenoviral vector, CEA, tumor

OV-4

A Targeted Nanopore Sequencing Method for Multiplex Detection of Respiratory Viruses in Severe Acute Respiratory Infections

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Background and aim: Severe acute respiratory infection (SARI) is a leading cause of morbidity and mortality globally. Sequencing technologies, particularly nanopore sequencing, offer great potential for the detection of viral pathogens in clinical settings. This study aimed to develop and validate a multiplex detection method using nanopore sequencing to identify SARI-related viruses, including SARS-CoV-2, Influenza A, Influenza B, RSV, and others. The method's sensitivity, specificity, and detection limits were assessed, and its effectiveness was validated using clinical samples.

Methods: Oropharyngeal swab samples were collected from patients suspected of having severe acute respiratory infections (SARI). Viral genomic RNA was extracted and subjected to conventional RT-PCR assays to amplify target viral regions. For multiplex detection, barcoded sequencing libraries were prepared using a customized primer pool for eight SARI-related viruses: SARS-CoV-2, Influenza A (H1N1, H3N2), Influenza B, human respiratory syncytial virus (RSV), human adenoviruses, human enteroviruses, and human parainfluenza viruses. These libraries were then sequenced using the MinION device. Sensitivity was evaluated by testing various sample dilutions, while specificity was determined using distinct primer pools. Data were analyzed using bioinformatic tools for read alignment and viral typing. A validation step involved sequencing 20 clinical samples with known positive results.

Results: During 12 hours of MinION sequencing, a total of 711,000 reads passed quality filters (Q-score 7). Eleven out of twelve target genes were successfully identified in clinical samples, with most viruses showing over 90% coverage. The method achieved a detection limit for SARS-CoV-2, Influenza A (H1N1, H3N2), Influenza B, and human respiratory syncytial virus (RSV), with the sensitivity reaching near 100%. The specificity of the method was 99.9%, as confirmed by using serial dilutions and different primer pools. The Q30 value of all detected viruses was consistently above 1%, indicating high-quality sequence data. Validation with 20 clinical samples demonstrated the accuracy and reliability of the multiplex detection approach. This method successfully identified all targeted viruses with high coverage, highlighting its potential for clinical application in detecting respiratory pathogens in SARI cases.

Conclusion: This study developed and validated a novel multiplex detection method using Oxford Nanopore Technologies for identifying SARI-related respiratory viruses.

keywords: Nanopore sequencing; NGS, SARI, Respiratory virus

OV-5

Detection of Epstein-Barr Virus Small RNA Genes in Oral Squamous Cell Carcinoma and Non-Cancerous Oral Cavity Samples

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Background and aim: Epstein-Barr Virus (EBV) is a human oncogenic virus linked to cancers in both lymphoid and epithelial cells, with a potential role in oral cavity lesions like oral squamous cell carcinoma (OSCC). However, its exact etiological relationship remains unclear. This study aimed to investigate the presence of EBV, its viral load, and sequence variations in EBV-encoded small RNA (EBER) in tissue samples from OSCC patients and those with other oral lesions, including oral lichen planus (OLP) and oral irritation fibroma (OIF).

Methods: A total of 88 oral cavity samples, including 23 from OSCC patients, 29 from those with OLP, and 36 from individuals with OIF, were analyzed using Real-Time PCR, with some samples also undergoing sequencing.

Results: EBER sequences were detected in 6 of the 23 OSCC samples (31.4%), 6 of the 29 OLP samples (20.7%), and 3 of the 36 OIF samples (8.3%). The mean EBV copy number was highest in OSCC samples ($1.2 \times 10^{-2} \pm 1.3 \times 10^{-2}$ copies/cell), followed by OLP ($2.2 \times 10^{-3} \pm 2.6 \times 10^{-3}$ copies/cell) and OIF ($2.4 \times 10^{-4} \pm 2.0 \times 10^{-4}$ copies/cell), although the differences were not statistically significant ($P = 0.318$). The EBER gene was successfully amplified and sequenced from 5 OSCC, 3 OLP, and 2 OIF samples with high viral loads. Sequence analysis revealed nucleotide variations (C6834T, C6870T, C6981T, C7085T, C7085G, and C7094T) in one OSCC, two OLP, and two OIF isolates compared to the EBV-WT and AG876 prototype sequences.

Conclusion: In our study, the detection of multiple genome copies per tumor cell suggests a potential role for EBV infection in oral cancers. However, further research is needed to fully elucidate the involvement of EBV in the carcinogenesis of OSCC.

keywords: Epstein-Barr Virus; Oral squamous cell carcinoma; Oral lichen planus Oral,ancer

OV-6

Seroepidemiological Study of Hepatitis B and Hepatitis C Infections in Semnan, 2023-2024

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Background and aim: Viral hepatitis is associated with complications such as liver cirrhosis, hepatocellular carcinoma, liver fibrosis, and steatosis. These viruses are significant global health concerns, particularly in developing countries such as Iran. The purpose of this study was to investigate the seroepidemiology of HBV and HCV infections, as well as the simultaneous prevalence of these infections.

Methods: This cross-sectional study included 4944 individuals who visited the Semnan Health Reference Laboratory between 2023 and 2024. Demographic data of the participants were collected, and they were tested for the presence of hepatitis B surface antigen (HBS-Ag) and hepatitis C antibody (HCV-Ab).

Results: Among the tested samples, 1.8% were positive for HBs-Ag, and 0.8% were positive for HCV-Ab. No significant association was observed between gender and HBS-Ag (P 0.05) or HCV-Ab (P 0.05). However, a significant association was found between age and HBS-Ag status, indicating a statistically significant difference between age groups and HBS-Ag status (negative/positive) (P 0.001). This suggests that the likelihood of HBS-Ag positivity increases with age. No relationship was observed between age and HCV-Ab status (P 0.05). Additionally, no concurrent HBV and HCV infections were detected among the participants.

Conclusion: Based on the findings of this study, the prevalence of HBV and HCV in Semnan City was lower than that reported in other regions of Iran. These results may assist policymakers and public health authorities in the planning and evaluation of hepatitis B and C control programs in Semnan City. Furthermore, additional large-scale studies are recommended to confirm and extend these findings.

keywords: Hepatitis B, Hepatitis C, Seroprevalence, Iran

OV-7

Inhibition of herpes simplex virus type 1 infection by Sambucus ebulus extract in vitro

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Background and aim: The emergence of drug-resistant strains of herpes simplex virus type 1 (HSV-1) has been increasingly reported. Therefore, attempts to discover new antiviral agents in particular from natural compounds are required. In this study, we evaluated the possible inhibitory effects of hydroalcoholic extract of Sambucus ebulus (S. ebulus) against HSV-1.

Methods: S. ebulus extract was produced by maceration method. MTT assay was used to evaluate the cytotoxicity effects of the S.ebulus extract; also, antiviral effects were measured both by test TCID50 and quantitative real-time PCR methods. To study the inhibitory impact of S. ebulus extract on the expression of HSV-1 antigens, indirect immunofluorescence assay (IFA) was also performed. All analyses were performed using the GraphPad Prism software v. 7.0.

Results: In the postexposure assay of HSV-1 with S. ebulus extract at the highest nontoxic concentration (75 µg/mL), S. ebulus extract led to 2.6 log10 TCID50 reduction in infectious virus titer. At the highest nontoxic concentration, the S. ebulus extract led to inhibition rates of 91.2%, based on the quantitative real-time PCR assay results (p0.001). Also, in the immunofluorescence assay, a significant reduction was observed in fluorescence emission intensity in HSV-1-infected cell treated with S. ebulus extract compared to the control group.

Conclusion: S. ebulus extract is a novel and effective natural compound in reducing HSV-1 titer and future studies should be conducted to discover the complete mechanism of antiviral effect of this natural compound.

keywords: Herpes simplex virus, Antiviral activity, Sambucus ebulus

OV-8

Genetic characterization of rotavirus A strains circulating in children under 5 years of age with acute gastroenteritis in Tehran, Iran, in 2023–2024: dissemination of the emerging equine- like G3P[8]-I2- E2 DS- 1- like strains

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Background and aim: Rotavirus A is a leading cause of acute gastroenteritis in children under five, especially in low- and middle-income countries. Common G–P genotypes include G1P[8], G2P[4], G3P[8], G4P[8], G9P[8], and G12P[8]. Rotavirus genetic diversity arises mainly through reassortment. In Iran, despite recent vaccine introduction, genotype prevalence has shifted over time, with G3P[8] becoming more common, highlighting the dynamic nature of rotavirus circulation and the importance of continuous molecular surveillance.

Methods: Specimen collection Between October 2023 and October 2024, a total of 300 faecal were collected from children 5≤ who were hospitalized for acute gastroenteritis at Tehran Children's Hospital. Viral RNA extraction and cDNA synthesis Viral RNA was extracted from 10% suspension prepared in phosphate-buffered saline (PBS) using a commercial kit. Subsequently, CDNA was synthesized using one-step kit. Rotavirus detection and genotype determination Rotavirus screening was performed by RT- PCR. Positive samples were further genotyped for G and P typing by semi-nested multiplex RT- PCR with type- specific primers. For I and E genotyping, amplification of the VP6 and NSP4 genes was carry out using specific primers. Sequence analysis To understand variants of circulating G3 strains, samples (n=47) were selected for Sanger sequencing of their VP7 and VP4 genes. The obtained sequencing was genotyped and analysis using phylogenetic methods

Results: Among 300 stool samples, 32% were rotavirus-positive, with G3P[8] as the predominant genotype (72.9%). Phylogenetic analysis showed Iranian G3 strains clustered into two lineages: human-like lineage I and equine-like lineage IX, with equine-like strains becoming dominant during 2023–2024. VP4 and VP7 analyses confirmed close clustering within lineage III.

Conclusion: This study investigated the genotype diversity of rotavirus A in Iranian children under five during 2023–2024. Equine-like G3P[8] DS-1–like strains were dominant, accounting for 72.9% of RVA-positive cases, replacing human Wa-like strains. Genetic analysis suggests these strains emerged not be related to selection pressure from rotavirus vaccination, but rather to cross- border migration of rotavirus strains due to population movements. The findings highlight emphasize the need for ongoing molecular surveillance to monitor rotavirus evolution and inform vaccination strategies.

keywords: Wa-like, DS- 1- like; equine G3 strain; rotavirus

OV-9

Evaluation of the expression levels of cellular genes involved in the mismatch repair (MMR) pathway (MSH2 and MLH1) in HeLa cells transfected with an EBNA1-expressing plasmid, compared to cells transfected with a control plasmid

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Background and aim: Cervical cancer remains one of the most common cancers among women, with persistent infection by high-risk human papillomaviruses (HPVs) as its primary cause. Increasing evidence also suggests that Epstein–Barr virus (EBV) may act as a co-factor in cervical carcinogenesis. Among EBV proteins, EBV nuclear antigen-1 (EBNA1) is continuously expressed and can influence host gene regulation. This study explored how EBNA1 affects the expression of mismatch repair (MMR) genes MLH1 and MSH2 in HeLa cells.

Methods: HeLa cells were transfected with an EBNA1-expressing plasmid and a control plasmid. After confirming successful transfection, total RNA were extracted then residual plasmid DNA were removed by using DNase. After converting RNA to cDNA, we examined the expression of MLH1 and MSH2 by using quantitative RT-PCR.

Results: EBNA1 expression was clearly detected in transfected HeLa cells. Real-time PCR analysis revealed that the presence of EBNA1 led to an increase in the transcriptional levels of MLH1 and MSH2 compared with control cells. Although these changes were not statistically significant, the pattern suggests a possible role of EBNA1 in modulating components of the DNA mismatch repair system.

Conclusion: The findings indicate that EBNA1 may subtly alter the regulation of DNA repair pathways by enhancing the expression of MLH1 and MSH2. Such modulation could provide advantages for viral persistence and potentially contribute to genomic instability in cervical cells co-infected with HPV.

keywords: HBsAb titer, Hepatitis B, Fars province, PWUD

OV-10

The miRNA-ACE2 Axis in COVID-19: Investigating miR-190a, miR-200c-3p, and miR-421-5p Expression and an Unexpected Vitamin D Finding

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Background and aim: Introduction: Angiotensin-converting enzyme 2 (ACE-2) has been shown to be a serves as the receptor by which coronaviruses can enter the cytoplasm of cells. However, the host cells' antiviral responses depend heavily on specific miRNAs. Additionally, research has shown an association between viral infections and vitamin D. This study looked at the expression levels of ACE-2, miR-190a, miR-200c-3p, miR-421-5p, and vitamin D concentration in COVID-19 patients and evaluated how they related to the control group.

Methods: Methods: This case-control study included 32 COVID-19 patients who were admitted to Razi Hospital, as well as 16 control individuals who were referred to Allameh Karmi Hospital of Ahvaz between March 2022 and April 2023. The expression level of miR-190a, miR-200c-3p, miR-421-5p, and ACE-2 was measured by real time PCR method. In addition, vitamin D concentration was measured in by ELISA method.

Results: Results: The relative expression of miR-190a, miR-200c-3p and miR-421-5p was significantly increased in the patient group compared to the controls (P0.001 for all three). The relative expression of ACE2 was significantly reduced in the patient group compared to the controls (P0.001). However, the concentration of vitamin D was significantly higher in the patient group than the control group (P=0.002).

Conclusion: Conclusion: In comparison to control subjects, the study discovered that COVID-19 patients had lower levels of ACE-2 and higher levels of miR-190a, miR-200c-3p, and miR-421-5p. Remarkably, vitamin D levels were also higher in COVID-19 patients than in controls, which defies earlier findings and calls for more investigation.

keywords: Keywords: SARS-CoV-2, COVID-19, MicroRNAs, Vitamin D, Angiotensin-Converting Enzyme 2.

OV-11

Serological and molecular prevalence of Hepatitis E virus among blood donors in Iran

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Background and aim: The hepatitis E virus (HEV) is proven to be one of the principal causative agents of acute viral hepatitis across the globe, especially in developing countries. The major mode of transmission of the virus is the fecal-oral route that takes place via infected water and/or food; however, there have been reports of transfusion-transmitted HEV (TT-HEV) among blood donors. The purpose of this study is to examine the reports that calculate the prevalence of anti-HEV IgG/IgM and HEV RNA among blood donors in Iran.

Methods: The literature search involved a wide-ranging search through several databases, including PubMed, Scopus, Science Direct, Google Scholar, Scientific Information Database (SID), IranMedex, and Magiran, for relevant literature in English or Persian up to December 16, 2025.

Results: This systematic review collected the data of nine studies, along with 4,429 blood donors. The sample population included a range of Iranian zones such as Bushehr, Babol, Arak, Birjand, Tehran, Khuzestan, Tabriz, and Shiraz. The studies included sample sizes of 340 to 700 participants. The studies varied in duration, starting from 2007 in Tabriz to 2022 in Babol. Serological measurements of all nine studies conducted Enzyme-linked Immunosorbent Assay (ELISA) of anti-HEV IgG, with only one study checking anti-HEV IgM levels too. The anti-HEV IgG seroprevalence levels varied between 1.6% and 16.7%, with Babol having the lowest prevalence and Bushehr having the highest prevalence, while anti-HEV IgM showed 0.71% prevalence in Fars, 2016. Various studies showed detection levels of HEV-RNA of up to 12% in Fars, with Tehran having the least at 2.35%.

Conclusion: A significant HEV infection burden among Iranian blood donors has been revealed, with a wide range of IgG seroprevalence in certain geographic locations. HEV viremia detected in previous studies sparks concern about TT-HEV infection, especially among immunocompromised population. There is a serious gap for extensive research across multiple regions of a country using molecular screening for HEV RNA to better estimate to scope of HEV infection and TT-HEV seroprevalence in Iran.

keywords: Hepatitis E virus , Blood Donation, Iran, Blood safety, Viremia

OV-12

Alterations of the Gut Virome Across Disease Severity in Ulcerative Colitis and Crohn's Disease: A Metagenomic Study

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Background and aim: Inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease, is a chronic inflammatory condition associated with intestinal immune dysregulation. Although bacterial dysbiosis has been extensively studied, the role of the gut virome remains insufficiently understood. Emerging evidence suggests that alterations in bacteriophages and eukaryotic viruses may influence microbial balance and disease severity. The aim of this study was to characterize gut virome composition and diversity in patients with mild and severe IBD compared with healthy controls using metagenomic sequencing, and to evaluate virome features as potential non-invasive biomarkers for disease stratification.

Methods: This cross-sectional observational study was conducted on fifty participants recruited from an IBD referral center, including patients with mild and severe ulcerative colitis, mild and severe Crohn's disease, and healthy controls (n=10 per group). Disease activity was assessed using the Mayo score for ulcerative colitis and the Crohn's Disease Activity Index for Crohn's disease. Fresh stool samples were collected, processed for viral particle enrichment, and subjected to viral DNA extraction. Metagenomic libraries were prepared and sequenced using the Illumina NovaSeq platform. Quality control, host read removal, and de novo assembly were performed using standard bioinformatics pipelines. Viral contigs were taxonomically classified, and diversity metrics were calculated. Differential abundance analysis and functional annotation were conducted, and machine-learning models were applied to evaluate virome-based discrimination of disease status and severity.

Results: Fifty participants were analyzed with no significant differences in age or sex distribution among groups. Virome alpha diversity indices were significantly reduced in patients with severe ulcerative colitis and Crohn's disease compared with healthy controls (p 0.05), whereas mild disease groups showed diversity values closer to controls. Beta diversity analysis demonstrated a clear separation between severe IBD and healthy individuals (PERMANOVA, p 0.001), while mild cases largely overlapped with controls. Taxonomic analysis revealed depletion of crAss-like phages and Microviridae in IBD patients, alongside enrichment of Caudovirales families, particularly Siphoviridae and Myoviridae, in severe disease. Anelloviridae abundance increased in severe IBD, and Herpesviridae enrichment was observed specifically in severe ulcerative colitis. Functional analysis showed higher representation of lytic phage-related proteins in severe disease. Virome-based random forest models demonstrated good accuracy in distinguishing IBD and disease severity.

Conclusion: This study demonstrates that inflammatory bowel disease is associated with significant alterations in the gut virome. Severe disease is characterized by reduced viral diversity, depletion of core bacteriophages, and enrichment of lytic phages and selected eukaryotic viruses. These changes correlate more strongly with disease severity than disease type. Overall, the findings support the potential utility of virome-based signatures as non-invasive biomarkers for assessing disease activity and stratifying patients with inflammatory bowel disease clinically. This work was supported by the National Institute for Medical Research Development (NIMAD) with grant numbers [979157].

keywords: Gut virome, Inflammatory bowel disease, Ulcerative colitis, Crohn's disease, Metagenomics

OV-13

Association of Cytomegalovirus Infection With Inflammatory Cytokine Responses in Ulcerative Colitis

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Background and aim: Ulcerative colitis is a chronic inflammatory bowel disease in which viral infections may influence disease activity and treatment response. Cytomegalovirus reactivation has been frequently reported in patients with severe or steroid-refractory ulcerative colitis; however, its immunological impact remains incompletely defined. Cytokines play a central role in mucosal inflammation and systemic immune responses in ulcerative colitis. Understanding how cytomegalovirus infection affects cytokine regulation may clarify its role as a pathogenic factor rather than a bystander. The aim of this study was to evaluate mucosal gene expression and serum levels of selected pro- and anti-inflammatory cytokines in cytomegalovirus-positive and cytomegalovirus-negative ulcerative colitis

Methods: This case-control study was conducted on 190 patients with confirmed ulcerative colitis who were recruited from a tertiary inflammatory bowel disease center. Ninety patients with tissue-proven cytomegalovirus infection and 100 cytomegalovirus-negative patients were included. Cytomegalovirus status was determined using quantitative real-time PCR on colonic biopsy specimens, complemented by plasma CMV DNA detection and serological IgM testing. Disease activity was evaluated using the Mayo scoring system. Total RNA was extracted from colonic biopsy samples and reverse-transcribed into cDNA. Gene expression levels of selected cytokines were quantified using real-time PCR and normalized to GAPDH expression. In parallel, serum levels of TNF-α, IL-1β, IL-6, and IL-17A were measured using enzyme-linked immunosorbent assay. Statistical analyses were performed to compare mucosal and systemic cytokine profiles between cytomegalovirus-positive and cytomegalovirus-negative groups.

Results: A total of 190 ulcerative colitis patients were analyzed, including 90 cytomegalovirus-positive and 100 cytomegalovirus-negative individuals, with no significant differences in age, sex distribution, baseline laboratory parameters, or medication history between groups. Cytomegalovirus tissue viral load was significantly higher in patients with moderate to severe disease compared with those with mild disease and showed a strong positive correlation with plasma viral load ($r = 0.664$, p 0.01). Colonic gene expression analysis demonstrated significantly increased mRNA levels of TNF-α, IL-1β, IL-6, and IL-17A in cytomegalovirus-positive patients compared with cytomegalovirus-negative controls (all p 0.05). In contrast, IFN-γ, TGF-β, IL-8, IL-12, and RANTES expression did not differ significantly between groups. Consistent with tissue findings, serum concentrations of TNF-α, IL-1β, IL-6, and IL-17A were significantly elevated in cytomegalovirus-positive patients. Receiver operating characteristic analysis showed good diagnostic performance for TNF-α, IL-1β, and IL-6 in distinguishing cytomegalovirus-positive ulcerative colitis.

Conclusion: This study demonstrates that active cytomegalovirus infection in ulcerative colitis is associated with selective upregulation of key pro-inflammatory cytokines at mucosal and systemic levels. Elevated TNF-α, IL-1β, IL-6, and IL-17A characterize cytomegalovirus-positive patients, whereas regulatory cytokines remain unchanged. These findings suggest that cytomegalovirus acts as an immune amplifier rather than a bystander and support cytokine profiling as a useful tool for risk stratification and clinical management in affected ulcerative colitis patients. This study was supported by Grant No. 979157 from the National Institutes for Medical Research Development (NIMAD), Tehran, Iran.

keywords: Inflammatory Bowel Diseases, Gene expression, Inflammation, Tumor Necrosis Factor

OV-14

HPV-16 Viral Load–Driven Immune Dysregulation During Cervical Neoplastic Progression

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Background and aim: Persistent infection with human papillomavirus type 16 is a key determinant of cervical lesion progression, and increasing viral load has been associated with higher disease severity. However, the host immune and inflammatory mechanisms underlying escalating viral burden remain incompletely characterized. HPV-16 can modulate antiviral immunity, promote chronic inflammation, induce angiogenesis, and facilitate immune evasion, thereby supporting viral persistence and neoplastic progression. Understanding how these molecular pathways relate to viral load may improve risk stratification. The aim of this study was to investigate the association between HPV-16 viral load and cervical expression of antiviral, inflammatory, angiogenic, and immune-evasion–related genes across histopathological

Methods: This cross-sectional study included 150 women classified as healthy controls, CIN-I, CIN-II, CIN-III, or invasive cervical carcinoma. Cervical specimens were collected prior to treatment for DNA and RNA extraction. HPV-16 genotyping was performed using multiplex PCR, and viral load was quantified by TaqMan real-time PCR targeting the E6 gene, normalized to β-globin and expressed as log10 copies per 10^3 cells. Expression of IFNB1, IFNG, TLR9, IL6, IL8, TNF, VEGFA, and PD-L1 was measured by quantitative real-time PCR and normalized to GAPDH using the 2−ΔΔCt method. Group comparisons were performed using ANOVA or Kruskal–Wallis tests as appropriate. Spearman correlation assessed associations between gene expression and viral load. Multivariable regression models identified independent predictors, and receiver operating characteristic analysis evaluated diagnostic performance for distinguishing high-grade lesions. Statistical significance was defined at p less than 0.05 using SPSS and GraphPad Prism software throughout analyses with two-sided testing and multiple comparison corrections applied.

Results: HPV-16 viral load increased significantly across histopathological stages, showing a clear ascending gradient from CIN-I and CIN-II to CIN-III and invasive cervical carcinoma (p0.001). Antiviral genes IFNB1, IFNG, and TLR9 exhibited progressive downregulation with advancing disease and demonstrated negative correlations with viral load, reaching statistical significance for IFNB1 and TLR9. In contrast, inflammatory cytokines IL-6, IL-8, and TNF showed stepwise upregulation and correlated positively with viral burden, with strongest associations observed for IL-6 and IL-8. Genes related to angiogenesis and immune evasion, VEGFA and PD-L1, remained unchanged in early lesions but were markedly increased in CIN-III and carcinoma and correlated positively with viral load. Multivariable regression identified IL-6, IL-8, VEGFA, and PD-L1 as independent predictors of higher viral burden. Receiver operating characteristic analysis demonstrated moderate diagnostic accuracy for individual markers and improved discrimination for a combined four-gene model in identifying high-grade cervical lesions across diverse patient subgroups overall consistently.

Conclusion: Increasing HPV-16 viral load is closely associated with coordinated suppression of antiviral responses and activation of inflammatory, angiogenic, and immune-evasive pathways in cervical tissue. Elevated IL-6, IL-8, VEGFA, and PD-L1 expression characterizes high-grade lesions and independently predicts higher viral burden. A combined multigene expression signature improves discrimination of advanced disease compared with single markers. These findings highlight viral load–driven immune remodeling and support gene-expression profiling for stratification and monitoring of HPV-related cervical disease progression. This study was supported by National Institute for Medical Research Development (NIMAD) under Grant No. 989185.

keywords: Papillomavirus, HPV16, Cervical Intraepithelial Neoplasia, Viral Load, Immunity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OV-15

Epidemiology and Clinical Features of Respiratory Viruses in Hospitalized Iranian Children During the COVID-19 Pandemic

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Background and aim: Acute respiratory infections (ARIs) are a significant global health concern, especially in children under five, causing approximately 4.3 million annual deaths. ARIs are mainly caused by respiratory viruses. The coronavirus disease 2019 (COVID-19) has altered the circulation of respiratory viruses. This study investigates the epidemiology and clinical features of respiratory viruses in hospitalized children during the COVID-19 pandemic in Gorgan, Iran.

Methods: A total of 264 nasopharyngeal swab samples were collected from hospitalized children between October 2021 to March 2022 at Taleghani Children's Hospital, Gorgan, Iran. The frequency of various respiratory viruses, including human parainfluenza viruses (HPIV1-4), influenza viruses A and B (FLU-A, B), human metapneumovirus (HMPV), human rhinovirus (HRV), respiratory syncytial virus (RSV), and severe acute respiratory syndrome-associated coronavirus 2 (SARS-CoV-2) was detected using a SYBR green-based real-time PCR assay.

Results: Out of the 264 hospitalized children, 88.2% (233) tested positive for at least one respiratory virus, with 60.2% (159) showing co-infections and 28% (74) having single infections. The most frequently detected were HRV (56.4%), HMPV (53%), and RSV (18.2%). The proportions of HPIV-1, HPIV-2, HPIV-3, HPIV-4, FLU-A, FLU-B, and SARS-CoV-2 were 8.7%, 12.9%, 8%, 7.6%, 1.9%, 0%, and 15.2%, respectively. There was a clear association between specific viruses and some clinical symptoms, such as RSV with pneumonia, and HPIV-1 with cyanosis. Co-infections were linked to severe outcomes, including pneumonia and seizures. Among all 264 patients, 5 died, and 3 of them had underlying diseases. All fatal cases tested positive for at least one virus, with HMPV being the most frequently detected.

Conclusion: This study highlights the considerable impact of ARIs among children under five in Golestan Province, Iran, during the COVID-19 pandemic. The findings underscore the importance of early detection and ongoing surveillance, particularly in high-risk pediatric populations and across diverse geographic areas

keywords: acute respiratory tract infection, children, COVID-19, epidemiology

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

OV-16

Determination of Antibody Response against a Conserved EPI Epitope in Patients Infected with HCV Genotype 1a

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Background and aim: Hepatitis C Virus (HCV) employs extensive genetic diversity, particularly in its envelope glycoproteins, to evade host neutralizing antibodies, presenting a significant barrier to vaccine development. However, the EP1 epitope within the E2 glycoprotein is highly conserved, targeted by broadly neutralizing antibodies, and crucial for viral receptor binding. This study investigated the IgG antibody response against a conserved EP1-derived peptide in genotype 1a infection using an optimized in-house ELISA. Analyzing this response aims to identify key immunogenic targets, which could inform the development of both diagnostic tools and vaccines capable of inducing cross-reactive neutralizing antibodies against HCV.

Methods: An in-house indirect ELISA was optimized and performed to assess serum IgG reactivity against a conserved epitope (aa 412–426; QLINTNGSWHINSTA) within the HCV E2 glycoprotein. A synthetic peptide (Biomatik, 90% purity) was reconstituted and used as the coating antigen. Checkerboard titration determined optimal conditions. Blocking and dilutions were performed with skim milk-based buffers. The assay was applied to 75 serum samples from HCV genotype 1a-infected patients and 30 HCV-negative controls. The cut-off was defined as the mean optical density (450 nm) of negative controls + 0.5 × standard deviation. All samples were tested in duplicate.

Results: Optimal ELISA conditions were determined using a pre-confirmed positive serum. The checkerboard titration identified 20 µg/mL of the EPI peptide, a serum dilution of 1:50, and an anti-human HRP conjugate dilution of 1:80,000 as optimal parameters. Blocking was performed with 5% skim milk. The assay cutoff was established as the mean OD450 of 30 HCV-negative controls + 2SD, calculated to be 0.115. When 75 serum samples from HCV genotype 1a-infected patients were tested, 24 samples (32%) showed an OD450 above the cutoff, indicating a positive antibody response against the conserved EPI epitope. The remaining 51 samples (68%) were negative.

Conclusion: This corresponds to a seroprevalence of 32% (24/75) for antibodies targeting this specific E2 epitope in the tested Iranian population infected with HCV genotype 1a. The results demonstrate that this conserved epitope is immunogenic in a subset of patients, suggesting its potential for inclusion in an epitope cocktail to be used for HCV diagnosis and vaccine development.

keywords: Hepatitis C Virus, EP1, Antibody, Genotype 1

Mini-Oral (Poster) Presentation Abstracts

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-1

The role of PET/CT scan in the follow-up of patients with differentiated thyroid cancer by using radiomix features and machine learning

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Background and aim: Differentiated thyroid cancer (DTC) is the most common endocrine malignancy, and despite the generally favorable prognosis achieved with total thyroidectomy and radioiodine ablation, a considerable number of patients continue to exhibit elevated serum thyroglobulin levels while demonstrating negative radioiodine whole-body scans. This clinical scenario poses significant diagnostic challenges, as the detection of recurrent or metastatic lymph-node involvement becomes highly dependent on more advanced imaging modalities. Although ^{18}F-FDG PET/CT has emerged as a crucial tool in this setting

Methods: In first step of our study (25 patients: 63 lymphnodes (local or distant) were evaluated: 41 benign and 22 malignant (pathology proven)) an extensive radiomics-driven analysis was applied to the PET/CT images of DTC patients by extracting a large spectrum of quantitative image features—including gray-level co-occurrence matrices (GLCM), gray-level run-length matrices (GLRLM), histogram-based descriptors, and multi-level wavelet transformations—following expert manual segmentation of suspicious lymph nodes. These high-dimensional features were integrated with multiple machine-learning classifiers, supported by rigorous feature-selection strategies designed to identify the most informative and diagnostically relevant parameters. Histopathological and cytological findings were used as the gold standard for evaluating model performance

Results: The primary results in 25 patients were shown promising outcomes. After the running the 5 classifiers to evaluation of our primary models the results were shown in this way. The accuracy of K-neighbor classifier (KNN), support vector classifier (SVC) and Random Forest (RF), NuSVC and Extra classifier (ETC) were respectively 63%, 63%,69%, 66% and 68%. As RF had the highest accuracy it showed the highest sensitivity and specificity with 70% and 68% respectively

Conclusion: The analysis demonstrated that radiomics combined with machine learning substantially enhances the discriminatory power of ^{18}F-FDG PET/CT, with several classifiers achieving accuracy rates exceeding 90% in distinguishing malignant from benign lymph nodes(while we were only in first step of our study). These findings underscore the potential of radiomics-enhanced ^{18}F-FDG PET/CT as a powerful, non-invasive diagnostic strategy that may reduce reliance on fine-needle aspiration, improve early detection of recurrent or distant nodal metastases, and support more precise risk stratification in the follow-up of DTC patients. This integrative approach may ultimately contribute

keywords: 18F-FDG, PET/CT scan, DTC, Radiomics, Machine learning

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-2

From Early Warning to Public Health Response: Bridging the Signal to Action Gap in Integrated Epidemic Intelligence Systems

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Background and aim: Advances in epidemic intelligence, including genomic surveillance, wastewater based epidemiology, digital epidemiology, and One Health environmental data, have substantially improved early outbreak detection. Despite these advances, many warning signals fail to trigger timely public health interventions, revealing a persistent "Signal to Action" gap. This gap limits the operational value of modern surveillance systems. This scoping review aimed to systematically map existing evidence on multi source epidemic intelligence systems and to identify the technical, institutional, ethical, and governance barriers that prevent surveillance signals from being translated into public health action.

Methods: This scoping review was conducted according to the Joanna Briggs Institute (JBI) methodology and reported following the PRISMA ScR guidelines. A comprehensive search was performed in PubMed, Web of Science, and Scopus for studies published between January 1, 2019, and October 25, 2024. Gray literature from major public health organizations, including WHO, CDC, Africa CDC, and ECDC, was also reviewed. No language restrictions were applied. Eligible sources addressed population level surveillance systems integrating clinical, genomic, environmental, digital, or One Health data. Data were synthesized using narrative and thematic analysis.

Results: The evidence demonstrated a rapidly expanding but fragmented surveillance landscape. Four key themes emerged: (1) technical barriers such as heterogeneous metadata standards, limited interoperability, and delayed turnaround times; (2) institutional and governance fragmentation across health, environmental, veterinary, and infrastructure sectors; (3) ethical and equity challenges related to digital bias, privacy, and global inequities in genomic data sharing; and (4) operational models including tiered decision matrices and federated data architectures. Wastewater based epidemiology showed strong potential as a population level anchor signal, while digital surveillance offered speed but limited independent action ability.

Conclusion: The primary weakness of contemporary epidemic intelligence lies not in detection capability but in the absence of operational frameworks linking signals to decisions. Bridging the Signal to Action gap requires predefined action thresholds, integrated governance structures, and equity centered data sharing mechanisms.

keywords: Epidemiological Surveillance, Wastewater Based Epidemiology, Genomic Surveillance Digital Health

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-3

Evaluation of miRNAs Involved in Cardiac Fibrosis: Approach Based on Machine Learning

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Background and aim: Defective cardiac function can lead to the excessive accumulation of extracellular matrix proteins in the heart. This study aimed to investigate and analyze the miRNAs involved in cardiac fibrosis using machine learning algorithms.

Methods: A dataset related to the expression of miRNAs in healthy individuals and patients with cardiac fibrosis was collected from public sources and relevant clinical databases. We selected a study population of 50 individuals, comprising 25 healthy controls and 25 patients with cardiac fibrosis. Different machine learning algorithms, including support vector machines, random forests, and artificial neural networks were employed to analyze, categorize, and predict the role of miRNA expression changes in cardiac fibrosis. The validation of the machine learning model through both leave-one-out cross-validation and an independent dataset effectively supports the robustness of the results. The reported metrics for accuracy, sensitivity, and specificity were impressive.

Results: A total of 78 miRNAs were found to be differentially expressed (adjusted P 0.05) between the two groups, with 47 miRNAs upregulated and 31 miRNAs downregulated in the cardiac fibrosis group compared to the control group. The top 10 miRNAs selected by each method were compared, and a consensus set of 5 miRNAs (miR-21-5p, miR-29a-3p, miR-29c-3p, miR-30b-5p, and miR-133a-3p) was identified as the most informative features for distinguishing between cardiac fibrosis and control samples. Based on the results, the expression of miR-21-5p, miR-29a-3p, and miR-29c-3p was increased in cardiac fibrosis patients compared to the control group. On the contrary, it was found that the expression of miR30b-5p and miR-133a-3p was increased in normal subjects compared to patients. The SVM algorithm with a radial basis function kernel was found to be the best-performing model, with an accuracy of 92%, sensitivity of 88%, specificity of 96%, and area under the receiver

Conclusion: In general, the evaluation of miRNAs in patients can be used as a biomarker for monitoring patients and applying treatment strategies.

keywords: miRNAs, Cardiac Fibrosis, Machine Learning, Network Analysis, Biomarkers

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-4

Integration of Artificial Intelligence with Whole Genome Sequencing for Pathogen Diagnostics: Advanced Best Practices for Predicting Antimicrobial Resistance in the Genomic Era

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Background and aim: The clinical implementation of Whole Genome Sequencing (WGS) has generated massive datasets that exceed the interpretative capacity of traditional bioinformatics. While NGS provides the genomic blueprint of a pathogen, predicting the functional resistome remains a significant challenge. Artificial Intelligence (AI) and Machine Learning (ML) have emerged as essential catalysts in transforming raw genomic data into actionable clinical insights. This review evaluates the best practices for integrating AI-driven models with WGS to optimize laboratory diagnosis and the precision prediction of antimicrobial resistance (AMR) markers.

Methods: Databases such as PubMed, Google scholar, and Medline were searched by key words Whole Genome Sequencing, Artificial Intelligence, Machine Learning, Antimicrobial Resistance, and Bioinformatics pipelines for this review. The analysis specifically evaluated the performance of Deep Learning (DL) architectures and Explainable AI (XAI) frameworks in predicting Minimum Inhibitory Concentrations (MIC) directly from genomic sequences.

Results: The integration of AI with WGS offers superior diagnostic resolution compared to conventional rule-based pipelines. Current evidence indicates that Convolutional Neural Networks (CNNs) can predict resistance phenotypes with 90% accuracy for high-priority pathogens. Key best practices identified include: 1) Implementation of automated AI-driven quality control (QC) for library preparation, 2) Utilization of "Explainable AI" to ensure transparency in clinical decision-making, and 3) The application of hybrid assembly models to resolve complex plasmid-mediated resistance. Furthermore, AI-augmented WGS significantly reduces the turnaround time for identifying hospital-acquired infection (HAI) clusters in real-time.

Conclusion: The synergy between NGS technology and Artificial Intelligence represents the pinnacle of precision microbiology. Transitioning to AI-augmented interpretation is essential for modern laboratories to provide rapid, accurate, and personalized therapeutic recommendations. These advanced genomic strategies must be considered of utmost importance for the future of infection control and mitigating the global burden of drug-resistant pathogens.

keywords: Whole Genome Sequencing; Artificial Intelligence; Machine Learning; Antimicrobial Resistance

PAI-5

Integrative Systems Biology Analysis of Gene Expression Reveals Metabolic Pathway Alterations in Breast Cancer

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Background and aim: breast cancer (BC) progression is accompanied by extensive molecular and metabolic alterations that influence tumor growth and therapeutic response. Dysregulation of energy and lipid metabolism has been shown to play a key role in tumor biology. This study aimed to integratively analyze gene expression profiles from multiple microarray datasets to identify differentially expressed genes and altered metabolic pathways in breast cancer.

Methods: Two publicly available microarray datasets (GSE3744 and GSE42568), including 151 breast tumor samples and 24 normal breast tissues, were retrieved from the Gene Expression Omnibus (GEO) database. After preprocessing and normalization, batch effects between datasets were corrected using the ComBat algorithm. Differential gene expression analysis was performed using the Limma linear modeling approach. Genes with an adjusted P-value 0.05 were considered statistically significant, and genes with an absolute log2 fold change greater than 1 were regarded as biologically meaningful. Functional enrichment analyses using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases were conducted to identify overrepresented biological processes and signaling pathways.

Results: Out of 33,520 analyzed genes, 8,281 were significantly differentially expressed between tumor and normal tissues. Among these, 728 genes were upregulated and 362 genes were downregulated in tumor samples with |log2 fold change| 1. Enrichment analyses highlighted metabolic and energy-related pathways, including the Peroxisome Proliferator-Activated Receptor (PPAR) signaling pathway, AMP-activated protein kinase (AMPK) signaling, fatty acid degradation, glycolysis/gluconeogenesis, and adipocytokine signaling. Key lipid metabolism genes such as PPARG, FABP4, CD36, and LPL showed significant upregulation in the analyzed tumor samples, indicating metabolic reprogramming in breast cancer.

Conclusion: Overall, this integrative gene expression analysis reveals substantial alterations in metabolic pathways in breast cancer, particularly those related to lipid and energy metabolism. The enrichment of the PPAR signaling pathway suggests its potential involvement in reshaping tumor cell metabolism. These identified genes and pathways provide valuable insight into metabolic vulnerabilities and may support the development of metabolism-targeted therapeutic strategies.

keywords: Keywords: Breast cancer, Gene expression, Metabolic pathways, Bioinformatics

17th International Congress of Lab. and Clinic
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PAI-6

Advances in Artificial Intelligence for Microbiological Data Analysis

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Background and aim: Recent advances in microbiology, including whole-genome sequencing, metagenomics, MALDI-TOF mass spectrometry, and high-resolution microscopy, have generated large and complex datasets that challenge conventional analytical methods. Traditional approaches are often time-consuming and limited in handling high-dimensional data. Artificial intelligence (AI), particularly machine learning techniques, has emerged as a solution to improve data processing and interpretation. AI-based methods have shown performance in microbial identification, antimicrobial resistance prediction, and clinical diagnostics. The aim of this study is to review recent advances in AI applications for microbiological data analysis and to discuss their benefits, limitations, and future perspectives globally.

Methods: A narrative review was conducted using peer-reviewed articles published between 2020 and 2025. Relevant studies were retrieved from PubMed, ScienceDirect, and Google Scholar using keywords related to artificial intelligence, machine learning, microbiology, metagenomics, and antimicrobial resistance. Selected articles focused on AI applications in microbial genomics, metagenomics, clinical diagnostics, and antimicrobial susceptibility testing. Studies involving real-world microbiological data, including genomic sequences, microscopy images, microbiome profiles, and mass spectrometry data, were qualitatively analyzed to identify key methodologies, applications, advantages, and challenges related to data quality and implementation.

Results: The reviewed studies show that artificial intelligence significantly improves microbiological data analysis. AI-based models enhance microbial identification using genomic, metagenomic, and imaging data, especially in clinical laboratories. Several studies report effective prediction of antimicrobial resistance through machine learning applied to genomic and phenotypic data. AI-assisted analysis of MALDI-TOF mass spectrometry and microscopy images enables faster pathogen detection and shorter diagnostic turnaround times. Additionally, machine learning supports microbiome analysis and epidemiological surveillance by identifying complex patterns. However, challenges remain, including data heterogeneity, lack of standardization, and limited clinical validation.

Conclusion: Artificial intelligence is an important complementary tool in microbiological data analysis, improving accuracy, efficiency, and scalability. Its applications in genomics, clinical diagnostics, antimicrobial resistance prediction, and microbiome analysis show strong potential for advancing research and healthcare. However, challenges such as data quality, algorithm transparency, and integration into routine laboratory workflows remain. Addressing these issues through standardized data, interdisciplinary collaboration, and clinical validation is essential for the effective and responsible use of AI in microbiology.

keywords: Artificial intelligence; Microbiology; Machine learning; Antimicrobial resistance; Metagenomics

PAI-7

Applications of Artificial Intelligence in Personalized Cancer Diagnosis, Prognosis, and Treatment: A Systematic Review and Future Prospects

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Background and aim: Clinical pathology continues to be the foundation of definitive cancer diagnosis, even though cancer is one of the major causes of mortality from a global perspective. The emergence of digital pathology, in conjunction with the exponential rise in medical data, has opened the potential for the use of artificial intelligence (AI) and deep learning methods. The purpose of this systematic review is to assess the uses of AI in cancer diagnosis, prognosis, and clinical pathology, as well as the obstacles that it faces and the opportunities that lie ahead.

Methods: This study was conducted as a systematic review of the literature using the scientific databases PubMed, Scopus, and Google Scholar. Articles published between January 2020 and September 2025 were searched using the keywords “artificial intelligence”, “deep learning”, “digital pathology”, “cancer diagnosis”, “cancer prognosis”, and “precision oncology”. Eligible studies focused on the clinical application of AI in the analysis of histopathological images, genomic data, or electronic health records of cancer patients.

Results: According to the 23 included studies, AI is increasingly transforming all phases of cancer management. In diagnostic pathology, deep learning–based algorithms can detect, classify, and grade cancerous lesions (such as breast, prostate, and colorectal cancers) on digital pathology slides with accuracy comparable to or surpassing that of expert pathologists. Furthermore, AI systems can extract subtle micro-morphological features that are often imperceptible to the human eye. In prognostic applications, AI models that integrate histopathological, genomic, and clinical data provide more accurate predictions of treatment response, disease recurrence, and patient survival. In the context of personalized therapy, AI also facilitates the identification of molecular biomarkers and the prediction of responses to targeted therapies and immunotherapy.

Conclusion: Artificial intelligence has become a powerful and potentially transformative assistant in clinical pathology and oncology. AI has taken a major step towards personalized cancer medicine by increasing accuracy, efficiency, and objectivity in diagnosis. The future success of this field will depend on establishing standardized frameworks, resolving legal and ethical challenges, and effectively integrating AI models as complementary tools that augment, rather than replace, pathologists' expertise in advanced digital pathology laboratories.

keywords: Artificial intelligence, deep learning, digital pathology, cancer diagnosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-8

Evaluation of Insurance Policies Based on Diagnostic Data Using Artificial Intelligence

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Background and aim: The integration of diagnostic data into healthcare decision-making has the potential to optimize insurance policies, reduce unnecessary costs, and improve patient outcomes. Traditional approaches to insurance policy evaluation often rely on retrospective data and expert judgment, which may not fully capture complex patterns in patient diagnostics. Artificial intelligence (AI) offers advanced tools for analyzing large-scale diagnostic datasets and predicting risk, enabling evidence-based and data-driven insurance policy assessment. This study aimed to evaluate insurance policies using AI-based analysis of diagnostic data to identify opportunities for cost optimization and policy improvement.

Methods: A retrospective dataset comprising diagnostic records, claims data, and patient demographics from a national insurance database was collected. Machine learning algorithms, including random forest, gradient boosting, and neural networks, were developed to analyze patterns of healthcare utilization, predict high-cost patients, and assess the effectiveness of existing insurance policies. Model performance was evaluated using accuracy, area under the receiver operating characteristic curve (AUC), and precision-recall metrics. Policy scenarios were simulated to assess potential improvements based on AI-driven insights.

Results: AI models identified key diagnostic and demographic factors associated with high insurance costs and suboptimal coverage. Predictive analysis enabled stratification of patients by risk, revealing areas where current insurance policies may lead to overutilization or undercoverage. Simulation of policy adjustments based on AI predictions suggested potential reductions in unnecessary claims and improved alignment between coverage and patient needs. The models demonstrated high predictive performance with AUC values exceeding 0.85 across validation datasets.

Conclusion: Artificial intelligence can effectively evaluate insurance policies using diagnostic data, providing actionable insights to optimize coverage, reduce costs, and enhance healthcare delivery. Integration of AI-driven analysis into insurance decision-making has the potential to support data-informed policy reform and improve outcomes for both insurers and patients. Future work should explore real-time AI integration and longitudinal assessment of policy impact.

keywords: Artificial Intelligence; Insurance Policy Evaluation; Diagnostic Data; Machine Learning; Risk

PAI-9

Early Detection of Acute Kidney Injury Using Trend-Based Routine Biochemical Panels and Machine Learning: A Lab→Bedside Approach

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Background and aim: Acute kidney injury (AKI) is a frequent complication in hospitalized patients and often becomes clinically apparent only after significant renal function deterioration. Because early biochemical changes are subtle, reliance on single laboratory values may delay recognition. This study aimed to develop a clinically practical machine-learning model that uses temporal patterns in routine laboratory tests to enable earlier detection of AKI and support timely preventive interventions.

Methods: We performed a retrospective cohort study including adult inpatients with sequential, time-stamped laboratory measurements. Routinely available biochemical and hematological parameters—such as serum creatinine, blood urea nitrogen, electrolytes, estimated glomerular filtration rate, liver enzymes, lactate, and inflammatory indices—were extracted from the laboratory information system. Instead of isolated values, trend-based features were derived, including short-term deltas, rates of change, variability measures, and cumulative deviations over rolling 24–72 hour windows. Machine-learning models, including gradient-boosted decision trees and temporal sequence models, were trained to predict AKI onset within the subsequent 24 hours. AKI was defined according to KDIGO criteria. Model evaluation was performed using patient-level cross-validation and external validation, with an emphasis on clinically relevant metrics. Feature attribution techniques were applied to enhance interpretability and identify laboratory trends driving risk predictions.

Results: The proposed model achieved robust predictive performance, with an external validation AUC-ROC greater than 0.85 and high sensitivity at clinically acceptable alert thresholds. The system identified patients at increased risk a median of 12–24 hours before standard clinical diagnosis. Dynamic increases in creatinine, rising urea-to-creatinine ratios, electrolyte instability, and inflammatory marker trends were the strongest contributors to risk prediction. Importantly, alert frequency remained manageable, minimizing the risk of alarm fatigue.

Conclusion: Temporal machine-learning analysis of routine biochemical panels enables earlier and clinically actionable detection of AKI. This laboratory-driven, interpretable approach can be readily integrated into existing clinical workflows, helping clinicians initiate renal-protective strategies sooner and improving patient outcomes.

keywords: Acute kidney injury; Machine learning; Laboratory medicine; Trend analysis; Clinical

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-10

Automated Detection of Opportunistic Parasitic Infections Using Deep Learning in Immunocompromised Patients

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Background and aim: Immunocompromised patients, including individuals with HIV/AIDS, organ transplant recipients, and patients undergoing immunosuppressive therapies, are at increased risk of opportunistic parasitic infections. Early and accurate diagnosis is critical to reducing morbidity and mortality in these vulnerable populations. Conventional diagnostic methods, such as microscopy and antigen-based assays, are labor-intensive, time-consuming, and highly dependent on expert interpretation. Recent advances in deep learning offer promising tools for automated image analysis and pattern recognition, potentially enhancing the detection of opportunistic parasites. This study aimed to evaluate the application of deep learning techniques for the automated diagnosis of opportunistic parasitic infections in immunocompromised patients.

Methods: Microscopic images obtained from stool and tissue samples of immunocompromised patients were used to develop deep learning–based classification models. Convolutional neural networks (CNNs) were trained to identify common opportunistic parasites, including Cryptosporidium spp., Cystoisospora belli, Cyclospora cayetanensis and Toxoplasma gondii. The dataset was divided into training, validation, and testing sets. Model performance was evaluated using accuracy, sensitivity, specificity, precision, and the area under the receiver operating characteristic curve (AUC). Model interpretability was assessed using visualization techniques such as Grad-CAM.

Results: The deep learning models demonstrated high diagnostic performance in distinguishing parasitized from non-parasitized samples. CNN-based classifiers achieved high accuracy and AUC values across multiple opportunistic parasites. The automated approach reduced inter-observer variability and showed consistent performance across different staining methods. Visualization analyses highlighted parasite-specific features used by the models for classification, supporting their interpretability and clinical relevance.

Conclusion: Deep learning–based automated detection systems offer a reliable and efficient approach for diagnosing opportunistic parasitic infections in immunocompromised patients. These tools have the potential to support clinical decision-making, reduce diagnostic delays, and improve patient outcomes. Integration of deep learning models into routine diagnostic workflows may enhance the accuracy and accessibility of parasitological diagnostics in high-risk patient populations.

keywords: Deep Learning; Opportunistic Parasites; Immunocompromised Patients; Automated Diagnosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-11

Application of Artificial Intelligence in Assessing the Risk of Parasitic Diseases among Afghan Migrants Living in Iran

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Background and aim: Human migration is a key determinant in the epidemiology of parasitic diseases, particularly in regions experiencing large-scale population movements. Iran hosts a substantial population of Afghan migrants, many of whom originate from areas endemic for various parasitic infections. Traditional surveillance systems often face challenges in timely risk assessment due to heterogeneous data sources and complex interactions between demographic, environmental, and socio-economic factors. Artificial intelligence(AI) offers advanced tools to integrate diverse datasets and improve risk prediction for parasitic diseases in migrant populations. This study aimed to evaluate the application of AI-based-models in assessing the risk of parasitic infections among Afghan migrants(live-in-Iran).

Methods: Demographic, clinical, and epidemiological data of Afghan migrants were combined with environmental and spatial variables obtained from national surveillance systems and public health records. Machine learning algorithms, including logistic regression, random forest, and gradient boosting models, were developed to estimate the risk of parasitic diseases. Model performance was assessed using accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC). Feature importance analysis was conducted to identify key predictors associated with infection risk.

Results: AI-based models demonstrated improved predictive performance compared to conventional statistical approaches. Ensemble learning methods achieved the highest AUC values for identifying individuals and communities at increased risk of parasitic infections. Key risk factors identified included duration of residence in Iran, living conditions, access to sanitation, region of origin, and proximity to endemic areas. The models enabled stratification of migrant populations into different risk categories, facilitating targeted screening and intervention strategies.

Conclusion: Artificial intelligence provides an effective approach for assessing the risk of parasitic diseases among Afghan migrants living in Iran. AI-driven risk models can support early detection, optimize screening programs, and enhance public health decision-making. Integrating AI into migrant health surveillance systems may contribute to more efficient and equitable control of parasitic diseases in host communities.

keywords: Artificial Intelligence; Parasitic Diseases; Migration; Afghan Migrants; Machine Learning

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-12

Classification of Stroke and Recurrent Stroke Risk Using Irregular Fuzzy Cellular Automata: A Five-Year Analysis of Hospital Data in Ahvaz

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Background and aim: Stroke stands as the second leading cause of death globally, presenting a major public health challenge that necessitates precise predictive tools for preventing both primary and recurrent incidents. This study aimed to develop a novel explanatory classification method for stroke and recurrent stroke risk using Irregular Fuzzy Cellular Automata (FICA).

Methods: In a retrospective descriptive-analytical study, we analyzed the epidemiological data of 384 patients admitted to the neurology wards of teaching hospitals affiliated with Ahvaz Jundishapur University of Medical Sciences, Iran, from 2019 to 2024. Patients were selected based on a definitive diagnosis confirmed by clinical symptoms and CT scan imaging. The data were pre-processed using SPSS software. Key variables included age (mean 66.58 ± 14.31 years), gender (55.2% male), hypertension (68%), diabetes (42.4%), dyslipidemia (19%), history of myocardial infarction (34.1%), previous stroke (26.3%), family history (43.5%), and low physical activity (95.1%).

Results: Our FICA model represented the data as an irregular graph and classified risk into low, medium, and high levels using fuzzy rules and the centroid defuzzification method. The FICA-RISK algorithm, which incorporates voting, classification, and update steps, achieved an accuracy of 92.3% for primary stroke risk (AUC-ROC=0.95) and 88.7% for recurrent stroke (AUC-ROC=0.92). These results surpassed those of logistic regression (85.6%) and neural networks (89.2%). Statistical analysis revealed significant associations, such as between age and diabetes (P=0.002) and family history with recurrent stroke (P=0.001).

Conclusion: By managing the uncertainty inherent effectively in medical data, our recommended model provides a valuable tool for personalized prediction and preventive interventions in similar populations, having the potential to reduce the burden of stroke.

keywords: Stroke; Irregular Fuzzy Cellular Automata; Epidemiology; Predictive Modeling

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-13

Integrated Bioinformatics and Machine Learning Approaches for the Identification of Dysregulated miRNA Biomarkers in Lung Cancer

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Background and aim: Lung cancer, a leading global cause of cancer mortality, demands innovative strategies for early detection and treatment. This study integrates bioinformatics and machine learning to analyze RNA sequencing data from the GEO dataset GSE164174, identifying dysregulated microRNAs (miRNAs) in lung carcinogenesis.

Methods: Our materials and methods (~500 words) detail data preprocessing, differential expression analysis, and model development using 50 lung cancer and 30 normal tissue samples.

Results: Differential expression analysis revealed 2,565 significantly altered miRNAs, including hsa-miR-4481 (upregulated, logFC = 2.23) and hsa-miR-5100 (downregulated, logFC = -3.91). Pathway enrichment highlighted miRNA-mediated mRNA destabilization (GO:0035279, p = 4.20E-63) as a key mechanism driving tumor progression. Machine learning models, notably random forests, achieved high diagnostic accuracy (AUC 0.90) for top miRNAs, underscoring their potential as non-invasive biomarkers. Results (~700 words) demonstrate that upregulated miRNAs like hsa-miR-4481 correlate with oncogenic pathways such as PI3K/Akt, while downregulated miRNAs like hsa-miR-5100 suggest tumor-suppressive roles.

Conclusion: The discussion (~1000 words) compares these findings with existing lung cancer literature, emphasizing clinical implications for early detection via liquid biopsies and personalized therapies. This study bridges computational insights with biological mechanisms, offering a framework for advancing lung cancer diagnostics and therapeutics. By identifying actionable miRNA targets, we contribute to precision oncology, aiming to improve survival rates and patient outcomes in this devastating disease.

keywords: Lung cancer, microRNAs (miRNAs), Bioinformatics, Machine learning, Biomarker discovery, Precision

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-14

Artificial Intelligence for Predicting Antimicrobial Resistance from Genomic Data: Current Advances, Challenges, and Future Perspectives

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Background and aim: AMR is one of the significant problems associated with global health and imposes huge burdens on health and economies all over the world. Antimicrobial susceptibility testing in the conventional sense involves culture and may be lengthy, reducing its usefulness for making quick decisions. In the era of genome sequence analysis, the identification of complete genomes has become possible; nonetheless, it is difficult to interpret genetic characteristics and translate them into accurate resistance phenotypes. AI and ML provide novel means to bridge the genotypic to phenotypic gap. The goal of this narrative review is to provide updates regarding advancements, applications, barriers,

Methods: A narrative review was performed based on fifteen seminal articles on the use of artificial intelligence for antimicrobial resistance prediction in the genomic era that have been published from 2018 to 2025. The reviewed literature comprised original research articles and methodology studies related to topics such as whole genome sequencing, metagenomics, machine learning, deep learning, graph neural network, and genotype-to-phenotype prediction. The studies were critically analyzed in terms of genomic feature extraction techniques, which involved antimicrobial resistance genes, single nucleotide polymorphism, pangenome, mobile genetic elements, and k-mers. Computational tools used included random forest, XGBoost, support vector machine, set covering machine, deep neural network, and graph neural network. Issues such as model performance, model interpretation, minimum inhibitory concentration prediction, biomarker identification, clinical translation, validation methods, and limitations of the current research were taken into account in this analysis.

Results: From the reviewed literature, it was found that machine learning models have been shown to predict both the antimicrobial resistance phenotype and the minimum inhibitory concentration using genomics alone. Some of the machine learning models that showed high predictive performance in this context include random forest, XGBoost, and set covering machines. Deep learning models improved on the detection of complex genomic patterns as well as the identification of the resistome at scale. The use of graph neural networks for machine learning helped improve prediction accuracy through consideration of the interaction among genes, mutations, and pathways. Novel biomarkers for resistance beyond known antimicrobial resistance genes were successfully identified in some studies. There is still need for improvement in various aspects such as dataset bias, population stratification, class imbalance, and model interpretability, among others.

Conclusion: Genomic prediction of antimicrobial resistance using artificial intelligence has become a revolutionary strategy, enabling faster and more efficient methods than traditional approaches. The latest studies have provided proof of improved performance of AI models in the prediction of resistance, biomarker identification, and targeted antimicrobials. However, problems related to the quality of data, generalizability, interpretability, and validation remain major challenges for the widespread use of these solutions. Future success in this sphere will require the introduction of such technologies as explainable AI, graph neural networks, multi-omics approaches, foundation models, and benchmark

keywords: Artificial Intelligence; Antimicrobial Resistance; Whole-Genome Sequencing; Machine Learning; Genomic Prediction

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-15

The Application of Convolutional Neural Networks in Diagnosing Cutaneous Fungal Infections: A Systematic Review of Diagnostic Accuracy

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Background and aim: Cutaneous fungal infections are prevalent worldwide, posing diagnostic challenges in clinical and laboratory settings. These infections, including tinea infections, onychomycosis, and fungal keratitis, often rely on conventional methods like potassium hydroxide (KOH) examinations, microscopy, and culture, which can be time-consuming, resource-intensive, and subject to human error. Recent advancements in artificial intelligence, particularly convolutional neural networks (CNNs), have revolutionized the field of dermatology by providing automated, accurate, and real-time diagnostic tools. This systematic review explored the application, efficacy, and diagnostic performance of CNN-based models for identifying and classifying cutaneous fungal infections.

Methods: A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science databases to identify studies applying CNNs for diagnosing cutaneous fungal infections using keywords such as "convolutional neural networks", "cutaneous fungal infections", "deep learning", "diagnosis", "artificial intelligence" and related MeSH terms. Inclusion criteria were studies published in peer-reviewed journals, focusing on CNN-based approaches for fungal skin, nail, or corneal diseases. Seven studies were included after assessing quality using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) for diagnostic studies and the PROBAST tool for AI-related methodologies.

Results: The included studies demonstrated high diagnostic performance of CNNs in detecting cutaneous fungal infections. Reported accuracy ranged from 88.1% to 99.95% across various datasets, with sensitivity values between 70.2% and 99% and specificity ranging from 72.7% to 100%. Models applied to microscopic images achieved mean accuracy rates of 88.10% and 88.78%, outperforming dermatologists with an accuracy of 74.53% (p 0.0001). Sensitivity and specificity for these models reached 75.04% and 93.78%, respectively. In the diagnosis of fungal keratitis, CNN frameworks achieved near-perfect accuracy, with values as high as 99.95%, while improving real-time diagnostic performance. For dermoscopic and clinical image-based diagnosis of onychomycosis, CNN models demonstrated sensitivity of 70.2% and specificity of 72.7%, achieving comparable accuracy to dermoscopic examination (AUC = 0.751). Overall, the included studies highlighted CNN models' ability to provide superior accuracy, sensitivity, and specificity compared to conventional methods, including dermatological assessments.

Conclusion: CNN-based models have shown significant potential in accurately diagnosing cutaneous fungal infections, including tinea infections, onychomycosis, and fungal keratitis, using clinical, dermoscopic, and microscopic images. These models achieve superior diagnostic performance compared to conventional methods and, in many cases, outperform dermatologists in accuracy and specificity. Despite these promising results, large-scale, multicenter studies are required to validate CNN performance further and facilitate its clinical integration.

keywords: Convolutional Neural Networks; Deep Learning; Cutaneous Fungal Infections; Tinea; Onychomycosis

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PAI-16

AI-Driven QSAR Modeling and Virtual Screening for Identification of Potential JAK1 Inhibitors

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Background and aim: Inflammatory diseases are a broad group of chronic conditions that significantly impact patient quality of life. Janus kinase 1 (JAK1) has emerged as a key therapeutic target due to its central role in inflammatory signaling pathways. Identification of novel or repurposed inhibitors of JAK1 can facilitate the development of more effective treatments. Artificial intelligence (AI)-driven Quantitative Structure-Activity Relationship (QSAR) modeling has shown promise as a computational approach to predict biological activity based on molecular structure. This study aimed to develop and apply an AI-based QSAR model to identify potential small-molecule inhibitors of JAK1.

Methods: Approximately 9,000 small-molecule compounds with reported JAK1 inhibitory activity were retrieved from the ChEMBL database, focusing on human JAK1-specific binding and functional assays with high confidence annotations. Compounds were categorized based on half-maximal inhibitory concentration (IC_{50}) values as active (IC_{50} 1,000 nM) or inactive (IC_{50} 10,000 nM), while intermediate compounds (IC_{50} between 1,000 and 10,000 nM) were excluded to reduce noise and improve model robustness. IC_{50} values were transformed into pIC_{50} values for regression analysis. Physicochemical properties were calculated according to Lipinski's rule of five, and molecular descriptors were generated using PaDEL-Descriptor software. A QSAR model was constructed using Random Forest regression to predict pIC_{50} values from molecular descriptors, integrating AI-based learning to capture complex structure-activity relationships. Model performance was evaluated using a hold-out test set and cross-validation. The validated model was subsequently applied to an external drug dataset for virtual screening and potential drug repurposing.

Results: The Random Forest model demonstrated strong predictive performance, achieving a coefficient of determination (R^2) of 0.89 on validation data. Virtual screening identified Daptomycin as one of the top-ranked compounds with a predicted pIC50 value of 7.52, identifying it as a candidate for further experimental evaluation as a potential JAK1 inhibitor. Daptomycin is a widely available and cost-effective drug, and its predicted activity suggests potential off-target interactions with JAK1.

Conclusion: These findings indicate that AI- QSAR modeling allows prioritization of existing drug for JAK1 inhibition, representing a novel computational approach in this context. The identification of Daptomycin as a candidate for further experimental evaluation as a potential JAK1 inhibitor may reflect previously unrecognized off-target kinase interactions, highlighting the utility of computational screening approaches. However, experimental validation through in vitro and in vivo studies is required to confirm the predicted activity. Overall, this study demonstrates that integrating of AI and QSAR methodologies can accelerate early-stages drug discovery and support the identification

keywords: Inflammatory diseases, QSAR modeling , Artificial intelligence, Daptomycin

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PAI-17

Identification of a Transcriptional Signature Linked to Bone Marrow-Derived Mesenchymal Stem Cell-Mediated Metastatic Progression in Breast Cancer

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Background and aim: Bone marrow-derived mesenchymal stem cells (BM-MSCs) are an important component of the breast tumor microenvironment. It has previously shown that BM-MSCs promote metastatic progression by generating reversible phenotypic alterations in cancer cells. Being aware of molecular changes during metastasis mediated by BM-MSCs can help to understand mechanisms of breast cancer progression and to locate potential therapeutic targets.

Methods: Gene expression profiles of human breast tumor samples from the Gene Expression Omnibus (GEO) dataset GSE8977 were examined using Python-based bioinformatics methods. Boxplots and density plots were used for quality control of the normalized expression data (22,880 genes) to examine data distribution and normalization consistency across samples. Sample clustering and transcriptional differences across experimental groups were assessed by principal component analysis (PCA).

Results: Differential expression analysis was applied using adjusted p-value and log2 fold-change thresholds of 0.05 and $|\log2FC| \geq 1$ respectively. Using volcano plots and heatmaps, pointed out 572 significantly different genes (DEGs), including 316 upregulated and 256 downregulated genes. GPM6B was the most significant DEG and COL11A1 had the highest fold change. Quality control studies showed similar expression patterns. Conclusion: Integrated analysis of GSE8977 identified a specific transcriptional signature associated with the effect of bone marrow generated mesenchymal stem cells on breast cancer progression.

Conclusion: The detected DEGs give insight into the molecular mechanisms of tumor microenvironment contribution to metastatic dissemination and are potential biomarkers and therapeutic targets for metastatic breast cancer.

keywords: Python, Bioinformatics, Breast cancer, gene expression

PBa-1

Epidemiologic investigation of Human Immunodeficiency Virus and Tuberculosis co-infection in Golestan province, Iran

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Background and aim: Tuberculosis (TB) is the most common opportunistic infection in people with Human Immunodeficiency Virus (HIV). Although anti-TB drugs effectively cure TB, treatment failure and mortality remain high in TB/HIV co-infected patients. This study aimed to estimate the epidemiological characteristics of TB/HIV co-infection in Golestan Province, Iran.

Methods: Demographic and clinical data from TB cases referred to the Golestan province Regional Reference Tuberculosis Laboratory between 2013 and 2020 were analyzed. Drug susceptibility testing for rifampicin, isoniazid, ethambutol, and streptomycin was performed using the proportion method on Lowenstein–Jensen media.

Results: Of 495 individuals diagnosed with TB, 7 (1.4%) had TB/HIV co-infection. Among these co-infected cases, all were male, with an average age of 38 ± 8.2 years. Six (85.6%) were Iranian and one (14.3%) was from Afghanistan. All co-infected patients were susceptible to anti-TB drugs; however, one patient (14.3%) experienced treatment failure, and one (14.3%) died during anti-TB treatment.

Conclusion: To accelerate treatment and reduce transmission, it is crucial to integrate HIV and TB control programs to minimize diagnostic delays and improve early case detection. Therefore, regular screening programs and linkage to care for HIV patients require special attention. Further investigation with a larger sample size is recommended to determine the epidemiologic characteristics of TB/HIV co-infected cases.

keywords: Mycobacterium tuberculosis, Tuberculosis, Human Immunodeficiency Virus, Golestan Province

PBa-2

Antimicrobial resistance of pathogens causing bloodstream infections: Emergence of a major challenge in the medical field

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Background and aim: Among the hospital-acquired infections (HAI). Bloodstream infections (BSIs) are among the most serious HAI. Antibiotics are the drug choice for bloodstream infections. Nowadays, overuse and misuse of antibiotics lead to the emergence of drug resistance in bacteria, especially in hospitals. For this reason, this study aimed to assess the frequency and antibiotic resistance pattern of bacteria isolated from BSIs at Imam Khomeini Hospital in Ardabil city in 2024.

Methods: This cross-sectional study was conducted at Imam Khomeini Hospital in 2024. Blood samples were collected from patients suspected of BSIs and cultured on Castellani's biphasic medium. Bacterial identification was performed using biochemical tests and Gram staining. Antibiotic susceptibility patterns were determined by the Agar disk diffusion method according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. The results were analyzed to determine the frequency and resistance patterns of bacterial isolates.

Results: Out of 186 positive blood cultures, the most frequently isolated bacteria were Staphylococcus species (44.1%), including 22 Staphylococcus aureus and 60 coagulase-negative Staphylococci (CoNS), followed by Escherichia coli (22.6%), Klebsiella pneumoniae (12.9%), Acinetobacter baumannii (7.5%), Enterococcus faecalis (9.6%), and Citrobacter freundii (3.2%). Antibiotic susceptibility testing revealed high resistance of CoNS and S. aureus to penicillin (90% and 100%, respectively), while meropenem remained the most effective agent. E. coli showed the highest resistance to ampicillin (71.4%), and K. pneumoniae to ampicillin (75%). A. baumannii displayed extensive resistance to multiple antibiotics (85.7%) but retained partial susceptibility to meropenem and piperacillin/tazobactam (28.5%). C. freundii remained fully susceptible to meropenem and ceftazidime. Overall, 48.3% of isolates were multidrug-resistant (MDR), including 63.6% of S. aureus, 77.7% of E. faecalis, 71.4% of E. coli, 75% of K. pneumoniae, and 100% of A. baumannii. No MDR strains were detected among CoNS or C. freundii.

Conclusion: our results revealed that Staphylococcus spp. were the most frequent pathogens causing BSIs. High resistance was observed to commonly used antibiotics such as ampicillin and trimethoprim-sulfamethoxazole, while meropenem and piperacillin/tazobactam remained more effective. The notable prevalence of multidrug-resistant strains highlights the need for strict antibiotic stewardship, ongoing resistance surveillance, and robust infection control measures in hospitals.

keywords: Bloodstream infection, drug resistance, Disk diffusion, Antibiotic

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-3

Antibiotic Resistance Patterns of Bacterial Pathogens Causing Bloodstream Infections in Northern Iran: A Three-Year Retrospective Study (2021–2024)

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Background and aim: Background: Bloodstream infections (BSIs) are life-threatening conditions with increasing antimicrobial resistance (AMR) in low- and middle-income countries. Local surveillance data are essential to guide empirical therapy and antimicrobial stewardship. Aim: To determine the microbial etiology and current antibiotic resistance patterns of BSIs in two tertiary hospitals in northern Iran over a three-year period (March 2021–March 2024).

Methods: A three-year retrospective study was conducted on 792 non-duplicate positive blood cultures collected from March 2021 to March 2024 at Bou-Ali Sina Hospital and Razi Hospital. Bacterial identification and antimicrobial susceptibility testing were performed using standard microbiological techniques and the Kirby–Bauer disk diffusion method, interpreted according to CLSI 2023 guidelines. CoNS were considered true pathogens only if isolated from ≥2 separate bottles or in patients with intravascular devices and clinical signs of sepsis.

Results: Gram-positive bacteria predominated, with coagulase-negative staphylococci (CoNS) being the leading pathogens (340/792, 42.9%; S. epidermidis 37.5%). Among Gram-negatives (45%), Pseudomonas aeruginosa (11.1%), Enterobacter spp. (10.2%), Klebsiella spp. (9.2%), and Escherichia coli (9.0%) were most common. Resistance rates were alarmingly high: MRSA 58.8%, oxacillin-resistant CoNS 25.3%, MDR Enterobacterales 71.3%, MDR P. aeruginosa 59.1%, and MDR Acinetobacter spp. 88.9%. Amikacin showed the best activity against Gram-negatives (resistance 15.8–26.1%)

Conclusion: In northern Iran, device-associated BSIs caused by resistant staphylococci and MDR Gram-negative bacilli predominate. Third-generation cephalosporins are no longer suitable for empirical monotherapy. Vancomycin plus amikacin (with or without piperacillin-tazobactam/carbapenem) is recommended as initial therapy for suspected healthcare-associated BSIs pending susceptibility results.

keywords: Bloodstream infection, antimicrobial resistance, coagulase-negative staphylococci, multidrug-resistant Gram-negative bacteria, antimicrobial

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-4

The Role of crusial Genes in the multiplication Cycle, Immune Evasion, and Development of Novel Treatments in Intracellular Bacteria Chlamydia: A Focus on Chlamydia trachomatis

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Background and aim: Chlamydia species are known to cause significant health challenges in humans, including respiratory tract infections and sexually transmitted diseases. Among these, Chlamydia trachomatis (C. trachomatis) is one of the most prevalent sexually transmitted pathogens worldwide. Although C. trachomatis exhibits minimal documented antibiotic resistance, the development of advanced therapeutic strategies, such as peptide-based drugs and vaccines, presents promising avenues for mitigating resistance and enhancing treatment outcomes.

Methods: This study investigated the role of key genes involved in Chlamydia biology, including TNT, FtsK, Euo, and ClpX, through a comprehensive review of scientific literature from reputable databases, such as Google Scholar. Diagnostic methods such as polymerase chain reaction (PCR), ligase chain reaction (LCR), and nucleic acid sequence-based amplification (NASBA) were highlighted for their accuracy in detecting pathogenic factors such as the type III secretion system (T3SS).

Results: The analysis demonstrated that Chlamydia possesses sophisticated immune evasion mechanisms by targeting neutrophils, dendritic cells, and macrophages. The reproductive cycle of C. trachomatis and its genetic components were found to be intricately linked to its pathogenicity. Furthermore, understanding immune evasion strategies and key genes related to the bacterial lifecycle provides valuable insights into disease progression and potential therapeutic targets.

Conclusion: Therefore, effective strategies for the prevention and management of chlamydial infections are crucial. This study investigates the defense mechanisms employed by C. trachomatis to evade the human immune system as well as its replication cycle. Furthermore, this study explores the potential of novel antibiotic- and peptide-based therapies to address the emerging issue of antibiotic resistance in C. trachomatis. By understanding the intricate mechanisms of chlamydial pathogenesis, this study aims to facilitate the development of more effective treatment options. This study also discussed how preventive medicine measures could help interrupt transmission

keywords: Chlamydia trachomatis, Immune evasion, Antibiotic therapy, Virulence gene

PBa-5

High Prevalence of Multidrug-Resistant Uropathogenic Escherichia coli with Marked Gender-Associated Resistance Patterns: A Retrospective Study from Northern Iran

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Background and aim: Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, with Escherichia coli (E. coli) accounting for up to 90% of cases. Risk factors include anatomical differences, poor hygiene, pregnancy, urinary obstruction, catheter use, urethral reflux, and spermicidal contraceptives. Common empiric treatments include amoxicillin, ciprofloxacin, amoxicillin/clavulanic acid, nitrofurantoin, and trimethoprim, but increasing antimicrobial resistance (AMR) complicates therapy. This study aimed to evaluate in vitro resistance patterns of common antimicrobials against uropathogenic E. coli and assess trends over time to inform empiric treatment strategies.

Methods: This retrospective, record-based study analyzed culture and sensitivity (C/S) reports of urine samples from inpatients at hospitals in Sari, Iran, from March 2021 to the end of 2022. Ethical approval and laboratory permission were obtained. E. coli was identified using standard microbiological and biochemical methods. Antimicrobial susceptibility testing used the Kirby-Bauer disk diffusion method on Mueller-Hinton agar per CLSI 2021 guidelines, testing penicillins, cephalosporins, quinolones, aminoglycosides, sulfonamides, carbapenems, and nitrofurantoin. Data were compiled year-wise, with statistical analysis via IBM SPSS version 20.

Results: Of 1,804 E. coli-positive isolates, 64.7% were from females and 35.3% from males; age was recorded for 1,627 patients, with 41-60 years most frequent (33.3%). Highest susceptibility was to amikacin (92.0%), nitrofurantoin (83.7%), and gentamicin (80.3%); highest resistance to ampicillin (93.4%), ceftriaxone (66.1%), ciprofloxacin (63.9%), cefotaxime (63.8%), and cotrimoxazole (62.4%). Resistance was significantly higher in females for most agents, including ciprofloxacin (78.0% vs. 36.8%) and nitrofurantoin (84.4% vs. 3.0%, p=0.027). Over 70% of isolates were MDR. Intermediate susceptibility was low (0.0-3.2%). Highest resistance rates occurred in patients with 7-10 day hospital stays.

Conclusion: Monitoring antibiotic resistance is crucial in combating AMR. E. coli isolates from UTIs highlighted the greatest sensitivity to amikacin and nitrofurantoin, while exhibiting the most resistance to ampicillin. A higher incidence of resistant strains was found in females than in males, indicating that antibiotic treatments should be customized according to patient characteristics, such as sex, age, existing health conditions, and prior antibiotic use. Future prospective studies incorporating detailed clinical data, molecular characterization of resistance mechanisms, and community-based sampling are required to refine personalized treatment strategies.

keywords: Uropathogenic Escherichia coli, Antimicrobial resistance, Multidrug-resistant

PBa-6

Evaluation of Phage-Induced Degradation of the Extracellular Polymeric Substance Matrix in Chronic Prosthetic Joint Infections

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Background and aim: Chronic prosthetic joint infections (PJIs) are challenging to eradicate due to biofilms composed of extracellular polymeric substances (EPS), which protect bacterial communities and harbor dormant persister cells. This study systematically evaluated biofilm architecture, regulatory mechanisms, and therapeutic strategies targeting chronic PJI biofilms

Methods: Methods: A systematic literature review was conducted using PubMed, Scopus, and Web of Science for articles published from 2020 to 2025. Keywords included “prosthetic joint infection,” “biofilm,” “extracellular polymeric substance,” “phage therapy,” “DNase,” “antibiotics,” and “persister cells.” Data on biofilm structure, regulatory pathways (RsmA, quorum sensing, two-component systems), persister cell characteristics, and therapeutic interventions were extracted. Quantitative outcomes were integrated using a predictive PAN model to assess synergistic effects of combined therapies. The review adhered to PRISMA guidelines.

Results: Results: PJI biofilms exhibited onion-like stratified structures with interspersed channels. Persister cells demonstrated ~95% ATP reduction. Therapeutic evaluation indicated complete Varidase activity, AZM at 1/256 MIC reduced viability, and bacteriophage at 5.8 log PFU further decreased biofilm populations. PAN modeling predicted 99.8% eradication with a combined phage × DNase × AZM strategy.

Conclusion: Multi-modal therapies targeting both EPS matrices and persister cells provide near-complete eradication of chronic PJI biofilms, offering a quantitative framework for rational design of anti-biofilm strategies.

keywords: Prosthetic joint infection, Biofilm, Extracellular polymeric substance, Phage therapy, DNase

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-7

Identification of novel antimicrobial peptide from Asian sea bass (Lates calcarifer) by in silico and activity characterization

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Background and aim: The global crisis of antibiotic resistance increases the demand for the new promising alternative drugs such as antimicrobial peptides (AMPs). Accordingly, we have described a new, previously unrecognized effective AMP, named dicentracin-like, from Asian sea bass and characterized its antimicrobial activity by comparison with moronecidin

Methods: Researchers initiated an in silico search using the conserved signal peptide of moronecidin as a query in BLASTP against Asian sea bass databases, identifying dicentracin-like (XM_018688317.1), followed by sequence analysis with tools like ORF finder, SignalP, CAMP, and ProtParam to predict its structure, motifs, and physicochemical properties such as charge (+6), hydrophobicity, and amphipathicity. The gene was cloned from fish tissue RNA via RT-PCR, sequenced after insertion into pET28b vector, and its expression confirmed in immune tissues (e.g., head kidney, skin) by semi-quantitative RT-PCR using EF1 as control. Peptides were chemically synthesized (Fmoc method, 95% purity), and antimicrobial properties assessed through MIC broth microdilution against Gram-positive/negative bacteria and yeasts, time-kill kinetics, binding affinity via fluorometric ELISA (5-FAM labeled), antibiofilm/antibiofilm assays (crystal violet), salt/pH effects, and hemolytic activity on human RBCs. All experiments followed ethical guidelines and used statistical analysis (ANOVA, p0.05).

Results: Moronecidin and dicentracin-like exhibited a higher antibacterial activity against gram-positive bacteria relative to gram-negative ones, while both peptides showed a greater binding ability to gram-negative bacteria compared to gram-positive ones. This contradiction between antibacterial activity and binding affinity may be related to the outer membrane from gram-negative bacteria. Compared with moronecidin, dicentracin-like peptide showed more potent binding ability to all gram-positive and gram-negative bacteria. In addition, dicentracin-like peptide exhibited a high antibacterial activity against the investigated microorganisms, except against Staphylococcus aureus. A direct relationship was found between the binding affinity/cationicity and the antibiofilm activity of the peptides wherein an elevation in pH corresponded to a decrease in their antibiofilm property.

Conclusion: In the present study, In Silico comparative sequence analysis and antimicrobial characterization led to identify a new, previously unrecognized antimicrobial function for named dicentracin-like peptide by comparison with moronecidin, representing a possible template for designing new effective AMPs and improving known ones.

keywords: antimicrobial peptide, in silico, antibiotic resistance

PBa-8

Staphylococcus haemolyticus: Tackling Multidrug Resistance and Biofilm Hurdles – Advances in Antimicrobial Strategies

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Background and aim: Staphylococcus haemolyticus, an emerging coagulase-negative staphylococcus (CoNS), drives hospital-acquired infections (HAIs) in immunocompromised patients and those with indwelling devices, fueled by its multidrug resistance (MDR) and robust biofilm formation. Despite its clinical significance, S. haemolyticus remains understudied compared to other staphylococci.

Methods: A systematic literature review was conducted using PubMed and Google Scholar from 2020 to 2025. Keywords included Staphylococcus haemolyticus AND (multidrug resistance OR biofilm OR phage therapy OR 'antimicrobial peptides). The inclusion criteria comprised peer-reviewed articles on mechanisms, epidemiology, or therapies in humans and animals. The initial search yielded 1,247 hits; after the removal of duplicates (n=312) and title/abstract screening, 156 full texts were assessed.

Results: S. haemolyticus exhibits multidrug resistance primarily through mecA-mediated methicillin resistance and horizontal gene transfer (HGT). Biofilm formation enhances antibiotic tolerance and immune evasion. Key virulence factors, including surface proteins and phenol-soluble modulins, contribute significantly to its pathogenesis. Novel therapeutic approaches, such as antimicrobial peptides and bacteriophage therapy, demonstrate promising efficacy against MDR strains in preclinical studies.

Conclusion: : This review highlights S. haemolyticus as an underestimated threat in HAIs, emphasizing the need for targeted therapies and advanced diagnostics. Future research should focus on clinical trials for novel antimicrobials, global epidemiology, and omics-driven drug discovery to combat this resilient pathogen.

keywords: Staphylococcus haemolyticus, Multidrug Resistance, Biofilm, Antimicrobial Peptides, Phage Therapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-9

In vitro evaluation of chlorhexidine-EDTA combination against gram-negative bacilli isolated from hemodialysis patients with catheter-related bloodstream infections

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Background and aim: Catheter-related bloodstream infections are a significant source of morbidity and mortality in the end-stage renal disease population, particularly those receiving hemodialysis (HD). The aim of this study is to evaluate the in vitro synergistic activity of chlorhexidine and EDTA against Gram-negative bacilli isolated from hemodialysis patients with catheter-related bloodstream infections (CRBSIs), in order to explore their potential role in improving catheter care and infection control strategies.

Methods: Patients undergoing hemodialysis with temporary or permanent catheters at the dialysis units of Velayat and Bouali Teaching Hospitals, Qazvin, Iran, from December 2023 to November 2024, were enrolled in this study. Blood and catheter tip cultures were analyzed, and antibiotic susceptibility was tested using the disk diffusion method (CLSI 2025). Biofilm formation was assessed via the crystal violet microtiter plate assay. The antibacterial activities of chlorhexidine, EDTA, and their combination were evaluated using the broth microdilution method to determine the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC).

Results: Of the 120 hemodialysis patients studied, 61.7% developed catheter-related bloodstream infections (CRBSIs), with 52.7% caused by Gram-negative bacteria and 54.05% were due to Gram-positive organisms. Klebsiella pneumoniae (53.8%) and Pseudomonas aeruginosa (23.1%) were the most prevalent Gram-negative pathogens. Among these isolates, 59% were multidrug-resistant, and 69.2% exhibited strong biofilm-forming ability. The MIC_{90} of chlorhexidine alone was 0.03%, which significantly decreased to 0.004% when combined with EDTA, indicating enhanced antibacterial activity (p 0.05).

Conclusion: Chlorhexidine–EDTA showed strong in vitro activity against MDR Gram-negative bacilli from catheter infections in hemodialysis patients, suggesting its potential as a cost-effective disinfectant. However, invivo studies are required to confirm its clinical applicability.

keywords: Catheter-related bloodstream infection, Hemodialysis, Nosocomial infections, gram-negative bacilli, Multidrug-resistant

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-10

Investigating the Antimicrobial Peptide Production, Anti-biofilm, and Anti-adhesion Activities of Indigenous Probiotic Lactobacillus Strains Against Bacterial Isolates from Burn Wounds and Diabetic Foot Ulcers

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Background and aim: The increasing incidence of antibiotic-resistant bacterial infections, especially in burn wounds and diabetic foot ulcers, has created a significant challenge in clinical treatments. Accordingly, the use of probiotics and their supernatants (postbiotics), as non-chemical agents with minimal toxicity and side effects, is considered a new approach to control pathogens and reduce the problems caused by antibiotic resistance, among which lactobacilli can be mentioned. Therefore, considering the importance of controlling infectious skin diseases and also considering that the genetics of pathogens, like climate, vary from one region to another, regional studies can significantly contribute to improving the quality of medical services.

Methods: This study was conducted with a total of 95 isolates from wounds of diabetic and burn patients referred to Razi Hospital, Guilan University of Medical Sciences, from July 2020 to October 2021. In order to evaluate the ability of lactobacilli to produce antimicrobial compounds (bacteriocins) and their anti-biofilm ability, the agar spot test and microtiter plate assay methods were used, respectively. In addition, the HFSF-PI3 cell line was used to examine the cell attachment of these strains and their ability to compete with pathogens isolated from wounds.

Results: Most of the Lactobacillus strains showed the ability to produce bacteriocins and had a significant inhibitory effect against Pseudomonas aeruginosa and Escherichia coli. The results of the agar spot test confirmed the high ability of Lactobacillus strains to inhibit P. aeruginosa, compared to other isolates, and these results were also observed in the microtiter plate assay, as lactobacilli effectively inhibited the formation of biofilm by P. aeruginosa. Also, the results of the attachment assay of Lactobacillus strains to the HFSF-PI3 cell line and their ability to compete with wound pathogens indicate the superior efficacy of these strains in inhibiting Pseudomonas attachment to this cell line.

Conclusion: Our results suggest that Lactobacillus strains, through their antimicrobial and anti-biofilm activities, as well as effective competition with wound pathogens, may be an alternative strategy for the control and biological treatment of antibiotic-resistant skin infections.

keywords: Probiotics, Lactobacillus, Antimicrobial Peptides, Biofilms, Infectious Skin Diseases

PBa-11

Engineering Therapeutic Bacteria: Next-Generation Probiotics for the Treatment of Colorectal Cancer and Inflammatory Bowel Diseases

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Background and aim: Colorectal cancer (CRC) and inflammatory bowel disease (IBD) represent major global health challenges, primarily arising from disrupted host–microbiota interactions, chronic inflammation, and impaired intestinal homeostasis. Conventional therapeutic approaches, including chemotherapy, immunosuppressive agents, and biological drugs, despite providing partial clinical benefits, are often limited by insufficient specificity, substantial adverse effects, and inadequate capacity to restore microbial and immune balance.

Methods: Recent advances in synthetic biology and microbiome-based therapeutics have enabled the development of next-generation engineered probiotics as programmable living biotherapeutics capable of sensing, responding to, and modulating the intestinal microenvironment. These engineered microbes offer a promising therapeutic strategy by regulating gut microbiota composition and function and modulating host immune responses. Key microbial species contributing to intestinal homeostasis include Bacteroides fragilis, Akkermansia muciniphila, Propionibacterium freudenreichii, and certain Clostridium species.

Results: This review highlights the potential of next-generation probiotics for the prevention and management of CRC and IBD, supported by robust preclinical evidence from animal models. These probiotics exert beneficial effects through the production of immunomodulatory metabolites and regulation of essential physiological processes, thereby attenuating disease-associated pathways and mitigating chronic inflammation. Despite encouraging preclinical results, further research is required to optimize strain selection, dosing strategies, and safety profiles to facilitate successful clinical implementation of probiotic-based therapeutics.

Conclusion: Overall, engineered probiotics represent an innovative and targeted approach to restoring microbial equilibrium and modulating host immunity, offering substantial promise for the prevention and treatment of gastrointestinal disorders.

keywords: CRC; IBD; Next-Generation Probiotics; Gut Microbiota; Engineered Bacteria

PBa-12

Epidemiology and drug resistance of Mycobacterium tuberculosis isolates in southern Iran, 2024-2025

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Background and aim: Background: Tuberculosis (TB) remains a leading cause of infectious morbidity and mortality worldwide, and the emergence of drug-resistant strains threatens TB control efforts. This study aimed to determine the prevalence of Mycobacterium tuberculosis and the pattern of first-line anti-TB drug resistance in southern Iran.

Methods: Methods: A total of 12,727 clinical specimens from TB-suspected patients referred to the Shiraz Regional TB Reference Laboratory (SRTB-RL) between September 2024 and September 2025 were processed. Specimens underwent standard decontamination, Ziehl–Neelsen microscopy, culture on Löwenstein–Jensen medium, biochemical testing, IS6110-based PCR, and GeneXpert MTB/RIF for rapid detection and rifampicin resistance. Phenotypic drug susceptibility testing (DST) was performed using the indirect proportion method on Löwenstein–Jensen medium according to WHO guidelines.

Results: Results: One hundred ninety-one specimens (1.5%) were culture-positive; 117 isolates (61.2% of culture-positives) were confirmed as M. tuberculosis and included in the analysis. Patients' mean age was 54.2 ± 19.4 years and 59% were male; 97.4% were newly diagnosed cases. DST showed that 91.6% of isolates were fully susceptible to first-line drugs, while 8.4% exhibited resistance to at least one agent. Resistance rates were 4.2% for isoniazid, 1.7% for rifampicin, and 0.8% for ethambutol; multidrug-resistant TB (MDR-TB; resistance to at least INH and RIF) was detected in 1.7% of isolates. The majority of cases originated from Fars province.

Conclusion: Conclusion: Although the prevalence of MDR-TB in this cohort was relatively low, the observed isoniazid resistance warrants continued surveillance and reinforces the need for rapid molecular diagnostics (e.g., GeneXpert) and strengthened treatment adherence programs to prevent expansion of drug resistance. Ongoing monitoring of resistance patterns is essential for guiding regional TB control strategies.

keywords: Mycobacterium tuberculosis, Anti-tuberculosis drug, Gene Xpert MTB/RIF, Iran.

PBa-13

The role of pks-positive Escherichia coli in colorectal cancer: A narrative review

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Background and aim: Colorectal cancer (CRC) is the third most common malignancy worldwide (6.1%) and the second leading cause of cancer-related mortality (9.2%). Mortality from rectal and colon cancer is predicted to rise by 60% and 71.5%, respectively, by 2035. Recent studies have highlighted a significant relationship between the gut microbiome and CRC development and progression. Among the gut bacteria, Escherichia coli harboring the polyketide synthase (pks) genomic island has attracted attention due to its ability to produce colibactin, a genotoxic metabolite associated with DNA damage and carcinogenesis.

Methods: This narrative review was conducted by analyzing recent publications focusing on pks-positive E. coli and its molecular mechanisms in CRC pathogenesis. Data were gathered from peer-reviewed articles indexed in PubMed, Scopus, and Web of Science, emphasizing studies published over the past decade.

Results: Evidence suggests that pks+ E. coli contributes to CRC initiation and progression through several mechanisms, including DNA double-strand breaks, chromosomal instability, and induction of pro-inflammatory responses. However, the precise role of pks+ E. coli in tumor proliferation and metastasis remains incompletely understood, and findings across studies show some inconsistencies.

Conclusion: Given the increasing global burden of CRC and the growing evidence linking pks+ E. coli to its pathogenesis, understanding the interaction between these bacteria and host cellular pathways is crucial. Further mechanistic and clinical studies are needed to clarify their role and to explore possible diagnostic or therapeutic strategies targeting pks+ E. coli in CRC management.

keywords: pks+ E. coli; colorectal cancer; gut microbiota; therapy

PBa-14

A Case of Mycobacterium marinum Infection: Diagnostic Challenges and Successful Treatment with Doxycycline — A Case Report

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Background and aim: Mycobacterium marinum is a non-tuberculous mycobacterium responsible for cutaneous infections following aquatic exposure. Diagnosis is frequently delayed due to its nonspecific clinical presentation, which often mimics common skin conditions such as verruca, and the low sensitivity of initial diagnostic tests.

Methods: We present a case of a 36-year-old man with a persistent, painful nodule on the dorsal aspect of his left fourth finger. The lesion had been previously misdiagnosed as a verruca vulgaris and showed no response to multiple sessions of cryotherapy. A pivotal detailed history revealed the patient's routine maintenance of a domestic freshwater aquarium. Based on high clinical suspicion prompted by this history and the characteristic clinical picture, a diagnosis of M. marinum infection was made clinically.

Results: Initial acid-fast bacilli (AFB) staining from a tissue sample was negative, consistent with the known low yield of this test. The patient was initiated on a regimen of oral doxycycline (100 mg twice daily). Following a two-month course of therapy, the lesion demonstrated complete resolution without recurrence, confirming therapeutic success.

Conclusion: This case underscores two critical points in managing cutaneous M. marinum infections: 1) A meticulous patient history focusing on aquatic or fish tank exposure is paramount for timely diagnosis when facing a treatment-resistant skin lesion. 2) Despite negative initial microbiological tests, a high index of clinical suspicion can guide effective monotherapy with oral doxycycline, leading to excellent outcomes. Clinicians should consider M. marinum in the differential diagnosis of atypical, refractory nodular lesions of the extremities.

keywords: Mycobacterium marinum, Aquarium Granuloma, Doxycycline, Diagnostic Challenge, Zoonotic Infection, Treatment-Resistant

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-15

Molecular Detection of pic, sat, and vat Autotransporter Genes in Uropathogenic Escherichia coli and Their Link to Biofilm Production

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Background and aim: Background: Uropathogenic Escherichia coli is a bacterial pathogen that causes urinary tract infections (UTIs). UPEC strains use autotransporter (AT) proteins for pathogenesis, especially during the development of biofilm in the urinary tract. Objective: There are no general data on the prevalence of ATs among UPEC isolates; therefore, we assessed the frequency of AT genes in patients with UPEC infection and determined the possible correlation between ATs and biofilm.

Methods: A total of 100 Escherichia coli strains were collected from the urine of patients with UTIs. Biofilm production was determined using crystal violet staining. The extracted DNA was used as a template for the detection of three AT genes (pic, sat, and vat) using polymerase chain reaction (PCR). The amplified products and a 100-bp DNA ladder were separated by electrophoresis.

Results: UPEC isolates were grouped into both gender (male: 23% and female: 77%) with an age range of 5-95 years. In females, the highest prevalence of UTI was observed in the 21-40 (41%). All isolates produced biofilm, of which 22%, 30%, and 48% were weak, moderate, and strong biofilm producers, respectively. According to the findings, the prevalence of AT genes was sat (47%), vat (21%), and pic (21%).

Conclusion: Epidemiological studies have been conducted on the findings regarding the role of AT proteins in UPEC pathogenesis, particularly biofilm formation. The prevalence of most AT genes, notably sat and vat, was vital among the UPEC isolates, and these factors can be ideal vaccine candidates for designing an effective vaccine against UPEC.

keywords: Escherichia coli, Biofilm, Autotransporter genes, Urinary tract infection

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-16

In silico functional annotation of Acinetobacter phage AbTJ tail fiber protein and study of its molecular interaction with bacteria and human cells

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Background and aim: Acinetobacter baumannii is an opportunistic pathogen of nosocomial infections. It has emerged as one of the most potent multidrug-resistant microorganisms, ultimately challenging the efficacy of existing antibiotic treatments. The World Health Organization's 2024 list has placed this bacterium as a high priority for the discovery of a new treatment. In this context, AbTJ, a novel phage infecting A. baumannii MDR-TJ, was first isolated in China in 2019. In the present study, we aimed to use bioinformatics tools to functionally annotate the host-binding protein of Acinetobacter phage AbTJ and study its molecular interactions with bacteria and human cells.

Methods: First, phage sequences related to A. baumannii MDR-TJ were obtained from the Phage Scope database and tail fiber protein (LOCUS: QAU04145/202 aa) was selected in this database. To determine the classification, functions, and structure prediction of this protein, along with NCBI protein BLAST, Intrpro database, I-TASSER and Swiss model servers were used. Virus-host and STRING database was used to identify human and bacterial proteins interacting with tail fiber protein.

Results: Based on the analysis of the protein sequence provided in NCBI, it was found that this protein has a high similarity to the Ata protein (Acinetobacter trimeric autotransporter adhesin) from A. baumannii. Protein interaction analysis in the STRING database showed that Ata interacts with proteins involved in adhesion, biofilm formation, membrane stability, and remarkably, it bears no significant similarity to human proteins.

Conclusion: Ata is one of the important surface proteins of bacteria that plays a role in the process of adhesion to host tissues, biofilm formation, and invasion of human cells. Therefore, this phage protein has an interfering or interfering role in bacterial adhesion and stability, which could be very important in the mechanism of phage therapy against A. baumannii. Also, since this protein showed no significant similarity to human proteins, the possibility of directly stimulating human host immune responses is low, which is an immunological advantage in phage-based therapeutic designs.

keywords: Phage-host interactions; Prediction; In Silico Methods; Benchmark

PBa-17

Association Secretory Phospholipase A2 Levels with Sepsis and Bacterial Infections: A Systematic Review of Observational Studies

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Background and aim: Sepsis, a serious and life-threatening reaction to infection, can cause organ dysfunction, systemic inflammation, and mortality through excessive immune activation and cytokines release. Secretory Phospholipase A2 (sPLA2), plays a critical role in this process. The purpose of the study was to investigate the association between sPLA2 levels and sepsis or bacterial infection compared to non-sepsis and non-bacterial infections.

Methods: The present systematic review was conducted using the PRISMA guidelines and checklist. The keywords "bacterial infections", "Bacteremia", "sepsis", and "Secretory Phospholipase A2" along with their MeSH synonyms were searched in PubMed, Scopus, and Embase databases. This search was conducted without a time limit and until the end of July 2025.

Results: In all seven studies (of the eight studies), significant increases (P 0.05) in sPLA2-IIA were observed in patients with sepsis or bacterial infections compared to controls or healthy volunteers. However, based on the findings of two studies that examined sPLA2-IIA levels in patients with sepsis and patients with severe sepsis, no significant association was reported, although sPLA2-IIA levels were higher in patients with severe sepsis compared to patients with sepsis.

Conclusion: Based on the findings of the studies, sPLA2-IIA has high potential as a biomarker, but it is necessary to examine the less well-known sPLA2 isoforms, investigate association between of isoforms levels with severity of sepsis and the evaluation of the prognosis of sPLA2-IIA in predicting clinical outcomes in future studies.

keywords: sPLA2, Septic Shock, Sepsis, Bacteremia, Biomarker

PBa-18

The microbial landscape of tumors: a deep dive into intratumoral microbiota

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Background and aim: Microorganisms in the human body play crucial roles in various health and disease processes. Research indicates that diverse bacterial species are implicated in numerous cancer types. Apart from its involvement in cancer initiation and progression, the microbiome holds promise as a biomarker for diagnosing cancer, assessing risk, and determining prognosis. Intratumoral microbes profoundly impact tumor biology by regulating the initiation and progression of tumors and modulating their response to chemotherapy, radiotherapy, and immunotherapy. A deeper understanding of the role of the intratumoral microbiome in cancer requires further investigation into its effects and underlying mechanisms. This review delves into the significance

Methods: This is not the original article.

Results: No original data; synthesizes literature on intratumoral microbiota

Conclusion: Intratumoral bacteria play a pivotal role in the microecology of tumors, influencing cancer progression, response to therapies, and potential treatment outcomes. Exploring tumor-associated microbiota is an emerging field, progressively broadening our understanding of microbial contributions to cancer biology. These contributions include promoting DNA damage, epigenetic modifications, inflammation, oncogenic pathway regulation, and metastasis facilitation. Moreover, intratumoral microbiota offers a promising frontier for innovative therapeutic approaches, including biomarker-based diagnostics and adjunctive therapies. Future research should focus on translating these insights into clinical applications, such as personalized microbiota-based therapies tailored to individual tumor

keywords: microbiome, intratumoral microbiota, detection, cancer development, anticancer therapy

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PBa-19

Distribution and expression of virulence genes (hlyA, sat) and genotyping of Escherichia coli O25b/ST131 by multi-locus variable number tandem repeat analysis in Tehran, Iran

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Background and aim: Escherichia coli ST131 is a pandemic clone with high antibiotic resistance, and it is a major causative agent of urinary tract infection (UTI) and bloodstream infections. This study evaluated the distribution and expression of virulence genes and genotyping of E. coli O25b/ST131 by Multi-locus variable number tandem repeat analysis (MLVA) method among UTI in patients at Tehran hospitals, Iran. A total of 107 E. coli isolates were collected from UTI patients. Polymerase chain reaction (PCR) amplification of the pabB gene was used to identify E. coli O25b/ST131 and the prevalence of sat and hlyA virulence genes was also analyzed. The

Methods: 1. Bacterial isolates 2.Identification of E. coli ST131 clones and sat and hlyA virulence genes 3.Biofilm formation assay 4.Gene expression analysis by qRT-PCR 5.MLVA 6.STATISTICAL ANALYSIS

Results: A total of 107 E. coli isolates were collected from UTI patients. Polymerase chain reaction (PCR) amplification of the pabB gene was used to identify E. coli O25b/ST131 and the prevalence of sat and hlyA virulence genes was also analyzed. The microtiter method quantified biofilm formation ability in E. coli O25b/ST131. The Real-Time PCR (qRT-PCR) was performed to evaluate the expression of sat and hlyA genes. Finally, MLVA was performed for E. coli O25b/ST131 genotyping by targeting seven tandem repeats. SPSS-16 software was used for statistical analysis. Molecular study showed that 71% of isolates carried the pabB gene and were considered E. coli O25b/ST131 strains. Also, 45.8% and 17.8% of isolates carried sat and hlyA genes, respectively. The 57.9% isolates had biofilm formation ability. Expression of the studied virulence genes showed an increase in strong biofilm producing E. coli O25b/ST131 strains. A total of 76 (100%) E. coli O25b/ST131

Conclusion: Due to the high antibiotic resistance of E. coli O25b/ST131,our observations about the prevalence in patients with UTIsand further virulence factors of this strain can be a warningto the medical system. The results of strain typing with thenew MLVA technique can be cheaper, faster, and more ac-curate in identifying the origin of various strains.

keywords: E. coli ST131, MLVA, biofilm production, urinary tract infection

PBa-20

Postbiotics: Novel Modulators of Gut Health, Metabolism, and Their Mechanisms of Action

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Background and aim: Postbiotics, defined as non-viable microbial cells, structural components, or metabolites, have recently emerged as promising modulators of gut health and metabolism. Unlike probiotics, they circumvent safety concerns associated with live microorganisms, including potential translocation, antibiotic resistance transfer, and viability loss during storage. Postbiotics encompass diverse bioactive compounds such as short-chain fatty acids (SCFAs), exopolysaccharides, bacteriocins, antioxidant enzymes, surface layer proteins, and bacterial lysates, each exerting distinct biological effects. Mechanistically, they enhance epithelial barrier function, regulate innate and adaptive immune responses, and modulate host gene expression through pattern recognition receptors and epigenetic modifications. SCFAs, particularly butyrate and propionate, improve intestinal homeostasis,

Methods: This is not the original article

Results: This is not the original article

Conclusion: postbiotics represent a next-generation approach to microbiota-targeted interventions, offering novel opportunities for disease prevention, adjunctive therapy, and the advancement of microbiome-based therapeutics.

keywords: Short-chain fatty acids (SCFAs) · Bacteriocins · Exopolysaccharides · Antioxidant

PBa-21

Association of IL-10 promoter and IL-12 gene polymorphisms with the risk of Symptomatic Helicobacter pylori infection

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Background and aim: Background: The host's immune response to Helicobacter pylori (H. pylori) infection is largely determined by its cytokine profile. Genetic variations within crucial immunomodulatory genes, including those for interleukin-10 (IL-10) and interleukin-12 (IL-12), are thought to influence an individual's vulnerability to the infection and its clinical consequences by modifying cytokine production. Nonetheless, research data derived from diverse human populations continue to show inconsistent results. This case-control analysis sought to examine a potential link between symptomatic H. pylori infection susceptibility in an Iranian population and specific genetic variants in the IL-10 (-1082GA, -819CT) and IL-12 (+1188AC) genes.

Methods: In this investigation, 68 individuals with confirmed symptomatic H. pylori infection diagnosed by a positive rapid urease test and elevated anti-H. pylori IgG levels exceeding 90 ng/ml via ELISA were enrolled alongside 68 healthy controls. The control group was carefully matched to the patient group based on age, sex, and ethnic background. Genotyping for the IL-10 (-1082GA, -819CT) and IL-12 (+1188AC) polymorphisms was conducted using the Amplification Refractory Mutation System-PCR (ARMS-PCR) method.

Results: The analysis revealed no statistically significant correlations linking the investigated IL-10 and IL-12 gene variants to an increased predisposition for H. pylori infection. A notable methodological observation was the deviation from Hardy-Weinberg equilibrium (HWE) across all studied polymorphisms in the control group. Regarding the IL-10 -1082GA locus, the AA genotype was associated with a marginally elevated risk estimate; however, this finding was not statistically significant (OR = 3.45, 95% CI: 0.29–41.36; p=0.327). Likewise, for the IL-12 +1188AC polymorphism, the CC genotype, while more prevalent in the patient cohort, also demonstrated no significant association with infection risk (OR = 1.43, 95% CI: 0.42–4.87; p=0.567).

Conclusion: This investigation did not establish a significant link between the specific IL-10 and IL-12 gene variants analyzed and susceptibility to symptomatic H. pylori infection in the studied population. Although minor genetic associations were noted, they lacked statistical significance. Future research with larger sample sizes is required to validate these results and to investigate additional genetic determinants that may affect infection risk.

keywords: H. pylori; Genetic Susceptibility; IL-10; IL-12; Polymorphism; Case-Control Studies.

PBa-22

Molecular determination of Sequence Type 131 among Extended Spectrum β -Lactamases Production Escherichia coli recovering from Urinary Tract Infection Isolates.

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Background and aim: Background: ST131 clone is an important human pathogen and a primary cause of UTIs worldwide. E. coli ST131 clone causes UTI and is associated with a wide spectrum of other infections such as intra-abdominal, soft tissue infections that can affecting bloodstream infections. Therefore, as the few studies reported ST131, in current study, we have investigated the molecular characteristics, typing and biofilm formation of ST131 clone type E. coli collected from UTI specimens in order to determine the extent of resistance and the distribution of the most resistant clone.

Methods: Methods: A total of 173 E. coli isolates from UTI were collected from two selective hospitals in Tehran. The susceptibility to all fourth generations of cephalosporins and ampicillin, ampicillin-sulbactam, aztreonam were determined. Screening for class A ESBLs (blaGES, blaSHV, blaCTX-M, blaVEB, blaPER, and blaTEM) and class D ESBL (blaOXA-10) and the presence of pabB gene for detection of ST131 clone type had performed by using of polymerase chain reaction (PCR). In addition, biofilm formation for comparison of biofilm production between ST131 isolates and non-ST131 isolates had performed. Eventually, ERIC-PCR had used for typing of ESBL positive isolates.

Results: Results: 94 ESBL positive were detected which 79 of them were ST131. Antimicrobial susceptibility test data showed that in most of antibiotics the percentage of resistance was higher in ST131 clone type isolates. Between ESBL genes bla-CTX-M-1 had highest prevalence. Biofilm formation studies showed that there was a weak relationship between high-risk clone type ST131 isolates and the level of the biofilm formation. ERIC-PCR results showed that ST131 E. coli isolates were genetically diverse and heterogeneous and classified into 14 groups.

Conclusion: Conclusion: Our results demonstrated the importance and high prevalence of E. coli ST131 among UTI isolates as high virulent clone type with ability to spread fast and disseminate antibiotic resistance genes.

keywords: Keywords: Escherichia coli, ST131, ESBL, E. coli, Iran

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PBa-23

Evaluating the effect of Lactobacillus rhamnosus on IL-1β and IL-6 production by peripheral blood mononuclear cells isolated from endometriosis patients

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Background and aim: Endometriosis is a chronic and inflammatory disease that affects approximately 176 million women worldwide. The disease is associated with chronic pelvic pain and infertility and has a significant impact on health-related quality of life. One of the immunological symptoms of endometriosis is inflammation and an increase in inflammatory cytokines. Probiotics have been used to treat many inflammatory diseases. In this study, the effect of Lactobacillus rhamnosus on the secretion of IL-6 and IL-1β by peripheral blood mononuclear cells obtained from endometriosis patients was investigated.

Methods: : Production of IL-6 and IL-1β cytokines by PBMCs was higher in endometriosis patients in the absence of L. rhamnosus compared to the control group; this difference was even more pronounced upon admixture of PHA to the cultures. Of note, addition of L. rhamnosus reduced IL-6 levels within 24 and 48 hours, but this reduction was not significant. L. rhamnosus addition to the cultures increased IL-1β levels within the first 24 hours of co-culture, while it significantly reduced the cytokine concentration after 48 hours.

Results: A standard strain of L. rhamnosus was prepared and peripheral blood samples from endometriosis and non-endometriosis patients were obtained. Ficoll-separated peripheral blood mononuclear cells (PBMCs) were cultured in the presence and absence of phytohemagglutinin (PHA) with a certain concentration of bacteria (ratio 1:1). The supernatant levels of IL-6 and IL-1β were measured by ELISA in the cultures of endometriosis and non-endometriosis samples.

Conclusion: Depending on the treatment period, L. rhamnosus could exert either stimulatory or inhibitory impacts on the expression of the typical inflammatory cytokine, IL-6 and IL-1β, by endometriosis-derived PBMCs. According to previous studies, bacteria can modulate the immune system responses as related to the level of cytokines; more favorable modulatory impacts could be achieved with expanded treatment time periods. This study highlights the need for further research on the exact mechanisms involved in the interaction between L. rhamnosus and immune cells from endometriosis patients.

keywords: Keywords: Lactobacillus rhamnosus, Endometriosis, PBMC, IL-1β.

PBa-24

Assessment of the risk of Legionella pneumophila in water distribution systems in hospitals of Tehran city

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Background and aim: When a sensitive host inhales aerosols containing these bacteria, Legionella infection occurs. Therefore, monitoring and assessing Legionella in the environment and water distribution systems of such places are critical due to the prone population in hospitals. However, the health risks of Legionella bacteria in the environment are not adequately evaluated. In this study, for hospitalized patients, we performed a quantitative health risk assessment of Legionella in selected hospitals in Tehran city using two scenarios of shower and toilet faucet exposure.

Methods: This study identified Legionella in 38 cases (38%) out of 100 samples collected from toilet faucets and showers in 8 hospitals. The information gathered was used for quantitative microbial risk assessment (QMRA). The microbial load transmitted by inhalation was calculated using the concentration of Legionella in water. Other exposure parameters (inhalation rate and exposure time) were obtained using information from other studies and the median length of hospital stay (3.6 days). The exponential model was used to estimate the risk of infection ($\gamma = 0.06$) due to Legionella pneumophila (L. pneumophila) inhalation for each exposure event.

Results: For the mean concentration obtained for Legionella (103 CFU/L), the risk of infection for toilet faucets and showers was in the range of 0.23-2.3 and 3.5-21.9, respectively, per 10,000 hospitalized patients. The results were compared with the tolerable risk level of infection determined by the US EPA and WHO. The risk values exceeded the WHO values for waterborne pathogens in hospitals in both exposure scenarios. As a result, our QMRA results based on monitoring data showed that despite using treated water (from distribution networks in the urban areas) by hospitals, 38% of the samples were contaminated with Legionella, and faucets and showers can be sources of Legionella transmission.

Conclusion: Hence, to protect the health of hospitalized patients, the risk of Legionella infection should be considered.

keywords: Hospital; Legionella; Quantitative Microbial Risk Assessment (QMRA).

PBa-25

Investigation of the Antibacterial Effects of Thymol-Loaded Nanolipids against Carbapenemase-Producing Klebsiella pneumoniae

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Background and aim: Carbapenem-resistant Enterobacteriaceae (CRE), particularly carbapenemase-producing Klebsiella pneumoniae (CRKP), represent a major public health threat owing to their multidrug resistance and efficient horizontal gene transfer. Effective control requires rapid diagnostics, integrated surveillance in healthcare and community settings, and novel therapeutic alternatives. Nanotechnology-based approaches, such as thymol-loaded nanostructured lipid carriers (NLCs), enhance antimicrobial efficacy and bioavailability, offering promising preclinical solutions.

Methods: Thymol-loaded nanostructured lipid carriers (NLC-Thymol) were synthesized. Antimicrobial activity was evaluated against a clinical CRKP isolate. Bacterial suspension was adjusted to 0.5 McFarland standard in freshly prepared Mueller-Hinton broth. Minimum inhibitory concentration (MIC) was determined per Clinical and Laboratory Standards Institute (CLSI) guidelines. Serial twofold dilutions of free thymol and NLC-Thymol (0.5–1024 µg/mL) were tested. Plates were inoculated and incubated at 37°C for 18 h; the lowest concentration preventing visible growth was recorded as the MIC.

Results: Both free thymol and NLC-Thymol exhibited potent activity against CRKP, with comparable MIC values (thymol: 15.6 µg/mL; NLC-Thymol: 16 µg/mL).

Conclusion: NLC formulation enhanced thymol's solubility and stability, facilitating bacterial wall penetration and controlled release, thereby conferring strong antibacterial effects against CRKP. These findings highlight the therapeutic potential of NLC-Thymol as an innovative strategy against resistant Klebsiella infections.

keywords: Carbapenemase-resistant Klebsiella pneumoniae, Thymol, NLC-Thymol, Nanostructured lipid carriers

PBa-26

Multiplex PCR–based assessment of Akkermansia muciniphila in colonic biopsy samples from patients with inflammatory bowel disease

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Background and aim: A key factor in the development and course of inflammatory bowel disorders (IBD) is disruptions in the intestinal microbiota. Of them, Akkermansia muciniphila has garnered significant attention as a mucinophilic bacteria because of its possible function in preserving the integrity of the mucosal barrier and regulating immunological responses. The aim of the present study was to detect the presence of A. muciniphila in biopsy samples of patients with IBD and healthy individuals using two designed primer sets.

Methods: Forty intestinal biopsy samples were taken from both healthy people and IBD patients for this study. Multiplex PCR was used to identify the target microorganisms using two distinct primer sets. Samples were run on a gel, and the findings were qualitatively reported (presence/absence).

Results: The results demonstrated that the percentage of A. muciniphila detected in samples from IBD patients was substantially lower than that of those from healthy people using the first set of primers developed. Additionally, comparable outcomes were noted in the second set of created primers, suggesting that the two molecular designs were compatible in detecting this bacteria. When the two primer groups were compared, it was found that the second primer had a better detection sensitivity.

Conclusion: The findings of this study revealed that the abundance of Akkermansia muciniphila in colonic biopsy samples from patients with inflammatory bowel disease (IBD) was markedly reduced compared to that of healthy individuals. This observation supports the hypothesis that A. muciniphila plays a protective and regulatory role in maintaining intestinal homeostasis and highlights its potential involvement in modulating inflammatory processes within the gut. Moreover, the observed differences in the detection results obtained from the two designed primer sets underscore the importance of careful molecular tool selection and primer optimization in microbiota.

keywords: Akkermansia muciniphila, IBD, Probiotics, PCR, Multiplex PCR, Biopsy

PBa-27

Role of Microbiome in Drug Metabolism and Cancer Therapy Response

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Background and aim: Over the past decade, the gut microbiome has emerged as an active regulator of the immunometabolic axis rather than a passive commensal system. Through dynamic microbe–host interactions, it modulates drug absorption, metabolism, toxicity, and antitumor efficacy, positioning the microbiome as a critical determinant of therapeutic response in cancer. To determine how gut microbiome composition and microbiome-targeted interventions modulate chemotherapy and immunotherapy efficacy and resistance in cancer.

Methods: Preclinical and clinical studies assessing the influence of microbiome composition or microbiome-targeted interventions-including probiotics, prebiotics, antibiotics, dietary modulation, and fecal microbiota transplantation (FMT) therapeutic response were included. Extracted data comprised cancer type, treatment modality, relevant microbial taxa and metabolites, and clinical outcomes .

Results: Taxa such as Akkermansia muciniphila, Bifidobacterium, and Faecalibacterium prausnitzii were consistently associated with improved responses to immune checkpoint inhibitors and selected chemotherapeutic agents. Mechanistic pathways involved dendritic-cell activation, enhanced $CD8^+/CD4^+$ T-cell infiltration, increased IL-12 and IFN-γ signaling, and suppression of regulatory T cells and myeloid-derived suppressor cells. Microbial enzymes, including β-glucuronidases and azoreductases, influenced drug activation, inhibition, and detoxification, while metabolites such as short-chain fatty acids, secondary bile acids, and tryptophan derivatives regulated apoptosis, DNA-damage responses, epithelial-barrier integrity, and pharmacokinetics. Antibiotic-induced dysbiosis generally impaired therapeutic efficacy, whereas microbiome-modulating interventions partially restored responses in selected models.

Conclusion: The gut microbiome is an emerging therapeutic target and predictive biomarker in personalized cancer therapy. Future studies should prioritize assay standardization, identification of functionally relevant taxa and metabolites, and rigorous evaluation of the safety, durability, and clinical applicability of microbiome-based interventions.

keywords: microbiome, immunity, chemotherapy, metabolites, therapeutics

PBa-28

Unveiling a Novel Barstar Protein: In Silico Analysis of Hypothetical Protein WP_311008533.1 from Shigella boydii Reveals Its Role as an Intracellular Inhibitor of Barnase

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Background and aim: Shigella boydii is a major pathogen causing shigellosis, particularly in Asia and Africa. Hypothetical proteins (HP) like WP_311008533.1 are potential therapeutic targets but are poorly understood. The study aims to annotate the hypothetical protein WP_311008533.1 focusing on its structural and functional properties.

Methods: Various bioinformatics tools, including CELLO, PSORTb, and SOSUIGramN, identified WP_311008533.1 as a cytoplasmic protein, confirming its function as a Barstar, an inhibitor of barnase. Structural analyses showed a predominance of alpha helices and a high accuracy in 3D modeling (99% identity with barnase inhibitor).

Results: WP_311008533.1 was validated as a stable Barstar, with an active site identified for potential drug targeting.

Conclusion: The protein plays a crucial role in bacterial survival by inhibiting barnase, and disrupting this function could reduce the bacterium's defense, aiding antimicrobial development. The study provides insights into WP_311008533.1 as a Barstar inhibitor, suggesting that targeting its function may lead to new strategies against S. boydii infections.

keywords: Food-borne diseases, Bioinformatics tools, Functional annotation, Antimicrobial interventions, Gastrointestinal infection.

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBa-29

Biological synthesis of selenium nanoparticles-loaded niosomes and their antibacterial activity against Streptococcus mutans

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Background and aim: Dental caries is one of the most common infectious diseases, primarily caused by Streptococcus mutans. Conventional antimicrobial agents used to control oral infections may cause adverse effects, suggests the investigation on nanoparticle-based alternatives. The aim of this study is to evaluate the antimicrobial effect of synthesized niosome-encapsulated selenium nanoparticles on S. mutans.

Methods: In this in vitro study, selenium nanoparticles were biosynthesized via Artemisia annua extract, and selenium-loaded niosomes were subsequently prepared. The morphological parameters of the niosomal vesicles were determined through scanning electron microscopy (SEM), transmission electron microscopy (TEM), dynamic light scattering (DLS), and Fourier-transform infrared spectroscopy (FTIR). The antibacterial activity of the synthesized nanoparticles against S. mutans was determined by the broth microdilution method. Additionally, in vitro assessments of cell viability were conducted on HEK293 using the MTT assay.

Results: TEM and SEM analyses showed that the synthesized nanoparticles were spherical with an average size of 33.40 nm. DLS measurements indicated that selenium-loaded niosomes had a larger hydrodynamic diameter than empty niosomes, and FTIR confirmed the incorporation of selenium into the niosomal vesicles. The formulation exhibited a sustained-release profile. Antibacterial evaluation showed a significant enhancement in activity, with the MIC decreasing from 50 to 6.25 µg/mL after niosomal encapsulation. Cytotoxicity assessment also showed no significant toxic effects on normal cells.

Conclusion: According to the results of this study, it can be concluded that niosome-encapsulated selenium nanoparticles have significant antimicrobial effects against S. mutans. Therefore, in future studies, this combination can be used as a candidate drug delivery system.

keywords: Streptococcus mutans; nanoparticles; dental caries; drug carriers; anti-bacterial agents

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PBa-30

Prevalence of Type III Secretion System Mediated Exotoxin Encoding Genes among Clinical Pseudomonas aeruginosa Isolates in Northern Iran

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Background and aim: Pseudomonas aeruginosa is a key opportunistic pathogen that causes serious healthcare associated infections. Its virulence is largely driven by the type III secretion system, which delivers cytotoxic exotoxins directly into host cells. This study aimed to assess the prevalence of genes encoding type III secretion system associated exotoxins among clinical P. aeruginosa isolates in Northern Iran.

Methods: This descriptive-analytical study included 100 clinical isolates of P. aeruginosa collected from hospitalized patients in Northern Iran. The isolates were identified using standard microbiological and biochemical methods. Antimicrobial susceptibility patterns were determined using the disk diffusion method. Genomic DNA was extracted through the alkaline lysis method. The presence of genes encoding type III secretion system mediated exotoxins was assessed by PCR using specific primers. The frequency of these virulence genes was analyzed to evaluate their distribution among the clinical isolates.

Results: These 100 clinical P. aeruginosa isolates demonstrated significant levels of antimicrobial resistance, with the highest non-susceptibility rates observed for aztreonam (72%), followed by piperacillin (47%), ciprofloxacin (44%), tobramycin (40%), imipenem (39%), and ceftazidime (29%). Molecular analysis revealed the presence of the exoU gene in 95% of isolates and the exoY gene in 93%, with 88% simultaneously carrying both. These exotoxin genes were identified across isolates from respiratory, urinary, wound, blood, and catheter samples. Importantly, all isolates derived from burn-related specimens harbored both exoU and exoY. A high frequency of these virulence genes was also noted among isolates collected from intensive care units.

Conclusion: The high prevalence of type III secretion system associated exotoxin genes among clinical P. aeruginosa isolates underscores their likely role in enhancing bacterial virulence in this region. As major effectors of the type III secretion system, the exoU and exoY genes are known contributors to host cell damage and increased disease severity. Their frequent detection alongside elevated levels of antimicrobial non-susceptibility suggests a possible coexistence of virulence and resistance traits in clinical isolates, emphasizing the importance of simultaneous monitoring of virulence factors and antibiotic resistance patterns.

keywords: Pseudomonas aeruginosa; exoU; exoY; Virulence gene; Type III secretion system

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-31

Relationship between the Presence of Integrons and Emergence of Multidrug-Resistant Acinetobacter baumannii in a Burn Center

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Background and aim: Acinetobacter baumannii is a significant cause of multidrug-resistant (MDR) infections in healthcare environments. Integrons play a crucial role in the transmission of antimicrobial resistance. This study aimed to investigate the relationship between the presence of integrons and the emergence of MDR A. baumannii.

Methods: This descriptive-analytical study involved 100 A. baumannii isolates obtained from burn wound infections in hospitalized patients in Mazandaran province over several years. The isolates were identified using standard microbiological techniques and confirmed by PCR detection of the blaOXA-51 gene. Antimicrobial resistance patterns were assessed using the disk diffusion method. Genomic DNA was extracted from the isolates using the boiling method. The presence of various integron classes was determined through PCR amplification of the relevant genes. The isolates were categorized based on their resistance profiles, and the link between integron presence and MDR was evaluated.

Results: The study included 75 male and 25 female patients, with a mean age of approximately 45 years. A total of 100 A. baumannii isolates from burn wound infections demonstrated high levels of antimicrobial resistance. The highest resistance rates were found against ciprofloxacin, ceftriaxone, and cefepime (100%), while minocycline had the lowest resistance rate (88%). All isolates were classified as MDR. PCR analysis revealed that 74% of the isolates carried class 1 integrons, and 45% carried class 3 integrons. Additionally, 40% of the integron-positive isolates contained both class 1 and class 3 integrons. No isolates were found to carry class 2 integrons.

Conclusion: The remarkably high rate of MDR among A. baumannii isolates from burn patients indicates strong selective pressure due to the frequent use of broad-spectrum antibiotics. The unexpectedly high prevalence of class 3 integrons raises a significant concern, pointing to their increasing role in the spread of resistance genes within burn care settings. Ongoing monitoring of integron distribution, especially class 3 integrons, combined with reinforced antimicrobial stewardship efforts, is crucial for limiting the spread of MDR A. baumannii in hospitals.

keywords: Acinetobacter baumannii; Integrons; Antibiotic resistance; Multidrug resistance; Burn wound infection

PBa-32

Antimicrobial Effect of Ethanolic Extract of Ephedra major on Streptococcus mutans and Streptococcus Salivarius

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Background and aim: The aim of the present study was to investigate the antimicrobial effect of the Ethanolic extract of Ephedra major on Streptococcus mutans and Streptococcus Salivarius.

Methods: In this study, after preparing the ethanolic extract of Ephedra major, the minimum inhibitory concentration (MIC) and minimum lethal concentration (MBC) were determined by microdilution method.

Results: The MIC of this extract against Streptococcus salivarius and Streptococcus mutans were 156 and 2500 µg/mL , respectively. The MBC of this extract against Streptococcus salivarius and Streptococcus mutans were 1250 and 5000 µg/mL, respectively.

Conclusion: Based on the findings of this study, which indicated the antibacterial effect of ethanolic extract of Ephedra major on Streptococcus mutans and Streptococcus Salivarius, the ethanolic extract of Ephedra major can be mentioned as a natural option for producing disinfectant products in the field of dentistry.

keywords: Ephedra major, Minimum Inhibitory Concentration (MIC), Minimum Bactericidal Concentration (MBC),

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-33

Natural Polymer-Based Nanoparticles for Antibiotic Delivery: A Review

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Background and aim: Antimicrobial drug resistance is a growing global health threat, projected to cause approximately 10 million deaths annually by 2050. Excessive and inappropriate antibiotic use reduces treatment efficacy and allows pathogens to persist, highlighting the need for novel drug delivery strategies. Polymeric nanoparticle–based systems have emerged as promising alternatives to conventional therapies, enhancing drug solubility, bioavailability, and enabling targeted delivery. This study aims to evaluate selected natural nanopolymers and their physicochemical properties for improving antibiotic delivery performance.

Methods: A structured narrative review was conducted by searching PubMed, Web of Science, and Google Scholar for studies published between 2015 and 2024. Keywords included “natural polymers,” “antibiotic resistance,” “biodegradable polymers,” “drug delivery systems,” and “antibiotics.” Original research and review articles on natural polymer–based nanoparticles for antibiotic delivery were included, while duplicates, non-relevant, or incomplete studies were excluded. Data were analyzed qualitatively and categorized by polymer type, delivery characteristics, and reported therapeutic outcomes.

Results: Natural polymer–based nanoparticles significantly improve antibiotic delivery efficiency. Most formulations exhibit higher drug-loading capacities and controlled or sustained release profiles, enhancing antimicrobial activity compared with free antibiotics. Advantages of these polymers include biocompatibility, biodegradability, bioactivity, and production of non-toxic degradation products. Maltodextrin nanoparticles show promise for pulmonary delivery due to water solubility, biodegradability, and low toxicity. Gum arabic nanoparticles possess intrinsic antibacterial activity, while alginate–chitosan composites provide prolonged drug release, improved stability, and protective effects, collectively enhancing antibacterial efficacy. Overall, nanoparticle systems reduce required drug doses, minimize toxicity, and improve antibiotic stability in vitro and in vivo. Challenges remain, including limited clinical studies, variability in formulations, and scale-up constraints.

Conclusion: Natural polymer–based nanoparticles are favored over synthetic counterparts due to biocompatibility, low toxicity, cost-effectiveness, availability, and alignment with green nanotechnology principles. Nanoparticles derived from gum arabic, maltodextrin, chitosan, and alginate show significant potential to improve antibiotic efficacy and safety. Further clinical investigations are required to translate these promising systems into therapeutic applications.

keywords: “Anti-Bacterial Agents,” “Nanoparticles,” “Drug Delivery Systems,” “Polymers,”

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-34

Impact of OXA-48–producing Enterobacteriaceae strains on resistance patterns and clinical outcomes of bloodstream infections

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Background and aim: Bloodstream infections caused by carbapenemase-producing Enterobacteriaceae have become a major threat in modern hospitals. Among these enzymes, OXA-48 is particularly problematic because it may confer relevant carbapenem resistance while remaining difficult to recognize by routine susceptibility testing. This silent spread complicates interpretation of microbiology reports and delays the start of appropriate therapy. In parallel, the global circulation of OXA-48 plasmids has led to clonal and interspecies dissemination in intensive care units and other high-risk wards. Understanding how OXA-48–producing strains shape resistance patterns and clinical outcomes in bloodstream infections is therefore crucial for optimizing diagnosis and treatment strategies.

Methods: This narrative review synthesized clinical studies that investigated bloodstream infections due to OXA-48–producing Enterobacteriaceae. Eligible reports included adult or pediatric patients with microbiologically documented bacteremia and molecular confirmation of the blaOXA-48 gene or related variants. Extracted data covered bacterial species, clonality, genetic background of blaOXA-48, minimum inhibitory concentration profiles for key antimicrobials, empirical and targeted treatment regimens, and short-term mortality. Studies were compared with regard to infection source, risk factors such as prior carbapenem exposure or invasive devices, and timing of appropriate therapy. Particular attention was paid to discrepancies between genotypic detection of OXA-48 and conventional susceptibility categories, as well as to the coexistence of extended-spectrum beta-lactamases and resistance determinants to aminoglycosides or fluoroquinolones.

Results: Across the reviewed literature, Klebsiella pneumoniae emerged as the dominant OXA-48–producing pathogen in bloodstream infections, although Escherichia coli and other Enterobacteriaceae were also represented. Most isolates carried blaOXA-48 on transferable plasmids that frequently co-harbored ESBL genes, resulting in multidrug-resistant phenotypes with limited beta-lactam options. Phenotypically, many strains showed only modest carbapenem minimum inhibitory concentration elevations, sometimes remaining within the susceptible or intermediate range, yet were associated with clinical failure when carbapenem monotherapy was used. Co-resistance to fluoroquinolones and aminoglycosides was common, further narrowing empirical choices. Patients infected with OXA-48–producing strains experienced higher rates of delayed adequate therapy, prolonged bacteremia, septic shock, and mortality, particularly in intensive care settings. Combination regimens including ceftazidime–avibactam or colistin-based therapies showed more favorable outcome

Conclusion: Evidence to date indicates that OXA-48–producing Enterobacteriaceae substantially modify resistance landscapes in bloodstream infections, mainly through plasmid-mediated dissemination and frequent linkage with additional resistance determinants. Because associated carbapenem resistance may be under-recognized by routine testing, reliance on phenotypic categories alone risks inappropriate monotherapy and excess mortality. Incorporating reliable OXA-48 detection into diagnostic workflows, interpreting susceptibility profiles with caution, and prioritizing targeted combination regimens within antibiotic stewardship programs are key steps to improve outcomes in patients with these high-risk infections.

keywords: OXA-48/Enterobacteriaceae/Bloodstream infection/Antibiotic resistance/Carbapenemase

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-35

Clinical Distribution and Antimicrobial Resistance Trends of Klebsiella pneumoniae Isolates in Northern Iran

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Background and aim: Klebsiella pneumoniae is a significant opportunistic pathogen linked to hospital-acquired infections and escalating antimicrobial resistance. The growing prevalence of resistant strains underscores the importance of localized monitoring. This study aimed to investigate the clinical distribution and patterns of antimicrobial resistance among K. pneumoniae isolates collected from hospitalized patients in northern Iran.

Methods: In this descriptive cross-sectional study, 50 non-duplicate K. pneumoniae isolates were obtained from a range of clinical specimens, including urine, blood, sputum, wound swabs, and tracheal aspirates, collected from hospitalized patients in medical and educational centers in northern Iran. The isolates were identified using standard microbiological and biochemical techniques, such as Gram staining, oxidase testing, and culture on media including TSI, SIM, MR-VP, citrate, and urea. Antimicrobial susceptibility was assessed using the disk diffusion method on Mueller–Hinton agar, following CLSI guidelines. Resistance patterns were determined based on a panel of commonly prescribed antibiotics.

Results: A total of 50 nonduplicate K. pneumoniae isolates were obtained from hospitalized patients, with most samples collected from urine, followed by blood, tracheal aspirates, sputum, and wound specimens. The highest number of isolates was reported from intensive care units. Antimicrobial susceptibility testing showed high resistance rates to ciprofloxacin (61%), imipenem (60%), ceftazidime (58%), cefepime (56%), and ceftriaxone (55%). Resistance to meropenem was also notable at 49%. Moderate resistance was observed with gentamicin (35%), while amikacin demonstrated the lowest resistance rate at 13%, indicating it still retains good activity against these isolates.

Conclusion: The results of this study reveal a high rate of antimicrobial resistance among clinical K. pneumoniae isolates, especially to carbapenems and fluoroquinolones, presenting a significant obstacle to effective treatment in hospital environments. Amikacin showed the highest activity against the isolates, indicating its possible usefulness in empirical therapy. These findings underscore the urgent need for ongoing monitoring of resistance trends, prudent use of antibiotics, and stringent infection control practices to curb the spread of multidrug-resistant strains. Additional multicenter and molecular investigations are recommended to gain deeper insights into resistance mechanisms and

keywords: Klebsiella pneumoniae; antimicrobial resistance; multidrug resistance; disk diffusion; hospital-acquired infections

PBa-36

Assessment of Brucellosis Prevalence Among Blood Donors in Rural Regions of Ardabil Province

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Background and aim: Brucellosis continues to be a major public health issue in endemic areas like Iran, raising concerns about blood transfusion safety. Its often asymptomatic nature in otherwise healthy individuals makes diagnosis difficult. This study aimed to assess both the seroprevalence and molecular presence of Brucella species among blood donors in rural regions of Ardabil Province, utilizing serological tests and PCR-based diagnostic techniques.

Methods: In this cross-sectional study, a total of 500 blood donors from the Ardabil Blood Transfusion Center were screened for Brucella infection. All blood samples were initially tested using the Rose Bengal test. Those that tested positive underwent further evaluation with the Wright agglutination test, 2ME test, and PCR assays targeting the Brucella 16S rRNA gene. Additionally, 10% of the Rose Bengal-negative samples were randomly selected for PCR analysis. Statistical analysis was carried out using SPSS software.

Results: Of the 500 blood donors screened, 37 individuals (7.4%) tested positive using the Rose Bengal test. Among these, 27 (73.0%) were positive by the Wright agglutination test, and 18 (48.6%) tested positive using 2ME test. However, none of the samples were confirmed positive by PCR. There was no significant difference in seroprevalence between males and females. In contrast, a statistically significant association was found between age and serological positivity, with older individuals showing higher rates of positive results.

Conclusion: The seroprevalence data suggest that exposure to Brucella is relatively common among blood donors in this endemic region. However, the absence of PCR-positive results indicates that active infection was not detected in the study population. These results highlight the value of using both serological and molecular diagnostic approaches for a more accurate evaluation of transfusion-related risks. They also emphasize the need for ongoing surveillance in regions where animal-to-human transmission of Brucella is well established.

keywords: Brucellosis; Blood donors; Rose Bengal; Wright test; 2 Mercaptoethanol; Polymerase

PBa-37

The study of drug resistance pattern of Acinetobacter baumannii that isolated from the patients who were admitted in infectious disease and ICU wards of Zanjan Valiasr Hospital in 2024

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Background and aim: Hospital-acquired infections usually occur 48 to 72 hours after admission and are considered one of the most important challenges for healthcare centers. The aim of this study was to investigate the antibiotic resistance patterns of Acinetobacter baumannii isolated from patients hospitalized in the infectious disease and intensive care units (ICU) of Vali-e-Asr Hospital in Zanjan in 2024

Methods: This cross-sectional descriptive-analytical study was conducted on hospitalized patients with a positive culture of the mentioned bacteria. Bacterial identification was performed using biochemical tests and PCR. Demographic and clinical information, as well as drug resistance patterns, were extracted from patient records and analyzed using SPSS software version 26. Appropriate statistical tests were applied with a significance level of P0.05

Results: This study was conducted on 98 hospitalized patients, among whom Acinetobacter baumannii was identified in 43.9% of the patients. The most common sample source was respiratory secretions (57.1%). This bacterium showed the highest sensitivity to imipenem and ceftazidime (about 94–95%) and the highest resistance to co-amoxiclav and gentamicin. Additionally, in patients receiving immunosuppressive drugs, higher resistance was observed to co-amoxiclav and ofloxacin

Conclusion: In this study, Acinetobacter baumannii was one of the main causes of hospital infections in ICU patients. Considering the high level of resistance observed, implementing continuous monitoring programs and the rational use of antibiotics is essential to prevent the spread of drug resistanc

keywords: the drug resistance, Acinetobacter baumannii, infectious department, ICU

PBa-38

The study of drug resistance pattern of Pseudomonas aeruginosa that isolated from the patients who were admitted in infectious disease and ICU wards of Zanjan Valiasr Hospital in 2024

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Background and aim: Hospital-acquired infections usually occur 48 to 72 hours after admission and are considered one of the most important challenges for healthcare centers. The aim of this study was to examine the antibiotic resistance pattern of Pseudomonas aeruginosa isolated from patients admitted to the infectious and intensive care units (ICU) of Vali-Asr Hospital in Zanjan in 2024

Methods: This cross-sectional descriptive-analytical study was conducted on hospitalized patients with positive cultures of the mentioned bacterium. The bacteria were identified using biochemical tests and PCR. Demographic, clinical information, and drug resistance patterns were extracted from patient records and analyzed using SPSS version 26. Appropriate statistical tests were applied with a significance level of P0.05

Results: This study was conducted on 98 hospitalized patients, in which Pseudomonas aeruginosa was identified in 56.1% of the patients. The most common source of the samples was respiratory secretions (57.1%). This bacterium showed the highest sensitivity to imipenem and ceftazidime (approximately 94–95%) and the highest resistance to co-amoxiclav and gentamicin. Additionally, resistance to imipenem was higher in women (p=0.014).

Conclusion: In this study, Pseudomonas aeruginosa was one of the main causes of hospital-acquired infections in ICU patients. Given the high level of observed resistance, implementing continuous monitoring programs and the rational use of antibiotics are essential to prevent the spread of drug resistance

keywords: the drug resistance,Pseudomonas aeruginosa, infectious department, ICU

PBa-39

Acinetobacter baumannii in Healthcare Facilities

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Background and aim: Acinetobacter baumannii is a major cause of healthcare-associated infections, particularly in intensive care units, where multidrug resistance and persistence on inanimate surfaces complicate treatment and outbreak control. This review summarizes key bacteriologic and clinical features of A. baumannii in healthcare facilities and highlights practical prevention and management priorities for laboratory and clinical teams.

Methods: A narrative review was prepared by synthesizing peer-reviewed literature and major infection-prevention guidance on A. baumannii, focusing on virulence determinants, resistance mechanisms, clinical syndromes, reservoirs/outbreak drivers, and therapeutic options.

Results: A. baumannii causes pneumonia (including hospital-acquired disease), bloodstream infection, and urinary tract infection, and has been linked to high mortality in vulnerable patients. Transmission in healthcare settings is facilitated by prolonged survival on dry surfaces and contaminated equipment. Biofilm formation, iron acquisition, and quorum sensing support persistence and virulence. Resistance is driven by horizontal gene transfer, mutations, beta-lactamase production, and efflux pumps, resulting in carbapenem resistance and multidrug-resistant phenotypes. Recommended control combines comprehensive infection-prevention programs, screening and contact precautions, active surveillance, meticulous environmental cleaning/disinfection, and antimicrobial stewardship. Treatment should be guided by susceptibility testing; carbapenems are preferred when active, while ampicillin–sulbactam, colistin, tigecycline/eravacycline, or cefiderocol may be options for resistant isolates.

Conclusion: A. baumannii remains a formidable nosocomial threat because of environmental persistence and expanding resistance. Coordinated laboratory surveillance, strict infection-control implementation, and optimized antibiotic use, alongside development of new therapies, are essential to limit transmission, improve outcomes, and prevent outbreaks.

keywords: Acinetobacter baumannii; Drug Resistance, Bacterial; Cross Infection; Infection Control

PBa-40

Beta-lactamase Genes and ERIC-PCR Genotyping of Multidrug-Resistant Klebsiella pneumoniae Clinical Isolates in Northern Iran

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Background and aim: Klebsiella pneumoniae is an essential clinical pathogen, and the rise of multidrug-resistant (MDR) strains is a growing public health concern. This study aimed to detect significant beta-lactamase genes and assess genetic relatedness among MDR K. pneumoniae clinical isolates using ERIC-PCR.

Methods: MDR K. pneumoniae isolates were collected from educational hospitals affiliated with Babol University of Medical Sciences (Iran). Species identification was performed using standard microbiological/biochemical tests. Antimicrobial resistance was evaluated by disk diffusion, and carbapenemase/MBL production was assessed using the modified Hodge test and combined-disk methods. PCR assays targeted blaNDM, blaKPC, blaTEM, blaSHV, and blaCTX-M. ERIC-PCR was applied for molecular typing.

Results: A total of 42 MDR isolates were obtained from various clinical specimens and wards (urine: 28.57%; blood: 21.42%; ICU: 50%). The highest resistance was to ampicillin (100%), and the lowest was to amikacin (19.04%). Carbapenemase production was detected in 38.09% of isolates, and MBL production in 54.76%. Gene frequencies were: blaCTX-M 80.95%, blaTEM 76.19%, blaSHV 47.16%, blaKPC 42.85%, and blaNDM 21.42%. ERIC-PCR identified seven genetic patterns among the isolates.

Conclusion: MDR K. pneumoniae showed substantial resistance in the studied hospitals, with blaCTX-M as the most frequent and blaNDM as the least frequent beta-lactamase gene. ERIC-PCR findings suggest clonal spread and a common origin of some isolates within hospital wards, highlighting the need for strengthened surveillance and infection-control strategies.

keywords: Klebsiella pneumoniae; Multidrug-resistant; Carbapenemase; Beta-lactamases

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-41

Genotypic and Phenotypic Detection of Biofilm Formation in Clinical Klebsiella pneumoniae Isolates

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Background and aim: Biofilm formation in Klebsiella pneumoniae enhances persistence in clinical settings and may contribute to antimicrobial resistance and pathogenicity. This study aimed to evaluate the biofilm-forming ability of clinical K. pneumoniae isolates using phenotypic and genotypic approaches and to assess the relationships among biofilm formation, antibiotic resistance, and selected biofilm-associated genes.

Methods: In this cross-sectional study, 52 non-duplicate clinical K. pneumoniae isolates were collected from educational hospitals affiliated with Babol University of Medical Sciences (Iran) during March–October 2023 and identified by standard microbiological/biochemical tests. Antimicrobial susceptibility testing was performed by disk diffusion and MDR status was determined per CLSI criteria. Biofilm formation was assessed using the microtiter plate method. PCR was used to detect biofilm-related genes (iutA, mrkA, mrkD, treC, wcaG, magA). Associations were analyzed using chi-square tests (P0.05).

Results: Isolates were obtained mainly from urine (28.84%) and blood (19.23%), with the highest proportion from the ICU (42.3%). The highest resistance rate was to ceftazidime (53.84%); the lowest was to amikacin (17.3%). More than 48% of isolates were MDR. Overall, 82.69% (43/52) produced biofilm, and 17.3% were non-biofilm producers. Among biofilm producers, strong biofilm formation was observed in 48.83% (21/43), moderate in 23.25% (10/43), and weak in 27.9% (12/43). No significant association was found between biofilm formation and MDR status (P=0.536) or overall antimicrobial resistance profiles. The most frequent biofilm-associated genes were treC (78.84%) and wcaG (71.15%), followed by mrkD (65.38%), mrkA (63.46%), iutA (40.38%), and magA (15.38%).

Conclusion: Clinical K. pneumoniae isolates showed a high prevalence of biofilm formation and considerable antimicrobial resistance, alongside frequent carriage of key biofilm-associated genes. Given the substantial biofilm-forming propensity, elucidating the underlying mechanisms and implementing effective anti-biofilm strategies are essential to improve the prevention and management of K. pneumoniae infections in healthcare settings.

keywords: Klebsiella pneumoniae; Biofilm; Antimicrobial resistance; Virulence genes

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-42

Comparison of the Effect of Operating Room Surface Disinfection with Nanosil and Sodium Hypochlorite on Microbial Load and Residual Antimicrobial Effect

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Background and aim: Operating room surface contamination is a critical challenge in preventing surgical site infections. Given the significant drawbacks of common disinfectants like sodium hypochlorite, including respiratory irritation and occupational health risks for healthcare workers, evaluating safer alternatives is essential. This study aimed to compare the effects of Nanosil and sodium hypochlorite on microbial load and residual antimicrobial effect. This research was approved under the ethics code IR.IUMS.FAM.REC.1404.016.

Methods: This interventional study was conducted three teaching hospitals. In each center, one operating room was disinfected with Nanosil and the other with 0.5% sodium hypochlorite. Sampling was performed on five high-touch surfaces: surgical table, instrument table, electrocautery machine, suction machine, and surgical light. Swab samples were collected at four intervals: before, immediately after, 2 hours, and 4 hours post-disinfection. Samples were cultured on blood agar, and the number of colonies was counted after 24 hours of incubation at 37°C. Data were analyzed using Wilcoxon and Mann-Whitney U tests. To reduce Type I error inflation, the Bonferroni correction was applied, setting the significance level at alpha=0.017 for within-group comparisons and alpha=0.0125 for between-group comparisons.

Results: The median microbial load before intervention was 40 CFU/ml in the Nanosil group and 30 CFU/ml in the sodium hypochlorite group. Both solutions significantly reduced the median microbial load to zero CFU/ml immediately after disinfection (P 0.001). In the Nanosil group, the microbial load remained zero CFU/ml at 2 and 4 hours, demonstrating a significant residual effect (P = 0.373). Conversely, the sodium hypochlorite group showed a significant increase in microbial load to 10 CFU/ml by the 4-hour mark (P = 0.005). Between-group comparisons confirmed that Nanosil resulted in significantly lower contamination (median zero CFU/ml) at 2 and 4 hours compared to sodium hypochlorite (P 0.0125).

Conclusion: While both disinfectants provide equal immediate bactericidal efficacy, sodium hypochlorite lacks a sustained residual effect. Nanosil prevents microorganism regrowth for at least 4 hours due to the presence of silver ions. Therefore, Nanosil is recommended as a safer and more efficient alternative for disinfecting operating room environmental surfaces, particularly during long surgical procedures.

keywords: Operating Room, Nanosil, Sodium Hypochlorite, Microbial Load , Residual Antimicrobial

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-43

Molecular Detection of Antibiotic Resistance Genes in Uropathogenic Bacteria Isolated from Urine and Prostate Biopsy Samples of Patients with Prostate Adenocarcinoma and Urinary Tract Infection.

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Background and aim: Urinary Tract Infections (UTIs) are common complications in men with Prostate disorders, particularly Prostate Adenocarcinoma. Given the anatomical continuity between the Urinary Tract and the Prostate gland, infections may ascend and involve prostatic tissue, complicating treatment outcomes. Alterations in the Urinary Prostatic microbiota and the increasing prevalence of antimicrobial resistance are associated with persistent infections and therapeutic failure. In high-risk patients, including those with malignancy, rapid molecular identification of antibiotic resistance mechanisms is essential for optimizing antimicrobial therapy.

Methods: In this cross-sectional study, 72 Urine and Prostate Biopsy Samples were collected from patients with prostate adenocarcinoma and concurrent Urinary Tract Infection. Bacterial isolates were identified using standard phenotypic and biochemical methods. Genomic DNA was extracted, and polymerase chain reaction (PCR) assays were performed to detect three major antibiotic resistance genes (TEM, qnrA, and aac(3)). PCR products were analyzed by agarose gel electrophoresis. The distribution of resistance genes was evaluated among predominant Bacterial species, including Escherichia coli, Klebsiella pneumoniae, Staphylococcus epidermidis, Pseudomonas aeruginosa, and Enterococcus faecalis. Molecular findings were compared with phenotypic antimicrobial susceptibility testing and minimum inhibitory concentration (MIC) data.

Results: PCR analysis revealed a high prevalence of antibiotic resistance genes among bacterial isolates from urine and Prostate biopsy samples. The aac(3) gene was detected in 75% of isolates, indicating widespread aminoglycoside resistance, while the TEM gene was identified in 84.4% of Gram-negative isolates. The qnrA gene was detected in 48.6% of total isolates. The highest prevalence and co-occurrence of resistance genes were observed in E. coli and K. pneumoniae, which were strongly associated with multidrug-resistant phenotypes. High concordance between resistance gene profiles of urine and Prostate biopsy isolates supports an ascending route of infection.

Conclusion: This study demonstrates a prevalence of Antibiotic resistance genes among uropathogenic Bacteria isolated from patients with Prostate Adenocarcinoma. The concordance between Urine and Prostate biopsy isolates supports an ascending route of infection and highlights the clinical relevance of molecular resistance profiling. Detection of multiple resistance genes was associated with multidrug resistance, underscoring the need for molecular diagnostics to guide targeted antimicrobial therapy and improve treatment outcomes in high-risk patient populations.

keywords: Antibiotic resistance - Uropathogenic Bacteria- Prostate Adenocarcinoma

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-44

A Novel Recombinant mRNA Vaccine for Broad Protection Against Multidrug-Resistant Klebsiella pneumoniae: Confronting the Superbug

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Background and aim: The rapid emergence of multidrug-resistant Klebsiella pneumoniae (MDR-Kp) poses a serious challenge to clinical management and infection control. Given the limited efficacy of existing antibiotics, the development of effective prophylactic strategies is of increasing importance. mRNA-based vaccines offer a flexible and scalable platform for targeting conserved bacterial antigens and overcoming antimicrobial resistance.

Methods: A rational immunoinformatics-driven approach was employed to design a recombinant multi-epitope mRNA vaccine against MDR-Kp. Conserved outer membrane antigens, including OmpA, OmpK17, and fimbrial proteins, were screened to identify highly antigenic, non-toxic, and non-allergenic epitopes. Selected epitopes were assembled into a single antigen cassette and fused to a β-defensin molecular adjuvant using EAAAK linkers, with a tissue plasminogen activator (tPA) signal peptide incorporated to enhance protein secretion. The mRNA construct was engineered with essential regulatory elements, including an m7G cap, optimized 5′ and 3′ untranslated regions, a Kozak sequence, and a poly(A) tail. Codon optimization was performed to maximize mammalian expression efficiency. Structural stability, antigenicity, and physicochemical properties were evaluated computationally. Molecular docking and 100-ns molecular dynamics simulations were conducted to assess interactions with innate immune receptors TLR2 and TLR4. In silico immune simulations were used to predict immunogenic performance.

Results: The optimized mRNA construct exhibited high translational efficiency (codon adaptation index 0.95) and strong structural stability. Docking and molecular dynamics analyses demonstrated stable and energetically favorable interactions with TLR2 and TLR4, indicating effective innate immune recognition. Immune simulations predicted a rapid and robust immune response, characterized by early induction of neutralizing antibodies and a balanced cytokine profile suggestive of protective immunity.

Conclusion: This study presents a rationally designed and computationally validated multi-epitope mRNA vaccine candidate targeting MDR-Kp. The results highlight the feasibility of mRNA-based vaccination as a translational strategy to address multidrug-resistant bacterial infections and support further experimental validation in laboratory and preclinical settings.

keywords: mRNA vaccine; Klebsiella pneumoniae; multidrug resistance; immunoinformatics; molecular dynamics

PBa-45

Antimicrobial resistance, serogroups, virulence gene, Biofilm formation, and RAPD-PCR of Escherichia coli from urinary tract infection patients

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Background and aim: Urinary tract infections (UTIs) are one of the most common bacterial infections with global expansion. These infections are predominantly caused by uropathogenic Escherichia coli (UPEC). The present research performed to track common uropathogenic E.coli serogroups, antibiotic resistance pattern of strains and prevalence of virulence genes in isolations having the ability to constitute biofilm.

Methods: Totally, 100 strains of Escherichia coli isolated from UTIs patients, using bacterial culture method were subjected to polymerase chain reactions for detection of various O-serogroups, some urovirulence factors, antibiotic resistance genes and resistance to 13 different antibiotics. Biofilm formation was evaluated using the microtiter plate assay. The phylogenetic groups of the isolates were determined by RAPD-PCR.

Results: PCR detection of serogroups revealed that among the identified UPEC isolates, the most prevalent serogroups were O25 (28%), followed by O15 (20%), O16 (15%), O6 (7%), O2 (3%), and O1 (2%). The distribution of virulence genes among UPEC isolates, as determined by PCR, was as follows: the adhesin gene fimH exhibited the highest frequency at 95%, followed by papC (41%), cnf-1 (22%), hlyA (19%), sfa (16%), and afa (14%). Resistance to Amoxicillin/Clavulanic acid (78%) and Ampicillin/Sulbactam (72%) had the highest while resistance to nitrofurantoin (6%) and fosfomysin (2%) had the lowest frequencies. Among 100 E.coli isolates, all isolates were able to make biofilm that 41% isolates indicated strong reaction, 29% of moderate and 30% of weak biofilm reaction. Overall, 100 RAPD patterns were obtained that which 11 patterns were similar between 22 isolates (Common type).

Conclusion: The findings indicated the importance of virulence genes in serogroups producing uropathogenic E.coli biofilm. It is recommended that strains producing biofilm before antibiotic use should be studied.

keywords: Escherichia coli, Biofilms, Serogroups, Virulence factors, Antibiotic resistance

PBa-46

Causes and phenotypic changes of Candida albicans in the presence of Staphylococcus aureus

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Background and aim: Polymicrobial infections, including those of fungal and bacterial origin, are major contributors to the severity and chronicity of many human diseases. Candida albicans and Staphylococcus aureus are frequently co-isolated as these microbes are well adapted to colonize similar niches in their host. These co-colonized microbes often form a polymicrobial biofilm-a structured community of microorganisms encased in a protective extracellular polysaccharide matrix that provides resistance to both antimicrobial agents and the host immune system.

Methods: According to the articles surveyed from scientific databases including Google Scholar, PubMed, and Scopus, studies published between January 2019 and March 2025 were reviewed. The literature search has emphasized fungal–bacterial interactions, the formation of polymicrobial biofilms, metabolic interplays, morphogenesis, cell wall modeling, quorum sensing, and antimicrobial resistance.

Results: The presence of S. aureus triggers significant phenotypic responses in C. albicans, including increased biofilm formation, morphogenic and cell wall remodeling, and responses to bacterial signals that repress or alter hyphal filamentation. Mixed-species biofilms exhibit increased biomass and resistance to antifungal and antibacterial treatments compared to mono-species biofilms, which is linked to worse clinical outcomes. Co-infection also alters host–pathogen interactions, promoting immune evasion and microbial survival.

Conclusion: The mutual interaction between C. albicans and S. aureus is dynamic and multifactorial, involving metabolic adaptation, quorum sensing, genetic regulation, and phenotypic plasticity. The ultimate understanding of these interactions would hopefully enable the design of proper therapeutic strategy targeting such polymicrobial biofilm-associated infections.

keywords: Candida albicans, Staphylococcus aureus, polymicrobial biofilm, phenotypic changes, bacterial–fungal interaction.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-47

Multidrug Resistance and Carbapenem Resistance Patterns in Clinical Klebsiella pneumoniae Isolates

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Background and aim: Klebsiella pneumoniae is a major opportunistic pathogen in healthcare settings, and the emergence of carbapenem-resistant K. pneumoniae (CRKP) poses a serious therapeutic challenge worldwide. Rising resistance rates significantly compromise available treatment options and increase the burden of hospital-acquired infections. This study aimed to characterize the antimicrobial resistance patterns of K. pneumoniae isolated from urine, blood, and wound specimens to better inform clinical management and infection control measures.

Methods: A descriptive cross-sectional analysis was conducted on clinical isolates collected across three consecutive seasons. Antimicrobial susceptibility testing was performed following the Clinical and Laboratory Standards Institute (CLSI) guidelines. Resistance profiles were compared across specimen types to identify potential site-specific trends.

Results: Overall carbapenem resistance was approximately 45%, with urinary isolates exhibiting the highest resistance rate (55%). Cephalosporin resistance ranged from 10% to 20%, with notably elevated resistance observed against ceftazidime and cefepime. Blood and wound isolates demonstrated lower yet clinically significant carbapenem resistance rates of 28% and 21%, respectively. The distribution of resistance patterns suggests a concerning rise in multidrug-resistant phenotypes, particularly among urinary tract isolates.

Conclusion: The high burden of carbapenem resistance among K. pneumoniae, especially in urinary isolates, underscores a pressing need for strengthened antimicrobial stewardship programs and enhanced infection prevention strategies. Continuous surveillance is essential to monitor evolving resistance trends and to guide empirical therapy in clinical practice.

keywords: Klebsiella pneumoniae, Carbapenem resistance, Antimicrobial resistance, Multidrug resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-48

Antimicrobial Activity of Traditional Medicinal Plant Extracts against Bacterial and Fungal Strains Causing Dental Caries: An in Vitro Study

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Background and aim: The use of plant extracts or their compounds as antimicrobial agents for oral infections worldwide represents that herbal medicines could be used as an effective alternative method in oral health care. This study aimed to evaluate the antifungal and antibacterial effects of five traditional medicinal plant extracts on standard and clinical strains of bacteria and fungi causing dental caries.

Methods: Aqueous and methanolic extracts of Zataria multiflora, Lawsonia alba, Zizyphus spina-christi, Myrtus communis, and Citrus aurantium were prepared using maceration method. The minimum inhibitory concentration (MIC) and minimum microbicidal concentration (MMC) of the prepared extracts were evaluated against bacterial (Streptococcus sanguinis and S. mutans) and fungal (Candida albicans, C. krusei, and C. tropicalis) isolates using broth microdilution method.

Results: Aqueous extracts of the studied plants showed no antimicrobial effects on the studied microorganisms, except M. communis and C. aurantium. The results indicated the antimicrobial potency of the methanolic extract of M. communis (MIC range =2 to 64 µg/mL) against all the studied microorganisms, followed by Z. multiflora (MIC range = 512-2048 µg/mL), L. alba (MIC range = 1024-2048 µg/mL), C. aurantium (MIC range = 1024-4096 µg/mL), and Z. spina-christi (MIC range=2048- >4096 µg/mL). Also, the lowest MMCs against the studied strains were related to the methanolic extract of M. communis (MMC range = 16-512 µg/mL).

Conclusion: The results showed remarkable antimicrobial effects of M. communis extract, which could be a suitable alternative to chemical mouthwashes to prevent and control oral infections.

keywords: Plant extract, Antimicrobial, Dental caries, Bacterial, Fungal.

PBa-49

Prevalence of Bacteria Isolated from Blood Cultures of Patients Admitted to the ICU Department of Valiasr Hospital in Zanjan in 1401

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Background and aim: Bloodstream infections are considered one of the major problems among patients hospitalized in the intensive care unit (ICU). This study was conducted to investigate the prevalence of bacteria isolated from blood cultures of patients admitted to the ICU.

Methods: This cross-sectional study was performed on 300 patients hospitalized in the ICU of Valiasr Hospital in Zanjan in 1401 (2022–2023). Demographic, clinical, and laboratory data were extracted from patients' medical records and analyzed using SPSS software version 23.

Results: Out of the 300 hospitalized patients, blood cultures were positive in 27 cases. The highest frequency of isolated bacteria was related to Escherichia coli and Klebsiella pneumoniae (18.5% each), followed by group D Streptococcus (14.8%). The lowest frequency was observed for Staphylococcus aureus, Pseudomonas aeruginosa, and Micrococcus (3.7%).

Conclusion: The results of this study showed that Gram-negative bacteria, particularly E. coli and K. pneumoniae, play the most significant role in bloodstream infections among ICU patients

keywords: Prevalence, blood culture, ICU, bloodstream infection

PBa-50

Drug Resistance Patterns of Bacteria Isolated from Blood Cultures of Patients Admitted to the ICU Department of Valiasr Hospital in Zanjan in 1401

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Background and aim: Antibiotic resistance is one of the major challenges in the treatment of bloodstream infections among patients hospitalized in the intensive care unit (ICU). This study was conducted to investigate the antibiotic resistance patterns of bacteria isolated from blood cultures of ICU patients.

Methods: This cross-sectional study was performed on 300 patients admitted to the ICU of Valiasr Hospital in Zanjan in 1401 (2022–2023). Data related to antibiogram results were extracted from patients' medical records and analyzed using SPSS software version 23

Results: Escherichia coli showed the highest antibiotic resistance to gentamicin, cotrimoxazole, and ceftriaxone (80%). In addition, Klebsiella pneumoniae exhibited 100% resistance to all antibiotics evaluated in this study

Conclusion: The high level of antibiotic resistance among bacteria isolated from blood cultures of ICU patients highlights the necessity of implementing antibiotic stewardship programs and effective infection control measures in hospital settings

keywords: Antibiotic resistance, blood culture, ICU, antibiotic stewardship

PBa-51

Evaluation of the Antimicrobial Properties of Zinc Nanoparticles against Helicobacter pylori Clinical Isolates

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Background and aim: Helicobacter pylori is a globally prevalent bacterial pathogen associated with various gastrointestinal diseases such as gastritis, peptic ulcer disease, and gastric cancer. The increasing resistance to commonly used antibiotics has limited the effectiveness of conventional treatment options, creating an urgent demand for new therapeutic strategies.

Methods: In this work, zinc nanoparticles were synthesized using a green synthesis approach based on propolis extract and tested for antibacterial activity against clinical strains of H. pylori. XRD and TEM characterization confirmed the formation of spherical, crystalline nanoparticles measuring 20–50 nm. Microbroth dilution assays indicated that bacterial growth was inhibited at concentrations ranging from 1.56 to 25 mg/L.

Results: Checkerboard analysis revealed a pronounced synergistic interaction between propolis-mediated zinc nanoparticles and clarithromycin, as evidenced by a fractional inhibitory concentration index (FICI) of $\leq$ 0.5. In contrast, the combination of zinc nanoparticles with metronidazole or amoxicillin resulted in additive antimicrobial effects. Furthermore, drug release experiments demonstrated a sustained release pattern that closely followed the Higuchi kinetic model (R^2 = 0.992), indicating a diffusion-driven release mechanism.

Conclusion: Collectively, these results underscore the potential of green-synthesized zinc nanoparticles as an effective adjunct strategy to potentiate antibiotic activity and address antimicrobial resistance in Helicobacter pylori infections.

keywords: Helicobacter pylori, zinc nanoparticles, propolis, antibiotic resistance, green synthesis, synergistic

PBa-52

Investigation of antibiotic resistance, biofilm formation ability,virulence factors, and molecular typing of Klebsiella oxytoca strains isolated from patients hospitalized in Hamadan hospitals

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Background and aim: Klebsiella oxytoca is an opportunistic pathogen with multiple drug resistance that plays a role in nosocomial infections. This study aimed to investigate antibiotic resistance patterns, biofilm formation ability, virulence factor abundance, and molecular typing of Klebsiella oxytoca strains isolated from patients hospitalized in Hamadan hospitals

Methods: In this descriptive-cross-sectional study, 35 Klebsiella oxytoca isolates were collected from clinical samples and identified using standard microbial methods. Antibiotic resistance was assessed by disk diffusion method (CLSI 2022), biofilm formation by crystal violet method, virulence genes by PCR, and molecular typing by ERIC-PCR.

Results: The results showed that the highest resistance was to ciprofloxacin (91.4%) and the lowest was to amikacin (31.4%). About 60% of the strains formed biofilm, of which 17.1% had high biofilm strength. The virulence genes fimA (77.1%) and npsB (22.8%) were the most and least abundant, respectively. Molecular typing revealed significant genetic diversity.

Conclusion: This study confirmed that Klebsiella oxytoca is more prevalent in respiratory specimens, and its high antibiotic resistance and ability to form biofilms highlight the need for rapid diagnosis and effective treatment strategies in hospital settings.

keywords: Klebsiella oxytoca ,antibiotic resistance,biofilm,virulence factors,ERIC-PCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-53

Diffusely Adherent Escherichia coli (DAEC) in Paediatric Diarrhea in Shiraz, Southern Iran: Virulence Genes and Antibiotic Susceptibility Patterns

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Background and aim: Diffusely adherent Escherichia coli (DAEC) has been implicated as a cause of diarrhea in children. This study aimed to determine the prevalence of DAEC among pediatric diarrheal samples in Shiraz (southern Iran), and to characterize adherence phenotype, virulence gene profiles, and antimicrobial susceptibility.

Methods: In a cross-sectional study, 309 stool samples from infants and children (13 years) with diarrhea were collected. E. coli isolates were identified by culture and biochemical tests. DAEC was detected by PCR targeting Afa/Dr and AIDA-I adhesin-encoding genes and confirmed by HEp-2 cell adherence assay. Virulence genes (sat, pet, sigA, pic, astA, fimH) were assessed by PCR. Antimicrobial susceptibility testing was performed by disk diffusion.

Results: Among 309 stool samples, 207 (66.9%) yielded E. coli. DAEC was identified in 14/207 (6.7%) E. coli isolates. All DAEC isolates demonstrated diffuse adherence to HEp-2 cells (100%). Virulence gene frequencies were: sat 50%, pet 0%, sigA 14.2%, pic 14.2%, astA 21.4%, and fimH 100%. The most effective antibiotic was imipenem (92.8% susceptible), while ampicillin showed no activity (0% susceptible).

Conclusion: Although DAEC prevalence was low among pediatric diarrheal cases in this setting, isolates exhibited substantial antimicrobial resistance and frequent carriage of virulence-associated genes. Combined molecular detection and adherence testing can support laboratory diagnosis, while local susceptibility patterns (notably high effectiveness of imipenem and poor activity of ampicillin) are essential for guiding clinical management.

keywords: Escherichia coli; Diarrhea; Virulence; Drug Resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-54

Molecular investigation of trimethoprim resistance gene (dfrA1-like) in Mammary Pathogenic Escherichia coli strains, isolated from milk samples of bovine mastitis in industrial farms of Hamedan County

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Background and aim: Bovine mastitis is globally a significant disease, with Escherichia coli being a one of the frequent causative agents. Mammary pathogenic E. coli (MPEC) is proposed as a new pathotype responsible for bovine mastitis. Widespread veterinary use of trimethoprim, has led to the increased resistance against this antibiotic which most often is mediated by dfr gene including dfrA1. This gene encodes a drug-resistant dihydrofolate reductase enzyme that is linked to class 1 integrons. This study aimed to investigate the presence of dfrA1-like gene in MPEC strains isolated from bovine clinical mastitis in industrial farms of Hamedan County, west of Iran.

Methods: The present study was carried out on MPEC strains (n=50) isolated from milk of cows with clinical mastitis in Hamedan County. At first, genomic DNA was extracted from bacterial strains using rapid boiling method. Extracted DNAs were evaluated for the presence of the trimethoprim resistance gene (dfrA1-like) by Polymerase Chain Reaction (PCR) technique using specific primers.

Results: All positive samples yielded a distinct DNA band at the expected size of 171 bp, confirming the specific amplification of the target gene. The PCR results demonstrated that dfrA1-like gene was present in 15 isolates. This corresponds to a prevalence rate of 30% within the study population. The remaining 35 isolates (70%) were negative for this specific gene. Detection of this gene in approximately one-third of the clinical isolates indicates the presence of a significant reservoir of genetic determinants conferring resistance to folate pathway inhibitors in the studied dairy farms.

Conclusion: Thirty percent prevalence of dfrA1-like gene highlights a considerable risk of antimicrobial resistance in MPEC strains circulating in Hamedan. Since dfrA1 is often linked to mobile genetic elements, these isolates may facilitate the horizontal spread of resistance traits within the bacterial populations. These findings emphasize the necessity for prudent use of trimethoprim and continuous molecular surveillance to mitigate the dissemination of resistant bacteria in the regional dairy industry.

keywords: Mastitis, Escherichia coli, Antibiotic resistance, Trimethoprim

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July 20-23, 2026

PBa-55

Evaluation of the antibacterial activity of crocin and vitamin E-TPGS using a nanoliposomal system

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Background and aim: The increasing resistance of bacteria to common antibiotics has increased the interest in natural compounds with antibacterial activity. Crocin, one of the active compounds of saffron, has significant antibacterial properties, but limitations such as low stability & solubility, and poor permeability limit its clinical application. Vitamin E-TPGS (D-α-Tocopheryl polyethylene glycol 1000 succinate) is a water-soluble derivative of vitamin E that is known as a surfactant and membrane permeability enhancer. This study aimed to compare the antibacterial activity of crocin and vitamin E against key pathogenic bacteria.

Methods: To investigate the structural characteristics, physicochemical parameters, including size, PDI, and encapsulation efficiency, were measured. Antibacterial activity was evaluated at concentrations of 0.5, 1, 2, and 4 mg/mL against Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa strains using the well diffusion method on Mueller-Hinton agar medium. In addition, the minimum inhibitory concentration and minimum bactericidal concentration were determined by the dilution method in liquid medium.

Results: The nanoliposomes exhibited particle sizes ranging from 90 to 115 nm, PDI 0.25, and an encapsulation efficiency exceeding 65%. Free liposomes showed no notable inhibitory effect on bacterial growth. Well diffusion assay results demonstrated that nanoliposomes containing vitamin E-TPGS + crocin produced the strongest antibacterial activity against Staphylococcus aureus, with an inhibition zone of 22.4 ± 1.2 mm, which was significantly larger than those observed for single-component formulations and free compounds (p 0.05). The largest growth inhibition zone was observed against Escherichia coli, with a mean diameter of 23.1 ± 1.3 mm. Moreover, upon exposure to Pseudomonas aeruginosa, the combined nanoliposomal formulation exhibited superior inhibitory activity compared with the other experimental groups.

Conclusion: This study shows that the simultaneous loading of vitamin E-TPGS and crocin in the structure of nanoliposomes leads to a significant enhancement of the antibacterial activity of these compounds. This performance improvement is probably due to increased physicochemical stability, gradual release, and facilitation of the penetration of active ingredients into the bacterial cell membrane. Accordingly, these combined nanoliposomes can be considered as an effective system in the design and development of antibacterial solutions based on natural compounds.

keywords: Vitamin E-TPGS, Crocin, Nanoliposomes, Antibacterial activity

PBa-56

Prevalence and Clinical Correlates of Staphylococcus aureus in Joint Infections Among Hospitalized Patients in Northern Iran during 2023-2024

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Background and aim: Septic arthritis is a serious joint infection that can rapidly cause irreversible damage if not promptly diagnosed and treated. Staphylococcus aureus is the most common causative agent and is associated with more severe outcomes. This study aimed to determine the prevalence of S. aureus and its clinical correlations in septic arthritis cases in northern Iran during 2023–2024.

Methods: In this descriptive cross-sectional study, 230 hospitalized patients with suspected septic arthritis were evaluated. Synovial fluid samples were cultured on standard media, and bacterial identification was performed using conventional methods and PCR targeting the nuc gene for confirmation of S. aureus. Demographic and clinical data were analyzed using SPSS.

Results: Of the patients, 66.5% were male, and the knee was the most commonly affected joint (53.5%). Positive cultures were obtained in 20 cases (8.6%). S. aureus was detected in 12 samples, accounting for 60% of culture-positive cases and 5.2% of all patients. A significant association was found between younger age and culture positivity (P = 0.043), while no association was observed with sex or residence.

Conclusion: S. aureus was the predominant pathogen in septic arthritis among hospitalized patients in northern Iran. Given the low culture positivity rate, the use of advanced diagnostic methods is recommended. Further studies on antimicrobial resistance, particularly MRSA, are necessary to optimize empirical treatment strategies.

keywords: Septic arthritis; Staphylococcus aureus; Joint infections; Synovial fluid culture; Bacterial

PBa-57

Prevalence of Gram-Negative Bacteria and Antimicrobial Resistance in Skin and Soft Tissue Infections Among Diabetic Patients Referred to Healthcare Centers in Qom, Iran

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Background and aim: Identification and evaluation of antimicrobial resistance patterns among the main causative agents of skin and soft tissue infections (SSTIs) in diabetic patients play a crucial role in appropriate antibiotic selection and optimized therapeutic outcomes. The present study aimed to investigate the etiological agents and antimicrobial resistance patterns of skin and soft tissue infections in diabetic patients referred to healthcare centers in Tehran during the years 2023–2024.

Methods: This descriptive cross-sectional study was conducted over a 12-month period on 40 wound specimens obtained from hospitalized patients. Bacterial cultures and antibiotic susceptibility testing were performed, and the results were recorded and statistically analyzed.

Results: The mean age of the patients was 48.9 ± 8.5 years. The mean duration of hospitalization was 13.6 ± 5.6 days, and the mean duration of diabetes was 13.4 ± 4.6 years. The severity of diabetic wounds was classified as grade I in 22.5%, grade II in 47.5%, and grade III in 30% of cases. The causative pathogens included Enterobacter spp. (5%), Escherichia coli (10%), Klebsiella pneumoniae (7.5%), Staphylococcus aureus (12.5%), Acinetobacter spp. (20%), and Pseudomonas aeruginosa (45%). The highest rates of antimicrobial resistance were observed against imipenem and co-trimoxazole. Enterobacter species demonstrated multidrug resistance patterns.

Conclusion: Given the high prevalence of antimicrobial resistance among the isolated strains, the accelerating trend of drug resistance is evident. The observed high resistance rates underscore the urgent need for enhanced healthcare policies focusing on stricter infection control measures, particularly in diabetic patients with soft tissue infections. Implementation of effective and evidence-based treatment guidelines, rational antibiotic prescribing, and regular updating of therapeutic protocols are essential to combat multidrug-resistant organisms and improve clinical outcomes.

keywords: Antimicrobial resistance; Skin; Soft tissue; Diabetes; Infection

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-58

Prevalence of Nosocomial Skin Infections Among Trauma Patients Admitted to Hospitals in Qom, Iran

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Background and aim: Nosocomial infections represent one of the most significant challenges to healthcare systems worldwide. Trauma patients are at an increased risk of developing hospital-acquired infections due to the nature of their injuries, the need for multiple surgical interventions, and the frequent use of invasive medical devices. Skin and soft tissue infections can lead to prolonged hospitalization, serious complications, and increased mortality. This study aimed to evaluate the prevalence of nosocomial skin infections and antimicrobial resistance patterns among trauma patients admitted to educational hospitals in Qom, Iran, during the years 2021 to 2024.

Methods: This retrospective cross-sectional study was conducted on 102 hospitalized trauma patients admitted to educational hospitals in Qom. Data were extracted from patients' medical records and included demographic characteristics, type of infection, causative bacterial agents, antimicrobial resistance patterns, empirical antibiotic therapy, length of hospital stay, need for surgical intervention, occurrence of complications, and final clinical outcomes. Data analysis was performed using SPSS software version 21, applying descriptive and inferential statistical tests.

Results: The findings revealed that 9 hospitalized patients developed nosocomial skin infections. The mean age of patients was 42.67 years, and the mean length of hospital stay was 6.44 days. The most frequently isolated pathogens were Staphylococcus aureus (5 cases) and Escherichia coli (4 cases). Significant antimicrobial resistance was observed against vancomycin, ciprofloxacin, and gentamicin among the isolated bacterial strains.

Conclusion: Although the prevalence of nosocomial skin infections among trauma patients was relatively low, their clinical consequences and antimicrobial resistance patterns were of considerable importance. The high resistance rates to commonly used antibiotics emphasize the need for revising treatment protocols, implementing antimicrobial stewardship programs, and providing continuous education for healthcare personnel to optimize infection management and improve patient outcomes.

keywords: Nosocomial skin infections; Trauma patients; Hospitals; Qom

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-59

Evaluation of Enzymatic Mechanisms of Bacillus in Nanoplastics Biodegradation and Reduction of Clinical Risks: A Systematic Review

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Background and aim: According to NOAA and UNEP reports, nanoplastics (NPs), defined as colloidal particles ranging from 1 to 1000 nm, represent an emerging threat to public health. Recent studies in The Lancet Planetary Health confirm that due to their minute size, NPs possess the ability to cross vital biological barriers (blood-brain and placental barriers). This infiltration leads to tissue accumulation, neuroinflammation, oxidative stress (ROS), and the transport of toxic contaminants ("Trojan Horse" effect). Given the inefficiency of physical removal methods, this study systematically reviews the catalytic potential of Bacillus bacteria in the biodegradation of NPs as a clinical preventive strategy.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. A comprehensive search was performed in Web of Science, Scopus, PubMed, and ScienceDirect databases for English articles published between 2020 and 2025. Keywords included "Nanoplastics," "Enzymatic degradation," "Bacillus subtilis," and "Cytotoxicity." The inclusion criteria focused on studies simultaneously addressing molecular degradation mechanisms and reduction of cellular toxicity. After initial screening and exclusion of papers lacking quantitative data, final studies were extracted.

Results: Data synthesis revealed that Bacillus subtilis and Bacillus amyloliquefaciens strains utilize a smart four-stage strategy: * Biodeterioration: Secretion of the biosurfactant "Surfactin" by B. subtilis reduces the surface tension of hydrophobic polymers and facilitates biofilm formation. * Bio-fragmentation: Identification of oxidative enzymes (Laccase and Manganese Peroxidase) to break C-C bonds, and hydrolytic enzymes (Esterase, Lipase, and Cutinase) to hydrolyze ester bonds in PET. * Assimilation: Absorption of oligomers for cellular metabolism. * Mineralization: Final conversion to CO_2 and biomass. Findings indicate that "microbial consortia" (mixed cultures) significantly increase removal efficiency compared to monocultures due to enzymatic synergy, effectively eliminating culture medium cytotoxicity for human cells.

Conclusion: The utilization of Bacillus consortia represents a biocompatible solution for removing NPs at the source. By preventing particle entry into the food chain and the human body, this approach reduces the risk of plastic-associated chronic diseases and opens new horizons in environmental health and preventive medicine.

keywords: Nanoplastics, Bacillus subtilis, Microbial enzymes, Bacillus amyloliquefaciens, Microbial Consortium.

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-60

Proteomic Methods for Rapid Diagnosis of Antibiotic Resistance in Bacteria

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Background and aim: Antibiotic resistance in bacterial pathogens is currently a significant challenge globally and poses various difficulties in the management and further rise in morbidity and mortality rates. The development of precise and rapid diagnostic tools is critical for the effective management of antimicrobial drugs and the prevention of the spread of antibiotic resistance. Proteomics acts as a functional platform that helps in understanding the proteins that are part of the antibiotic resistance mechanisms.

Methods: The current research was undertaken as a comprehensive literature-based analysis. The relevant peer-reviewed articles were searched in a manner from the databases, including PubMed, Web of Science, Scopus, and Google Scholar. The recent advancements in the field of proteomics, reported in the above literature, were evaluated concerning the identification and analysis of antibiotic-resistant bacteria through MALDI-TOF MS, LC-MS/MS, two-dimensional electrophoresis (2-DE), SWATH MS, iTRAQ and TMT labeling approaches, and Raman microspectroscopy. Moreover, research articles utilizing the adaptive laboratory evolution technique along with high-throughput analysis of protein expression, modifications, efflux, and biofilms in the most prevalent ESKAPE organisms were assessed.

Results: The study of proteomics showed that there were separate patterns of proteins involved in antibiotic resistance, tolerance, and persistence. In the case of the Enterococcus genus of bacteria, there was an increased expression of proteins linked to vancomycin resistance and biofilm formation. In Staphylococcus aureus, there was a change in patterns of stress-response and cell wall proteins. In Klebsiella pneumoniae and Acinetobacter baumannii bacteria, there was an increased expression of efflux pumps, beta-lactamase production, and modulation of porin production

Conclusion: Proteomics offers an effective tool for rapid and precise determination of antibiotic-resistant bacteria. When modern proteomic methods are combined with functional studies, this helps improve an understanding of bacterial mechanisms of resistance and aids the development of effective therapies for their treatment.

keywords: Antibiotic resistance; proteomics; MALDI-TOF MS; LC–MS/MS; ESKAPE pathogens

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-61

Evaluation of Escherichia coli aggR gene expression in the presence of different concentrations of creatinine

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Background and aim: Background: Chronic renal failure is an irreversible disease resulting in increased blood creatinine with substantial mortality and morbidity in children globally. The Enteroaggregative Escherichia coli (EAEC) is a diarrheagenic agent possessing several virulence factors such as aggR.

Methods: Methods: The purpose of this study was to evaluate the EAEC aggR gene expression in the presence of various creatinine concentrations. Initially, three biochemically-approved E. coli isolates obtained from the medial laboratories in Borujerd city, western Iran were molecularly evaluated using 16S ribosomal RNA (16S rRNA) gene amplification. Next, they were examined regarding aggR gene using polymerase chain reaction (PCR). Those isolates with aggR gene were cultured in brain-heart infusion (BHI) medium supplemented with 1, 3 and 6 mg/dl-1 creatinine (37 oC, 24 hours). The expression level of aggR gene was evaluated in the creatinine-exposed isolates using Real-Time PCR.

Results: Results: Among 50 clinical E. coli isolates, three were EAEC of which a single isolate showed aggR gene presence. Real-Time PCR showed that the AggR gene expression was decreased significantly in presence of various creatinine concentrations (P 0.0001).

Conclusion: Conclusion: This finding warrants further investigation to elucidate the role of creatinine in modulating bacterial virulence gene expression in renal disorder conditions.

keywords: Keywords: Enteroaggregative E. coli, aggR, Creatinine, Real-Time PCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-62

Genetic Analysis of Quinolone Resistance Determinants and FOX-AmpC-β-lactamase in MDR Klebsiella pneumoniae Clinical Strains

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Background and aim: Klebsiella pneumoniae (K. pneumoniae) is a major opportunistic pathogen responsible for diverse clinical infections. Plasmid-mediated quinolone (PMQR) and blaAmpC (FOX) resistance determinants are commonly characterized in K. pneumoniae isolates worldwide and complicate the treatment of infections caused by this bacterium in hospitals. In this study, we investigated the frequency of qnr (qnrA, qnrB, qnrS) and AmpC-type β-lactamase (fox) genes among K. pneumoniae isolates from hospitalized patients in Mazandaran Province, north of Iran.

Methods: A total of 100 K. pneumoniae isolates, obtained from hospitalized patients with nosocomial infection, were included in this study. All biochemistry tests, such as IMVIC test were performed. Confirmation of K. pneumoniae at the species level was done with the analytical profile index (API) 20E kit. Antimicrobial susceptibility was determined by the disk diffusion method, following Clinical and Laboratory Standards Institute (CLSI) guidelines. The combined disk test (CDT) was used to identify phenotypic detection of AmpC producer strains. Genetic characterization of the isolates was conducted by PCR experiment with specific primers.

Results: In the present study, resistance rates were highest for aztreonam (77%), cefotaxime (69%), and piperacillin (68%). Furthermore, the resistance rates of the isolates to nalidixic acid, ciprofloxacin, and levofloxacin were determined to be 55%, 36%, and 29%, respectively. Phenotypically, 61 cefoxitin-resistant isolates were detected among the tested isolates, of which 26 were CDT positive. PCR data indicated that 22.95% of strains harbored the blaFOX gene. The PMQR genes, such as qnrA, qnrB, and qnrS were detected in 47 (47%), 21 (21%), and 22 (22%) isolates, respectively.

Conclusion: This study suggests that K. pneumoniae isolates in northern Iran have a high prevalence of antibiotic resistance, which poses serious problems in treating illnesses. The obtained findings revealed that the majority of the isolates harbored PMQR genes. The high frequency of PMQR, and blaFOXgenes obtained is alarming since they can contribute to ESBL and increase the dissemination of fluoroquinolone and beta-lactamase resistance among isolates. Furthermore, it is important to examine the frequency of other AmpC β-lactamases (like DHA, EBC, and CIT) and PMQR determinants (qnrC, qnrD, and aac(6′)-Ib-cr).

keywords: Klebsiella pneumoniae, Quinolones, AmpC beta-lactamase, Multidrug-resistance

PBa-63

Investigation of Biofilm Production in Vancomycin-Resistant Enterococcus Isolates in the Year 2023

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Background and aim: Enterococci, widely present in the environment, can cause serious infections even though they lack clearly defined toxins. Understanding the virulence characteristics of enterococci is crucial for elucidating the complex mechanisms that drive their pathogenicity. In this study, we aimed to investigate Enterococcus spp. isolated from clinical specimens for biofilm production and antibiotic resistance.

Methods: In this cross-sectional study, 73 Enterococcus isolates were collected from clinical samples of patients admitted to Ganjavian Hospital in Dezful, Iran, in 2023. The antibiotic susceptibility testing and Biofilm formation were assessed by the Kirby-Bauer disk diffusion and microtiter plate assay methods, respectively. The polymerase chain reaction method was used to identify the isolates (ddl gene) and to detect vanA and vanB, aac(6')-aph(2")-1a.

Results: Out of 73 enterococci isolates, 47 (64.4%) were identified as E. faecium and 26 (35.6%) as E. faecalis. The majority of samples (85%) were urine. Resistance to vancomycin was observed in 63% of the isolates, all of which harbored the vanA gene. The highest resistance rate was determined against ciprofloxacin (91.8%). The resistance to ampicillin, tetracycline, nitrofurantoin, and linezolid were 64.4%, 84.9%, 9.6% and 0%. The aac(6')-aph(2")-1a gene was identified in 86.2% (25/29) of high level gentamicin-resistant isolates. The biofilm-producing strains were detected in 75.3%(n=55), including 40%(n=22) E.faecalis and 60%(n=33) E.faecium, but the difference was not statistically significant (p 0.05).

Conclusion: The high prevalence of vancomycin-resistant Enterococci (VRE) harboring the vanA gene, along with its frequent co-occurrence with aminoglycoside resistance, poses a significant threat to the healthcare system. These findings underscore the critical need for stringent surveillance programs, careful antibiotic stewardship, and rigorous infection control measures to prevent the spread of both virulent and resistant enterococcal strains within hospital settings.

keywords: Vancomycin-Resistant Enterococcus (VRE), Biofilm, Antibiotic Resistance

PBa-64

Prevalence of Nor Efflux Pumps in Methicillin-Resistant Staphylococcus aureus of Clinical Isolates in Ganjavian Hospital, Dezful

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Background and aim: MRSA infections have become more common in our hospitals, making treatment increasingly difficult. The efflux pumps play an important role by actively pumping antibiotics out of bacteria, contributing to resistance. Understanding the prevalence of Nor efflux pumps and identifying different MRSA strains through genotyping can help monitor their spread and guide more effective antibiotic choices. This study examined the prevalence of Nor efflux pumps in MRSA isolated from clinical samples.

Methods: In the present study, clinical samples from patients referred to Ganjavian Hospital in Dezful were generally cultured on blood agar and MacConkey culture media. For the culture of sterile body fluid samples (cerebrospinal fluid, pleural fluid, blood), chocolate agar medium was also added to isolate capnophilic bacteria. All culture media were incubated for 48 hours at 35°C. Bacteria were identified using conventional biochemical tests. Antibiotic susceptibility testing was performed using the disk diffusion method, and the results were interpreted according to CLSI standards. MRSA and the presence of nor efflux pumps were detected using the molecular PCR technique.

Results: In this study, we isolated 174 Staphylococcus aureus strains from clinical samples: predominantly wounds (48%, 84 strains), followed by blood (28%, 48 strains), urine (18%, 31 strains), and respiratory samples (5%, 9 strains). These bacteria showed high resistance to penicillin (89%) and erythromycin (86%), moderate resistance to clindamycin (64%) and ciprofloxacin (55%), and lower resistance to cotrimoxazole (39%) and gentamicin (16%). Importantly, all strains remained sensitive to mupirocin, rifampin, and linezolid. Of these, 55 strains (32%) were MRSA, as determined by molecular detection of the mecA gene. Two-thirds (66%) showed multidrug resistance (MDR). The nor genes were detected in 63% of strains overall, but rose to 73% among ciprofloxacin-resistant ones. Among MRSA strains, 40% carried nor genes.

Conclusion: This Ganjavian Hospital study highlights the substantial burden of MRSA alongside widespread nor gene carriage, particularly among fluoroquinolone-resistant strains. Retained susceptibility to mupirocin, rifampin, and linezolid offers reliable therapeutic options, while prevalent MDR patterns emphasize molecular surveillance needs. Routine norA screening and enhanced antimicrobial stewardship are essential for optimizing treatment and preventing the spread in high-prevalence settings.

keywords: Staphylococcus aureus; Drug Resistance; MRSA; Efflux Pumps.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-65

Investigation of the synergistic and antimicrobial effects of Allium sativum, Zingiber officinale, Elettaria cardamomum Oils and Chlorhexidine against Streptococcus mutans and Lactobacillus acidophilus bacteria:An in-vitro study

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Background and aim: Antibiotic resistance complicates treating infections from bacteria like Streptococcus mutans and Lactobacillus acidophilus, key in dental caries. This study aimed to evaluate the antimicrobial and synergistic effects of plant extracts from garlic (Allium sativum), ginger (Zingiber officinale), cardamom (Elettaria cardamomum), and chlorhexidine against these bacteria, with the goal of identifying natural alternatives for managing bacterial resistance in oral infections..

Methods: Essential oils were extracted via steam distillation. In this in vitro study, the antimicrobial effects of garlic, ginger, and cardamom essential oil extracts (individually and in combination) were evaluated against Streptococcus mutans (PTCC 1683) and Lactobacillus acidophilus (PTCC 1643), Antimicrobial activity against standard strains was tested using disk diffusion and broth microdilution under anaerobic conditions, with 2% chlorhexidine as a control.

Results: All extracts were effective individually. Garlic showed the highest potency (MIC = 0.5 and 1 µg/mL against S. mutans and L. acidophilus, respectively), outperforming chlorhexidine (MIC = 1 and 2 µg/mL). The synergistic combination of all three extracts significantly reduced MICs to 0.25 and 0.5 µg/mL (FICI 0.5). Combining extracts with chlorhexidine enhanced its efficacy 2-4 fold. In diffusion assays, garlic produced inhibition zones up to 20 mm, with the combination increasing zones by 30-50%.

Conclusion: Garlic, ginger, and cardamom extracts possess substantial potential as natural antimicrobial agents against Streptococcus mutans and Lactobacillus acidophilus. These compounds could serve as suitable alternatives or adjuncts to conventional dental therapies, aiding in the mitigation of bacterial resistance. However, clinical trials are essential to validate efficacy under real-world conditions and to standardize the extracts.

keywords: Antibiotic resistance, Allium sativum, Streptococcus mutans, Lactobacillus acidophilus, dental caries

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-66

The Potential of Gut Microbiota-Derived Postbiotics as Diagnostic Biomarkers and Therapeutic Targets in Metabolic Syndrome: A Narrative Review

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Background and aim: Microbiome research is shifting from live probiotics toward their functional byproducts, known as "Postbiotics." These metabolites, including short-chain fatty acids (SCFAs) and cell wall components, offer higher stability and a more predictable safety profile. Since metabolic syndrome is closely linked to gut dysbiosis, postbiotics present a promising frontier. This review examines their dual role as quantifiable laboratory biomarkers and targeted therapeutic agents.

Methods: This review analyzes literature from PubMed and Scopus (2018–2025) using MeSH terms including "Gastrointestinal Microbiome", "Metabolic Syndrome", and "Insulin Resistance". The selection focused on studies investigating the biochemical quantification and clinical efficacy of postbiotic derivatives in metabolic disorders.

Results: Evidence indicates that postbiotics, particularly Butyrates and Propionates, directly modulate systemic inflammation and insulin sensitivity. Unlike live bacteria, these compounds are stable and measurable via standard laboratory techniques, providing a reliable "biochemical snapshot" of metabolic health. Furthermore, postbiotics reinforce the intestinal barrier and attenuate low-grade inflammation, offering a standardized and safer alternative to traditional probiotic interventions.

Conclusion: Based on these findings, postbiotics solve the two main challenges of using live bacteria: clinical safety and measurement difficulty. Because they are stable and quantifiable, they are ideal for routine laboratory use to monitor metabolic syndrome. Moving forward, using postbiotics as standardized biomarkers will allow for more predictable and personalized treatments, moving "from the lab to the bedside" with greater precision.

keywords: Postbiotics; Gastrointestinal Microbiome; Metabolic Syndrome; Biomarkers; Insulin Resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-67

Investigating the potential of λ phage in inhibiting pathogenic strains of Clostridioides difficile

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Background and aim: Clostridioides difficile is the most common cause of healthcare-associated and antibiotic-associated diarrhea worldwide. The production of highly resistant spores and antibiotic-induced dysbiosis of the gut microbiota increases colonization and infection rates. Standard antibiotic therapies are not universally effective, promote antimicrobial resistance, and also disrupt the intestinal microbiota. Although faecal microbiota transplant represents a successful treatment option, it could be ineffective or dangerous for immunocompromized patients. Thus, the search for targeted alternative therapies is a priority. Bacteriophages and phage-based products, inspired by model phages such as λ, have emerged as promising, specific antimicrobial alternatives.

Methods: In this study, λ phage-based techniques are assessed for their ability to inhibit pathogenic C. difficile strains, utilizing current information on phages, genomes, and lytic mechanisms. For phage-mediated bacterial suppression, phage infection kinetics, gene expression regulation, and endolysin action on the bacterial cell wall were emphasized. Studying temperate and integrase-deficient phages and identifying lysogeny-related genes shed light on potential inhibitory mechanisms for λ phage applications.

Results: Evidences from past research works have shown that the C. difficile bacteriophages possess the capability to influence the bacterial viability, pathogenicity, and expression level. The endolysins from bacteriophages have shown promising results against antibacterial activity and the capacity to damage C. difficile bacterial cell walls. Even though most of the C. difficile bacteriophages studied were temperate viruses, results have shown that integrase deficient or genomic-modified bacteriophages possess improved antimicrobial activity. These results suggest that it is possible to utilize λ phage-like systems to control C. difficile.

Conclusion: The inhibititory potential of λ phage derived methods underscores the potential of phage therapy and phage-derived antibiotics in overcoming the drawbacks of antibiotics in C. difficile treatment. The use of a λ phage as a model phage offers valuable information on phage life cycles and regulatory control of phage genes necessary for phage therapy. In spite of the drawbacks such as host specificity and lysogeny of phage therapy, breakthroughs in genomics and bioinformatics allow phage therapy to target C. difficile intestine infections

keywords: λ phage (Lambda bacteriophage) Clostridioides difficile Phage therapy Bacteriophage-derived endolysins

PBa-68

Ramadan Intermittent Fasting: Modulation of Gut Microbiome, Metabolic Profiles, and Clinical Biomarkers

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Background and aim: Ramadan intermittent fasting (RF), a form of time-restricted eating, is practiced globally and has been associated with beneficial metabolic and physiological changes. This study aimed to investigate the impact of RF on gut microbiome composition, metabolic parameters, and clinical biomarkers in healthy adults.

Methods: A structured literature review was conducted to summarize current evidence on the effects of Ramadan intermittent fasting on gut microbiome composition, metabolic parameters, and clinical biomarkers. Peer-reviewed human and animal studies were analyzed, focusing on microbiome profiling, anthropometric changes, biochemical markers, and metabolic adaptations reported during and after Ramadan fasting.

Results: RF significantly increased microbial diversity, particularly enhancing butyrate-producing families such as Lachnospiraceae and Ruminococcaceae. Key taxa such as Akkermansia muciniphila, Bacteroides fragilis, and Prevotella showed population-specific enrichment. Fasting led to reductions in body weight, waist circumference, triglycerides, LDL cholesterol, and inflammatory markers (hs-CRP, TNF-α), along with increases in HDL cholesterol and autophagy-related proteins (Beclin-1). Metabolomic analyses revealed shifts in amino acid, carbohydrate, lipid, and vitamin-related pathways, reflecting metabolic adaptations to RF. No adverse effects were observed on hematological or biochemical parameters.

Conclusion: RF promotes favorable modifications in gut microbiota, supports metabolic health, enhances lipid profiles, and activates autophagy pathways without compromising clinical safety. These findings suggest that RF may serve as a safe and effective non-pharmacological intervention to improve metabolic and immunological outcomes.

keywords: Ramadan fasting, intermittent fasting, gut microbiome, metabolic adaptation, lipid profile,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-69

Molecular typing of Acinetobacter baumannii and Staphylococcus aureus isolates forming biofilm at the same time using multilocus variable-number tandem repeat analysis (MLVA) method

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Background and aim: Diabetic foot ulcers are among the most common complications of diabetes, often leading to chronic and treatment-resistant infections. Staphylococcus aureus and Acinetobacter baumannii are among the predominant bacteria isolated from these wounds, both capable of forming biofilms and exhibiting synergistic interactions that complicate treatment. This study aimed to investigate the genetic diversity of these isolates using the Multiple-Locus Variable number tandem repeat Analysis (MLVA) method and to assess their ability to form single- and dual-species biofilms.

Methods: As part of a previous project (Ethical approval code: IR.UMSHA.REC.1401.809), 27 Acinetobacter baumannii and 31 Staphylococcus aureus isolates were collected from patients with diabetic foot ulcers. Biofilm formation was assessed using the microtiter plate assay, and dual-species biofilms were developed to evaluate simultaneous biofilm formation. Genomic DNA was extracted, and genetic typing was performed through analysis of VNTR loci using the MLVA method. Data were analyzed with BioNumerics software employing the UPGMA clustering algorithm.

Results: All isolates demonstrated the ability to form biofilms, with several capable of establishing dual-species biofilms that exhibited enhanced structural integrity. MLVA analysis revealed that isolates forming dual-species biofilms frequently clustered together genetically, suggesting that genetic relatedness may play a role in cooperative biofilm development and increased antibiotic resistance.

Conclusion: : Identification of genetic profiles and assessment of single- and dual-species biofilm formation provide valuable insights for understanding microbial interactions in diabetic foot infections. These findings can contribute to the design of more effective, targeted therapeutic strategies and help prevent the dissemination of resistant bacterial isolates.

keywords: Diabetic foot ulcer, Staphylococcus aureus, Acinetobacter baumannii, MLVA

PBa-70

Probiotic-Derived Exosomes: Emerging Theranostic Nano-Postbiotics for Obesity Management: A Narrative Review

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Background and aim: Obesity is a chronic and multifactorial disease characterized by excessive accumulation of body fat that imposes substantial health risks. Dysbiosis is known to be a major factor in obesity. Probiotics exert beneficial effects through modulation of gut microbiota composition, reinforcement of intestinal barrier function, regulation of immune and metabolic responses, and production of bioactive proteins. However, their precise molecular mechanisms remain incompletely elucidated. Probiotic-derived extracellular vesicles (PDEs) are nanosized, cell-free structures containing lipids, proteins, and regulatory RNAs that mediate intercellular communication. This narrative review explores the emerging role of PDEs in obesity pathophysiology and their diagnostic and therapeutic (theranostic) potential.

Methods: PubMed, Scopus, and Web of Science were searched for peer-reviewed studies published from 2018 to 2024 using terms related to probiotic-derived exosomes/vesicles, obesity, metabolic inflammation, and nano-postbiotics. In vitro, in vivo, and ex vivo studies on vesicles from probiotic bacteria, primarily Lactobacillus and Bifidobacterium spp., were included when they examined adipogenesis, insulin resistance, intestinal barrier integrity, and/or systemic inflammation. Data extraction focused on cargo composition, implicated signaling pathways, diagnostic relevance, therapeutic outcomes, and reported advantages over live probiotic therapy.

Results: Across multiple studies, PDEs have been shown to cross the intestinal barrier and exert systemic effects on key metabolic tissues. PDEs strengthen gut barrier function by upregulating tight-junction proteins such as ZO-1 and occludin, thereby limiting metabolic endotoxemia. Their bioactive components mitigate inflammation through the downregulation of pro-inflammatory cytokines, including TNF-α and IL-6, and enhance insulin sensitivity via activation of the AKT/PI3K signaling pathway. In adipose tissue, PDEs promote the browning of white fat by increasing UCP1 expression, stimulating fatty acid oxidation, and suppressing lipogenesis. Notably, strain-specific differences in PDE abundance and circulating levels have been associated with obesity severity, highlighting their potential as non-invasive biomarkers for metabolic health.

Conclusion: PDEs represent a promising theranostic platform integrating microbiome-based diagnosis with targeted nanotherapeutic delivery for precision obesity management. Future work should standardize isolation and characterization workflows, clarify structure–function relationships, and translate robust preclinical findings into well-designed clinical trials.

keywords: Probiotic-derived exosomes, obesity, nano-postbiotics, extracellular vesicles, gut microbiota

PBa-71

Antimicrobial Resistance of Klebsiella pneumoniae Clinical Isolates from ICU and Non-ICU Hospitalized Patients in Tehran Hospitals During a Two-Year Surveillance Period Identified by MALDI-TOF MS

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Background and aim: Klebsiella pneumoniae is a major cause of healthcare-associated infections, particularly in intensive care units (ICUs), and is associated with significant morbidity and mortality. The increasing prevalence of antimicrobial resistance in this pathogen has severely limited treatment options and complicated empirical antibiotic therapy. Continuous local surveillance of resistance patterns is essential to support clinical decision-making and antimicrobial stewardship programs. The aim of this study was to evaluate and compare antimicrobial resistance patterns of Klebsiella pneumoniae clinical isolates obtained from ICU and non-ICU hospitalized patients in Tehran hospitals.

Methods: In this multicenter laboratory-based surveillance study, a total of 7,445 Klebsiella pneumoniae clinical isolates were collected from ten hospitals in Tehran during a two-year period (April 2023 to October 2025). Isolates were recovered from routine clinical specimens obtained from hospitalized patients. Bacterial identification was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Antimicrobial susceptibility testing was primarily conducted using the disk diffusion method, and minimum inhibitory concentration (MIC) testing was performed when required. Interpretation of susceptibility results was carried out according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. Resistance patterns were analyzed descriptively, with particular attention to isolates recovered from ICU settings.

Results: Among the 7,445 Klebsiella pneumoniae isolates analyzed, a high level of antimicrobial resistance was observed. Overall susceptibility to carbapenems was 17%, indicating a substantial burden of carbapenem-resistant isolates. Susceptibility to fluoroquinolones and piperacillin/tazobactam was below 25%, demonstrating limited effectiveness of these agents. Amikacin retained partial activity, with a susceptibility rate of approximately 30%. Resistance to third-generation cephalosporins was widespread across the isolates. A marked multidrug-resistant phenotype was frequently identified, particularly among isolates recovered from ICU patients, reflecting a higher resistance burden in critical care settings.

Conclusion: This multicenter surveillance study demonstrates a concerning level of antimicrobial resistance among Klebsiella pneumoniae clinical isolates in Tehran hospitals. The observed resistance patterns markedly restrict available empirical treatment options in critically ill patients, underscoring the importance of continuous local resistance monitoring. Rapid species-level identification using MALDI-TOF MS facilitates efficient antimicrobial resistance surveillance and supports timely laboratory reporting and antimicrobial stewardship efforts in hospital settings.

keywords: Klebsiella pneumoniae; Antimicrobial Resistance; ; MALDI-TOF MS

17th International Congress of Lab. and Clinic
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PBa-72

Bacteriological and Molecular Analysis of Staphylococcus aureus and Pseudomonas aeruginosa Isolated from Diabetic Foot Ulcers in Al-Zahra Hospital, Isfahan.

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Background and aim: Diabetic foot infections (DFIs) are a major complication of diabetes mellitus, commonly involving opportunistic bacterial pathogens with significant virulence and antibiotic resistance. Staphylococcus aureus and Pseudomonas aeruginosa are clinically significant due to their antibiotic resistance, biofilm-forming ability, and virulence factors. Accurate identification and antimicrobial resistance profiling are essential for effective management of DFU infections. This study investigated antimicrobial resistance patterns, biofilm formation capacity, and molecular detection of the nuc and toxA genes in S. aureus and P. aeruginosa isolates obtained from DFU patients at Al-Zahra Hospital, Isfahan.

Methods: So far, 33 bacterial isolates have been recovered from DFU specimens, including 28 Staphylococcus aureus and 5 Pseudomonas aeruginosa. Initial identification was performed using conventional microbiological methods. Molecular confirmation was carried out by PCR amplification of the nuc gene for S. aureus and the toxA gene for P. aeruginosa. Antimicrobial susceptibility testing was conducted using the disk diffusion method according to CLSI guidelines. Biofilm formation was assessed using the crystal violet microtiter plate assay, and isolates were categorized as weak, moderate, or strong biofilm producers based on optical density values.

Results: Among the 33 isolates, S. aureus was the predominant pathogen (84.8%). S. aureus isolates showed high resistance to penicillin (95%), while the highest susceptibility was observed to linezolid (89%). Methicillin resistance was detected in 50% of S. aureus isolates, and 68% were classified as multidrug-resistant (MDR). All P. aeruginosa isolates were MDR, with complete resistance to ciprofloxacin (100%) and the highest susceptibility to imipenem (40%). Biofilm analysis demonstrated that 89% of S. aureus isolates were strong biofilm producers. Among P. aeruginosa isolates, 60% showed strong, 20% moderate, and 20% weak biofilm formation. Molecular characterization of nuc and toxA genes will be presented in the full manuscript.

Conclusion: This study highlights a high prevalence of antibiotic-resistant and strong biofilm-producing S. aureus and P. aeruginosa in DFU infections. The presence of MDR strains and MRSA poses significant therapeutic challenges. Comprehensive microbiological and molecular characterization of DFU pathogens is crucial to guide effective antimicrobial therapy and improve patient outcomes.

keywords: Staphylococcus aureus, Pseudomonas aeruginosa, Diabetes Mellitus, Antibiotic resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
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PBa-73

Antibacterial efficacy of Graphene Oxide–Silicon Dioxide (GO: SiO2) nano hybrids against Escherichia coli

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Background and aim: Background: Emerging resistance demands nano-enabled antimicrobials. Graphene oxide (GO) offers oxidative activity, yet aggregation limits potency. Therefore, this study hypothesized that SiO_2 decoration would disperse GO, thereby enhancing antibacterial efficacy against Escherichia coli.

Methods: Method: Graphene oxide was synthesized via a modified Hummers' route and hydrothermally coupled with SiO_2 (1:2, 1:1, 2:1 GO: SiO_2 w/w). Nano-hybrids were characterized by XRD, FTIR, and SEM-EDS. Antibacterial activity against E. coli was quantified by disk diffusion (n = 9) and microdilution MIC/MBC assays. Data were analyzed by one-way ANOVA followed by Tukey's HSD test.

Results: Result: The GO: SiO_2 (1:1) hybrid exhibited the strongest antibacterial activity against E. coli (20.0 ± 1.0 mm inhibition zone), significantly larger than all other formulations (p 0.001). It was recognized that antimicrobial potency is not monotonically related to GO content; rather, it is related to balanced oxygenated edges and SiO_2 mediated dispersion that maximized ROS generation and membrane disruption. It also demonstrated the lowest MIC (0.7 ± 0.05 % v/v) and MBC, with a bactericidal index of 1.9 that is indicating potent bactericidal action. In contrast, the GO:SiO_2 (2:1) showed the lowest antimicrobial performance, with the highest MIC and MBC. Statistical analysis confirmed significant inter-formulation differences ($F \geq 402$, p 0.001), identifying the 1:1 composite as the most effective antibacterial agent.

Conclusion: Conclusion: It was concluded that the GO: SiO_2 (1:1) hybrid constitutes a first-in-class, synergistic nanocomposite that converts two weakly biocidal precursors into an ultra-potent anti-E.coli agent at 1 % v/v doses, offering an immediately translatable platform for next-generation, graphene-based topical antimicrobials.

keywords: SiO2, GO, Nano hybrid, E. coli, antibacterial resistant

PBa-74

Biosynthesis of Molybdenum oxide Nanoparticles as a Potential Antibacterial Agent Against Clinical Isolates of Multidrug-Resistant Klebsiella pneumoniae and Acinetobacter baumannii

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Background and aim: The global rise in infections caused by multidrug-resistant (MDR) Gram-negative bacteria, particularly Klebsiella pneumoniae and Acinetobacter baumannii, represents a serious threat to public health. These pathogens are frequently associated with hospital-acquired infections and exhibit high levels of resistance to multiple classes of antibiotics, including carbapenems, which severely limits available treatment options. Consequently, there is an urgent need to develop alternative antimicrobial strategies. This study aimed to investigate the antibacterial activity of biogenically synthesized Molybdenum against clinical isolates of MDR Klebsiella pneumoniae and Acinetobacter baumannii.

Methods: Molybdenum nanoparticles were biosynthesized using an aqueous Rosa damascena extract as a reducing and stabilizing agent, with microwave irradiation to improve synthesis efficiency. The nanoparticles were characterized by FESEM, XRD, EDX, FTIR, DLS, and UV–Vis spectroscopy. Their antibacterial activity against clinical MDR Klebsiella pneumoniae and Acinetobacter baumannii isolates was assessed using the broth microdilution method to determine MIC values.

Results: FESEM analysis demonstrated that the biosynthesized molybdenum nanoparticles were predominantly spherical with an average particle size of approximately 20–25 nm. XRD patterns confirmed the crystalline structure of arsenic oxide, while FTIR spectra revealed functional groups related to plant-derived biomolecules involved in nanoparticle stabilization. DLS analysis showed a narrow size distribution, indicating good dispersion stability. The antibacterial evaluation demonstrated that the minimum inhibitory concentration (MIC) of molybdenum nanoparticles were 1600 µg/ml, 800 µg/ml, 800 µg/ml, and 400µg/ml for three carbapenem-resistant clinical strains and one standard strain of Klebsiella pneumoniae. The antibacterial assays revealed that the minimum inhibitory concentrations (MICs) of molybdenum nanoparticles against three carbapenem-resistant clinical isolates of Acinetobacter baumannii were 1600 µg/ml, 1600 µg/ml, and 800 µg/ml, whereas the MIC value for the standard strain was 400 µg/ml.

Conclusion: The findings of this study demonstrate that biogenic molybdenum nanoparticles possess significant antibacterial activity against clinical isolates of multidrug-resistant Klebsiella pneumoniae and Acinetobacter baumannii. These results highlight the potential of molybdenum nanoparticles as promising alternative antimicrobial agents and support further investigations into their mechanisms of action, toxicity profiles, and potential clinical applications in combating MDR bacterial infections.

keywords: molybdenum nanoparticles; Multidrug-resistant bacteria; Klebsiella pneumoniae; Acinetobacter baumannii; Biosynthesis

PBa-75

The role of viridans streptococci in infective endocarditis: from pathogenesis to treatment

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Background and aim: In developing countries, VGS remains the leading cause of IE and the second most common cause of infectious endocarditis worldwide. The viridans group streptococci can infect the cardiovascular endothelium, which can lead to infectious endocarditis and possibly atherosclerosis.

Methods: The fibrin and platelet matrix that covers the streptococci that grow on the surfaces of heart valves (causing infective endocarditis) can cause valve perforation, arrhythmias in cardiac conduction, valve ring abscesses, pericarditis, aneurysm of the sinus of Valsalva, and the release of peripheral emboli. The matrix forms macroscopic, wart-like lesions. In men and those over 45, they account for 40–60% of all endocarditis cases affecting the healthy valves. We have developed a tool that aids doctors in determining when to perform echocardiography by identifying which patients with non-beta-hemolytic streptococcal bloodstream infections (BSIs) are most likely to develop IE, as echocardiography has been the cornerstone of IE diagnosis.

Results: Infectious endocarditis was always fatal before the invention of antibiotics. The key to treating this condition is selecting the correct bactericidal regimen and administering it for the appropriate duration. Published guidelines recommend similar regimens for prevalent organisms, and they are mostly based on cohort studies and experience rather than controlled trials.

Conclusion: Numerous professional groups from across the globe have produced publications on the prevention of endocarditis; some of these publications offer very different viewpoints on the evidence. As a result, it is essential to carefully analyze the published recommendations and evaluate them in light of the current state of scientific knowledge.

keywords: Viridans group streptococci (VGS), Infective endocarditis (IE), Cardiovascular endothelium infection

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-76

Investigating the Antibiotic Resistance Pattern and Broad-Spectrum β-Lactamase Genes in Enterobacter species Isolated from Infants with Sepsis from Ahvaz, Southwest Iran

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Background and aim: The global challenge of neonatal sepsis caused by antibiotic resistant Gram negative bacteria is a significant concern, primarily due to the high mortality rates and increased hospital costs that accompany it. The elevated resistance rate can be attributed to the existence of extended-spectrum beta-lactamases (ESBLs) within Enterobacteriaceae family. The antibiotic resistance patterns of Gram negative bacteria that lead to neonatal sepsis can vary depending on the hospital setting and the timeframe. This study aimed to investigate the antibiotic resistance pattern and ESBL genes in Enterobacter isolates collected from infants with sepsis from Ahvaz, southwest Iran.

Methods: In this study, Enterobacter isolates were collected from blood samples of infants with sepsis admitted in Imam Khomeini and Abuzar teaching hospitals located in Ahvaz city. The identification of isolates was performed with standard bacteriology tests. Disc diffusion test was performed to evaluate the antibiotic resistance rate. Polymerase chain reaction (PCR) was performed to investigate the presence of ESBL genes.

Results: Among 850 neonates suspected of sepsis, a total of 41 (4.8%) Enterobacter isolates were collected. In this study, the highest and the lowest resistance rates were observed to ceftazidime and cefotaxime antibiotics (100%) and imipenem (70.7%), respectively. The PCR results showed the frequency rates of 9.8% (n = 4/41), 24.4% (n = 10/41), 31.7% (n = 13/41), and 58.5% (n = 24/41) for blaTEM, blaSHV, blaCTX-M14, and blaCTX-M15, respectively.

Conclusion: Considering the high rate of antibiotic resistance observed, it is suggested to adopt strict monitoring policies to prevent the increase of this trend and further spread of ESBL genes in neonatal care centers.

keywords: Antibiotic resistance, ESBLs, Klebsiella pneumoniae, Sepsis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-77

Artificial Intelligence (AI)-Driven Approaches to Antibiotic Resistance Prediction: Challenges and Practical Outlooks

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Background and aim: The rapid emergence and global dissemination of antibiotic-resistant pathogens pose a major challenge to clinical medicine and laboratory diagnostics. Conventional antimicrobial susceptibility testing methods are often time-consuming and limited in their ability to capture complex resistance mechanisms. Artificial intelligence (AI) has gained increasing attention as a transformative approach for predicting antimicrobial resistance through advanced data-driven modeling of biological and clinical information.

Methods: This study is based on an integrative analysis of recent peer-reviewed literature and experimental reports focusing on AI applications in antibiotic resistance prediction. Machine learning and deep learning models were evaluated for their ability to analyze genomic sequences, transcriptomic data, phenotypic susceptibility profiles, and electronic health records. Emphasis was placed on algorithm performance, data quality, model interpretability, and clinical applicability within laboratory medicine.

Results: AI-driven models demonstrated high predictive accuracy in identifying resistance phenotypes and underlying genetic determinants across multiple bacterial species. These approaches enabled early detection of resistance patterns and supported rapid decision-making in antimicrobial therapy. However, significant challenges were identified, including data heterogeneity, limited external validation, algorithmic bias, and insufficient model transparency. The evolving nature of resistance mechanisms further reduced model generalizability across diverse clinical settings.

Conclusion: AI-based antibiotic resistance prediction offers substantial potential to enhance diagnostic efficiency and antibiotic stewardship. Addressing challenges related to data standardization, explainability, and regulatory integration is essential for successful clinical implementation.

keywords: Artificial Intelligence, Antibiotic Resistance, Machine Learning, Laboratory Medicine, Predictive Modeling

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-78

Immunoinformatic evaluation for the development of a potent multi-epitope vaccine against bacterial vaginosis caused by Gardnerella vaginalis

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Background and aim: Bacterial vaginosis (BV) is the most common vaginal dysbiosis in fertile women, which is associated with side effects including the risk of premature birth. Gardnerella vaginalis (G. vaginalis) is a facultative anaerobic bacillus known as the main pathogen responsible for BV. In this study, using bioinformatics and immunoinformatics methods, a multi-epitope vaccine with optimal population coverage against BV caused by G. vaginalis was designed.

Methods: Amino acid sequences of two important virulence factors (Vaginolysin and Sialidase) of G. vaginalis were retrieved from NCBI and UniProt databases. At first, three online servers ABCpred, BCPREDS and LBtope were used to predict linear B-cell epitopes (BCEs) and IEDB server was used for T cells. Then the antigenicity, toxicity, allergenicity were evaluated using bioinformatics tools. After modeling the three-dimensional (3D) structure of the vaccine by Robetta Server, molecular docking and molecular dynamics were performed. Finally, immune simulation and in silico cloning were considered effective for the design of vaccine production strategy.

Results: In total, six epitopes of BCEs, eight epitopes from CD4+ and seven epitopes from CD8+ were selected. The designed multi-epitope vaccine was non-allergenic and non-toxic and showed high levels of antigenicity and immunogenicity. After the 3D structure was predicted, it was refined and validated, which resulted in an optimized model with a Z-score of -7.4. Molecular docking and molecular dynamics simulation of the designed vaccine revealed stable and strong binding interactions. Finally, the results of vaccine immunity simulation showed a significant increase in immunoglobulins, higher levels of IFN-γ and IL-2.

Conclusion: According to the findings, the candidate multi-epitope vaccine has stable structural features. It also has the potential to stimulate long-term immunity in the host, but wet-lab validation is needed to justify it.

keywords: Gardnerella vaginalis, Immunoinformatic , multi-epitope vaccine

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-79

Encapsulated Postbiotics as Next-Generation Therapeutics for Celiac Disease: A Narrative Review

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Background and aim: Celiac disease (CD) is a gluten-induced autoimmune enteropathy, caused by complex interplay of genetic and environmental factors, including gut dysbiosis. While a gluten-free diet (GFD) is the primary approach for managing CD, its limitations necessitate alternative strategies. Postbiotics have emerged as safer and more stable alternatives to live probiotics; however, their efficacy may be limited by degradation and low bioavailability. Encapsulation technologies, particularly liposomal systems, offer a promising approach to protect bioactive components, enhance targeted delivery, and improve translational potential. This narrative review summarizes recent evidence (2023–2025) in encapsulated postbiotic formulations as next-generation CD therapeutics.

Methods: A targeted literature search was conducted in PubMed, Scopus, and Web of Science (January 2023–December 2024) using keywords such as "Encapsulated postbiotic," "Postbiotic," "Celiac disease," "Gut barrier," and "Immunomodulation." Eligible studies included preclinical research using Caco-2 intestinal cell lines, animal models of gluten sensitivity, and early clinical trials. Extracted data evaluated formulation characteristics, bioactive components, and key mechanisms involving inflammatory signaling and intestinal barrier regulation.

Results: Preclinical evidence supports the therapeutic potential of probiotic- and postbiotic-based interventions in mitigating gliadin-induced intestinal injury. Postbiotics derived from Lactiplantibacillus plantarum and Lactobacillus rhamnosus GG attenuate inflammatory signaling through inhibition of NF-κB and mTOR pathways, while simultaneously enhancing intestinal barrier integrity via upregulation of tight junction proteins. In addition, selected Lactobacillus and Bifidobacterium strains contribute to gluten detoxification through the enzymatic degradation of immunogenic peptides. Encapsulation using nano- and microcarriers further enhances stability, bioavailability, and targeted gastrointestinal delivery.

Conclusion: In conclusion, encapsulated postbiotics, represent a novel and promising adjunctive strategy for CD, targeting both immunomodulation and barrier repair. To translate mechanistic insights into validated clinical applications, standardized formulations and biomarker-driven clinical trials are required to support clinical translation and extend therapeutic options beyond the GFD.

keywords: Celiac disease; Postbiotics; Drug delivery; Immunomodulation; Translational therapeutics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
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PBa-80

CRISPR-Enhanced Lateral Flow Immunoassay for Rapid Point-of-Care Detection of Antimicrobial-Resistant Bacteria: a Narrative Review

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Background and aim: Antimicrobial resistance (AMR) is a critical global public health threat. The time-consuming nature of conventional tests creates a demand for innovative rapid detection strategies. Lateral flow immunoassays (LFIAs) are rapid and user-friendly point-of-care (POC) testing methods, but due to low detection sensitivity, reliable detection of AMR genes is often compromised. This narrative review evaluates CRISPR-Cas (Cas12a/13a)-enhanced LFIAs for ultrasensitive, nucleic acid-based detection of key AMR determinants (e.g., blaNDM-1, mecA), critically assessing their diagnostic performance and practical POC applicability.

Methods: A search for relevant literature published (from Jan 2020 to Oct 2025) using the keywords CRISPR/Cas12a/Cas13a and lateral flow immunoassay/ LFIAs and antimicrobial resistance/AMR/ point-of-care was conducted in the PubMed, Scopus, the Web of Science, and Embase databases. Eligible papers included studies on the performance (sensitivity, specificity, or Limit of detection) and POC applicability of the CRISPR-LFIAs for detecting either AMR genes or resistant pathogens (e.g., MRSA, CRE) in clinical samples.

Results: CRISPR-Cas (Cas12a/13a)-enhanced LFIAs have shown considerable clinical potential for the rapid POC detection of AMR. They reliably detect critical resistance markers (e.g., KPC, NDM and mecA) directly from minimally processed clinical samples using isothermal amplification. Reported assays achieve excellent analytical sensitivity, with detection limits (down to a few gene copies or CFU/mL comparable or superior to conventional PCR-based methods, with total assay time of 30-90 minutes for pathogens like methicillin-resistant Staphylococcus aureus, carbapenem-resistant Klebsiella pneumonia, and drug-resistant Salmonella species. Design optimized assay minimizes non-specific signals and false positives, supporting reliable, low cost AMR monitoring, and offering a user-friendly and equipment-minimal alternative to conventional laboratory-based diagnostic methods.

Conclusion: CRISPR- enhanced LFIAs technology holds significant potential for the rapid, accurate and POC compatible detection of AMR. To realize this potential for effective AMR surveillance, key challenges in current technologies, such as the need for pre-amplification, cost reduction, and extensive field validation must be addressed.

keywords: Point-of-care (POC), Antimicrobial resistance (AMR), Lateral flow immunoassay (LFIAs), CRISPR-Cas

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
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PBa-81

Comparative analysis of antibiotic resistance gene patterns and their genomic context in Staphylococcus aureus

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Background and aim: Staphylococcus aureus is a Gram-positive bacterium that is part of the normal human flora and can cause infections ranging from mild skin conditions to severe diseases. The rise of antibiotic-resistant strains, particularly methicillin-resistant S. aureus (MRSA), poses a major public health concern. Resistance is mainly mediated by specific genes.. The aim of this study to perform a comparative in silico analysis of antibiotic resistance gene patterns in MRSA and methicillin-susceptible S. aureus (MSSA) strains among S. aureus isolates.

Methods: Genomic data of S. aureus strains, including MRSA and MSSA, were retrieved from the NCBI database, with a focus on antibiotic resistance genes. The selected strains were analyzed for the presence of genes such as ermC, tetK, tetM, aacA-aphD, msrA, vatA, vatB, vatC, and linA.

Results: Statistical analysis of MRSA and MSSA isolates using SPSS 26 revealed a high prevalence of the blaZ gene in both groups, reflecting widespread β-lactam resistance.Genes mecA, ermA, and ermB showed similar frequencies in both strains. tetM, tetK, and aacA-aphD were notably higher in MRSA, serving as key markers of resistance, while vatC was found only in MRSA, indicating strain-specific resistance patterns. Overall, the analysis highlights genes common to both strains and those predominantly associated with MRSA .Analysis of the prevalence of antibiotic resistance genes in MRSA and MSSA strains revealed that some genes are present in both strains, with differences in prevalence below 10%. Certain genes were found exclusively in MRSA, indicating greater diversity of resistance genes and higher antibiotic resistance in MRSA compared to MSSA. Additionally, some genes showed higher prevalence in MRSA strains.

Conclusion: These findings highlight the importance of continuous surveillance of antibiotic resistance genes, particularly in MRSA, to support clinical management and epidemiological monitoring of S. aureus infections.

keywords: Staphylococcus aureus, MRSA, MSSA, Gen, Antibiotic resistant

PBa-82

Yeast Vectors: The Next Frontier in Brucellosis Vaccine Design

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Background and aim: Developing safe and effective vaccines against intracellular pathogens remains a major challenge. Saccharomyces cerevisiae and Pichia pastoris have emerged as leading yeast platforms for next-generation vaccines, combining cost-effective, high-density fermentation with proper eukaryotic protein folding and post-translational modifications. Importantly, their β-glucan-rich cell walls confer intrinsic adjuvant properties, promoting dendritic cell maturation and robust T-cell responses. To assess their potential for brucellosis vaccine development, this review evaluates the efficacy of yeast-based vector vaccines against various infectious diseases.

Methods: This review followed the PRISMA standard for systematic reviews. We searched the PubMed, Scopus, and ISI Web of Science databases for original research articles published between 2005 and 2025. The search strategy included a combination of MeSH terms and free text keywords, such as “yeast expression system” or “Pichia pastoris platform” or “Saccharomyces cerevisiae” combined with “subunit vaccine efficacy” and “intracellular bacterial pathogen” or “brucellosis.” Only in vivo studies assessing immune profiles (cytokine/antibody titers) and protective effects (survival or bacterial load reduction) in animal models met inclusion criteria.

Results: The initial search yielded 1,240 records, of which 42 studies met the inclusion criteria. A systematic analysis demonstrated that the yeast platform is superior to E. coli has significantly higher seroconversion rates, primarily due to increased eukaryotic glycosylation and solubility. In particular, Brucella candidates (L7/L12-HSA, Omp10-Omp28, etc.) P. Pastoris and S. cerevisiae systems consistently induced a balanced Th1/Th2 immune profile with increased IFN-γ secretion and achieved up to 2.41 log protection in mouse models. This effectiveness extends to other intracellular pathogens as well. Whole yeast vaccines against Mycobacterium tuberculosis and Salmonella induced strong CTL and Th17 responses, thereby reducing histopathology. Furthermore, oral administration of yeast-presented antigens (such as H. pylori UreB/VacA) was successful in stimulating mucosal IgA and reducing colonization. Taken together, these results confirm that yeast vectors constitute a dual-functional platform that provides both high-quality antigen production and unique adjuvant properties.

Conclusion: Yeast-based systems have clear advantages over traditional prokaryotic vectors for recombinant vaccine production. This platform provides an excellent option for combating difficult intracellular pathogens such as Brucella due to its ability to generate well-folded antigens and its unique immunostimulatory properties. The most promising approach is to move from single antigenic subunits to multivalent drugs in yeast. To enhance the protective effect of P. pastoris or Saccharomyces cerevisiae for the expression of complex bacterial antigens should be prioritized in future vaccination strategies.

keywords: Yeast-based vaccine, Recombinant Vaccine, Yeast Vector, Pichia, Saccharomyces, Immunogenicity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-83

Frequency, phylogenetic groups and antimicrobial resistance patterns of Diarrheagenic Escherichia coli, obtained from patients with diarrhea in Kerman hospitals

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Background and aim: One of the main causes of infectious diarrhea and a major factor in childhood morbidity and mortality in underdeveloped nations is Escherichia coli. Several significant pathotypes of diarrheagenic E. coli, such as EHEC, EPEC, ETEC, EIEC, and EAEC, are linked to different virulence factors and pathogenic processes. Accurate identification, phylogenetic categorization, epidemiological surveillance, and antibiotic resistance monitoring all depend on molecular techniques. This study sought to ascertain the distribution of E. coli pathotypes, their phylogenetic groups, and antibiotic resistance patterns in diarrheal patients due to the scarcity of data from Iran, especially Kerman.

Methods: Over the course of six months, 325 diarrheal samples were gathered from Kerman hospitals for this cross-sectional study. The isolates were identified using conventional microbiological and biochemical methods. The genes lt, st, cvd432, aggR, eae, stx, and ipaH were found using polymerase chain reaction (PCR). Using the PCR technique, isolates were categorized into one of the four major phylogenetic groups of E. coli (A, B1, B2, and D). The disc diffusion method was used to conduct the antibiotic susceptibility test.

Results: According to our findings, diarrheagenic E. coli caused diarrhea in 53 out of 325 individuals. Enteroaggregative E. coli (EAEC) was the most common type, isolated from 28/53 patients with diarrhea (52.8%), followed by enteropathogenic (EPEC) from 14/53 (26/4%), enteroinvasive (EIEC) from 6/53 (11/3%), and enterotoxigenic (ETEC) from 5/53 (9/4%). There was no evidence of enterohaemorrhagic (EHEC) in any diarrheal patients. Phylogenetic groups B1 (49%) and A (39.6%) comprised the majority of the isolates. While 79/2% of the isolates had ampicillin resistance, none of them had imipenem resistance.

Conclusion: The study's findings demonstrated that EAEC is a significant contributor to diarrhea in Kerman. Additionally, this study validates the value of molecular techniques like PCR in identifying diarrheagenic Escherichia coli in stool samples. Group A and B1 include the majority of diarrheagenic E. coli strains.

keywords: Diarrhea, Diarrheagenic E. coli, Polymerase chain reaction, antibiotic resistance, phylogenetic

PBa-84

Emerging mechanisms of microbial resistance to nanoparticles: challenges and opportunities in antimicrobial nanomedicine

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Background and aim: The emergence of multidrug-resistant illnesses has increased interest in nanomaterials as antibacterial agents. This paper evaluates how microorganisms become resistant to antimicrobial nanoparticles critically, describing strategies for resistance include modifying the characteristics of the cell membrane, turning on efflux mechanisms, and enhancing the control of oxidative stress. Biofilm formation and nanoparticle sequestration also restrict antimicrobial interactions. Both genetic and phenotypic changes contribute to resistance. Despite advancements, significant information gaps remain due to non-standard methods and challenges in simulating realistic conditions. Understanding these mechanisms is essential for designing effective nanomaterials and ensuring therapeutic and environmental safety.

Methods:

Results:

Conclusion:

keywords: Nanoparticles; Antimicrobial resistance; Microbial adaptation; Nanomedicine; Biofilm; Efflux pumps

PBa-85

Role of Adherent invasive Escherichia coli in Pathogenesis of Crohn's Disease: A Systematic Review

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Background and aim: Crohn's disease (CD) is a chronic inflammatory disease affected by genetic and microbial factors. Adherent invasive Escherichia coli (AIEC) may be associated with CD because it can adhere to, invade epithelial cells, and survive in macrophages. However, prevalence and clinical impact of AIEC remain vary between studies. This systematic review evaluates current evidence on the role of AIEC in CD.

Methods: We've searched PubMed, Google Scholar, Web of Science, SID and Magiran databases from the year 1990 to 2025 for keywords such as adherent-invasive Escherichia coli, Crohn's disease, pathogenesis and inflammation to identify relevant studies.

Results: Most included studies reported a significantly higher prevalence of AIEC in patients with CD than in healthy controls, especially in the mucosa of the ileum. AIEC produces virulence factors that help it attach to and invade intestinal epithelial cells and survive inside macrophages, which increases the production of pro-inflammatory cytokines. Moreover, the higher levels of host receptors, such as CEACAM6, facilitate AIEC colonization of the gut. The presence of AIEC was associated with severe disease, ileal involvement, and a higher risk of relapse after surgery. However, considerable variation was observed among studies in the methods used to detect AIEC and study design.

Conclusion: Current studies show that AIEC colonization is strongly associated with CD severity, especially in the ileum. Therefore, targeting AIEC could help manage the disease and prevent recurrence.

keywords: Adherent-invasive Escherichia coli, Crohn's disease, Pathogenesis, Inflammation

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-86

Gut microbiota manipulation in colorectal cancer: A systematic review

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Background and aim: Colorectal cancer (CRC) is a complex disease affected by several risk factors, including the patient's characteristics and changes in the gut microbiota. Alterations in gut microbial composition play a key role in CRC development, and targeting the gut microbiota may improve treatment outcomes. This study aims to evaluate current knowledge on gut microbiota manipulation in CRC management.

Methods: We've searched PubMed, Google Scholar, Web of Science, SID and Magiran databases from the year 1990 to 2025 for keywords such as gut microbiota, colorectal cancer, probiotics, prebiotics, synbiotics, and microbiota manipulation to identify relevant studies.

Results: Most studies have found that targeting the gut microbiota through diet, prebiotics, probiotics, or synbiotics can induce beneficial microbial changes in CRC patients. In particular, probiotics, especially Lactobacillus and Bifidobacterium, can increase tumor-suppressive bacteria and reduce postoperative complications. Dietary interventions also promote the growth of short-chain fatty acid–producing bacteria, which may have protective effects. Manipulating the gut microbiota appears to enhance immune responses by boosting anti-tumor immune cells and decreasing pro-inflammatory cytokines. However, due to heterogeneity in methods and limited clinical data, further well-designed studies are needed.

Conclusion: Current evidence suggests that targeting the gut microbiota may improve treatment response, reduce inflammation, and enhance anti-tumor immunity in CRC patients. However, more rigorous studies are needed because current evidence is still limited and variable.

keywords: Gut microbiota, Colorectal cancer, Probiotics, synbiotics, microbiota manipulation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-87

Monitoring Hospital Indoor Air Bioaerosols to Isolate Nocardia Species from a tertiary care hospital in Iranshahr, Iran

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Background and aim: Bioaerosols are recognized as significant contributors to the transmission of infectious agents within hospital environments. While multiple studies have reported the isolation of Nocardia species from clinical specimens, investigations focusing on their presence in hospital indoor air remain limited. This study aimed to evaluate the species diversity of the Nocardia genus across different indoor air environments at Khatam Hospital, Iranshahr, Iran.

Methods: Particle concentrations in various hospital wards were measured using a direct reading approach. Bioaerosol sampling was conducted following NIOSH methods 0800 and 0801, employing Sauton's medium culture plates. Petri dishes were incubated upside down for three weeks at 25°C and 37°C. Phenotypic tests, including growth in lysozyme broth and degradation of tyrosine, xanthine, and hypoxanthine, were used to confirm Nocardia isolates, followed by molecular analyses for further validation.

Results: The orthopedic ward exhibited the highest particle concentration among all hospital wards. A total of 14 Nocardia isolates were recovered from hospital indoor air, including four from the emergency department, four from the infectious diseases ward, three from the surgery ward, two from the hemodialysis ward, and one from the orthopedics ward. Identified species included Nocardia cyriacigeorgica, N. asteroides, N. otitidiscaviarum, N. wallacei, N. kroppenstedtii, N. farcinica, and N. nova.

Conclusion: This study presents one of the earliest documented reports of pathogenic Nocardia species detected in hospital indoor air. The results underscore the potential for hospital environments to serve as reservoirs for opportunistic pathogens, posing a risk to susceptible patients. Therefore, routine monitoring of microbial diversity in hospital settings is recommended as a preventive measure against opportunistic infections.

keywords: Airborne Nanoparticles, hospital indoor air, Nocardia species

PBa-88

Synergistic Phage-Nanoparticle Hybrids: Bacteriophage-Mediated Nanomedicines to Combat Multidrug-Resistant Bacterial Infections

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Background and aim: Multidrug-resistant (MDR) bacterial infections pose a severe worldwide threat, demanding novel treatment options. This review examines the combined application of bacteriophages and nanoparticles as an innovative strategy against these challenging pathogens.

Methods: We conducted a systematic search of PubMed/MEDLINE, Scopus, Web of Science, Embase, and Google Scholar from database inception through October 2025. Search terms included "bacteriophage," "nanoparticle," "synergism," "MDR," and "biofilm." Eligible studies showed combined effects of phages and nanoparticles (such as silver, zinc oxide, or chitosan) on MDR bacteria or biofilms in vitro, ex vivo, or in vivo, with publication dates from 2000–2025 and measurable results. We excluded research without synergy data, targeting non-bacterial organisms, or lacking adequate details.

Results: Bacteriophages provide targeted killing and on-site replication as viable antibiotic substitutes, but they suffer from quick immune neutralization and instability outside hosts. Nanoparticles bolster phage performance through enhanced stability, precise targeting, and sustained release, alongside their own antibacterial effects. Progress in phage-carrying nanotechnologies—such as liposomes, polymer-based particles, dendrimers, and metal oxides—has shown better treatment outcomes and biofilm eradication. Multiple investigations confirm potent cooperative activity between these nanoparticles (silver, zinc oxide, chitosan) and phages versus tough bacterial isolates and biofilms. However, obstacles like drug kinetics issues, production at scale, formulation durability, and approval processes hinder progress toward patient use.

Conclusion: Upcoming studies should prioritize refined phage-nanoparticle combinations, in vivo performance analysis, and uniform guidelines for regulatory clearance. This cross-disciplinary tactic offers transformative potential for antimicrobial treatments, delivering precise, potent, and secure options to counter rising antibiotic resistance.

keywords: multidrug-resistant, phage, nanoparticle, antibacterial synergy, bacterial infections

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-89

A Two-Phase Smart Delivery Platform for Targeting P. aeruginosa PqsR and Host EGFR in Wound Infection Management

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Background and aim: Chronic wounds caused by Pseudomonas aeruginosa pose a major clinical challenge due to quorum sensing activation and disrupted tissue repair. The quorum sensing regulator receptor PqsR plays a key role in the virulence and biofilm formation of this bacterium, while the Epidermal Growth Factor Receptor (EGFR) is one of the main regulators of skin wound healing. Alongside antibiotics for initial infection control, simultaneous targeting of bacterial virulence and modulation of the host inflammatory-repair response is required to prevent recurrence and facilitate effective tissue regeneration. Repurposing FDA-approved drugs provides a fast, cost-effective route for developing such dual therapies after antibiotic clearance.

Methods: In this study, all FDA-approved drugs were extracted from the PubChem database and, after structural preparation, subjected to molecular docking. Ligand preparation included hydrogen addition, assignment of Gasteiger–Marsili charges, and generation of pdbqt files. The crystal structures of the human receptor EGFR1 (PDB ID: 3POZ) and the Pseudomonas aeruginosa receptor PqsR (PDB ID: 4JVI) were obtained from the RCSB-PDB database and prepared using AutoDock Tools. Molecular docking was performed using AutoDock Vina. Docking validation was conducted through redocking of crystallographic ligands and calculation of RMSD. The strongest complexes in terms of binding energy were selected for 100-nanosecond molecular dynamics simulations using GROMACS.

Results: Virtual screening revealed that dutasteride shows strong binding affinity to the active sites of both PqsR and EGFR1, forming stable interactions with key amino acids in each receptor. Redocking confirmed the protocol's accuracy with an RMSD below 2 Å. Molecular dynamics simulations demonstrated the structural stability of the dutasteride–PqsR and dutasteride–EGFR1 complexes, showing limited RMSD and RMSF fluctuations and a stable radius of gyration. These features designate dutasteride as an ideal post-antibiotic candidate to prevent infection recurrence via PqsR inhibition and enhance tissue regeneration through EGFR modulation.

Conclusion: Computational findings propose dutasteride as a dual-target agent for sequential therapy in P. aeruginosa wounds. After antibiotics, its intelligent topical use inhibits biofilm via PqsR while stimulating repair through EGFR. This supports developing smart, controlled-release delivery for the healing phase.

keywords: Dutasteride, PqsR, EGFR, molecular docking, molecular dynamics, infected wound.

PBa-90

Droplet digital PCR (ddPCR) in the diagnosis of septicemia/sepsis

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Background and aim: Sepsis is a life-threatening condition that requires rapid and accurate diagnosis. Conventional diagnostic methods, such as blood culture, suffer from long turnaround times and low sensitivity, particularly in patients with low pathogen load or prior antibiotic exposure. Droplet Digital PCR (ddPCR), as an emerging molecular tool, enables absolute quantification of pathogen DNA, multiplex detection, and identification of resistant infections with high precision. This abstract, based on a synthesis of existing studies, highlights the superior performance of ddPCR compared to traditional methods in improving the timeliness and reliability of sepsis diagnosis.

Methods: This review is based on a systematic review of articles from 2015 to 2024, focusing on recent advances in clinical microbiology, infectious diseases, molecular diagnostics, and health economics. Sources include systematic reviews, meta-analyses, prospective and retrospective clinical studies, and technical innovation reports. Data were primarily extracted from adult populations (with limited pediatric data) and focus on key parameters such as sensitivity, specificity, turnaround time, and clinical impact.

Results: ddPCR demonstrates sensitivity of 75–100% and specificity of 63–100%, whereas blood culture shows sensitivity of 60–80% with a turnaround time of 48–72 hours. Rapid molecular panels such as T2Bacteria provide sensitivity of 50–93% with a turnaround time of 1–5.5 hours. ddPCR improves multiplex pathogen detection (30–50%) and resistance gene identification, enables absolute quantification of pathogen load, and correlates with disease severity. Limitations include high cost, technical complexity, and context-dependent specificity.

Conclusion: ddPCR, with its rapid turnaround time (2.5–5 hours) and high sensitivity, is transforming sepsis diagnosis and facilitates early treatment, optimized antibiotic management, and outcome prediction. However, challenges such as high cost and limited accessibility in resource-constrained settings remain. Future research should prioritize large-scale studies, improved specificity, and technical innovations to enable broader clinical adoption. This approach holds significant potential to reduce mortality and enhance antimicrobial stewardship, though further validation across diverse populations is required.

keywords: Sepsis, Molecular diagnosis, Bacteremia, ddPCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-91

Clonal relatedness and third-generation cephalosporin-resistant Escherichia coli isolated from pediatric urinary tract infections

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Background and aim: Third-generation cephalosporins, β-lactam antimicrobials, are commonly used as the first-line treatment for Escherichia coli (E. coli) urinary tract infections (UTIs) in children. This study aimed to investigate the resistance patterns of E. coli strains isolated from pediatric UTIs to third-generation cephalosporins and to explore their genetic relationships.

Methods: A descriptive cross-sectional study was conducted, assessing antibiotic resistance and extended-spectrum beta-lactamase (ESBL) production. Polymerase chain reaction (PCR) was employed to detect resistance genes, including bla TEM, bla CTX-M, bla SHV, bla AmpC, bla GES, and bla IMI resistance genes. To determine the clonal relationship among the different isolated strains, ERIC-PCR fingerprinting was used.

Results: Among 60 E. coli isolates from children aged 1 month to 18 years (mean age: 6.8±1.2 years), 75% showed resistance to cefepime, and 71.7% exhibited an ESBL phenotype. ESBL-producing isolates harbored a significantly higher distribution of β-lactamase genes than non-ESBL strains. ERIC-PCR analysis identified six clusters (A-F), with cluster A demonstrating the greatest heterogeneity.

Conclusion: These findings underscore the importance of routine screening for resistant E. coli strains to guide treatment and highlight the genetic diversity and potential hospital dissemination of these pathogens.

keywords: Cephalosporins, Escherichia coli, Urinary Tract Infections, genetic relatedness.

PBa-92

Prevalence and Molecular Characterization of Extended-Spectrum β-Lactamase–Producing Escherichia coli Isolated from Dog Feces in Tehran, Iran

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Background and aim: The emergence and spread of extended-spectrum β-lactamase (ESBL)–producing Escherichia coli pose a serious public health threat worldwide. Companion animals, particularly dogs, are considered potential reservoirs for such multidrug-resistant bacteria, facilitating zoonotic transmission. This study aimed to determine the prevalence, antimicrobial resistance patterns, and molecular characteristics of ESBL-producing E. coli isolated from dog feces in Tehran, Iran.

Methods: In this cross-sectional study, 100 non-duplicate E. coli isolates were obtained from fecal samples of dogs (50 shelter dogs and 50 pet dogs) in Tehran. Phenotypic detection of ESBL production was performed using the double-disk synergy test (DDST) following CLSI (2023) guidelines. Genomic DNA was extracted from confirmed ESBL producers, and PCR was used to detect β-lactamase genes (blaTEM, blaCTX-M, blaOXA, and blaSHV). Antimicrobial susceptibility testing was conducted against four cephalosporins using the disk diffusion method.

Results: Of the 100 E. coli isolates, 58 (58%) were confirmed as ESBL producers. The most prevalent β-lactamase gene was blaTEM (77.5%), followed by blaCTX-M (62.7%), blaOXA (27.5%), and blaSHV (22.4%). Co-carriage of multiple resistance genes was a common finding: the combination blaTEM + blaCTX-M was the most frequent (46.6%, 27 isolates). Other notable combinations included blaTEM + blaOXA (22.4%, 13 isolates), blaTEM + blaSHV (17.2%, 10 isolates), and blaCTX-M + blaOXA (10.34%, 6 isolates). One isolate (1.72%) harbored all four genes (blaTEM + blaCTX-M + blaOXA + blaSHV*) simultaneously. Antimicrobial susceptibility testing revealed high resistance to cefotaxime (56%) and cefoxitin (41%), whereas cefepime showed the highest susceptibility (60%).

Conclusion: The high prevalence of ESBL-producing E. coli and the frequent co-occurrence of β-lactamase genes in dog feces highlight the potential role of companion dogs as reservoirs for multidrug-resistant bacteria. These findings underscore the need for continuous surveillance and the implementation of antimicrobial stewardship programs in veterinary practice to mitigate the risk of zoonotic transmission.

keywords: Antimicrobial resistance, ESBL, Escherichia coli, dogs, β-lactamase genes, co-carriage, zoonosis.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-93

Effect of Incorporating Platinum Nanoparticles into AH26 Sealer on Its Antimicrobial Performance, Solubility, and pH Changes

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Background and aim: The long-term success of root canal treatment is highly dependent on proper sealing of the root canal system. Endodontic sealers play a crucial role in preventing microleakage and eliminating residual microorganisms. Enterococcus faecalis is a resistant bacterium frequently associated with persistent endodontic infections and treatment failure. Platinum nanoparticles have demonstrated strong antibacterial properties against a wide range of pathogenic microorganisms. This study aimed to evaluate the antibacterial activity, biofilm formation, solubility, and pH changes of AH26 sealer containing different concentrations of platinum nanoparticles.

Methods: In this in vitro study, platinum nanoparticles were incorporated into the powder component of AH26 sealer at concentrations of 0% (control), 2.5%, 5%, and 10% by weight. Five samples were prepared for each group, resulting in a total of 20 specimens. Antibacterial activity against Enterococcus faecalis, biofilm formation, solubility, and pH variations over time were evaluated using standard laboratory methods. Statistical analysis was performed with the significance level set at P 0.05.

Results: The control group showed the lowest mean solubility, while the 2.5% nanoparticle group showed the highest; however, no statistically significant differences were observed among the groups (P = 0.196). Significant differences were found among the groups regarding biofilm formation, bacterial colony count, and pH variation (P 0.001). Biofilm formation differed significantly between all groups except between the control and the 10% nanoparticle group (P = 0.518). The strongest antibacterial activity at 24 hours was observed in the 10% nanoparticle group.

Conclusion: AH26 sealer containing 10% platinum nanoparticles demonstrated the most favorable antibacterial performance and acceptable physicochemical properties.

keywords: AH26 sealer, Platinum, Nanoparticle, Antibacterial, Solubility, and pH Changes

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-94

Hypervirulent Klebsiella pneumoniae: Biofilm Formation, Capsular Types, Virulence Genes, and Genotyping in Hospitals of Amol, Northern Iran

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Background and aim: Klebsiella pneumoniae is an important opportunistic pathogen responsible for a wide range of hospital-acquired infections, particularly among immunocompromised patients. The emergence of hypervirulent strains and their ability to form biofilms pose serious challenges to infection control.

Methods: A total of 70 K. pneumoniae isolates were collected from different hospital units and clinical specimens in Amol, northern Iran. Capsular types were identified following DNA extraction. Biofilm formation was assessed using a microtiter plate assay. Hypervirulent isolates were identified using the string test, and virulence-associated genes were detected by polymerase chain reaction (PCR). Genotypic diversity was evaluated using random amplified polymorphic DNA-PCR (RAPD-PCR) with two primers.

Results: Among the isolates, 44 (62.85%) were identified as hypervirulent K. pneumoniae (hvKP), showing a significant association with strong biofilm formation (P 0.05). The virulence genes entB and mrkD were detected in all isolates. No significant association was observed between virulence gene patterns and hvKP status, hospital units, or sample types (P 0.05). RAPD-PCR analysis revealed 25 and 19 distinct clusters, which were significantly associated with sample types, biofilm production levels, and certain virulence gene profiles.

Conclusion: This study demonstrated a high prevalence of hvKP and biofilm-producing isolates in hospital settings. The significant associations between specific genotypes, biofilm formation, and sample types highlight the need for continuous surveillance of virulence factors to improve infection prevention and control strategies.

keywords: Klebsiella pneumoniae; Biofilm Formation; Virulence Factors; Capsular Type; RAPD-PCR

PBa-95

The Burden of Vancomycin-Resistant Enterococci (VRE) in Iran: A Systematic Review and Meta-Analysis (2020-2025)

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Background and aim: Vancomycin-resistant enterococci (VRE) are a serious threat to public health, leading to high mortality. This systematic review and meta-analysis aimed to determine the cumulative prevalence and epidemiological distribution of VRE across different regions of Iran over the recent five-year period (2020-2025).

Methods: A comprehensive search was conducted in Medline/PubMed, Scopus, and Web of Science from January 2020 to May 2025. Primary studies reporting the prevalence of VRE in clinical samples in Iran were identified using inclusion and exclusion criteria. Statistical analysis was performed using Comprehensive Meta-Analysis (v3), and, due to high predicted heterogeneity, a random-effects model was used. Publication bias was assessed using Egger's and Begg's tests and the Trim and Fill method.

Results: Of the 137 initially identified records, 36 studies including 7379 clinical specimens were included in the final analysis. The overall prevalence of VRE in Iran was 33% (95% confidence interval: 26.1%-40.8%). Considerable heterogeneity was observed (I^2 = 96.4%). Subgroup analysis revealed significant geographical variation, with the highest prevalence in Tehran (42.5%) and Shiraz (38.2%). A significant temporal increase was observed, rising from 20.5% in 2012-2014 to a peak of 62.9% in 2020, coinciding with the COVID-19 pandemic. The comprehensive analysis found no evidence of significant publication bias.

Conclusion: This study demonstrates the high and increasing prevalence of VRE in Iran, which poses a challenge for the national healthcare system. Implementing robust national antimicrobial resistance surveillance programs, standardized diagnostic methods, and advanced infection control measures, especially in hospital settings, can help reduce this infection.

keywords: Enterococcus, Vancomycin Resistance, Meta-Analysis, Prevalence, Iran

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-96

Epidemiological and Clinical Insights into Genotypic Diversity, Antibiotic Resistance Determinants, and Capsular Types of Klebsiella pneumoniae Isolates from Hospitalized Patients in Amol, Northern Iran

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Background and aim: Klebsiella pneumoniae is a Gram-negative opportunistic pathogen and a leading cause of hospital-acquired infections. This study aimed to investigate the distribution, antibiotic resistance patterns, resistance genes, capsular types, and genotypes of K. pneumoniae isolates from hospitalized patients in Amol, northern Iran.

Methods: A total of 872 clinical samples were collected from inpatients across various hospital wards. K. pneumoniae isolates were identified, and antibiotic susceptibility testing was performed. Capsular typing and resistance gene detection were carried out, and enterobacterial repetitive intergenic consensus PCR (ERIC-PCR) was used for genotyping.

Results: K. pneumoniae was isolated from 70 (8.04%) samples, primarily from urine (58.6%) and sputum (25.7%). High resistance rates were observed to erythromycin (98.6%), ampicillin (92.9%), and cefazolin (68.6%), while all isolates were susceptible to colistin. Multidrug-resistant (MDR) and extensively drug-resistant (XDR) isolates comprised 55.71% and 15.71%, respectively, and carbapenem-resistant K. pneumoniae (CRKP) accounted for 55.7%. The most prevalent capsular type was K57. Forty-eight resistance gene patterns were detected, with tetB present in all isolates. ERIC-PCR genotyping revealed 24 distinct clusters.

Conclusion: This study highlights the prevalence of antibiotic-resistant K. pneumoniae with significant clonal diversity among hospital isolates. The findings emphasize the necessity of rigorous infection control measures, judicious antibiotic use, and continuous regional and multicenter surveillance to mitigate the spread of resistant strains.

keywords: Klebsiella pneumoniae; Antibiotic Resistance; Resistance Genes; Genotyping; Capsular Type

PBa-97

Diagnostic Accuracy and Clinical Impact of Multiplex Respiratory PCR Panels in Early Detection of Viral and Bacterial Respiratory Infections

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Background and aim: Rapid identification of respiratory pathogens is critical for guiding appropriate antimicrobial therapy and reducing unnecessary antibiotic use. Conventional diagnostics—including culture and antigen testing—often lack sensitivity or require extended turnaround times. Multiplex respiratory PCR panels have emerged as high-performance diagnostic tools capable of detecting a broad range of viruses and bacteria in a single run. This systematic review evaluates their diagnostic accuracy and real-world clinical impact in emergency and inpatient settings.

Methods: Scientific databases (PubMed, Scopus, Web of Science) were searched for studies published between 2014–2024. Inclusion criteria covered clinical trials, cohort studies, and laboratory validation reports assessing multiplex PCR respiratory panels. Data extraction focused on analytical sensitivity/specificity, time-to-result, antimicrobial stewardship outcomes, and effects on hospitalization metrics.

Results: Across the included studies, multiplex PCR panels showed 90% sensitivity for common respiratory viruses such as influenza A/B, RSV, and human rhinovirus, and superior detection rates for atypical bacterial pathogens including Mycoplasma pneumoniae and Bordetella pertussis. Turnaround times decreased from 24–72 hours (culture-based methods) to under 2–4 hours. Several clinical cohorts demonstrated a 20–45% reduction in unnecessary antibiotic prescriptions, alongside improved antiviral stewardship during influenza seasons. Hospital length of stay was modestly reduced, particularly when PCR testing was performed at the point of care. Limitations included high assay costs, occasional cross-reactivity in low-viral-load samples, and inconsistent detection of co-infections across platforms.

Conclusion: Multiplex respiratory PCR panels provide substantial improvements in pathogen detection, antimicrobial stewardship, and patient management. Their integration into routine clinical practice—particularly during high-burden respiratory seasons—can meaningfully improve outcomes, though cost and access disparities should be addressed in future research.

keywords: Diagnostic Accuracy, Clinical Impact, Respiratory PCR Panels, bacterial Respiratory Infections

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-98

Antibiotic resistance of Escherichia coli isolated from hospitalized patients to broad-spectrum β-lactam in Babol city in 2025

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Background and aim: Understanding drug resistance patterns in Escherichia coli is of particular importance for developing appropriate treatment strategies and preventing the spread of resistance. This research can help reduce these negative consequences through more accurate and rapid identification of resistant bacteria and prescribing appropriate antibiotics, improving the quality of healthcare services, and reducing costs. The present study aims to "Investigate antibiotic resistance of Escherichia coli to Broad-spectrum β-lactam antibiotics".

Methods: This descriptive-analytical-cross-sectional study was conducted in the first six months of 2025 in Ayatollah Rouhani Hospital (Mazandaran province, Babol, Iran), under the supervision of Islamic Azad University, Amol Branch (Thesis codes: 163066046). Microbial and biochemical tests were used to identify Escherichia coli. Antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method according to the Clinical and Laboratory Standards Institute guidelines, and resistance to broad-spectrum β-lactam antibiotics (imipenem (10µg), ceftriaxone (30 µg), ceftazidime (30 µg), cefotaxime (30 µg), cefpodoxime (30 µg), cefepime (10µg)) was examined. Data analysis was performed using SPSS-27 software, a frequency distribution table (%), and a chi-square test (p 0.05) (Ethical code: IR.IAU.BABOL.REC.1404.113).

Results: Of the 50 Escherichia coli strains, 36 (72%) were isolated from women and 14 (28%) from men. The highest frequency of antibiotic resistance was associated with broad-spectrum β-lactam antibiotics (ceftriaxone (n=37, 74%), cefotaxime (n=37, 74%), ceftazidime (n=34, 68%), cefpodoxime (n=32, 64%), cefepime (n=28, 56%), imipenem (n=25, 50%)). No significant relationship was observed between antibiotic resistance and the gender of female (p=0.067) and male (p=0.066) patients.

Conclusion: In the present study, more than half of the Escherichia coli strains were resistant to broad-spectrum β-lactam antibiotics. Therefore, appropriate antibiotics should be selected more carefully, and the indiscriminate use of antibiotics should be stopped.

keywords: Antibiotic resistance, Escherichia coli, Patients, Broad-spectrum β-lactam antibiotics

PBa-99

Surface modified niosomal quercetin with cationic lipid: an appropriate drug delivery system against Pseudomonas aeruginosa Infections

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Background and aim: Background: Increase in infection caused by resistant strains of Pseudomonas aeruginosa possesses a formidable challenge to global healthcare systems. P. aeruginosa is capable of causing seriously human infections across diverse anatomical sites, presenting considerable therapeutic obstacles due to its heightened drug resistance. Niosomal drug delivery systems offer enhanced pharmaceutical potential for loaded contents due to their desirable properties, particularly providing a controlled release profile. This study aimed to formulate an optimized niosomal drug delivery system incorporating stearylamine (SA) to augment the antibacterial and antibiofilm activities of quercetin (QCT) against both standard and clinical strains of P. aeruginosa.

Methods: Methods: QCT-loaded niosome (QCT-niosome) and QCT-loaded SA-nisomes (QCT-SA-nissome) were prepared by the thin-film hydration method, and their physicochemical properties were assessed by field emission scanning electron microscopy (FE-SEM), zeta potential measurement, entrapment efficacy (EE%), and in vitro release profile. The anti- P. aeruginosa activity of synthesized niosomes, was evaluated through minimum inhibitory and bactericidal concentrations (MICs/MBCs), compared to free QCT. Additionally, the minimum biofilm inhibitory and eradication concentrations (MBICs/MBECs) were carried out to analysis the efficacy of QCT-niosome and QCT-SA-niosome against P. aeruginosa biofilm. The cytotoxicity assay was conducted on L929 mouse fibroblasts cell line to evaluate the biocompatibility of the formulated niosomes.

Results: Results: FE-SEM analysis revealed that both niosomal formulations exhibited spherical morphology with different in sizes (57.4 nm for QCT-niosome and 178.9 nm for QCT-SA-niosome). The encapsulated efficiency of QCT in SA-niosomal formulation was 75.9%, whereas standard formulation reported EE% 59.6. Both formulations showed a sustained release profile in vitro, with QCT-SA-niosome exhibiting greater stability over a 4-month storage time compared to QCT-niosome. Microbial experiments indicated that the prepared formulations had higher antibacterial and anti-biofilm activities compared to QCT. Also. The QCT-SA-niosome exhibited greater reductions in MIC, MBC, MBIC, and MBEC values compared to QCT-niosome at equivalent concentrations.

Conclusion: Conclusion: This study supports the potential of QCT-niosome and QCT-SA-niosome as effective agents against P. aeruginosa infections, manifesting significant antibacterial and anti-biofilm efficacy alongside biocompatibility with L929 cell lines. Overall, our results suggest that optimized QCT-niosome with cationic lipid efficiently target P. aeruginosa cells with reduced cytotoxic effects in comparison to QCT-niosome.

keywords: Niosomal drug delivery system, Stearylamine, Quercetin, Pseudomonas aeruginosa, Drug-resistant infection

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-100

Plasma Bacterial Extracellular Vesicles as Early Diagnostic and Prognostic Biomarkers in Klebsiella pneumoniae Bloodstream Infection

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Background and aim: Delayed and non-specific diagnosis of bloodstream infection (BSI) remains a major challenge in septic patients despite the routine use of CRP, procalcitonin (PCT) and blood cultures. Bacterial extracellular vesicles (BEVs) released by Gram-negative pathogens such as Klebsiella pneumoniae carry LPS and bacterial DNA and may enter the circulation during sepsis. This study aimed to evaluate whether plasma levels and molecular features of K. pneumoniae-derived BEVs at the time of sepsis suspicion can improve early diagnosis of K. pneumoniae BSI and provide additional prognostic information beyond CRP and PCT in adult ICU patients.

Methods: In a prospective single-center study, adult patients with suspected sepsis who had blood cultures taken in the emergency department/ICU were enrolled and classified into three groups: confirmed K. pneumoniae BSI (KP-BSI), sepsis without bacteremia (No-BSI) and non-septic controls. At sepsis onset (T0), EDTA blood was collected; platelet-poor plasma was prepared and processed by differential centrifugation, 0.22 µm filtration and size-exclusion chromatography to isolate EV-enriched fractions compatible with ISEV recommendations. Nanoparticle tracking analysis quantified particle number and size. Endotoxin content was measured by chromogenic LAL assay and Klebsiella-related LPS by ELISA. K. pneumoniae-specific DNA was detected in BEV-enriched fractions using qPCR. Routine CRP and PCT values were retrieved from clinical records. Diagnostic accuracy for KP-BSI and association with early organ dysfunction and 28-day mortality were assessed using ROC curves and multivariable logistic regression.

Results: Overall, 52 KP-BSI, 56 No-BSI and 30 control patients were included. KP-BSI patients had higher median BEV particle counts than No-BSI and controls (5.8×10^9 vs. 3.9×10^9 vs. 1.7×10^9 particles/mL; p0.001), while modal size was similar between groups. LPS-equivalent levels in EV-enriched fractions were highest in KP-BSI (0.92 EU/mL), intermediate in No-BSI (0.51 EU/mL) and lowest in controls (0.18 EU/mL; p0.001). K. pneumoniae DNA was detectable in 78.8% of KP-BSI, 16.1% of No-BSI and 6.7% of controls (p0.001). For KP-BSI discrimination, AUCs were 0.73 for PCT, 0.68 for CRP, 0.82 for BEV-LPS and 0.85 for BEV-DNA; combining BEV markers with PCT/CRP increased AUC to 0.90. Higher BEV-LPS and BEV-DNA positivity independently predicted early organ dysfunction and 28-day mortality.

Conclusion: Plasma profiling of K. pneumoniae-derived BEVs at sepsis onset provided earlier and more specific information on K. pneumoniae bloodstream infection than CRP and PCT alone and was independently associated with short-term organ dysfunction and mortality. Although the current workflow is still technically demanding and single-center, these findings suggest that BEV-based assays may become a clinically relevant adjunct to conventional biomarkers and blood cultures for early risk stratification of septic patients and warrant validation in larger multicenter cohorts.

keywords: Bacterial extracellular vesicles,Klebsiella pneumoniae,Bloodstream infection,Sepsis,Biomarkers

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July 20-23, 2026

PBa-101

Prevalence of tuberculosis disease and underlying diseases in infected individuals in Zanjan county between 2015 to 2022

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Background and aim: Tuberculosis (TB) infection is one of the ten leading causes of death worldwide, with more than one million deaths per year. The present study was designed and implemented to investigate the prevalence of tuberculosis and the diversity of underlying diseases in infected individuals in Zanjan province between 2015 -2022.

Methods: In this cross-sectional study, a total of 220 patients diagnosed with pulmonary tuberculosis who were admitted to the TB center of Zanjan province were studied during 2015 -2022. The data collection tool was a checklist including demographic variables and underlying diseases such as diabetes, chronic renal failure, cancer, silicosis, chronic lung disease, chronic malabsorption syndrome, gastrectomy or jejunoileal bypass surgery, organ transplantation, HIV infection, hepatitis B and C, which were extracted from the patients' medical records by referring to the hospital's medical records department. After collection, the relevant data were entered and analyzed in SPSS26 software.

Results: The mean (±SD) age was 57.52 (±18.53) years, 58.6% of the patients were male, 71.8% were urban residents, and 40.5% were housewives. 3.2% had a history of previous exposure to tuberculosis. 1.8% had a history of addiction, and 0.9% had a history of prison. 1.4% had a history of corticosteroid use. The mean (±SD) age was 57.52 (±18.53) years. The mean (±SD) height and weight were 165.73 (±11.01) cm and 63.93 (±12.04) kg, respectively. 79.5% of the patients were married, 31.8% were illiterate, and 30% had primary education. None of the patients had a history of tuberculosis, blood transfusion, or HIV in their spouse. Diabetes, chronic kidney disease (CKD), chronic respiratory disease (CRD), cancer, and HIV were the most common underlying diseases at 14.5%, 4.1%, 3.2%, 2.3%, and 0.9%, respectively. The most common form of tuberculosis was smear-positive and smear-negative at 60% and 22.3%. The prevalence of extrapulmonary tuberculosis (EP-TP)

Conclusion: The present study showed that smear-positive pulmonary tuberculosis is the most common form of tuberculosis in patients with TB, and diabetes, chronic kidney disease (CKD), chronic respiratory disease (CRD), cancer, and HIV were the most common underlying diseases in these patients. Therefore, timely diagnosis and treatment of the aforementioned underlying diseases may be an effective step to prevent antibiotic resistance and provide better treatment for tuberculosis.

keywords: Frequency, tuberculosis, underlying disease

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-102

Prevalence of Nasal Carriage of Staphylococcus aureus and Its Antibiotic Resistance Pattern Among Medical Interns and Trainees

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Background and aim: Staphylococcus aureus is one of the most important causes of hospital-acquired infections and can exist as an asymptomatic nasal carrier, particularly among individuals in close contact with healthcare environments such as medical students. Given the increasing prevalence of antibiotic-resistant strains, identifying nasal carriers and determining their antibiotic resistance patterns among medical students is of particular importance. This study aimed to determine the prevalence of nasal carriage of Staphylococcus aureus and assess its antibiotic resistance profile among medical students at Valiasr Hospital, Qaemshahr, in 2024.

Methods: This descriptive cross-sectional study was conducted on 104 medical students (interns and trainees). Nasal swab samples were collected from the anterior nares of each participant and cultured on blood agar and mannitol salt agar media. Bacterial identification was performed using biochemical tests, including catalase, coagulase, and DNase. Antibiotic susceptibility testing was carried out using the Kirby–Bauer disk diffusion method according to CLSI guidelines. Data were analyzed using SPSS version 26, and the relationships between variables were evaluated using Chi-square and Fisher's exact tests.

Results: Among all participants, 21 (approximately 20%) were identified as nasal carriers of Staphylococcus aureus. Overall, 8 isolates (about 38% of the positive samples) showed antibiotic resistance. There was no significant relationship between carrier status and variables such as gender, blood group, or history of underlying diseases (p0.05); however, a significant association was observed with prior antibiotic use (p=0.02) and higher age (p=0.044).

Conclusion: The findings indicate that medical students may serve as a potential reservoir for Staphylococcus aureus transmission in hospital settings. The observed antibiotic resistance and its correlation with previous antibiotic use highlight the necessity of implementing regular screening programs, infection control education, and continuous monitoring of antibiotic resistance among healthcare-associated groups.

keywords: Staphylococcus aureus, nasal carriage, antibiotic resistance, medical students

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-103

Bacterial contamination of surfaces and medical equipment in different wards of Valiasr Hospital, Zanjan, Iran, in 1403

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Background and aim: Healthcare-associated infections are among the major challenges for health systems, and environmental surfaces and medical devices can serve as potential reservoirs for transmission. This study aimed to assess the extent and pattern of bacterial contamination of surfaces and therapeutic/diagnostic equipment in different wards of Valiasr Hospital (Zanjan) in 1403.

Methods: This descriptive cross-sectional study was conducted on 135 samples collected from hospital surfaces and equipment. Sampling was performed across several wards (internal medicine, ICU, oncology, surgery, infectious diseases, and neurology), hospital surfaces (trolley trays, computer keyboards, doorbells, hand surfaces before and after washing, refrigerators, bedside edges, tables, file folders, and sinks), and medical equipment (ventilators, pulse oximeters, masks, and Abslangs). Specimens were cultured on BHI and MacConkey media, and microorganisms were identified using standard microbiological methods. Data are presented as frequencies and percentages, and comparisons were made using the chi-square test.

Results: Of the 135 samples, 99 samples (73.3%) were taken from surfaces and 36 samples (26.7%) from equipment. On BHI medium, 80% of samples were culture-positive, whereas only 23% showed growth on MacConkey. Staphylococcus spp. was the most frequent isolate (54.6%), followed by Enterobacteriaceae (25%). Gram-positive bacteria accounted for 64.8% of isolates, while gram-negative organisms comprised 28.4%. The highest surface contamination was observed on staff hands after washing, and the highest equipment contamination was observed in the abslangs, masks, and pulse oximeters. All bacteria identified on surfaces were gram-positive, whereas the medical equipment were predominantly contaminated with gram-negative bacteria; the ventilator was the only device showing both groups (62.5% gram-negative and 37.5% gram-positive) (P 0.05).

Conclusion: The findings indicate substantial bacterial contamination of surfaces and equipment in Valiasr Hospital. Surfaces were mainly colonized by gram-positive organisms, with Staphylococci being the predominant contaminator of surfaces overall. Although diagnostic and therapeutic devices were more frequently contaminated by gram-negative bacteria, this pattern poses a serious risk for nosocomial transmission. These results underscore the need to strengthen infection-control protocols, perform continuous disinfection of equipment, and provide ongoing staff training on hand hygiene.

keywords: Cross Infection, Hospital Equipment, Environmental Microbiology, Bacterial Contamination, Health Facilities

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-104

Epidemiological study of vancomycin resistance genes in vancomycin-resistant enterococci isolated from clinical samples of Imam Hossein Hospital, Shahroud

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Background and aim: Enterococcus spp. are one of the important causes of hospital-acquired and community-acquired infections, and its treatment is associated with serious challenges due to its increasing resistance to antibiotics. The aim of the present study was to investigate antibiotic resistance and identify vancomycin-resistant genes in vancomycin-resistant enterococci collected from patients of Imam Hossein Hospital in Shahroud.

Methods: In a descriptive-cross-sectional study, 94 clinical isolates of Enterococcus were collected from different samples. Phenotypic and molecular identification of the species was performed and susceptibility to vancomycin was investigated using agar disk diffusion and MIC-MBC methods. Also, PCR was used to identify vanA, vanB, vanD, vanC, and vanC2/C3 genes.

Results: In the disk diffusion method, 89.7% Enterococcus faecium isolates and 83.3% Enterococcus faecalis isolates were resistant to vancomycin. In the MIC-MBC method, 78.4% E. faecium isolates and 66.6% E. faecalis isolates were resistant to vancomycin. PCR results showed that vanA gene in enterococci isolated from clinical samples was 66.6% of the isolates had the vanA gene. The vanC1 and vanD genes were not detected in any of the strains. The vanB and vanC2/C3 genes were each detected in 1.4% of the isolates.

Conclusion: The results indicate a high prevalence of vancomycin resistance among E. faecium isolates especially the vanA gene. The findings emphasize the need for rational use of antibiotics and continuous monitoring of resistance patterns.

keywords: Enterococci, Antibiotic resistance, Vancomycin, PCR method

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-105

Investigation of the antibacterial activity of hydroalcoholic extract of hawthorn leaf (Crataegus persica) in healing skin wounds infected with Staphylococcus aureus in rats

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Background and aim: Infected skin wounds, especially those caused by Staphylococcus aureus, are common clinical problems and their healing process is delayed due to bacterial infection. The use of herbal compounds with antibacterial and regenerative properties can be an effective and low-complication approach in the treatment of these types of wounds. This study aimed to evaluate the antibacterial activity and regenerative effect of hydroalcoholic extract of hawthorn (Crataegus persica) on S. aureus–infected skin wounds in a rat model.

Methods: In this experimental study, 18 male Wistar rats were randomly divided into three groups: positive control, negative control, and treatment group receiving hydroalcoholic extract of hawthorn (Crataegus persica) leaves. The positive control group consisted of healthy rats with no skin wounds created. In the negative control group, a full-thickness excisional skin wound (1.5 × 1.5 cm) was created on the back of the rats and inoculated with Staphylococcus aureus ATCC 25923, and the animals received no treatment or dressing. In the treatment group, after wound creation and bacterial inoculation, topical application of hawthorn leaf hydroalcoholic extract was performed for 14 days. The wound healing process was evaluated by measuring wound area and assessing macroscopic and microscopic changes.

Results: The results showed that the use of hydroalcoholic extract of hawthorn leaves significantly reduced the wound size compared to the control group. Also, the symptoms of local infection, including discharge, inflammation, and redness, were significantly reduced in the treatment group. These findings indicated the effective antibacterial effects of hawthorn leaf extract against S. aureus ATCC 25923 and accelerated the wound healing process.

Conclusion: Hawthorn leaf hydroalcoholic extract, with its antibacterial and regenerative properties, can be considered as a natural and effective treatment option for healing infected skin wounds. This herbal compound has good potential for the development of new therapeutic products in wound healing.

keywords: Crataegus persica, Staphylococcus aureus, Wound healing

PBa-106

Investigation of bacteria isolated from tracheal culture samples in people hospitalized in Golestan Hospital, Ahvaz city and their antibiotic resistance pattern during 1397-1400

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Background and aim: Antibiotic resistance is one of the major challenges in treating hospital-acquired infections, particularly in patients admitted to intensive care units (ICUs). The increase in antibiotic resistance among this group can lead to treatment failure, prolonged hospitalization, and increased mortality. This study examines the trends of antibiotic resistance in bacterial strains isolated from endotracheal tube cultures of hospitalized patients between 2018 and 2021.

Methods: This descriptive cross-sectional study analyzed data from endotracheal tube cultures of hospitalized patients over four consecutive years. Data were collected from the hospital's microbiology laboratory and included bacterial isolation rates, antibiotic resistance patterns, and trends across different hospital wards.

Results: The most frequently isolated bacteria were Klebsiella spp. (1366 cases), Pseudomonas spp. (496 cases), and Staphylococcus aureus (246 cases). Some antibiotics, such as nitrofurantoin (99.6%), azithromycin (99.7%), penicillin (99.7%), cefepime (98.2%), and chloramphenicol (99.3%), exhibited the highest resistance rates. In contrast, clindamycin showed the lowest resistance at 32.3%, with 67.7% of samples remaining sensitive. Among carbapenems, imipenem and meropenem, which are crucial for treating severe respiratory infections, displayed resistance rates of 90.7% and 91.8%, respectively, indicating their reduced effectiveness in hospitalized patients. Cefepime exhibited high resistance at 98.2%, while ceftriaxone showed a resistance rate of 97.6%, limiting their efficacy against respiratory infections. Gentamicin and ciprofloxacin, commonly used to treat gram-negative respiratory infections, showed resistance rates of 91.7% and 93%, respectively, further highlighting their decreased effectiveness in patients with respiratory tract infections. Analysis of resistance patterns across hospital wards revealed the highest resistance rates in ICU 1, ICU 2, and

Conclusion: : The results of this study indicate that antibiotic resistance in bacterial strains isolated from endotracheal tube cultures has been increasing over the past four years, with a relative decline in 2021. Clindamycin was the most effective antibiotic, with 67.7% sensitivity, while cefepime, nitrofurantoin, and azithromycin exhibited the highest resistance rates. The high resistance to carbapenems and third- and fourth-generation cephalosporins suggests a significant reduction in the efficacy of these drugs for treating respiratory infections in hospitalized patients. Therefore, precise antibiotic stewardship is necessary, and effective control strategies must be

keywords: Antibiotic resistance, hospital-acquired infection, endotracheal tube culture, intensive care

PBa-107

Evaluation of Antimicrobial and Anti-Endotoxin Activities of the Dengue Virus–Derived PepR Peptide against Pseudomonas aeruginosa In Vitro and Ex Vivo

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Background and aim: Bacterial infections caused by Gram-negative pathogens, particularly Pseudomonas aeruginosa, remain a major clinical challenge due to antibiotic resistance and sepsis-associated mortality. Excessive inflammatory responses triggered by bacterial endotoxins, such as lipopolysaccharide (LPS), contribute significantly to disease severity. Development of novel therapeutics with both antimicrobial and anti-endotoxin properties is urgently needed. PepR, a cationic amphipathic peptide derived from the Dengue virus capsid, has demonstrated antimicrobial activity; however, its anti-inflammatory and anti-endotoxin effects are less explored. Objectives: To evaluate the antimicrobial, anti-inflammatory, and anti-endotoxin activities of PepR against invasive P. aeruginosa infection under in vitro and ex vivo conditions.

Methods: Antimicrobial activity was assessed using CFU counts, radial diffusion assays, and MIC determination. Ex vivo anti-endotoxin effects were evaluated in macrophage cultures and whole blood stimulated with LPS in the presence or absence of PepR, measuring cytokines (IL-6, TNF-α, IL-10, MCP-1, IFN-γ) by ELISA.

Results: PepR showed potent antimicrobial activity against P. aeruginosa (MIC = 5.5 µM; MBC = 11.7 µM). Bacterial counts decreased in a concentration-dependent manner, with a 3-log reduction at 11.7 µM (P 0.001), and radial diffusion assays yielded ~12 mm inhibition zones at this concentration. Ex vivo, PepR (12 µM) suppressed LPS-induced release of TNF-α, IL-6, MCP-1, and IFN-γ by 30–40% (P 0.01) in macrophages and whole blood, without affecting IL-10.

Conclusion: PepR demonstrates strong antimicrobial activity against P. aeruginosa and effectively modulates LPS-induced inflammatory responses ex vivo. These findings support PepR as a promising dual-function therapeutic candidate for managing Gram-negative bacterial infections and sepsis.

keywords: Antimicrobial peptide, Inflamation, antiendotoxin, LPS

PBa-108

Prevalence of exoA, cepA, plcH, lasB, and algD virulence genes in clinical isolates of Pseudomonas aeruginosa from hospitals in Yasuj and Shiraz, Iran

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Background and aim: Background and Objectives: Pseudomonas aeruginosa, an opportunistic Gram-negative bacterium, is ubiquitous and represents one of the most challenging multidrug-resistant pathogens today. This multicenter study aimed to evaluate antibiotic resistance patterns, detect the cepA antibiotic resistance gene, and identify virulence factor genes (exoA, algD, lasB, and plcH) in clinical isolates of P. aeruginosa.

Methods: Materials and Methods: This experimental study analyzed 74 P. aeruginosa isolates obtained from clinical samples at Imam Sajad (Yasuj) and Namazi (Shiraz) hospitals, including 74 clinical isolates and one standard reference strain. Bacterial identification was performed using standard biochemical tests. Antibiotic susceptibility was assessed by the disk diffusion method according to CLSI 2018 guidelines. Genomic DNA was extracted by means of boiling method, and PCR assays were applied to detect exoA, cepA, plcH, lasB, and algD genes. Data were analyzed with chi-square tests, considering p0.05 as statistically significant.

Results: Results: Among 74 P. aeruginosa isolates, all carried the exoA gene, while algD, plcH, cepA, and lasB were detected in 95.6%, 94.6%, 93.2%, and 91.9% of isolates, respectively. High resistance was observed to aztreonam and ticarcillin, while cefiderocol showed the greatest sensitivity. A significant correlation was found between the cepA gene and antibiotic resistance (P = 0.03).

Conclusion: Conclusion: This study reveals a high prevalence of virulence genes and increasing antibiotic resistance among P. aeruginosa clinical isolates, highlighting the urgent need for effective therapeutic strategies to combat this pathogen.

keywords: Keywords: Antibiotic resistance; Virulence; Pseudomonas aeruginosa; Polymerase chain reaction

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-109

Systems-Biology Approaches to Identify Potential Gene Targets and Pathways in Hepatocellular Carcinoma through Microbiota–Metabolite Interactions

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Background and aim: Hepatocellular carcinoma (HCC) is the third-leading cause of cancer mortality worldwide. Growing evidence links gut dysbiosis and the metabolites it produces to chronic liver inflammation, oncogenic signalling and variable therapy response. We therefore set out to integrate real-world transcriptomic, microbiome and metabolomic layers to pinpoint modifiable genes and pathways in HCC.

Methods: We combined RNA-seq profiles from the TCGA-LIHC project covering 374 tumour and 50 matched non-tumour samples (portal.gdc.cancer.gov), then shotgun faecal metagenomes from 51 patients across Barcelona Clinic Liver Cancer stages A–D deposited under BioProject PRJNA1111312 (pmc.ncbi.nlm.nih.gov) and untargeted serum lipidomics from Metabolomics Workbench study ST001640 (31 HCC, 24 chronic-liver-disease, 13 healthy controls) (metabolomicsworkbench.org). Differential expression was computed with DESeq2 (FDR 0.01). Microbial abundances were profiled with MetaPhlAn 4, centred-log-ratio normalised and linked to genes via MaAsLin2. All three matrices were harmonised in DIABLO (mixOmics); module detection used WGCNA. Pathway enrichment relied on KEGG/Reactome, and drug–gene matches on DGIdb.

Results: The cross-omic network retained 1842 differentially expressed genes, 68 bacterial taxa and 112 lipids at Q 0.05. Bacteroides stercoris recently reported as depleted in late-stage HCC clustered inversely ($\rho = -0.45$, p 0.001) with a Wnt/β-catenin sub-module centred on CTNNB1 and ceramide species (Cer d18:1/16:0). Bile-acid chenodeoxycholic acid correlated positively with FXR (NR1H4) and negatively with pro-inflammatory IL1B (adj. $p = 0.004$), supporting bile-acid–microbe crosstalk in tumour immunity. Network centrality highlighted CTNNB1, TP53, SLC1A5 and FXR as high-betweenness nodes; DGIdb flagged available FXR agonists and Porcupine (Wnt) inhibitors as tractable therapeutics.

Conclusion: A multi-omic systems-biology framework uncovered a triad linking bile-acid metabolites, Bacteroides stercoris depletion and Wnt/β-catenin activation as a potential driver of HCC progression. The data nominate FXR modulation and Wnt pathway blockade as gene–metabolite targets amenable to microbiome-informed intervention in HCC.

keywords: Hepatocellular carcinoma; Gut microbiome; Metabolomics; Wnt/β-catenin signalling

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-110

Exploring the Mechanisms and Drivers of Antibiotic Resistance in Pathogenic Bacteria: A Growing Global Health Concern

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Background and aim: Antibiotic resistance in pathogenic bacteria is a growing global health concern that reduces the effectiveness of common antimicrobial treatments. The increase of multidrug-resistant (MDR) bacteria has caused treatment failures, longer hospital stays, higher healthcare costs, and increased mortality. This problem arises from a combination of genetic, biochemical, environmental, and clinical factors. Understanding these mechanisms is essential for planning effective strategies to control and prevent resistance.

Methods: A systematic review was conducted following standard scientific methods. Peer-reviewed articles published between 2014 and 2024 were searched in PubMed, Scopus, Web of Science, and Embase. Studies addressing genetic and biochemical mechanisms of antibiotic resistance, environmental and clinical contributing factors, and health outcomes were included. After screening for eligibility and quality, 95 articles were selected for detailed analysis.

Results: The review shows that antibiotic resistance is mainly caused by horizontal gene transfer through plasmids, transposons, and integrons, along with chromosomal mutations that change antibiotic targets or metabolic pathways. Other important mechanisms include production of beta-lactamase enzymes, efflux pumps, and biofilm formation, which reduce drug effectiveness. Environmental factors, such as excessive use of antibiotics in medicine, agriculture, and animal husbandry, along with weak infection control, also help spread resistant bacteria. Despite progress in genomics and proteomics, gaps remain in connecting laboratory findings to clinical and environmental situations.

Conclusion: Antibiotic resistance in pathogenic bacteria is a complex and rapidly growing threat. Controlling it requires an integrated approach, including new antibiotics, alternative treatments like bacteriophage therapy, improved laboratory diagnostics, strong antibiotic stewardship programs, and global surveillance. Cooperation among laboratory scientists, clinicians, and health policymakers is essential to prevent the spread of resistance and protect public health

keywords: Antibiotic resistance; Pathogenic bacteria; Multidrug resistance;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-111

Sub-Minimum Inhibitory Concentrations of Colistin Reduce Biofilm Formation and Host Cell Adherence in Acinetobacter baumannii: Insights from a Pediatric Study

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Background and aim: Acinetobacter baumannii is a critical multidrug-resistant pathogen, especially in pediatric and immunocompromised patients. Colistin remains a last-resort antibiotic, but its dose-dependent toxicity necessitates exploration of lower, sub-inhibitory concentrations. This study investigates the effects of sub-minimum inhibitory concentrations (sub-MICs) of colistin on biofilm formation, host cell adherence, and invasion in clinical isolates of A. baumannii from a pediatric referral hospital.

Methods: Seventy non-duplicate A. baumannii isolates were collected from pediatric patients. Biofilm formation was assessed using a microtiter plate assay with and without sub-MICs of colistin (¼ and ½ MIC). The presence of biofilm-associated genes (bap, abal, ompA, csuE, blaPER-1) was detected by PCR, and gene expression (ompA, csuE) was quantified via qPCR. Adherence and invasion to human laryngeal epithelial (HEp-2) cells were evaluated under sub-MIC conditions.

Results: Among the isolates, 80% were multidrug-resistant (MDR) and 35.7% extensively drug-resistant (XDR). Biofilm formation was observed in 92.9% of isolates, with 37.1% classified as strong producers. Exposure to sub-MICs of colistin significantly reduced biofilm formation and downregulated the expression of csuE and ompA genes. Adherence to HEp-2 cells was also diminished at sub-MICs, while no invasion was observed in any isolate. A weak positive correlation was found between biofilm formation and gene expression under antibiotic pressure.

Conclusion: Sub-MICs of colistin downregulate key biofilm-related genes and reduce the adherence capacity of A. baumannii, without promoting invasion. These findings support the potential use of lower colistin doses in combination therapies to manage biofilm-associated infections, particularly in pediatric settings, while mitigating toxicity and resistance development.

keywords: Acinetobacter baumannii, colistin, sub-MIC, biofilm, adherence, pediatric infections

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July 20-23, 2026

PBa-112

Understanding Antibiotic Resistance in Pathogenic Bacteria: Mechanisms, Contributing Factors, and Innovative Interventions

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Background and aim: The spread of antibiotic-resistant bacteria poses a serious challenge to modern healthcare, compromising the effectiveness of standard treatments and increasing the burden on health systems. Multidrug resistance leads to longer hospitalizations, treatment failures, and higher mortality. Resistance emerges through a combination of genetic adaptations, biochemical strategies, and environmental pressures, making it essential to understand these processes to design effective preventive and therapeutic approaches.

Methods: A systematic review was carried out using articles published between 2014 and 2024. Scientific databases including PubMed, Scopus, Web of Science, and Embase were searched for studies addressing resistance mechanisms, environmental and clinical drivers, and potential interventions. Studies were selected based on predefined criteria and methodological quality, resulting in 100 studies included for detailed analysis.

Results: The findings highlight that bacteria develop resistance through multiple mechanisms. Genetic changes and exchange of resistance elements among bacteria enhance survival under antibiotic exposure. Biochemical adaptations, including enzyme-mediated drug breakdown and active removal of antibiotics, along with biofilm formation, reduce treatment efficacy. Environmental and human-related factors—such as excessive antibiotic use in healthcare, agriculture, and animal production—further accelerate resistance. Novel interventions including bacteriophage therapy, antimicrobial peptides, and innovative drug combinations show promise, but challenges remain in translating research findings into practical clinical solutions.

Conclusion: Antibiotic resistance is a complex, evolving, and multifactorial problem. Effective control requires a combination of new therapeutic agents, alternative treatments, strengthened diagnostic and stewardship programs, and coordinated global monitoring. Collaboration between researchers, clinicians, and policymakers is essential to reduce resistance and maintain effective treatment options.

keywords: Antibiotic resistance, Pathogenic bacteria, Multidrug resistance, Resistance mechanisms, Biofilms, Antimicrobial

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-113

Investigation of Antibiotic Prescription Patterns in Hospitalized Children with Gastroenteritis at Shahid Rahimy Hospital, Khorramabad, Iran (2024)

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Background and aim: Acute gastroenteritis is predominantly a viral illness, and antibiotic prescription is often unnecessary. This study aimed to investigate the pattern of antibiotic prescription and its related factors in children hospitalized with a diagnosis of gastroenteritis at a teaching hospital.

Methods: This retrospective cross-sectional study was conducted on 323 medical records of children hospitalized with a diagnosis of gastroenteritis at Shahid Rahimy Hospital in Khorramabad in 2024. Demographic data, type of prescribed antibiotic, and laboratory findings (such as the presence of WBC in stool and ESR) were extracted from the records and analyzed using SPSS statistical software and the Chi-square test.

Results: Among the 323 studied children (mean age: 6.91 ± 2.40 years), 186 (57.6%) were boys. Overall, 272 patients (84.2%) did not receive any antibiotics. The most commonly prescribed antibiotic was ceftriaxone (34 patients, 10.5%), followed by metronidazole. A statistically significant association was found between the type of antibiotic used and the presence of WBC in stool (P 0.001), where all patients with positive stool WBC had received ceftriaxone. Significant associations were also observed between antibiotic prescription (especially ceftriaxone) and elevated ESR (P 0.001), as well as a history of blood in stool.

Conclusion: Although antibiotics were not prescribed in most cases (84.2%), which is a promising approach, in cases where antibiotics (particularly ceftriaxone) were prescribed, alignment with potential laboratory evidence of bacterial infection (such as WBC in stool or elevated ESR) was observed. However, there appears to be a need for continued education and the use of clinical guidelines to ensure more precise prescribing and prevent unnecessary antibiotic use in pediatric gastroenteritis.

keywords: Gastroenteritis, Children, Antibiotics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-114

Phenotypic and Genotypic ESBL Evaluation of Escherichia coli Strain Isolated from Patients in Tehran, Iran.

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Background and aim: Escherichia coli isolates that produce extended-spectrum β-lactamase (ESBL) enzymes contribute significantly to urinary tract infections. The present study aims to explore the phenotypic and genotypic properties of ESBLs in isolates obtained from patients with urinary tract infections in Iran.

Methods: A total of 50 non-duplicate E. coli isolates were obtained from urine specimens of patients in hospitals across Tehran from 2020 to 2022. E. coli isolates were identified by standard biochemical reactions. Antibiotic resistance was checked by disk diffusion as per guidelines by CLSI (2024). Phenotyping for ESBL production by Combined Disk Test was performed. The gene expressions for blaTEM, blaSHV, and blaCTX-M genes were detected by Polymerase Chain Reaction and verified by DNA sequencing.

Results: Isolates were mainly recovered from female (72%) and the remaining 28% were isolated from males. The highest resistance was found to piperacillin (92%) and ceftriaxone (86%), whereas the lowest resistance was found to fosfomycin (2%) and minocycline (4%). Phenotypic confirmation of ESBL producers confirmed that 66% of isolates belonged to ESBL producers. In terms of genetic characterization, blaTEM was found to be the most dominant (62%) gene among blaCTX-M (54%) and blaSHV (40%).

Conclusion: This research has shown that ESBL-producing E. coli is a prevalent issue in Tehran, mostly driven by the genes blaTEM, blaSHV, and blaCTX-M. The current findings emphasize the need for surveillance as well as prudent antibiotic use. Fosfomycin and minocycline show promise for the treatment of bacterial infections caused by these multi-drug-resistant bacteria.

keywords: Escherichia coli,ESBL,Antibiotic Resistance,Urinary Tract Infection

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-115

Multi-omics diagnostic strategies in gastritis: Advances in prognostic and diagnostic biomarkers

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Background and aim: Gastritis is a clinical disorder characterized by inflammation of the gastric mucosa. Etiological factors include infections, heavy alcohol drinking, and use of non-steroidal anti-inflammatory drugs (NSAIDs), tobacco exposure, and consumption of foods that irritate the gastrointestinal tract and provoke symptoms. Less common causes include: autoimmune disorders (such as pernicious anemia), backflow of bile into the stomach (bile reflux), cocaine use, eating or drinking caustic or corrosive substances (such as poisons), and viral infection, such as cytomegalovirus and herpes simplex virus (more often occurs in people with a weak immune system). Trauma or a severe, sudden illness such as major surgery,

Methods: The following search terms were utilized using databases PubMed, Scopus, Medline, and Google Scholar: “Gastritis”, “Helicobacter pylori”, “smoking”, “trauma”, “food induced gastritis”, “inflammatory drug usage”, “PCR”, “RT-PCR”, “ Biomarker” and “molecular diagnostics”. Literature obtained was systematically reviewed and analyzed

Results: Both invasive and non-invasive assays are suggested for the various diagnostic assays. Among non-invasive tests, stool antigen detection and urea Breath test are common tests utilized in laboratories. For the detection of Helicobacter pylori caused gastritis, PCR based are the most widely molecular tools. However, this test is utilized in most laboratories for research purpose. The assay has been proved sensitive and specific especially when performed as multiplex PCR for its detection and presence of antibiotic resistance genes. Target genes used are as follows: ureA, ureC (glmM), 16S rRNA, cagA, vacA for the detection of H.pylori as PCR and Nested PCR from gastric biopsy, gastric aspirate and stool specimens. Common resistance markers are indicated for clarithromycin resistance (23 rRNA mutations) and levofloxacin (gyr mutation) resistance. Real-Time PCR Quantitative PCR has proved much better for the quantitation of bacterial load as H.pylori is present as colonizer in some individuals. The assay

Conclusion: Molecular diagnostic strategies in gastritis have gained increasing importance due to their ability to detect disease-specific alterations at the genetic, epigenetic, and proteomic levels, thereby complementing conventional histopathological and serological methods. Traditional diagnosis of gastritis relies largely on endoscopic evaluation and biopsy-based histology; however, these approaches may lack sensitivity in early or subclinical disease and provide limited prognostic information. Molecular diagnostics address these gaps by enabling precise characterization of pathogenic mechanisms, disease severity, and risk stratification for disease progression.

keywords: Gastritis, Genetic, Epigenetic, Antibiotic resistance, Molecular Assay

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-116

Metabolism and Healthy Aging in Women: What impact the Gut Microbiota has on her Health?

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Background and aim: According to WHO, health of women is a concern because, in many societies, they are disadvantaged by discrimination rooted in sociocultural factors. Healthy aging in women is closely linked to metabolic regulation, particularly in physiologic transitions that introduces profound hormonal, immunological, and metabolic changes. The gut microbiota has been increasingly recognized as a critical determinant of human health, influencing a wide range of physiological processes. A healthy gut microbiota is essential for maintaining metabolic, immune, and gastrointestinal homeostasis, contributing to overall well-being. Alterations in its composition and functionality, often referred to as microbial dysbiosis, are strongly associated with the development

Methods: The following search terms were utilized using databases PubMed, Scopus, Medline, and Google Scholar: “Women”, “Gut Microbiota”, “Health”, “Metabolism”, “Menopause”, “Dysbiosis” and “longevity”. Literature obtained was systematically reviewed and analyzed.

Results: The role of gut microbiota homeostasis has a role in female health; with dysbiosis potentially leading to diseases among women. The gut microbiota significantly influences estrogen levels that exerts bidirectional interactions with the gut microbiome. Estrogens shape microbial composition and diversity, while microbial enzymes (collectively termed the “estrobolome”) regulate estrogen metabolism and enterohepatic circulation. Disruption of this balance with age, particularly during the menopausal transition, can contribute to metabolic dysregulation. The gut microbiota can both promote and inhibit inflammatory response thus affecting the onset and progression of female diseases. Through the breakdown of organic matter, gut microbiota produces metabolites the SCFA and bile acids. Butyric acid has been shown to regulate progesterone and estradiol secretion through the cAMP signaling pathway in porcine granulosa cells. Age-related shifts in the gut microbiota may exacerbate risks for cardiometabolic disease, osteoporosis, sarcopenia, and cognitive decline.

Conclusion: In summary, studies are required to determine the molecular mechanisms underlying associations between dysbiosis of gut microbiota and female diseases to realize precision medicine, with FMT emerging as a promising intervention. Moreover, the gut microbiota serves as a fundamental integrator of metabolism, hormonal signaling, and immune regulation in women, shaping trajectories of healthy aging. Advancing our understanding of sex-specific microbiome–metabolism interactions is essential for developing precision interventions aimed at extending health span and reducing the burden of age-related metabolic disease in women.

keywords: Women, Gut Microbiota, Health, Metabolism, Menopause, Dysbiosis and longevity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-117

In Vitro Evaluation of the Impact of Curcumin on Biofilm-Associated Genes in Pseudomonas aeruginosa Isolates

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Background and aim: Pseudomonas aeruginosa is known for its ability to form biofilms, which contribute to its persistence and resistance in infections. Curcumin, a natural compound with antimicrobial properties, has been studied for its potential to inhibit biofilm formation. This study aimed to evaluate the impact of curcumin nanoparticles on the expression of biofilm-associated genes in P. aeruginosa clinical isolates under laboratory conditions.

Methods: In an experimental setup, clinical isolates of P. aeruginosa were treated with curcumin nanoparticles. The effect on biofilm formation was assessed using standard biofilm quantification assays. Additionally, changes in the expression levels of key biofilm-related genes, including algD, were measured using molecular techniques such as PCR and gene expression analysis.

Results: The results demonstrated that treatment with curcumin nanoparticles significantly reduced biofilm formation in P. aeruginosa isolates. Correspondingly, the expression of biofilm-related genes, particularly algD, showed a marked decrease after curcumin exposure. These findings suggest that curcumin disrupts the biofilm formation process at the genetic level, potentially weakening the bacteria's defense mechanisms and reducing its pathogenicity.

Conclusion: Curcumin nanoparticles exhibit promising anti-biofilm activity against Pseudomonas aeruginosa by downregulating genes essential for biofilm production. This natural compound could serve as a valuable adjunct in managing biofilm-associated infections, especially those caused by antibiotic-resistant strains. Further studies are recommended to explore curcumin's clinical applications and mechanisms in detail.

keywords: Pseudomonas aeruginosa, curcumin, biofilm, algD gene, antimicrobial resistance

PBa-118

A Novel Therapeutic Strategy for Parkinson's Disease based on the Gut Microbiota: A Rreview Article

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Background and aim: The gut microbiota, which is now recognized as an important organ of the human body, can have an impact on various neurological outcomes such as cognition, learning, and memory. The aim of this study was to investigate the relationship between gut microbiota and Parkinson's disease and also to highlight appropriate microbiota-based therapeutic approaches for Parkinson's disease.

Methods: In this study, we searched and extracted the articles based on the keywords of "Parkinson's", "gut microbiota", "gut microbiome", "fecal microbiota", "fecal microbiome", "probiotic", and "gut-brain axis" from all data bases. Our inclusion criteria included English and Persian language articles, original articles and articles with open access, and the exclusion criteria of the study included articles other than English and Persian articles, articles without open access, meta-analysis and review articles. Finally, 38 articles were reviewed and analyzed.

Results: Fecal microbiota transplant and probiotics laid the groundwork for identifying the mechanisms underlying the ability of the gut microbiota to influence a host's brain and behavior. It could help in prevention or early diagnosis of Parkinson's disease possibly through some peripheral biomarkers.

Conclusion: Recent studies have also shown that patients with Parkinson's disease have a disruption in gut microbiota balance (dysbiosis), but its exact role in causing the neurological disorder is still unknown. However, new approaches based on gut microbiota can be developed to prevent and treat neurological disorders such as Parkinson's disease.

keywords: Microbiome, Gut-brain axis, Parkinson's disease, Probiotics

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July 20-23, 2026

PBa-119

Drug Resistance Patterns of Mycobacterium tuberculosis in Iran: A Systematic Review

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Background and aim: The emergence and spread of drug-resistant Mycobacterium tuberculosis pose a critical challenge to tuberculosis (TB) control in Iran. Given the country's epidemiological setting and cross-border movements, a comprehensive understanding of drug resistance trends is essential for effective public health interventions. This systematic review aimed to synthesize available data on the prevalence and patterns of anti-tuberculosis drug resistance in Iran, with a focus on multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB, and to explore associated risk factors and geographical hotspots.

Methods: This systematic review aimed to synthesize available data on the prevalence and patterns of anti-tuberculosis drug resistance in Iran, with a focus on multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB, and to explore associated risk factors and geographical hotspots.

Results: Among new TB cases, resistance to any drug averaged approximately 15%. Mono-resistance to isoniazid (INH) was the most common pattern (about 10%). The prevalence of primary MDR-TB (resistance to at least INH and rifampicin) averaged 3.5% (range: 1.8–6.5%). Among previously treated cases, MDR-TB prevalence was substantially higher, ranging from 15% to 30%. Approximately 8–15% of MDR-TB cases met the criteria for XDR-TB, indicating additional resistance to a fluoroquinolone and a second-line injectable agent. A consistent geographical pattern was identified, with the highest burdens of MDR-TB reported in eastern (Sistan and Baluchestan Province) and northern (Golestan and North Khorasan) border provinces. Major reported risk factors included a history of previous TB treatment, contact with an MDR-TB patient, and residence in high-burden border regions.

Conclusion: Iran faces a significant and evolving burden of drug-resistant TB, concentrated in specific geographical regions. The substantial proportion of MDR-TB among previously treated patients underscores weaknesses in treatment adherence and infection control. The presence of XDR-TB highlights the urgent need to enhance diagnostic capacity and improve access to newer drug regimens. These findings support the need for a reinforced and targeted national response, including scaling up rapid molecular drug susceptibility testing, strengthening surveillance systems, and implementing tailored control strategies in high-risk provinces to curb the spread of drug-resistant tuberculosis.

keywords: Tuberculosis, Drug Resistance, Iran

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-120

Comparative Diagnostic Accuracy of Commercial SARS-CoV-2 Molecular Kits: A Systematic Review and Meta-Analysis

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Background and aim: Background: The diagnostic performance of commercial SARS-CoV-2 molecular kits varies considerably due to differences in assay design, target genes, and analytical sensitivity. A comprehensive comparison of these kits is essential for reliable clinical decision-making. Objectives: This systematic review and meta-analysis aimed to evaluate and compare the diagnostic accuracy of commercially available SARS-CoV-2 detection kits used in clinical specimens.

Methods: Major databases, including PubMed, Embase, Web of Science, and Scopus, were systematically searched for studies published between 2019 and October 2021. Eligible studies reporting the sensitivity and specificity of commercial SARS-CoV-2 kits were included. A random-effects meta-analysis and bivariate model were applied to estimate pooled diagnostic indices.

Results: A total of 48 studies evaluating more than 50 commercial diagnostic kits were included. Most assays were RT-PCR–based and primarily targeted the N, E, and RdRp genes. The pooled sensitivity and specificity were 90.4% (95% CI: 87.8–92.4) and 98.3% (95% CI: 97.7–98.8), respectively. Diagnostic odds ratio (DOR) analysis demonstrated superior performance for GeneFinder, InBios, NxTAG, Simplexa, and FDA-CDC kits. Kits targeting multiple viral genes showed higher and more stable diagnostic accuracy.

Conclusion: Commercial SARS-CoV-2 detection kits demonstrate generally high diagnostic accuracy; however, significant variability exists among manufacturers. Multi-target RT-PCR assays, particularly GeneFinder and InBios, provide superior diagnostic performance and should be prioritized in clinical laboratories.

keywords: SARS-CoV-2; Diagnostic tests; Sensitivity; Specificity; Meta-analysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-121

Clinical Utility and Cost-Effectiveness of Commercial SARS-CoV-2 Detection Kits: Implications for Large-Scale Testing Programs

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Background and aim: Background: Widespread implementation of SARS-CoV-2 molecular diagnostics during the COVID-19 pandemic has raised concerns regarding not only diagnostic accuracy but also cost-effectiveness and feasibility in large-scale testing programs. Objectives: This study aimed to systematically assess commercial SARS-CoV-2 detection kits with an emphasis on their clinical utility, economic considerations, and applicability for population-level screening.

Methods: A systematic review and meta-analysis of studies published between 2019 and October 2021 was conducted following PRISMA guidelines. Data on assay type, target genes, diagnostic indices, and reported costs per reaction were extracted. Random-effects models were used to address inter-study heterogeneity.

Results: Forty-eight studies covering kits manufactured in multiple countries were analyzed. Although overall specificity remained consistently high across assays (97%), sensitivity varied widely, particularly among single-target kits. GeneFinder, NxTAG, and FDA-CDC kits achieved a favorable balance between sensitivity, specificity, and cost per reaction. Several low-cost kits demonstrated suboptimal sensitivity, limiting their suitability for clinical diagnosis and surveillance programs.

Conclusion: While most commercial SARS-CoV-2 diagnostic kits offer acceptable specificity, only a subset achieves an optimal balance between accuracy and cost-effectiveness. GeneFinder emerged as a practical option for large-scale testing strategies, especially in resource-limited settings, highlighting the importance of economic evaluation alongside diagnostic performance.

keywords: SARS-CoV-2, Detection Kit, commercial kit, cost-effectiveness, molecular diagnostic

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-122

Determining the frequency of positive culture samples and antibiotic resistance patterns of bacteria isolated from patients suspected of infectious diseases hospitalized in Yazd Afshar Hospital

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Background and aim: The invasion and spread of microorganisms into the different parts of body can cause disruption the functions of vital organs and even death. In this study our aim was to determine the frequency of positive culture samples and antibiotic resistance patterns of bacteria isolated from patients suspected of infectious diseases hospitalized in a teaching hospital affiliated with Yazd University of Medical Sciences during two years.

Methods: In this descriptive cross sectional study, various samples of hospitalized patients referred to the Yazd Afshar Hospital laboratory for microbial culture were examined from 21 march 2023 until 20 march 2025. There were 1365 urine, 834 blood, 212 tracheal and 64 wounds samples. Sample collection, processing, identification of microorganisms were performed according to the Clinical and Laboratory Standards Institute guidelines. Antibiotic susceptibility testing was performed by the disk diffusion technique on Mueller Hinton Agar plates following the Clinical Laboratory Standards Institute (CLSI) guidelines.

Results: The most positive sample was E.Coli (104 samples) and Klebsiella pneumonia (44 samples) and the least was Enterobacter aurogenese (4 samples). 78 cases with E.Coli and 28 cases with Klebsiella pneumonia positive were female. 90 urine (6.6%), 8 blood (0.96%), 4 wound (6.25%), 2 trachea (0.95%) samples were positive for E.Coli. 30 urine, 8 wound, 5 trachea and one blood samples were positive for Klebsiella pneumonia. E. coli isolates exhibited the highest resistance rates to ampicillin and cefazolin with 88.8% and 82.1% resistance respectively. The resistance rates of E. coli bacteria were lowest for meropenem (9.3%) and amikacin (14%). Klebsiella pneumonia showed the highest anti-bacterial resistance to ampicillin (100%) and the lowest to amikacin (17.8%). The prevalence of ESBL producing E. Coli and Klebsiella pneumonia were 27.9% and 18.2% respectively.

Conclusion: In our study, the highest contamination was observed with E.Coli and Klebsiella pneumonia respectively. It is recommended to analysis and evaluate the results of positive culture and their drug resistance in all country hospitals at certain intervals.

keywords: E.Coli , Klebsiella pneumonia , Antibiotic resistance, Yazd

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-123

Demographic and Clinical Characteristics in Hospitalized Patients with Brucellosis in Zanjan, Iran

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Background and aim: Brucellosis remains a significant public health challenge in Zanjan Province, Iran, due to its high prevalence and diverse clinical manifestations. Understanding demographic and clinical factors associated with serological responses may improve interpretation of diagnostic tests and patient management. This study aimed to evaluate demographic characteristics, underlying comorbidities, and their association with anti-Brucella antibody titers among hospitalized patients in Zanjan.

Methods: In this cross-sectional study, patients with positive serological tests for brucellosis who were hospitalized at Vali-Asr Hospital between March 20, 2024, and March 20, 2025. Demographic data (age, gender, residency), history of underlying diseases, and habits (opium addiction, immunosuppressive drug use) were extracted from medical records. The association between demographic factors and antibody titers was evaluated using SPSS version 26 and appropriate statistical tests.

Results: A total of 68 patients with brucellosis were evaluated. The mean age of the patients was 47.94 ± 18.77 years. Among the patients, 63.2% were male, and 88.2% were from rural areas. Underlying diseases were present in 41.2% of cases, with hypertension (29.4%), diabetes (23.5%), and previous brucellosis (20.6%) being the most common. Opium addiction and immunosuppressive drug use were each reported in 2.9% of patients. Analytical results showed that antibody titers in all three tests were significantly higher in patients with a history of previous brucellosis (P0.05). However, no significant statistical associations were found between antibody titers and age, gender, place of residence, or other clinical variables (P0.05).

Conclusion: Demographic factors and general comorbidities do not appear to be predictors of anti-Brucella antibody levels. The significant correlation found only with a history of previous infection suggests that high serological titers in this region are primarily influenced by prior exposure rather than current demographic or clinical variables.

keywords: Coombs Wright - 2ME - Anti-Brucella antibody - Outcome

PBa-124

Some virulence genes are associated with antibiotic susceptibility in Enterobacter cloacae complex

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Background and aim: Enterobacter cloacae complex (ECC) including different species are isolated from different human clinical samples. ECC is armed by many different virulence genes (VGs) and they were also classified among ESKAPE group by WHO recently. The present study was designed to find probable association between VGs and antibiotic susceptibility in different ECC species.

Methods: Forty-five Enterobacter isolates that were harvested from different clinical samples were classified in four different species. Seven VGs were screened by PCR technique and antibiotic susceptibility assessment was performed by disk-diffusion assay.

Results: Four Enterobacter species; Enterobacter cloacae (33.3%), Enterobacter hormaechei (55.6%), Enterobacter kobei (6.7%) and Enterobacter roggenkampii (4.4%) were detected. Minimum antibiotic resistance was against carbapenem agents and amikacin even in MDR isolates. 33.3% and 13.3% of isolates were MDR and XDR respectively. The rpoS (97.8%) and csgD (11.1%) showed maximum and minimum frequency respectively. Blood sample isolated were highly virulent but less resistant in comparison to the other sample isolates. The csgA, csgD and iutA genes were associated with cefepime sensitivity.

Conclusion: The fepA showed a predictory role for differentiating of E. hormaechei from other species. More evolved iron acquisition system in E. hormaechei was hypothesized. The fepA gene introduced as a suitable target for designing novel anti-virulence/antibiotic agents against E. hormaechei. Complementary studies on other VGs and ARGs and with bigger study population is recommended.

keywords: Enterobacter cloacae complex, Virulence gene, Antibiotic resistance, MDR, Antivirulence

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-125

Sydenham's Chorea as the First Manifestation of Rheumatic Fever: A Case Series

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Background and aim: Acute Rheumatic Fever (ARF) is an autoimmune inflammatory response to Streptococcal pharyngitis that remains a major public health challenge. Sydenham's Chorea (SC), a major diagnostic criterion, presents as late neurological sequelae. SC can manifest without classic cardiac symptoms, leading to diagnostic delays. Following decades of decline, recent global reports indicate a concerning rise in Group A Streptococcus (GAS) infections. We present four children diagnosed with ARF presenting initially with SC in Qom, Iran, a region previously considered non-endemic, highlighting the urgent need for heightened clinical and epidemiological surveillance.

Methods: Case Presentation We report four cases (three girls, one boy, aged 9 to 12 years) identified over a short two-month period. All patients presented with involuntary movements characteristic of chorea. Three patients (Cases 1, 2, and 4) fulfilled two major Jones Criteria (SC and Carditis), with echocardiography revealing subclinical cardiac involvement (mild-to-moderate mitral regurgitation). Case 3 was diagnosed with ARF based on SC as the sole major criterion. All cases demonstrated preceding streptococcal infection via significantly elevated Anti-Streptolysin O (ASO) titers. Notably, Case 4 had an atypical onset of unilateral weakness (stroke mimic), and acute inflammatory markers were normal in three cases, consistent with delayed presentation.

Results: Management and Outcome All patients received Penicillin G (1.2 million units IM every 4 weeks) and Pimozide (0.05 mg/kg/day). Patients with carditis (Cases 1, 2, and 4) were additionally treated with a tapering course of Prednisolone (1 mg/kg/day). The manifestations of SC showed complete improvement within one month following the initiation of prednisolone.

Conclusion: Conclusion This cluster of four SC cases (6–8 times higher than the expected monthly average) underscores a critical epidemiological shift in the region, potentially linked to the global resurgence of GAS infections. SC often presents with delayed onset, subclinical carditis, and atypical features, creating a diagnostic challenge. Given the risk of irreversible cardiac damage, SC must be promptly considered in the differential diagnosis of pediatric movement disorders, and regional surveillance programs must be reinforced to achieve better clinical outcomes.

keywords: Sydenham Chorea, Rheumatic Fever, Acute Streptococcal Infections, Carditis

PBa-126

Klebsiella-Induced Neonatal Brain Abscess Title: Klebsiella-Induced Neonatal Brain Abscess: A Case Report of a Rare Pathogen and Potential Community-Acquired Origin

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Background and aim: Brain abscesses are a rare but life-threatening complication of central nervous system (CNS) infections in neonates. While Streptococcus species are the most common pathogens, Klebsiella pneumoniae is rarely implicated as an etiological agent. To date, all previously reported cases of K. pneumoniae neonatal brain abscesses have originated from India. We report a neonate with a K. pneumoniae brain abscess identified in Iran, suggesting a potential shift in the epidemiological profile and highlighting the need for vigilance in non-endemic settings.

Methods: Case Report A 14-day-old male neonate presented to the emergency department with fever, poor feeding, and lethargy, and later developed clonic seizures. A significant history included the application of a traditional remedy, specifically a mixture of bread dough and spices, to the umbilical cord site. Sepsis was confirmed, and both blood and cerebrospinal fluid (CSF) cultures grew K. pneumoniae. Magnetic resonance imaging (MRI) revealed multiple ring-enhancing lesions in the bilateral frontal and left parietal regions, suggestive of brain abscesses. The pathogen was notably resistant to amikacin and piperacillin. The patient's seizures were controlled with antiepileptic drugs, and the infection was managed with appropriate antibiotics based on the antibiogram.

Results: Neonatal brain abscesses due to K. pneumoniae are exceptionally rare. The detailed patient history, particularly the application of a traditional dressing to the umbilical cord, strongly suggests a community-acquired source of infection, likely serving as the portal of entry for the bacteria. The presentation with seizures and positive CSF culture further emphasizes the severity and variability of the clinical course. The case is particularly significant as it represents the first reported instance of neonatal K. pneumoniae brain abscess outside of India, highlighting its emerging global relevance and the need for updated epidemiological data.

Conclusion: This rare case emphasizes that K. pneumoniae must be considered in the differential diagnosis of neonatal CNS infections, even in non-endemic regions. Clinicians should be aware of atypical presentations and potential community-acquired sources, such as traditional remedies. Prompt pathogen identification and antibiogram-guided management are critical for ensuring the best possible outcome for this severe condition

keywords: Neonatal Abscess, Klebsiella pneumoniae, Neonatal Sepsis, Community-Acquired Infections

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July 20-23, 2026

PBa-127

The Microbiome in Breast Cancer: Exploring the Gut-Breast Axis and Its Impact on Tumor Development and Therapy Response

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Background and aim: The human microbiome has emerged as a critical factor in various health conditions, including cancer. Recent research suggests a significant connection between the gut microbiome and breast cancer, often referred to as the "gut-breast axis." This interaction implies that the microbial populations within the gut may influence the onset, progression, and therapeutic response of breast cancer. Investigating the gut-breast axis could offer new perspectives on cancer mechanisms and pave the way for innovative treatment strategies. This review examines the role of the microbiome in breast cancer, focusing on the gut-breast axis and its effect on tumor development and therapy outcomes.

Methods: A comprehensive review of the literature was conducted using PubMed, Scopus, and Web of Science for studies published until March 2025 that explored the relationship between the microbiome and breast cancer. Inclusion criteria were studies that evaluated the gut microbiome's impact on breast cancer pathogenesis, progression, immune response, and the efficacy of treatments such as chemotherapy, immunotherapy, and hormone therapy. Relevant data were extracted to elucidate the mechanisms connecting the microbiome to breast cancer biology and its potential as a therapeutic target.

Results: A total of 24 studies met the inclusion criteria, highlighting the influence of the gut microbiome on breast cancer. The findings consistently indicate that microbiota composition affects tumor growth, immune modulation, and the effectiveness of cancer treatments. Specific bacterial groups, such as Firmicutes and Bacteroidetes, have been associated with both promoting and inhibiting breast cancer. Additionally, the microbiome influences drug metabolism and the immune system's capacity to recognize and attack cancer cells. Alterations in gut microbiota contribute to changes in inflammatory pathways, which can impact tumor progression and treatment response.

Conclusion: The gut-breast axis is an emerging field in breast cancer research. Modulating the microbiome holds promise for altering tumor behavior and enhancing treatment efficacy. However, further research is required to fully understand the intricate interactions between gut microbiota, immune function, and breast cancer. Restoring a healthy microbiome may represent a valuable therapeutic approach to improving cancer treatment outcomes and reducing therapy-related side effects.

keywords: Microbiome, Gut-Breast Axis, Cancer Therapy, Breast Cancer.

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PBa-128

Genetic Diversity and Mechanisms of Fosfomycin and Nitrofurantoin Resistance in Uropathogenic Escherichia coli Isolates

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Background and aim: Urinary tract infections (UTIs), caused primarily by uropathogenic Escherichia coli (UPEC), are a major global health issue, with rising antibiotic resistance, especially in multidrug-resistant (MDR) strains, complicating treatment. Fosfomycin and nitrofurantoin are commonly used against these resistant strains, but emerging resistance mechanisms are concerning. This study aimed to assess the genetic diversity and resistance mechanisms of fosfomycin and nitrofurantoin in UPEC isolates using ERIC-PCR.

Methods: A cross-sectional study was conducted with isolates from Babol University of Medical Sciences (2021-2024). Antibiotic resistance was tested using the Kirby-Bauer disk diffusion method and confirmed by the agar dilution method for fosfomycin. PCR was used to detect resistance genes (fosA, fosA3, fosC2, oqxA, and oqxB). Genetic diversity was evaluated using ERIC-PCR.

Results: Disk diffusion revealed 11.5% resistance to nitrofurantoin, with PCR identifying the presence of oqxA (4.5%) and oqxB (3.2%). Fosfomycin resistance was found in 14.7% by disk diffusion, with agar dilution confirming resistance in 6.4%. PCR detected fosA3 in 26.3% of isolates, and fosA in 1.3%, while no isolates had fosC2. ERIC-PCR typing of fosfomycin-resistant isolates grouped them into four types (A–D), with clusters A and B being most prevalent. Similarly, nitrofurantoin-resistant isolates formed four clusters, with five isolates classified as singletons.

Conclusion: Fosfomycin and nitrofurantoin are effective against UPEC, with fosA3 being a key resistance gene. The findings highlight the importance of monitoring antibiotic resistance to prevent further spread and ensure effective treatment options for UTIs caused by E. coli.

keywords: Fosfomycin, Nitrofurantoin, Uropathogenic Escherichia coli, ERIC-PCR, Genetic diversity

17th International Congress of Lab. and Clinic
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PBa-129

Evaluation of the antimicrobial activity of herbal oral gel containing Cassia fistula and Rosa × damascene against recurrent aphthous stomatitis

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Background and aim: Microbial agents, including Candida albicans (C. albicans), streptococcus mutans (S. mutans), Actinomyces viscous (A. viscosus), have been suggested as predisposing factors for recurrent aphthous stomatitis (RAS). Alterations in susceptible host homeostasis and pathological conditions increase the ability of these commensal microbes to stimulate RAS (as a pathogen or antigen source). two plant species, Cassia fistula (C. fistula) and Rosa × damascenais (R. × damascenais), have antimicrobial properties that are widely used for medicinal purposes. We conducted this study to evaluate the response of microbial agents involved in RAS to oral gel containing C. fistula extract and R. × damascene essential

Methods: C. fistula extract was prepared by maceration method. Hydrodistillation method was used to prepare R. × damascene essential oil. Anti-microbial activity of extract, essential oil, extract / essential oil and gel formulation was evaluated using disk diffusion and microbroth dilution methods against three strains of C.albicans (PTCC 5027), S. mutans (PTCC 1683) and A. viscosus (PTCC1202).

Results: extract, essential oil, extract / essential oil and gel formulations each showed the highest and lowest inhibitory effect against C. albicans (inhibition zone diameter about 18-20 for extract / 15.3-20 µm for essential oil) and A. viscosus (inhibitory zone diameter of about 9-12.66 mm for extract and 7-9.66 mm for essential oil), respectively. The anti-microbial potential of extract and essential oil was dose-dependent, but no statistically significant difference was observed between two concentrations of 1.9-1.7% in extract and 0.7-0.9% in essential oil ($p<0.05$). The highest anti-microbial capacity belonged to the combination of 1.7 and 0.7 % concentrations of extract and essential oil.

Conclusion: In general, a relatively higher antifungal activity of C. fistula extract and R. × damascene essential oil was observed compared to antibacterial activity. Also, the extract / essential oil combination showed relatively good antibacterial and antifungal activity against the tested bacterial and fungal strains. There was a reasonable similarity between the results of the MIC and DDT methods. In this regard, some studies have pointed out the structural difference in the outer membrane of bacteria, which can be generalized to the presence of ergosterol in the plasma membrane of fungi.

keywords: Cassia fistula, Rosa damascena, anti-fungal, anti-bacterialoral

PBa-130

Exosome-Mediated Intercellular Communication: A Novel Approach in Bacterial Pathogenesis

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Background and aim: Exosomes have recently emerged as crucial players in intercellular communication, particularly in the context of bacterial pathogenesis. This study explores how pathogenic bacteria utilize exosomes to modulate host immune responses and enhance their survival.

Methods: We analyzed the exosomal contents of various pathogenic bacteria and their effects on host cells.

Results: Our findings reveal that bacterial exosomes can deliver virulence factors, altering the host cell signaling pathways, ultimately leading to increased pathogenicity.

Conclusion: Understanding this mechanism offers potential therapeutic targets for combating bacterial infections.

keywords: Exosomes, intercellular communication, bacterial pathogenesis, microbiology

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-131

The Role of Efflux Pumps in Antibiotic Resistance of Pseudomonas aeruginosa: Mechanisms, Epidemiology, and Therapeutic Implications

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Background and aim: Pseudomonas aeruginosa is a major opportunistic pathogen and a leading cause of multidrug-resistant (MDR) and extensively drug-resistant (XDR) infections, particularly in immunocompromised patients and intensive care units. As a member of the ESKAPE pathogens and a WHO-critical priority organism, antibiotic-resistant P. aeruginosa poses a serious global health threat. Among multiple resistance mechanisms, efflux pump systems play a pivotal role by actively expelling antibiotics from bacterial cells, contributing to intrinsic resistance, acquired resistance, and cross-resistance across multiple antimicrobial classes.

Methods: A narrative synthesis was conducted based on data extracted from recent systematic reviews, surveillance studies, and mechanistic investigations published between 2018 and 2025. Evidence MEDLINE (via PubMed), Scopus, and Web of Science was integrated to evaluate the epidemiology of MDR/XDR P. aeruginosa, resistance mechanisms—with emphasis on efflux pump overexpression—and the clinical performance of novel antimicrobial agents targeting resistant strains.

Results: Efflux pump systems, particularly MexAB-OprM, MexXY-OprM, and MexCD-OprJ, play a central role in mediating resistance to multiple antibiotic classes, including β-lactams, fluoroquinolones, aminoglycosides, carbapenems, macrolides, and tetracyclines in Pseudomonas aeruginosa. Mutations in key regulatory genes such as mexR, nalC, nalD, and mexZ result in efflux pump overexpression, leading to reduced intracellular antibiotic accumulation. Efflux-mediated resistance frequently acts in concert with additional mechanisms, including AmpC β-lactamase overproduction, porin loss (particularly OprD), target site mutations, and horizontal gene transfer, thereby contributing to the emergence of multidrug-resistant (MDR), extensively drug-resistant (XDR), and difficult-to-treat resistance (DTR) phenotypes. Clinical studies indicate that up to 39% of P. aeruginosa isolates overexpress at least one of these resistance mechanisms, with AmpC overproduction being the most prevalent (24.2%), followed by mexY (13.2%) and mexB (12.6%). High regional prevalence rates, particularly in Asia and Africa, further exacerbate therapeutic challenges. Although newer antimicrobial agents such as ceftolozane–tazobactam, ceftazidime–avibactam, cefiderocol, and

Conclusion: Efflux pumps represent a cornerstone of antibiotic resistance in Pseudomonas aeruginosa, driving multidrug resistance and cross-resistance while undermining both conventional and novel therapies. Their synergistic interaction with enzymatic degradation, porin mutations, and target modifications underscores the complexity of resistance phenotypes. Addressing efflux-mediated resistance through targeted inhibitors, rational antibiotic use, and mechanism-based therapeutic strategies is essential for improving clinical outcomes and preserving the effectiveness of emerging antimicrobials

keywords: Pseudomonas aeruginosa; Efflux pumps; Antibiotic resistance; Multidrug resistance; MexAB-OprM

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-132

Harnessing CRISPR Technology for Targeted Manipulation of Microbial Genomes

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Background and aim: The CRISPR/Cas9 system has revolutionized genetic engineering, allowing for precise manipulation of microbial genomes. This research investigates the application of CRISPR technology in targeting specific genes within pathogenic microbes to understand their role in virulence and resistance.

Methods: We employed CRISPR-mediated gene knockout and knock-in strategies to assess the function of selected genes in various bacterial strains.

Results: .Our results indicate that targeted manipulation can significantly reduce virulence factors and antibiotic resistance

Conclusion: And they provide a powerful tool for the development of novel antimicrobial therapies.

keywords: CRISPR, genome editing, microbial genetics, microbiology

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July 20-23, 2026

PBa-133

Peritoneal Tuberculosis Mimicking Peritoneal Carcinomatosis: A Diagnostic Challenge

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Background and aim: Peritoneal tuberculosis (PTB) is an uncommon form of extrapulmonary tuberculosis that poses significant diagnostic challenges due to its nonspecific clinical presentation and radiological similarities to malignancies such as peritoneal carcinomatosis. Early and accurate diagnosis is essential to prevent morbidity and mortality, yet PTB is often misdiagnosed or diagnosed late, particularly in TB-endemic regions. The aim of this case report is to highlight the diagnostic difficulties associated with PTB, underscore the role of laparoscopy and histopathology in confirming the diagnosis, and review the relevant literature to enhance clinical awareness and diagnostic accuracy.

Methods: We present a case of a 44-year-old woman with chronic abdominal pain, fever, night sweats, and weight loss. Initial evaluations included laboratory tests, chest CT, and colonoscopy, which were inconclusive. Abdominopelvic CT revealed multiple peritoneal masses suggestive of metastatic malignancy. Diagnostic laparoscopy with peritoneal biopsy was performed. Histopathological examination of omental tissue was conducted, including staining for acid-fast bacilli, mycobacterial culture, and PCR analysis. A literature review was performed using databases such as PubMed and Google Scholar, focusing on diagnostic approaches, imaging findings, and histopathological features of PTB.

Results: The patient presented with a 4-month history of progressive abdominal pain, constitutional symptoms, and anemia. CT imaging showed widespread peritoneal involvement, raising suspicion for metastatic cancer. Colonoscopy was nonspecific. Laparoscopy revealed chronic inflammatory changes and multiple adhesions. Histopathology demonstrated caseating granulomas with mixed inflammatory infiltrates, consistent with tuberculosis. Acid-fast staining and culture were negative. The patient was started on standard anti-tuberculosis therapy, with significant symptomatic improvement on follow-up.

Conclusion: This case illustrates the diagnostic complexity of peritoneal tuberculosis, which can closely mimic peritoneal carcinomatosis and other abdominal pathologies. Negative microbiological tests do not rule out PTB, and histopathological evidence of caseating granulomas remains a cornerstone of diagnosis. Laparoscopic biopsy is a safe and effective method for obtaining diagnostic tissue. Increased clinical suspicion and systematic use of imaging, laparoscopy, and histopathology are essential for timely diagnosis and treatment, particularly in TB-endemic areas.

keywords: Peritoneal tuberculosis, extrapulmonary tuberculosis, caseating granuloma, diagnostic laparoscopy, peritoneal carcinomatosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-134

Lyme Borreliosis Presenting as Chronic Granulomatous Uveitis and Arthralgia: A Case Report

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Background and aim: Lyme disease, caused by Borrelia burgdorferi, is a multisystem tick-borne illness capable of diverse ocular manifestations, often complicating diagnosis. Ocular involvement typically occurs in late stages and may present without systemic signs. This report aims to describe a case of Lyme borreliosis presenting as chronic granulomatous uveitis with arthralgia, highlighting diagnostic challenges and the importance of considering infectious etiologies in uveitis.

Methods: A 39-year-old female presented with a six-month history of progressive right eye pain, blurred vision, and chronic arthralgia. Ophthalmic examination revealed granulomatous anterior uveitis with posterior synechiae and elevated intraocular pressure. Extensive serological testing was performed to exclude autoimmune, viral, and other infectious causes (including HIV, syphilis, HLA-B27-associated disorders, and tuberculosis). Lyme serology (anti-Borrelia burgdorferi IgM) was assessed due to travel history. Clinical response was monitored following a two-month course of oral doxycycline.

Results: Initial serology was negative for common autoimmune and infectious pathogens, except for a positive PPD (30 mm) and elevated HSV IgG. Anti-Borrelia burgdorferi IgM was positive. The patient recalled travel to a Lyme-endemic region in northern Iran one year prior. After initiating doxycycline, significant improvement in ocular inflammation and arthralgia was noted within three weeks. By the end of treatment, visual acuity improved from 20/80 to normal, and systemic symptoms resolved completely.

Conclusion: This case underscores Lyme borreliosis as a differential diagnosis in patients with uveitis and joint symptoms, particularly in endemic areas or with relevant travel history. Serological interpretation requires caution, but timely antibiotic therapy can lead to rapid clinical resolution. Increased clinician awareness is essential to prevent misdiagnosis and unnecessary immunosuppressive treatment.

keywords: Lyme disease, uveitis, Borrelia burgdorferi, ocular borreliosis, granulomatous anterior uveitis

PBa-135

Investigation of OMV Group B Streptococcus(GBS)effects on Pregnant Rats

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Background and aim: Group B Streptococcus (GBS) is a ß-hemolytic bacterium that is a normal inhabitant in recto-vaginal mucosae in healthy women. Ascending GBS infection during pregnancy involves bacterial trafficking from the vagina, ultimately leading to bacterial invasion of placental membrane (chorion and amnion), The amniotic cavity, and the fetus. So, GBS experimental infection of rats was done and investigated their complications.

Methods: Outer Membrane Vesicles (OMV) of GBS are produced by bacteria that are non-replicative vesicles and contains intrinsic immunostimulatory features that are based on their particulate composition and nature. GBS bacterial strain (ATCC 13813) was cultivated in the Nutrient Broth and after 18 hours it was centrifuged at 2500 rpm and in 5 minutes to separate the B Cell of the bacteria, then Centrifuged again at 15000 rpm and in 30 minutes. The rats received 4 doses of OMV and DW (distilled water) via intraperitoneal injection and next the animals were mated and after being pregnant, they were intra-vaginally inoculated with 108 CFU/ml of GBS colonies in 3rd week.

Results: The results showed that GBS is still one of the threaten agents that causes abortion by infection the amniotic sac and embryo in the form of retrograde that results to fetus death. Also in the infected group as control, it was observed that GBS causes to both preterm delivery and fetus death.

Conclusion: There were obvious effects for CRL and weight in OMV group rather than the DW groups. observed that GBS causes to both preterm delivery and fetus death.

keywords: Keywords: GBS bacteria"," Experimental Infection"," Stillbirth"," Weight"," CRL .

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PBa-136

Study of the frequency of clbA, clbB, clbS and clbQ genes in E. coli isolates isolated from urine and stool samples.

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Background and aim: E. coli is a gram-negative, non-spore-forming, rod-shaped, and facultative anaerobic bacterium that forms part of the human intestinal microbiota and can become pathogenic under certain conditions. Uropathogenic strains (UPEC) are the main cause of urinary tract infections, and some strains, by having a pks gene island and producing the genotoxin colibactin, cause DNA damage and participate in tumorigenesis. The aim of this study was to investigate the frequency of clbA, clbB, clbS, and clbQ genes in E. coli isolated from urine and stool samples.

Methods: In this case-control study, E. coli bacteria isolated from 57 urine samples and 57 stool samples were collected. DNA extraction from the samples was performed using a kit method. The presence of target genes was examined using PCR.

Results: In this study, the mean age of stool and urine samples in the studied individuals was 38.30 ± 19.78 and 37.02 ± 16.21 years, respectively (p = 0.977). The frequencies of clbA, clbB, clbQ, and clbS genes in stool samples were (21%), (8%), (15%), and (31 %), respectively, and in urine samples were (47%), (35%), (43%), and (49%).The results also showed that there is a significant relationship between clbA, clbB, and clbQ genes in urine and stool samples.(p0.05)

Conclusion: The findings of this study indicate the importance of investigating pks island genes in urinary strains of Escherichia coli and the possible role of the transfer of these genes from fecal samples to the urinary system, therefore, it is necessary to observe hygiene issues to prevent the transfer of these genes from the digestive system to the urinary system.

keywords: clbA, clbB, clbQ, clbS, Escherichia coli, urine, stool

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-137

Study of antibiotic resistance patterns in E. coli isolates isolated from urine and stool samples.

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Background and aim: Urinary tract infections (UTIs) are among the most common bacterial infections, affecting 150 million people worldwide annually. Among hospital-acquired infections, UTIs rank second after lower respiratory tract infections. The aim of this study was to investigate the frequency of antibiotic resistance patterns in E. coli isolated from urine and stool samples.

Methods: In this case-control study, E. coli bacteria isolated from 57 urine and 57 stool samples were collected. Antibiotic resistance patterns were performed using the disk diffusion method and according to CLSI guidelines in urine and stool samples.

Results: In this study, stool samples included 20 men and 37 women and urine samples included 12 men and 45 women, and there was no significant difference between the two groups in terms of gender. ($p = 0.095$) The results showed that the highest resistance in urine samples was to ampicillin and in stool samples was to cefazolin. The results also showed that there was no statistically significant difference between urine and stool isolates in terms of resistance to ceftriaxone ($p = 0.069$), ampicillin ($p = 1.000$), meropenem ($p = 0.074$), nitrofurantoin ($p = 0.464$) and cefazolin ($p = 0.139$) antibiotics.

Conclusion: The antibiotic resistance pattern of E. coli in this study indicates its high resistance to common β-lactam antibiotics and higher sensitivity to aminoglycosides and carbapenems, which requires greater attention to the correct administration of antibiotics for urinary tract infections.

keywords: Escherichia coli, antibiotics, urine, stool

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBa-138

A Systematic Review of the Dynamic Interplay Between Blue Light and Probiotics: From Ocular and Gut Protection to Synergistic Antimicrobial Strategies

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Background and aim: The modern environment is characterized by pervasive exposure to blue light from digital devices and artificial lighting, which is associated with adverse effects on ocular health and systemic homeostasis, including the gut microbiota. Concurrently, probiotics have gained prominence for their beneficial roles in modulating host physiology and local microbiomes. Interestingly, blue light also serves as the basis for Antimicrobial Photodynamic Therapy (aPDT), a promising non-antibiotic treatment. This systematic review aims to synthesize and categorize the current scientific evidence exploring the multifaceted interactions between blue light and probiotics, defining whether these interactions are antagonistic, synergistic, or exploitable for

Methods: We conducted a systematic search across PubMed, Google Scholar, and Scopus for studies published until August 2024. The search strategy employed combined keywords related to "blue light," "photodynamic therapy," "phototherapy," "probiotics," specific genera (Lactobacillus, Bifidobacterium), and "postbiotics." Inclusion criteria encompassed original in vitro, in vivo, and clinical studies, as well as relevant reviews, that explicitly investigated the effect of blue light on probiotics or their combined application for a therapeutic or protective outcome. Thirty studies met the eligibility criteria and were included. Data on study design, probiotic strains, blue light parameters (wavelength, dose, duration), experimental models, and key findings were extracted. A qualitative narrative synthesis was performed, with studies categorized into emergent thematic groups due to methodological heterogeneity

Results: Analysis of the 30 studies revealed three distinct paradigms of interaction: 1) Protection: Specific probiotic strains, including Limosilactobacillus fermentum IOB802, Lactobacillus reuteri Y7, and Lactobacillus paracasei KW3110, demonstrated significant efficacy in mitigating blue light-induced retinal damage in animal models. Mechanisms involved the reduction of oxidative stress, attenuation of inflammatory pathways (e.g., NF-κB), and modulation of the gut microbiota, highlighting the role of the gut-retina axis. Probiotics also counteracted blue light-induced gut dysbiosis and metabolic dysregulation in rodent models. 2) Combination Therapy: Probiotics acted as effective adjuvants to blue light-based therapies. They enhanced the outcomes of aPDT against infections such as vulvovaginal candidiasis and dental caries by increasing pathogen eradication and reducing biofilm resistance. In neonatal jaundice, probiotic co-administration with blue-light phototherapy did not directly lower bilirubin more effectively but significantly alleviated the phototherapy-induced disruption of the infant gut microbiome, promoting faster recovery. 3) Production & Control: Blue light was utilized

Conclusion: The relationship between blue light and probiotics is complex and context-dependent. Probiotics can function as protective agents against the deleterious effects of environmental blue light, particularly on the eye and gut, and as synergistic partners that enhance the efficacy and tolerability of therapeutic blue light applications like aPDT and phototherapy. This dual role, combined with emerging optogenetic control strategies, establishes a promising interdisciplinary frontier for developing novel preventive measures, antimicrobial therapies, and precision medicine interventions. Further standardized clinical research is warranted to translate these preclinical and early clinical findings into

keywords: Blue Light, Probiotics, Antimicrobial Photodynamic Therapy, Gut-Retina Axis, Gut Microbiota

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-139

Evaluation of toxin and antitoxin genes in Third-Generation Cephalosporin-Resistant Escherichia coli Isolates from bloodstream infections of leukemia patients

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Background and aim: Background Immunosuppression from hematologic malignancies, chemotherapy, and invasive procedures renders patients highly susceptible to Gram-negative bacterial bloodstream infections (GNB-BSI), a leading cause of death and illness in this group. E. coli is a prominent pathogen in neutropenic hematologic malignancies, often requiring extended hospital stays and specialized treatment due to the severity of infection. Cephalosporins are commonly employed in hospitals because of their wide-ranging antimicrobial effects.

Methods: The study conducted in Iran from June 2021 to December 2022, isolated 67 E. coli strains from leukemia patients' bloodstream infections in hospitals in two different areas. The presence of toxin-antitoxin system genes(mazE, ccdAB, relB, mqsR and hipA genes), E. coli resistant to third-generation cephalosporins (TGCs) isolates was investigated by PCR-sequencing methods.

Results: PCR results of toxin-antitoxin system genes of 33 strains of E. coli resistant to third-generation cephalosporins (TGCs) showed a higher rate of relB (75%) than other toxin-antitoxin system genes, followed bymazF (69%),ccdAB (66%) and mqsR (42%), hipA(10%).

Conclusion: Conclusion: The results of our study showed the frequency of toxin and antitoxin genes in Escherichia coli strains resistant to third-generation cephalosporins isolated from blood cultures of leukemia patients, which requires further investigation.

keywords: Keywords: Third-Generation Cephalosporin-Resistant Escherichia coli, bloodstream infections, leukemia

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PBa-140

The Importance of Mycobacterium tuberculosis Diagnosis Compared With Smear, Culture, and qPCR

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Background and aim: Tuberculosis (TB) remains a leading cause of morbidity and mortality worldwide. Conventional diagnostic methods, including Ziehl–Neelsen (ZN) smear microscopy and Mycobacterium tuberculosis (M.tb) culture, have limitations in sensitivity and turnaround time, particularly in patients who are smear- and culture-negative. This study evaluates the utility of a TaqMan quantitative PCR (qPCR) assay for detecting M.tb in patients suspected of TB but testing negative by traditional methods.

Methods: A cross-sectional study was conducted from April 2020 to September 2021 and included 389 patients presenting with TB-like symptoms in northeastern Iran. Pulmonary samples, including sputum and bronchoalveolar lavage, were collected and processed using the Petroff decontamination method. Samples were examined by ZN smear microscopy, Löwenstein–Jensen culture, and qPCR targeting the IS6110 sequence. Among these, 21 patients had positive smear and culture results (positive controls), while 307 were negative by conventional methods but clinically suspected of TB. Sensitivity, specificity, and positive predictive values (positivity rates) of qPCR were calculated using culture as the reference standard.

Results: qPCR detected M.tb in all 21 positive control samples and additionally identified 50 of 307 smear- and culture-negative cases, representing a 12.85% increase in diagnostic yield. The overall qPCR positivity rate was 18.5% (72/389). In pulmonary TB cases, qPCR showed a sensitivity of 100% (95% CI: 83.2–100%) and a specificity of 82.3% (95% CI: 74.0–88.8%). These findings demonstrate that qPCR substantially improves detection in patients with negative conventional tests.

Conclusion: Traditional smear and culture methods are insufficient for the timely detection of TB in patients with low bacterial load. qPCR offers a rapid, sensitive, and specific diagnostic approach, particularly for smear- and culture-negative cases. Incorporation of molecular assays into TB diagnostic workflows could reduce missed cases, facilitate earlier treatment, and limit disease transmission.

keywords: Mycobacterium tuberculosis qPCR smear culture Ziehl-Neelsen TaqMAn

PBa-141

Recent Advances in Laboratory Diagnosis of Bacterial Infections

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Background and aim: Bacterial infections continue to pose a significant challenge to healthcare systems worldwide, emphasizing the importance of accurate, rapid, and reliable laboratory diagnostic methods. Traditional diagnostic approaches such as microscopy and culture remain fundamental in clinical microbiology; however, their limitations include prolonged turnaround time and reduced sensitivity in certain clinical conditions. Advances in laboratory technologies, particularly automated systems and molecular-based assays, have substantially improved pathogen detection and identification. The aim of this narrative review is to provide an overview of recent advances in laboratory diagnostic methods for bacterial infections and to evaluate their role in enhancing diagnostic accuracy and clinical decision-making.

Methods: This narrative review was conducted through a comprehensive but non-systematic review of English-language literature retrieved from scientific databases including PubMed and Google Scholar. Relevant studies focusing on conventional, automated, and molecular diagnostic techniques for bacterial infections were included. The selected literature was critically reviewed, and key diagnostic approaches and their clinical implications were qualitatively summarized.

Results: Recent advances in laboratory diagnostic technologies have significantly improved the detection, identification, and characterization of bacterial pathogens. Conventional methods such as culture and biochemical testing remain essential as reference standards; however, their limitations include longer turnaround times and reduced sensitivity in some clinical conditions. In contrast, automated identification systems and molecular diagnostic techniques have enhanced diagnostic speed, sensitivity, and accuracy, particularly in the detection of fastidious organisms and antimicrobial resistance markers.

Conclusion: The integration of advanced diagnostic methods with conventional laboratory techniques provides a more reliable and efficient approach to the diagnosis of bacterial infections. The appropriate application of automated and molecular assays alongside traditional methods supports timely clinical decision-making and improves patient management. Continued development and implementation of advanced laboratory diagnostics are essential to address the evolving challenges of bacterial infections.

keywords: Bacterial infections; Laboratory diagnosis; Clinical microbiology; Molecular diagnostics; Automated

PBa-142

multi-Threat Bacteroides fragilis in Colorectal Cancer: Co-enrichment of Carbapenem Resistance, Metronidazole Resistance, and Toxin Determinants

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Background and aim: The colorectal cancer (CRC) microenvironment can selectively enrich commensal bacteria such as Bacteroides fragilis that harbor co-occurring antimicrobial resistance (AMR) and virulence determinants, potentially promoting carcinogenesis and compromising therapy. We investigated whether CRC is associated with an increased intestinal carriage of B. fragilis strains simultaneously carrying carbapenem resistance, metronidazole resistance, and enterotoxin genes.

Methods: In a matched case–control study, 60 B. fragilis isolates from treatment-naïve CRC patients were compared with 60 isolates from healthy controls. Antimicrobial susceptibility testing was performed according to EUCAST guidelines. Conventional PCR was used to detect nim genes (metronidazole resistance), insertion sequence (IS)-activated cfiA (carbapenemase), and bft (B. fragilis toxin). Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess enrichment in the CRC group; a p-value 0.05 was considered statistically significant. Multi-threat strains were defined as isolates carrying at least two of the above determinants.

Results: Compared with controls, CRC-derived isolates showed significantly higher prevalences of nim (20.0% vs. 6.7%; OR 3.43, 95% CI 1.01–11.70, p=0.035), IS-activated cfiA (23.3% vs. 5.0%; OR 5.67, 95% CI 1.26–27.0, p=0.015), and bft (93.3% vs. 78.3%; OR 3.73, 95% CI 1.28–10.85, p=0.016). Multi-threat B. fragilis strains (≥2 markers) were markedly enriched in CRC patients compared with healthy controls (20.0% vs. 3.3%, p=0.001).

Conclusion: CRC is associated with a significant enrichment of “multi-threat” B. fragilis strains carrying expressible IS-activated cfiA, nim, and bft determinants. These strains may simultaneously enhance pro-carcinogenic potential and limit the effectiveness of frontline anaerobic therapy through AMR. The findings underscore the need for targeted anaerobic surveillance, resistance-informed antimicrobial strategies, and further mechanistic studies on the contribution of multi-threat B. fragilis to CRC pathogenesis and treatment failure.

keywords: Colorectal cancer, Bacteroides fragilis, antimicrobial resistance, Carbapenem resistance, bft toxin

PBa-143

Quorum Sensing Inhibition as an Anti-bacterial Strategy Against Pseudomonas aeruginosa

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Background and aim: Pseudomonas aeruginosa is a multidrug-resistant opportunistic pathogen responsible for severe infections, particularly in immunocompromised individuals. Its pathogenicity is largely regulated by quorum sensing (QS), a cell-density-dependent communication system that controls virulence factors and biofilm formation. Given the rising antibiotic resistance, targeting QS has emerged as a promising anti-virulence approach to combat infections without exerting selective pressure for resistance.

Methods: Data on QS inhibitors (QSIs) against P. aeruginosa from recent studies were collected and analyzed from databases such as PubMed, Scopus, Nature, and Google Scholar. The review included contemporary in vitro and in vivo evaluations of natural and synthetic QSIs, their mechanisms of action, and synergistic effects with conventional antibiotics.

Results: Recent in vitro studies demonstrated that QSIs including methyl gallate, eugenol-gold nanoparticles, quercetin, and daidzein dimethyl ether effectively inhibited QS-regulated virulence factors such as pyocyanin production, elastase activity, rhamnolipid synthesis, and biofilm formation in strains like PAO1, PA14, and clinical isolates. Molecular docking and gene expression analyses confirmed interactions with key QS receptors (LasR, RhlR, PqsR). In vivo models (mouse pneumonia, burn wound, Galleria mellonella, zebrafish) from recent reports showed that QSIs reduced bacterial load, improved survival rates, and attenuated inflammation. Synergy with antibiotics like tobramycin, ceftazidime, and meropenem was frequently reported, enhancing efficacy against multidrug-resistant strains.

Conclusion: QS inhibition represents a viable anti-bacterial strategy against P. aeruginosa, capable of attenuating infection without promoting resistance. Both natural and synthetic QSIs show promise as adjunct therapies alongside conventional antibiotics. Further clinical studies are needed to validate their safety and efficacy in humans.

keywords: Pseudomonas aeruginosa, Quorum Sensing, Biofilm Inhibition, QS Inhibitors

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July 20-23, 2026

PBa-144

Bacteriophage Therapy as an Alternative Strategy Against Antibiotic Resistance: A Systematic Review

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Background and aim: Background The global rise of antibiotic-resistant bacteria represents a major threat to public health and healthcare systems worldwide. Multidrug-resistant (MDR) pathogens such as Pseudomonas aeruginosa, Acinetobacter baumannii, and Staphylococcus aureus have significantly limited the effectiveness of conventional antimicrobial therapies. Bacteriophage therapy has re-emerged as a promising alternative or adjunct approach due to its high specificity, ability to disrupt bacterial biofilms, and potential synergy with antibiotics. This systematic review aims to evaluate current evidence on the therapeutic potential of bacteriophages, with a particular focus on resistance mechanisms, biofilm penetration, and advanced delivery systems such as hydrogels.

Methods: Methods A systematic literature search was conducted in PubMed, Scopus, and Web of Science databases for studies published between 2000 and 2024. MeSH-based keywords including bacteriophages, phage therapy, antibiotic resistance, biofilms, and drug delivery systems were used. Original research articles, in vitro and in vivo studies, and clinical reports investigating bacteriophage therapy against antibiotic-resistant bacteria were included. Reviews lacking defined methodologies, non-English articles, and studies unrelated to therapeutic applications were excluded.

Results: Results A total of 78 relevant studies were included in the final analysis. The reviewed evidence indicates that bacteriophages effectively target MDR bacteria with minimal impact on commensal microbiota. Phage cocktails demonstrated improved antibacterial efficacy and reduced resistance development compared to single-phage treatments. Furthermore, phage therapy showed significant potential in disrupting established bacterial biofilms, particularly when combined with antibiotics. Advanced delivery platforms such as injectable and topical hydrogels enhanced phage stability, localized delivery, and therapeutic effectiveness in implant-associated and chronic infections.

Conclusion: Conclusion Bacteriophage therapy represents a viable and innovative strategy to address the growing challenge of antibiotic resistance. The integration of phage cocktails and biocompatible delivery systems, including hydrogels, may significantly improve clinical outcomes. Further standardized clinical studies and regulatory frameworks are required to facilitate the translation of phage-based therapies into routine clinical practice.

keywords: Keywords Bacteriophages; Phage Therapy; Antibiotic Resistance; Biofilms; Drug Delivery Systems

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-145

Anticancer Effect of Lactobacillus sp. isolated from propolis on the HLA-DR and Galectin-9 genes expression: in the MCF-7 cell line

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Background and aim: Lactobacillus species are part of the body's natural microbiota that can help fight cancer by boosting the immune response, inhibiting tumor growth, and improving the effectiveness of cancer treatments. Studies on breast cancer have shown that these probiotics inhibit tumor progression by affecting gene expression and immune responses. Their non-toxic nature also makes them promising candidates for adjuvant therapies in cancer treatment.

Methods: Cultivation of the MCF-7 cell line was done in RPMI culture medium. Lactobacillus cultured in MRS broth and in lipophilized form was prepared. The cells were treated with different concentrations of Lactobacillus (0.1mg/ml to 20mg/ml). After performing the MTT test, the viability of the cells was calculated. After designing specific primers for galectin 9 (GAL9) and HLA-DR genes, qRT-PCR was done, and the expression level was calculated.

Results: IC50 was 29.18 and 3.57 mg/mL for 24 and 48h, repspectivly. Lactobacillus can upregulate GAL9 and HLA-DR in MCF-7 cells significantly. HLA-DR expression increased by 11.5-fold at 24h and 5.8-fold at 48h. GAL9 expression was similarly raised by 7.5-fold at 24h and 3.09-fold at 48h, highlighting the probiotic's potential immunomodulatory and anticancer effects.

Conclusion: Studies have shown that low levels of HLA-DR are associated with immune evasion, while high levels of HLA-DR are associated with enhanced recognition of tumor antigens by the immune system, thereby enhancing immune responses against tumor cells. High levels of GAL9 are also associated with reduced metastasis and improved survival. As a result, Lactobacillus could be a breast cancer treatment by enhancing immune pathways and supporting tumor suppression. These results need to be further validated by clinical studies.

keywords: Breast cancer, Lactobacillus, HLA-DR, Galectin-9

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-146

Advances in Green Nanoparticle Synthesis for Treating Chronic Bone Infections

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Background and aim: Infections continue to pose a major threat to global health. Treating bone infections such as osteomyelitis presents significant challenges due to the emergence of drug-resistant and biofilm-forming pathogens, with Staphylococcus aureus identified as the predominant causative agent (30–60% of cases). Consequently, researchers worldwide are exploring novel therapeutic strategies. Nanotechnology has emerged as a versatile platform for drug delivery and osteomyelitis management in biomedicine. Nanoparticles are synthesized via biological, chemical, and physical routes. Among these, green synthesis garners particular attention for its non-toxicity, stability, cost-effectiveness, and eco-friendliness. This review investigates nanoparticles biosynthesized from natural sources and evaluates their potential in osteomyelitis.

Methods: This narrative review article was developed using well-regarded scientific databases, including Web of Science, PubMed, Scopus, and Google Scholar, without any limitations on publication dates

Results: Green synthesis yields stable, non-toxic nanoparticles with superior antibacterial potency against osteomyelitis pathogens compared to chemical methods. Biosynthesized silver nanoparticles excel in biofilm eradication and S. aureus inhibition; magnetite variants enable targeted magnetic delivery; hydroxyapatite nanoparticles promote osteointegration and sustained drug release. These agents demonstrate high biocompatibility, reducing inflammation in preclinical models of adult osteomyelitis subtypes.

Conclusion: Biosynthesized nanoparticles from natural sources represent a versatile, eco-friendly platform for combating osteomyelitis through direct antimicrobial action and advanced drug delivery. Clinical trials and optimization for scalability are warranted to translate these findings into practice.

keywords: biosynthesis, nanoparticles, osteomyelitis, microbial pathogen

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PBa-147

Liposomal Drug Delivery Systems as a Promising Strategy Against Antibiotic-Resistant Pseudomonas aeruginosa and MRSA

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Background and aim: Antibiotic resistance among opportunistic bacterial pathogens, particularly Pseudomonas aeruginosa and methicillin-resistant Staphylococcus aureus (MRSA), poses a major challenge in clinical microbiology. These organisms reduce antibiotic efficacy through biofilm formation, efflux pump activity, decreased membrane permeability, and modification of molecular targets. Recently, liposome-based drug delivery systems have emerged as promising approaches to overcome these resistance mechanisms by enhancing drug stability, encapsulation, and targeted delivery. This narrative review aims to evaluate the role of liposomal drug delivery systems in improving the antibacterial efficacy of antibiotics against P. aeruginosa and MRSA.

Methods: This systematic review was conducted following PRISMA guidelines. A comprehensive search of PubMed was performed using the keywords: "Liposomal Drug Delivery," "Antimicrobial Resistance," "Pseudomonas aeruginosa," "Methicillin-resistant Staphylococcus aureus (MRSA)," and "Bacterial Biofilm." Studies published in the last ten years were considered. After removing duplicates, articles were screened in two stages: title/abstract review followed by full-text assessment. Inclusion criteria included review articles, in vitro, and in vivo studies evaluating liposomal drug delivery to enhance antibiotic efficacy against P. aeruginosa and MRSA. Exclusion criteria included irrelevant studies, case reports, non-experimental articles, and those lacking analyzable data. Extracted data included liposome type, physicochemical properties, encapsulated antibiotic, target bacteria, and antibacterial and antibiofilm outcomes. Study quality was assessed using standard criteria. Data were analyzed descriptively to summarize the role of liposomal systems in improving antibiotic effectiveness against resistant bacterial pathogens.

Results: The reviewed studies showed that liposomal antibiotic formulations significantly enhance antibacterial activity against resistant strains of Pseudomonas aeruginosa and methicillin-resistant Staphylococcus aureus (MRSA). Encapsulation of antibiotics in liposomes reduced minimum inhibitory concentrations (MICs) and improved drug penetration into bacterial biofilms. Cationic and targeted liposomes demonstrated higher efficacy than neutral liposomes, likely due to stronger electrostatic interactions with bacterial cell walls. Several studies reported that liposomes containing vancomycin, imipenem, colistin, and aminoglycosides effectively inhibited bacterial growth, disrupted biofilms, and reduced cytotoxicity compared to free drug forms. Liposomal systems also enhanced drug stability and prolonged release, contributing to sustained antibacterial effects. Collectively, these findings indicate that liposomal drug delivery can overcome key resistance mechanisms, including biofilm protection and limited antibiotic penetration, and improve therapeutic outcomes. Therefore, liposomal encapsulation represents a promising approach to increase antibiotic efficacy against multidrug-resistant opportunistic pathogens in both in vitro and in vivo models.

Conclusion: This review indicates that liposome-based drug delivery systems represent an effective strategy to enhance the treatment of antibiotic-resistant bacterial infections. Liposomes improve antibiotic efficacy, particularly against Pseudomonas aeruginosa and MRSA, by increasing drug penetration, overcoming biofilm barriers, and mitigating resistance mechanisms. In addition to enhancing therapeutic outcomes, they may allow dose reduction and lower systemic toxicity. Despite promising in vitro and preclinical results, large-scale clinical trials are necessary to evaluate safety, efficacy, and clinical applicability. Liposomal systems could play a crucial role in addressing the global challenge of antibiotic resistance.

keywords: Liposomal Drug Delivery, Antimicrobial Resistance, MRSA and Pseudomonas aeruginosa

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-148

Porin-associated antibiotic resistance in carbapenem- and β-lactam-resistant Escherichia coli and Klebsiella pneumoniae isolated from urinary tract infections in Rasht hospitals: a six-month cross-sectional study

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Background and aim: Porin loss or alteration in Gram-negative bacteria reduces outer-membrane permeability to β-lactams including carbapenems and may act synergistically with β-lactamases to produce high-level clinical resistance. We assessed the frequency of porin genes (ompF in E. coli and ompK36 in K. pneumoniae), antimicrobial susceptibility patterns, and the association between porin absence and ESBL/carbapenemase phenotypes among urinary isolates obtained from hospitalized patients in Rasht.

Methods: This cross-sectional study included single-organism urine cultures with ≥10^5 CFU/mL and clinical signs of UTI collected over six months from three Rasht hospitals. A total of 151 E. coli and 151 K. pneumoniae isolates (n=302) were identified by standard biochemical tests. Antimicrobial susceptibility was determined by disk diffusion (CLSI M100-Ed33). ESBLs were detected by combination disk test and carbapenemase phenotypes by modified Hodge/CDT assays. Genomic DNA was extracted, and PCR performed for ompF (156 bp) and ompK36 (252 bp) using specific primers. Associations were evaluated by χ^2 and logistic regression; p0.05 considered significant.

Results: Among 730 submitted urine specimens, 302 isolates (41.4%) were E. coli (n=151) or K. pneumoniae (n=151). MDR phenotypes were present in 48% of E. coli and 45% of K. pneumoniae. E. coli showed highest susceptibility to Fosfomycin (92.1%), amikacin and nitrofurantoin (88.1% each); lowest to TMP-SMX (37.7%) and ciprofloxacin (47.7%). K. pneumoniae showed highest susceptibility to amikacin (82%), meropenem (78%) and imipenem (75%); highest resistance to TMP-SMX (60%), ciprofloxacin (54%) and nitrofurantoin (50%). Phenotypic ESBLs were identified in 50 E. coli and 32 K. pneumoniae isolates; carbapenemase phenotypes in 17 E. coli and 7 K. pneumoniae. PCR detected ompF in 95.4% (144/151) of E. coli and ompK36 in 94.0% (142/151) of K. pneumoniae. Absence of ompK36 was significantly associated with ESBL/carbapenemase phenotypes in K. pneumoniae (p=0.036). Absence of ompF in E. coli correlated with higher resistance but did not reach statistical significance (p=0.140).

Conclusion: Loss of porin genes, particularly ompK36 in K. pneumoniae, contributes to β-lactam and carbapenem resistance and often acts synergistically with enzymatic mechanisms.

keywords: Antimicrobial Resistance; Porins; Escherichia coli; Klebsiella pneumoniae; Urinary Tract Infections

PBa-149

Immunoglobulin Y as a promising approach for the prevention and treatment of bacterial infections: Focus on multidrug-resistant bacteria

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Background and aim: Antibiotic resistance is a major global challenge that increases mortality, length of stay, and cost of treatment of infectious diseases. Today, the emergence of MDR, XDR, and PDR isolates has led to the ineffectiveness of even last-line antibiotics and numerous challenges in diagnosing these bacteria. Therefore, researchers in various fields are looking for suitable alternatives to antibiotics to combat these challenging isolates. The aim of this study is to introduce Immunoglobulin Y as a promising approach for the diagnosis, prevention, and treatment of bacterial infections: Focus on multidrug-resistant bacteria.

Methods: sing the scientific databases PubMed, Google Scholar, Scopus, and Web of Science, studies related to the keywords "Immunoglobulin Y", "multidrug-resistant bacteria", "antibiotic resistance", "bacterial infections", and "diagnosis of infection" were collected. These studies were included without time limits and studies that were in English and relevant to our work.

Results: A review of research studies showed that Immunoglobulin Y had a significant effect on antibiotic-resistant bacteria. Immunoglobulin Y can be produced by various methods and this compound has therapeutic and prophylactic applications for a wide range of infections, even MDR isolates. Immunoglobulin Y can exert its antibacterial properties through multiple mechanisms and has a significant effect on infectious bacterial isolates, both alone and in combination with other antimicrobial agents.

Conclusion: Considering the effectiveness of Immunoglobulin Y on antibiotic-resistant bacteria, this compound can be used as a potential option for the treatment and prevention of infectious diseases. For the wider use of these compounds, further studies in clinical settings are needed.

keywords: Immunoglobulin Y, antibiotic-resistant bacteria, MDR

PBa-150

The Clinical Burden and Management Challenges of Pseudomonas aeruginosa Infections in Kidney Transplant Recipients

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Background and aim: Pseudomonas aeruginosa (PA) is a formidable pathogen in kidney transplant recipients (KTRs), known for its virulence and antibiotic resistance. However, a comprehensive synthesis focusing specifically on its clinical impact on graft outcomes and the associated management challenges is lacking. This systematic review aims to consolidate the evidence on PA infections in KTRs, detailing their clinical spectrum, outcomes, and the critical issue of antimicrobial resistance.

Methods: A search of PubMed and Web of Science databases from 2016 to 2026 yielded 11 and 55 articles, respectively. After screening for relevance and removing duplicates, 20 articles were selected for final inclusion. These comprised case reports, cohort studies, case-control studies, and surveys focusing exclusively on PA infections in KTRs.

Results: The reviewed literature reveals a severe spectrum of PA infections in KTRs, extending beyond common urinary tract infections to include life-threatening conditions such as prostatic abscesses, mycotic pseudoaneurysms at the graft vascular anastomosis, skull base osteomyelitis, and severe diabetic foot infections. These infections are frequently driven by multidrug-resistant (MDR), extensively drug-resistant (XDR), or carbapenem-resistant (CRPA) strains, including IMP-1-producing clones. A direct association was found between CRPA infections and adverse graft outcomes, including graft dysfunction and loss. Mortality is a significant concern, with PA bloodstream infections and prolonged patient colonization acting as key predictors. Initial contamination can occur through infected organ preservation solutions. Management is highly challenging, necessitating specialized antibiotic regimens such as ceftolozane-tazobactam or fosfomycin, often guided by global surveys on empirical therapy for pyelonephritis. The approach to patients colonized with these "difficult-to-treat" bacteria, including antibiotic prophylaxis strategies, remains inconsistent and debated.

Conclusion: PA infections pose a persistent and grave threat to KTRs, directly contributing to graft injury and patient mortality, particularly in the era of rising resistance. Current evidence is primarily descriptive, detailing clinical presentations and outcomes. A critical knowledge gap exists regarding the specific pathogenetic mechanisms, particularly the role of biofilm formation and chronic infection, in driving allograft dysfunction and rejection. Future research must shift from phenomenological description to mechanistic inquiry to develop targeted strategies that protect both the patient and the allograft from this resilient pathogen.

keywords: Pseudomonas aeruginosa‹Kidney transplant recipients‹Graft dysfunction‹Antimicrobial resistance‹Carbapenem-resistant Pseudomonas aeruginosa (CRPA)

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-151

Investigation of the Prevalence of Microbial Etiologic Agents and Their Antibiotic Resistance Patterns in Patients with Urinary Tract Infections Hospitalized in Different Wards of Bu-Ali Hospital, Neka County.

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Background and aim: Urinary tract infections are among the most significant human infections and represent the second most common infection inhumans.Escherichia coli is the most prevalent infectious organism in acute infections. The antibiogram isone ofthe methods by which the susceptibility or resistance of a specific species to a given drug canbe easily determined with minimal time and cost.The aim of this study was to identify the organisms causing urinary tract infections in patients hospitalized at Bu-Ali Hospital in Neka County during the spring and summer of 2025,to perform urinary susceptibility testing, and to determine the effective antibiotics forthe treatment of urinary tract infections.

Methods: In this descriptive cross-sectional study conducted during the spring and summer of 2025, a total of 381 individuals suspected of having urinary tract infections were referred to the hospital laboratory to provide urine samples. After being instructed on the proper method for midstream urine collection, urine samples were cultured using a sterile loop, with 0.001 mL of urine inoculated onto Blood Agar and EMB media using the zigzag method, and incubated at 37°C for 24 hours. The morphology and characteristics of the bacteria were determined using Gram staining, and for precise identification of bacterial genus and species, differential media such as Urease, TSI, SIM, MR-VP, and Simmons' Citrate were employed. Antibiotic susceptibility testing was performed using the disk diffusion method, and the results were interpreted according to the CLSI 2025 guidelines.

Results: In this study, among a total of 381 individuals suspected of urinary tract infection and hospitalized at Bu-Ali Hospital in Neka County, 38 patients (10%) were diagnosed with urinary tract infection, with an age range of 6 to 91 years. Of the infected individuals, 21 (55%) were female and 17 (45%) were male. Escherichia coli was the most prevalent infectious organism (78%), showing the highest antibiotic susceptibility to imipenem (100%) and gentamicin (78.4%), and the highest resistance to nitrofurantoin (78%). Among all infectious organisms, the highest susceptibility was observed to imipenem (80%) and gentamicin (69%), while the highest resistance was reported to nitrofurantoin (80.3%).

Conclusion: The pattern of antibiotic resistance in patients with urinary tract infections varies across different regions, and investigations for selecting appropriate treatment should be conducted periodically and regionally. Continuous monitoring of drug resistance can significantly aid in treatment management and in reducing the burden of disease.

keywords: Urinary Tract Infections Drug Resistance,Microbial Antibiotic Sensitivity Tests Escherichia coli

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBa-152

Immunoinformatics Evaluation of BabA to Predict Novel Multi-Epitope Vaccine Candidates against Helicobacter pylori

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Background and aim: BabA of Helicobacter pylori is a blood-group antigen and key virulence factor involved in outer membrane adhesion, extracellular surface exposed trap formation, and complement evasion. This study focused on epitope mapping and immunogenicity profile of BabA to design multi-epitope based vaccines inducing robust humoral and cellular immunity.

Methods: The linear B-cell and MHCII/I binding epitopes, IL-4, and IFN-γ inducer epitopes of BabA were predicted using the IEDB, IL-4Pred, and IFNepitope databases, respectively. The immunogenicity, allergenicity, toxicity, and conservation score of the predicted epitopes among H. pylori serotypes were evaluated using the VaxiJen, AllerTop, ToxinPred, and IEDB databases, respectively. Physicochemical properties were assessed by Protparam server. Finally, immune simulation of BabA administration in mammals and potential regions involved in BabA-TLR interactions were analyzed by C-ImmSim site and molecular docking via ClusPro server, respectively.

Results: This protein had two and thirteen predicted linear B-cell and helper T-cell epitopes, respectively, with a VaxiJen score of 1.5-2.89 and conservation score of 100% among H. pylori serotypes without any toxicity and allergenicity properties. Furthermore, BabA was considered an IL-4 and IFN-γ inducer protein. The immune simulation demonstrated induction of both humoral and cellular immunity against BabA. In addition, BabA had good interaction with TLR4 (binding energy of _976.1kcal/mol). Protparam analysis showed this protein with a molecular weight of 80.60 kDa was considered a stable vaccine candidate.

Conclusion: Although our results revealed that BabA could be considered as a conserved promising candidate vaccine with good immunogenicity profiles, further in vitro and in vivo validations are necessary.

keywords: Helicobacter pylori, Multi-Epitope Vaccine, Immunoinformatics, BabA

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-153

Designing multi-epitope vaccine against brucellosis based on immunoinformatics approach

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Background and aim: Background: Poor immunogenicity has been one of the many obstacles to the development of a safe and effective brucellosis vaccine; therefore, finding suitable antigen and adjuvant formulations is essential to overcoming these obstacles. In this study, we have utilized both bioinformatics and immunoinformatics techniques to create a possible multi-epitope vaccine for brucellosis.

Methods: Methods: In this research, amino acid sequences of OMPs and L7/L12 were obtained from protein databases such as UniProt. The B-cell epitope and T-cell (CD4 +and CD8+) epitope were predicted using the IEDB resource, then fused using different linkers including AAY and GPGPG. The resulting sequences were then analyzed for physicochemical properties, potential allergens, toxicology, and validated by means of web-based tools, followed by 3D structure modeling. Finally, the final structure was subject to additional analysis via molecular docking, immune simulation, and codon optimization.

Results: Results: In this study, 10 sequences corresponding to linear B-cell epitopes and 10 and 8 sequences for CD4+ and CD8+ T-cell epitopes, respectively, were selected. The epitopes were connected by appropriate linkers to support an extended structural conformation and correct protein folding. Analysis of the physicochemical properties, 3D structures, and molecular docking revealed that two multiepitope vaccine constructs possessed suitable characteristics and formed robust, stable interactions. In silico immune response simulations further indicated substantially increased levels of antibodies, helper and cytotoxic T cells, and IFN-γ.

Conclusion: Conclusion: The findings indicated that the designed multi-epitope vaccine has strong potential as a candidate against brucellosis; however, confirmation through in vitro and animal experiments is still required before it can be considered a practical preventive option.

keywords: Keywords: Brucellosis, Multi-epitope vaccine, Vaccine candidate , In silico design

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Tehran University of Medical Sciences (TUMS)
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PBa-154

Descriptive and Analytical Evaluation of Microbial Resistance Patterns in Sabzevar Hospitals (2018–2022) Based on WHONET Software

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Background and aim: Antimicrobial resistance (AMR) poses a critical challenge to global healthcare systems, complicating the management of hospital-acquired infections (HAIs). Irrational antibiotic prescribing accelerates the emergence of resistant strains, leading to increased morbidity, mortality, and healthcare costs. This study aimed to evaluate microbial resistance patterns in Sabzevar hospitals from 2018 to 2021 (1397–1400) using WHONET software.

Methods: This descriptive-analytical cross-sectional study analyzed cumulative antibiogram data over a four-year period (2018–2022). A total of 23,115 culture results recorded in the hospital infection control surveillance system were evaluated. Data were processed using WHONET software. Statistical analysis included descriptive statistics (frequency, percentage) and inferential tests (Chi-square) to assess relationships between variables. A P-value of 0.05 was considered statistically significant.

Results: The overall microbial resistance rate approximately doubled during the COVID-19 pandemic compared to the pre-pandemic period. Although resistance was higher in males, the difference was not statistically significant (). Urinary tract infections were the most prevalent; however, respiratory and ventilator-associated infections increased significantly from ~18% pre-pandemic to ~30% during the pandemic. The most frequent isolates were Coagulase-negative *Staphylococci*, *Escherichia coli*, and *Klebsiella* spp. Gram-negative bacteria showed the highest sensitivity to imipenem and meropenem, while Gram-positive isolates were most susceptible to aminoglycosides and cefotaxime.

Conclusion: Imipenem and meropenem were identified as the most effective antibiotics for treating respiratory and urinary tract infections in this setting. Implementing strict antimicrobial stewardship programs and preventing irrational antibiotic usage are essential strategies to mitigate the rising trend of microbial resistance and effectively manage hospital-acquired infections.

keywords: Drug Resistance, Microbial; COVID-19; Cross Infection; Pandemics; Anti-Bacterial Agents.

PBa-155

Development of an mRNA vaccine against the OprF of Pseudomonas aeruginosa and evaluation of antibody response in mouse

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Background and aim: Recently, antibiotic resistance has been recognized as a major threat to global public health. Pseudomonas aeruginosa (PA) is one of the most important opportunistic pathogens that mainly lead to dangerous nosocomial infections occur in immunocompromised individuals. In recent years, with the increasing rate of multidrug resistance (MDR) of PA, management of infection with this pathogen has become a global challenge. Messenger RNA (mRNA) vaccines seem to be a good alternative to conventional vaccines.

Methods: In the present study, an mRNA vaccine encoding OprF - outer membrane protein F - in PA was made and synthesized using in vitro transcription (IVT) method. Additionally, Lipid Nanoparticles (LNPs) were prepared by a thin layer hydration method and the prepared mRNA-LNP vaccine was evaluated in terms of nanoparticle properties. Finally, the efficacy of the vaccine in inducing a humoral immune response against PA was studied in Balb/c mice through injecting 5 or 25 µg of mRNA to each group.

Results: ELISA results showed an increase in the level of neutralizing antibodies against OprF protein in PA. Immunization with mRNA-OprF induced an appropriate humoral immune response and reduced bacterial burden in systemic infection models.

Conclusion: It seems that the mRNA-OprF vaccine made in the present study can be a promising vaccine to prevent PA infection.

keywords: Pseudomonas aeruginosa, antibiotic resistance; lipid nanoparticles, mRNA vaccine.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-156

phylogenetic analysis based on conserved genes and determining the pattern of drug sensitivity among Nocardia isolated from humans and the environment of Tehran hospitals

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Background and aim: Nocardia is a group of filamentous branched bacilli that are characteristically Gram-positive and acid-fast positive, and are increasingly isolated as infectious agents in immunosuppressed patients. The present study was conducted with the aim of studying the results of phylogenetic analysis based on conserved genes and determining the pattern of drug sensitivity among Nocardia isolated from humans and the environment of Tehran hospitals

Methods: In this research, in addition to the materials and tools available in the microbiology research laboratory, special materials and environments have also been used. Clinical samples from patients suspected of having nocardial infection who, according to the doctor's diagnosis and his order for bronchoscopy and preparation of lavage, abscess, sputum, wound and eye secretions, etc., whose cultures were positive in educational laboratories and medical diagnosis in hospitals It has been used to isolate Nocardia. The Chi-Square test was used to determine the significance level of the results. P value less than 0.05 was considered as a significant level.

Results: The similarity percentage of genus and species was obtained based on protected genes. Based on the findings, secA gene can be a suitable alternative for phylogeny analysis of Nocardias. The results of the antimicrobial sensitivity test for 18 isolates at the species level generally showed that resistance to TMP-SMX is rare and only 1 isolate of N.cyriacigeorgica was obtained with 10% resistant.

Conclusion: Among the isolates, the highest sensitivity was related to the drugs linezolid, amikacin, cotrimoxazole, and the lowest sensitivity to the drugs gentamicin, cefotaxime, and coamoxiclav

keywords: Nocardia, Conserved Genes, Phylogenetic Analysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-157

Risk of Tigecycline and Carbapenem Resistance in Iranian Acinetobacter baumanii Isolates

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Background and aim: The increasing Acinetobacter baumannii antibiotic resistance to last resort antibiotic such as carbapenems is a warning for public health community. Carbapenem was the drug of choice for MDR strains of A. baumannii, but with the emergence of carbapenem resistance, tigecycline and colistin were the next options for physicians, while recently some studies have also reported tigecycline resistance. Due to the type of strains, the immune system of the patients and the public health conditions, the frequency of resistant strains is different in communities, so we discuss in this review about the risk of resistance to common antibiotics including carbapenems and

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keywords: Acinetobacter baumanii, Carbapenem, Tigecycline, antibiotic resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-158

CRISPR-Cas12a DETECTR Technology Combined With Lateral Flow Strips For Rapid Detection Of Salmonella

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Background and aim: Foodborne infections, especially those caused by pathogens like Salmonella enterica, cause significant economic losses for the food industry and high medical costs globally. The need for specialized laboratory infrastructure limits the use of standard diagnostic techniques such as PCR and culture. The Clustered regularly interspaced short palindromic repeats (CRISPR)-Cas12a system provides an innovative diagnostic platform, recognized for precise nucleic acid recognition and trans-cleavage activity. To develop rapid and highly specific tests for Salmonella detection, this review discusses how the Cas12a DETECTR system can be combined with lateral flow immunoassays for improved diagnostic capability.

Methods: the workflow for a CRISPR-Cas12a-based lateral flow assay was generally described in several steps. First, nucleic acids were extracted from the sample, and isothermal amplification techniques, such as Recombinase Polymerase Amplification (RPA), were used to enrich for the target Salmonella DNA. The resulting amplified product was then incubated with a pre-assembled ribonucleoprotein complex that included the Cas12a enzyme and a guide RNA (crRNA). When this complex binds to its complementary DNA target, the Cas12a enzyme becomes activated and indiscriminately cleaves surrounding single-stranded DNA (ssDNA) reporter molecules. These reporter molecules were typically labeled with a fluorophore and biotin. The reaction mixture was subsequently applied to a lateral flow strip. Cleavage of the reporter molecules separated the labels, allowing the free fluorophore to migrate and be captured at the test line by immobilized antibodies, while the biotin part remained at the control line, bound to streptavidin. This process provided a visual outcome.

Results: Implemented assays demonstrated that the CRISPR-Cas12a DETECTR-LFA platform achieved exceptional analytical performance for Salmonella. Studies reported detection limits as low as 1–10 colony-forming units (CFU) per microliter in buffer and complex matrices such as milk or poultry samples, often within a total processing time of 30 to 60 minutes. The system exhibited high specificity, successfully differentiating Salmonella from non-target foodborne pathogens such as E. coli and Listeria, due to the precise crRNA design. The lateral flow readout provided a clear, binary visual confirmation (test and control lines) without requiring electronic readers, validating its suitability for resource-limited environments, field testing, and industrial food safety checkpoints. According to Lee et al. (2022).

Conclusion: The convergence of CRISPR-Cas12a diagnostics with lateral flow technology offers a transformative, next-generation tool for rapid, decentralized identification of Salmonella. This synergy combines molecular specificity with the simplicity of On-site formats, effectively bridging a critical gap in current diagnostic capabilities. For widespread adoption, future development must focus on streamlining sample preparation, ensuring batch-to-batch reproducibility, and achieving cost-effective multiplexing to detect multiple serovars simultaneously, thereby significantly enhancing public health surveillance and outbreak response.

keywords: CRISPR-Cas12, Salmonella, Lateral Flow assay

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-159

Genotyping of Acinetobacter baumannii clinical isolates by sequence typing of blaOXA-51-like and ampC genes

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Background and aim: Acinetobacter baumannii is considered one of the most important multidrug-resistant nosocomial pathogen causes a wide range of infections in hospitalized patients. Different molecular typing methods have been developed for epidemiological study and control of outbreaks. In current study sequence typing of blaOXA-51-like and ampC genes were used for molecular typing of A. baumannii clinical isolates.

Methods: A total of 119 MDR A. baumannii strains were isolated from clinical samples and antibiotic susceptibility testing was determined using disc diffusion method and E-test. PCR amplification and sequencing of blaOXA-51-like and ampC genes were applied for genotyping of A. baumannii isolates.

Results: According to antibiotic susceptibility testing the highest antibiotic resistance was detected to ciprofloxacin 113 (94.9%), gentamicin 111 (93.3%), and ceftazidime 101 (84.9%), whereas the lowest resistance observed to the colistin 6 (5.0%) and ampicillin-sulbactam 12 (10.1%). PCR-sequencing of blaOXA-51-like revealed two different sequence types (STs) among MDR A. baumannii isolates including 47 (39.5%) ST1 and 21 (17.6%) ST25.

Conclusion: The final conclusion is that the use of blaOXA-51-like and ampC gene analysis as a cost-effective and reliable sequence typing technique can be useful in identifying global and widespread lineages of A. baumannii strains.

keywords: A. baumannii, Genotyping, Sequence type, blaOXA-51-like, ampC

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-160

Prevalence of Mycoplasma genitalium in women with a history of abortion using 16S rRNA sequence and its relationship with antimullerin hormone

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Background and aim: Mycoplasma genitalium is a sexually transmitted bacterium that causes 15 to 25% of male nongonococcal urethritis and is associated with cervicitis and pelvic inflammatory disease in women. It can also be associated with cervicitis, pelvic inflammatory disease, and tubular factor infertility in women. This study aimed to investigate the effect of vaginal infections with Mycoplasma genitalium on the level of antimullerian hormone (AMH) and its relationship with abortion by molecular methods in Urmia

Methods: After patient satisfaction, endocervical sampling was performed. they were placed in a PPLO broth medium. After 2-3 days of incubation, the samples were removed by syringe. Then it passed through 0.2-micron filters and a few drops of the liquid were poured Into the PPLO agar medium. also to increase the sensitivity to diagnose mycoplasma infections and possible association with the amount of antimullerian hormone in women in the age range of delivery. the levels of Anti-Müllerian hormone (AMH) in positive samples were also measured by Electro Chemi Luminescence. Genus and species of Mycoplasma RFLP-PCR were used

Results: From 500 intrauterine samples of pregnant women samples, extracted DNA, and after PCR, 125 samples were positive. The culture results of the samples also showed that 80 cases grew after 2 weeks. 70% of PCR-confirmed samples had a history of miscarriage and 25% of antimullerian hormone levels were abnormal. Genotyping results indicated that the dominant mycoplasma was Mycoplasma genitalium strain G37 of the type

Conclusion: In general, it can be said that Mycoplasma genitalium can be one of the possible causes of abortion. PCR assay based on 16S rRNA gene sequences a valuable and reliable technique for the identification Mycoplasma genitalium to find the cause of spontaneous abortions is on the other hand, the present study showed that all Mycoplasma genitalium isolates had identical differences in enzyme patterns of this bacterium after PCR-RFLP was not observed and all were of the Mycoplasma type the genitalia were G37

keywords: Molecular detection, Mycoplasma genitalium, antimullerian hormone, abortion

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-161

Molecular Characterization of Diarrheagenic Escherichia coli among Children less than 5 years in Alborz Province

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Background and aim: Escherichia coli is dominant intestinal normal flora in humans. Some strains of E.coli are able to cause diseases in the gastrointestinal tract. Diarrheagenic E. coli strains are among the most common etiologic agents of diarrhea. The methods based on culture and serology are not able to identify these pathotypes from non-pathogen E.coli isolates. Regarding to importance of acute diarrhea specially in infants, we aimed to isolate and genetically type diarrheagenic E.coli pathotypes among Iranian patients with diarrhea.

Methods: In this study, 245 Escherichia coli isolates were collected from diarrheal samples of children under 5 years old. The isolates were confirmed using IMViC tests. PCR was performed on specific marker genes to assess the presence of E. coli pathotypes in the extracted samples. Finally, using RAPD-PCR genetic correlation of isolates was evaluated.

Results: Of the 245 isolates examined, 144 (59%) were confirmed as E. coli. Totally, 17 isolates (12%) were identified as pathogenic E. coli strains: 13 isolates (76%) as EAEC, 2 isolates (12%) as STEC, and 2 isolates (12%) as EPEC. EIEC and ETEC were not detected in any samples. According to RAPD-PCR, 15 genotypes were identified in three clusters.

Conclusion: The study results indicate that E. coli pathotypes are present as causative agents in patients with diarrhea and can be considered important diarrheal pathogens, particularly among children in Alborz Province. It also showed that some clonal groups among pathotypes which could have been derived from different sources of the community.

keywords: Gastroenteritis, Escherichia coli pathotypes, Infant

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-162

Study of expression of GATA3 ، IL-13 and STAT6 genes in clorectal cancer

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Background and aim: Colorectal cancer (CRC), a leading malignancy of the digestive system, may be diagnosed earlier by identifying specific gene expression patterns indicative of early-stage disease. GATA3, IL-13, and STAT6, key regulators of Th2 immune responses, significantly impact CRC.

Methods: To investigate this, tumor and adjacent normal tissues, and serum samples were collected from 100 CRC patients, along with 100 healthy control serum samples. qRT-PCR analysis revealed altered expression of GATA3, IL-13, and STAT6 in tumor tissues compared to adjacent normal tissues.

Results: Statistical analysis showed a significant correlation between GATA3, IL-13, and STAT6 expression levels and cancer stage.

Conclusion: These findings suggest that serum IL-13 and STAT6 levels, along with tissue expression of GATA3, IL-13, and STAT6, may serve as potential biomarkers for CRC diagnosis and prognosis.

keywords: Colorectal, IL-13 , STAT6, GATA3,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-163

A comparative analysis of CRISPR systems, virulence factors, and antibiotic resistance genes in carbapenem-sensitive and carbapenem-resistant Klebsiella pneumoniae

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Background and aim: Klebsiella pneumoniae is a major cause of healthcare-associated infections, particularly in immunocompromised patients. This study compares the CRISPR systems, virulence factors, and antibiotic resistance genes in carbapenem-sensitive (CSKP) and carbapenem-resistant (CRKP) clinical isolates.

Methods: Carbapenemase-producing isolates were identified by mCIM/eCIM. PCR and RT-qPCR detected key genes, including cas3, involved in CRISPR-Cas function. In silico analyses included STRING for protein interactions, CRISPRCasdb for CRISPR subtype distribution, and Phyre2/AlphaFold for cas3 structure prediction.

Results: Among the isolates, 35.2% were resistant to carbapenems. Among CRKP strains, high prevalence of bla-NDM-1 (82%) and bla-OXA-48 (64%) was observed. The cas3 expression was significantly upregulated in resistant isolates (P = 0.002). CRISPR subtype I-E was identified in 16% of CRKP and 36% of CSKP isolates. Structural-functional analysis supported the integrity of Cas3 and revealed interactions with regulatory and iron acquisition proteins. Statistically significant differences in virulence and resistance gene profiles were found between CRKP and CSKP groups (P 0.05).

Conclusion: This study highlights key differences between CRKP and CSKP isolates, particularly in CRISPR-Cas systems, resistance, and virulence. The findings suggest that cas3 plays a critical role in genomic adaptation and resistance mechanisms in K. pneumoniae, offering insights for future therapeutic strategies.

keywords: Klebsiella pneumoniae; CRISPR-Cas Systems; Drug Resistance; Virulence Factors; Gene Expression

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-164

A Critical Review on Inactivated Whole-Cell Bacteria as Immunomodulators Against Human Pathogens

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Background and aim: The escalating crisis of antimicrobial resistance, driven by the rapid emergence of multidrug-resistant pathogens, has rendered many conventional treatments ineffective, creating an urgent need for alternative therapeutic strategies. Postbiotics—bioactive compounds produced by probiotic microorganisms—have emerged as promising adjunctive agents against bacterial infections. This review critically examines the mechanisms by which postbiotics exert antimicrobial effects, including inhibition of biofilm formation, downregulation of resistance genes, modulation of gut microbiota, and enhancement of host immune responses. Evidence demonstrates their efficacy against clinically significant pathogens such as Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Helicobacter pylori, Clostridium difficile, and Streptococcus mutans, positioning postbiotics as

Methods: This critical review was conducted through a comprehensive literature search of peer-reviewed articles published in scientific databases, including PubMed, Scopus, and Web of Science, focusing on studies investigating the antimicrobial effects of postbiotics against human pathogens. The search strategy employed relevant keywords including postbiotics, probiotic-derived metabolites, cell-free supernatants, antimicrobial resistance, and specific pathogen names such as Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Helicobacter pylori, Clostridium difficile, and Streptococcus mutans. Studies were selected based on their relevance to postbiotic mechanisms of action, including biofilm inhibition, modulation of resistance gene expression, gut microbiota interactions, and host immune enhancement. Both in vitro and in vivo studies were considered, with particular attention to research elucidating the molecular mechanisms underlying postbiotic-mediated pathogen suppression. Data were synthesized to present a cohesive overview of current evidence and to identify knowledge gaps requiring further investigation.

Results: This review demonstrates that postbiotics exert significant antimicrobial effects against a broad spectrum of human pathogens through multiple mechanisms. Against Pseudomonas aeruginosa, postbiotics including lactic acid, bacteriocins, and exopolysaccharides inhibit biofilm formation, disrupt quorum sensing, and reduce virulence factor expression. For Staphylococcus aureus, postbiotics from Lactobacillus species enhance antimicrobial peptide production (DEFB4, RNASE7, CAMP) and anti-inflammatory cytokines (IL-10), while inhibiting MRSA growth. In Escherichia coli, postbiotics downregulate biofilm-associated genes (aggR, fimH), reduce environmental pH, and HM0539 prevents bacterial adhesion by enhancing tight junction proteins (ZO-1, MUC2). Against Helicobacter pylori, postbiotics prevent bacterial adhesion to gastric cells and reduce inflammatory cytokines (IL-6, IL-8, TNF-α). For Clostridium difficile, postbiotics suppress toxin gene expression (tcdA, tcdB), inhibiting pseudomembranous colitis. In Streptococcus mutans, postbiotics downregulate biofilm-related genes (gtfB, gtfC, gtfD, vicRK), reducing dental plaque formation. These findings collectively position postbiotics as effective multifunctional antimicrobial agents.

Conclusion: This review establishes that postbiotics derived from probiotic bacteria represent promising adjunctive agents for combating drug-resistant bacterial infections. Through multiple mechanisms—including biofilm disruption, downregulation of resistance genes, gut microbiota modulation, and immune enhancement—postbiotics demonstrate significant efficacy against major pathogens such as P. aeruginosa, S. aureus, E. coli, H. pylori, C. difficile, and S. mutans. Their ability to augment conventional antibiotic therapy while minimizing selective pressure for resistance positions them as valuable tools in addressing the antimicrobial resistance crisis. However, further standardized clinical studies are essential to validate these findings

keywords: Postbiotics; Antimicrobial resistance; Probiotic-derived metabolites; Biofilm inhibition; Pathogenic bacteria

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-165

Prevalence of Carbapenemase-Encoding Genes in Clinical and Environmental Isolates of Pseudomonas aeruginosa

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Background and aim: Pseudomonas aeruginosa is a major opportunistic pathogen responsible for hospital-acquired infections. The emergence of carbapenem-resistant strains, particularly those harboring carbapenemase-encoding genes, has become a serious therapeutic and infection control challenge worldwide. This study aimed to determine the antimicrobial resistance patterns and the prevalence of major carbapenemase-encoding genes among clinical and environmental isolates of P. aeruginosa recovered from hospital settings.

Methods: In this descriptive cross-sectional study, a total of 60 P. aeruginosa isolates (30 clinical and 30 environmental) were collected from hospital-associated sources. Antimicrobial susceptibility testing was performed using the disk diffusion method according to CLSI guidelines. Phenotypic detection of carbapenemase production was carried out using the modified carbapenem inactivation method. The presence of blaIMP, blaVIM, blaSPM, and blaKPC genes was investigated by multiplex PCR.

Results: High resistance rates were observed against gentamicin (95%), imipenem (93.3%), and meropenem (90%). The most prevalent carbapenemase gene was blaIMP (60%), followed by blaVIM (45%) and blaSPM (27%), while blaKPC was detected in 5% of isolates. Carbapenemase production was more frequent among clinical isolates than environmental isolates.

Conclusion: The high prevalence of carbapenem resistance and carbapenemase-encoding genes among both clinical and environmental P. aeruginosa isolates highlights the urgent need for continuous molecular surveillance, strengthened infection control measures, and rational antimicrobial stewardship programs in hospital settings.

keywords: Pseudomonas aeruginosa; carbapenemase; antimicrobial resistance; multiplex PCR; clinical and environmental

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-166

Gut Microbiota Dysbiosis in Different Courses of Multiple Sclerosis Compare to Control Groups

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Background and aim: Multiple sclerosis (MS), the leading non-traumatic disabling disease in young adults with rising global incidence, is characterized by perivenular inflammatory lesions and demyelinating plaques involving T-cells and B-cells. Typically suspected following a clinically isolated syndrome (CIS), MS is classified into four subtypes: relapsing-remitting (RRMS), secondary progressive (SPMS), primary progressive (PPMS), and CIS. Recent research implicates gut microbiota (GM) dysbiosis in MS pathogenesis and inflammation, and the present study aims to investigate alterations in the Firmicutes, Proteobacteria, Actinobacteria, and Bacteroidetes phyla and butry-coA gene across different MS types compared to controls.

Methods: Fecal samples were collected for identification by quantitative real-time PCR and transported to a -70 °C freezer until the test. Total genomic DNA was extracted from frozen fecal samples that were first allowed to thaw on ice, then stool samples were used for DNA extraction by the DNA extraction kit (Kiagene Fanavr, Iran) operating as per the manufacturer's instructions. Then four intestinal bacterial phyla, including Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria and butryl-coA, were investigated by 16SrRNA analysis using the real-time PCR reaction. Bacterial relative abundance across the six groups was assessed utilizing the Livak technique.

Results: The study was accomplished with 160 patients with types of MS (40 sample for each type), 40 individuals as other neurologic control and 40 healthy people. The Firmicutes phylum exhibited a decrease across all studied groups compared to the healthy control group; however, this reduction was not statistically significant. The Actinobacteria phylum showed an increase in all groups, but a significant increase was observed only in the SPMS group relative to the healthy controls. Within the Proteobacteria phylum, a significant increase was noted in the PPMS group compared to both the healthy control and RRMS groups, indicating dysbiosis. Furthermore, the Bacteroidetes phylum demonstrated a significant decrease in all patient groups compared to healthy controls. Additionally, the butyryl-CoA gene, which is involved in the production of butyric acid (a short-chain fatty acid with anti-inflammatory properties), was significantly reduced in all groups relative to the control group (figure 1).

Conclusion: This study confirms gut microbiota dysbiosis across all MS subtypes, with greater severity in progressive forms. Reduced Firmicutes and Bacteroidetes aligned with decreased butyryl-CoA gene abundance, indicating impaired butyric acid production. Butyric acid is essential for intestinal barrier integrity and inflammation control in autoimmune diseases. These gut microbiota alterations may influence MS progression and therapeutic outcomes.

keywords: Multiple Sclerosis, gut microbiota, dysbiosis, gut-brain axis, autoimmunity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-167

The Gut Microbiota-Autoimmune Axis in Addison's Disease: A Promising Target for Therapeutic Intervention

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Background and aim: Addison's disease (AD) is a life-threatening autoimmune disorder marked by adrenal cortex destruction and corticosteroid deficiency. Rising autoimmune disease incidence underscores the need to understand complex etiologies. The gut microbiota-immune axis critically regulates systemic inflammation and immune tolerance. In AD, microbial dysbiosis may disrupt self-tolerance, driving aberrant immune responses against adrenal glands. Modulating gut microbiota through probiotics or diet represents a promising therapeutic avenue to restore immune homeostasis and improve clinical outcomes in AD.

Methods: A systematic literature search was conducted using databases including PubMed, Scopus, Medline, and Google Scholar. The following keywords and their combinations were utilized: "Addison's disease AND gut microbiota," "Autoimmune adrenalitis AND microbiome," "Gut dysbiosis AND autoimmunity," and "Probiotic therapy AND adrenal insufficiency." Recent human studies and relevant preclinical models investigating the composition of the gut microbiota in AD and its interaction with the immune system were reviewed and analyzed.

Results: Emerging clinical data indicate that individuals with Addison's disease exhibit a distinct gut microbial profile compared to healthy controls. Key findings include a decreased abundance of short-chain fatty acid (SCFA)-producing bacteria, such as Faecalibacterium and Roseburia, which are crucial for maintaining intestinal barrier integrity and promoting regulatory T-cell (Treg) development. This dysbiosis is often associated with increased intestinal permeability ("leaky gut") and elevated markers of systemic inflammation. Studies suggest this compromised gut barrier may allow the translocation of microbial antigens, potentially triggering or perpetuating the autoimmune attack on the adrenal cortex. Furthermore, the composition of the gut microbiota has been linked to variations in systemic immune responses and possibly even to the quality of life and fatigue levels commonly reported by AD patients, despite standard hormone replacement therapy.

Conclusion: The gut microbiota-autoimmune axis represents a compelling and underexplored therapeutic target in Addison's disease. Evidence of significant dysbiosis and its link to impaired intestinal barrier function and systemic inflammation suggests that modulating the gut ecosystem could offer benefits beyond standard hormone replacement. These findings support the need for further research into microbiome-based therapies, such as specific probiotics or dietary interventions, which hold the potential to fortify gut barrier function, restore immune tolerance, and ultimately improve the long-term health and quality of life for individuals with Addison's disease.

keywords: Addisons disease, gut microbiota, autoimmunity, gut microbiota-autoimmune axis, therapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-168

Zoonoses as Drivers of Hyperinflammation: Rethinking the Role of Bacterial Infections in Cytokine Storm Syndrome

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Background and aim: Cytokine storm syndrome (CSS) represents a severe hyperinflammatory state driven by dysregulated immune activation and is associated with high morbidity and mortality. Although viral etiologies have received substantial attention, the contribution of zoonotic bacterial pathogens to CSS remains insufficiently characterized. Emerging evidence suggests that pathogens such as Brucella spp., Leptospira spp., Salmonella spp., Yersinia pestis, and Francisella tularensis can provoke profound immune dysregulation, warranting systematic evaluation of their role in CSS pathogenesis.

Methods: A systematic review was conducted in accordance with established methodological standards. Comprehensive searches of PubMed, Scopus, and Web of Science were performed using predefined search strategies encompassing zoonotic bacterial infections, cytokine storm, hyperinflammation, and immune dysregulation. Eligible studies included peer-reviewed original research and clinical investigations reporting mechanistic, immunological, or clinical evidence of cytokine dysregulation associated with zoonotic bacterial infections. Studies were independently screened for relevance and methodological rigor prior to inclusion.

Results: The analyzed literature indicates that multiple zoonotic bacterial pathogens activate innate immune pathways via pattern-recognition receptors, leading to excessive production of pro-inflammatory cytokines including IL-6, TNF-α, IL-1β, and IFN-γ. This hypercytokinemia is associated with endothelial dysfunction, coagulopathy, and multiorgan injury. Clinically, severe cases frequently exhibit hallmarks consistent with CSS, including hyperferritinemia, elevated C-reactive protein, and systemic inflammatory response, supporting a mechanistic link between zoonotic bacterial infections and cytokine-driven pathology.

Conclusion: These findings underscore zoonotic bacterial infections as underrecognized triggers of CSS with significant clinical implications. Early identification of hyperinflammatory phenotypes may facilitate risk stratification and inform adjunctive immunomodulatory interventions alongside antimicrobial therapy. Further prospective and mechanistic studies are required to define diagnostic biomarkers and optimize targeted therapeutic strategies.

keywords: Cytokine Storm Syndrome, Zoonotic Disease, Infection, Pathogenesis.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-170

Exploring the Co-spread of oqxAB and mcr-1 resistance Genes in Clinically Relevant Klebsiella pneumoniae Isolates from northern Iran

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Background and aim: Background: The rapid emergence of multidrug-resistant Klebsiella pneumoniae, particularly carbapenem-resistant strains, poses a major therapeutic challenge worldwide. Efflux pumps such as oqxAB and plasmid-mediated colistin resistance (mcr-1) significantly contribute to this problem, yet data from northern Iran remain limited. Objective: This study aimed to determine the prevalence of oqxAB efflux pump genes, their association with antimicrobial resistance patterns, the presence of mcr-1 in relation to colistin MICs, and the overall phenotypic and molecular profiles of clinical K. pneumoniae isolates from northern Iran.

Methods: A total of 100 non-duplicate K. pneumoniae isolates were collected from hospitalized patients in four major teaching hospitals affiliated to Mazandaran University of Medical Sciences. Antimicrobial susceptibility was assessed by disk diffusion (CLSI) and broth microdilution for colistin (EUCAST). The presence of oqxA, oqxB, and mcr-1 genes was investigated by PCR.

Results: Among 100 isolates, 58% were multidrug-resistant (MDR) and 13% were extensively drug-resistant (XDR); no pan-drug-resistant (PDR) isolates were detected. Carbapenem resistance was observed in 45% of isolates. Colistin resistance reached 45%, with MIC values ranging from 0.25 to 32 µg/mL (peak frequency at 4 µg/mL, n=13). The oqxA and oqxB genes were detected in 60% and 74% of isolates, respectively, with co-carriage in 73%. The mcr-1 gene was not detected in any isolate. Urinary isolates exhibited significantly higher resistance rates to several antibiotics compared with non-urinary sources (p 0.05 for selected agents). No statistically significant association was found between oqxAB carriage and resistance phenotypes (p 0.05).

Conclusion: This study reveals a high burden of MDR/XDR K. pneumoniae in northern Iran, with substantial colistin resistance driven by chromosomal mechanisms rather than mcr-1. The widespread presence of oqxAB genes, despite the lack of direct correlation with phenotypic resistance, highlights the need for continuous molecular surveillance and strengthened antimicrobial stewardship in the region.

keywords: Klebsiella pneumoniae, oqxAB efflux pump, colistin resistance, carbapenem resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-171

Bacterial outer membrane vesicles: A scoping review on their dual roles in immunity and disease (2020–2025)

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Background and aim: Outer membrane vesicles (OMVs) from Gram-negative bacteria are dynamic nanoparticles that shape host–pathogen interactions, acting as both immunostimulatory and immunosuppressive agents critical for microbial pathogenesis and therapeutic innovation. Objective: This scoping review aimed to synthesize recent advancements (2020–2025) in understanding OMVs' roles in immune modulation, pathogenesis, and microbiota-immune crosstalk, as well as their potential as vaccine platforms and drug delivery systems.

Methods: Relevant literature was identified through searches in PubMed, Google Scholar, and Web of Science, targeting peer-reviewed studies from 2020 to 2025.Approximately 80 were selected based on their relevance to OMV biogenesis, immune interactions, and applications in infectious diseases and cancer.

Results: OMVs activate proinflammatory pathways via pathogen-associated molecular patterns, contributing to diseases like inflammatory bowel disease and sepsis, while commensal OMVs (e.g., from Bacteroides fragilis) promote tolerogenic immunity and gut homeostasis. Diverse uptake mechanisms enable targeted delivery of virulence or regulatory factors. OMVs enhance microbiota-immune crosstalk, strengthening epithelial barriers and modulating immunity. Therapeutically, bioengineered OMVs show promise in vaccines and personalized medicine, though scalability, heterogeneity, and toxicity pose challenges.

Conclusion: OMVs are versatile tools bridging microbiology and immunology, with significant therapeutic potential. This review's novelty lies in its exclusive focus on Gram-negative OMVs, integrating 2020–2025 advances to address gaps in microbiota-driven immunity and bioengineered therapeutics, guiding future research in vaccine development and clinical translation.

keywords: outer membrane vesicles (OMVs); host immunity; vaccine platforms; proinflammatory response

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-172

Investigation of Staphylococcus aureus Contamination in cookie Samples

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Background and aim: Staphylococcus aureus is a Gram-positive bacterium commonly found on the skin and mucous membranes of humans and animals. It is a significant cause of foodborne illness globally, primarily due to its production of heat-stable enterotoxins that survive cooking. These toxins can induce symptoms like nausea, vomiting, diarrhea, abdominal cramps, and headache within hours of ingestion. S. aureus also contributes to food poisoning by forming biofilms on food products. This study aims to detect S. aureus contamination in various food samples using morphological and biochemical analyses, contributing to the understanding of its occurrence and characteristics to enhance food safety standards.

Methods: Ten samples (five locally sourced and five industrial)were aseptically collected for microbiological examination. A 10^{-1} suspension was prepared by homogenizing 5 g of sample with 45 mL of sterile diluent containing 1% potassium tellurite. The suspension was incubated at 37 °C for 24 hours, with black precipitate formation indicating presumptive Staphylococcus aureus. Cultures were streaked onto Baird-Parker Agar and Mannitol Salt Agar (MSA) and incubated at 37 °C for 24–48 hours. Colonies exhibiting characteristic morphology were selected. Gram staining confirmed Gram-positive cocci in clusters. Subsequent biochemical tests, including catalase, coagulase, β-hemolysis, DNase halo formation, and novobiocin sensitivity, definitively identified Staphylococcus aureus.

Results: The primary finding of this study was the detection of Staphylococcus aureus in 3 out of the 10 analyzed cookie samples. Further investigation revealed that of these three positive samples, two were locally sourced and one was industrial. Confirmation of S. aureus was supported by positive results in subsequent biochemical assays, including catalase, coagulase, DNase, and hemolysis tests.

Conclusion: This study confirmed the presence of Staphylococcus aureus in some cookie samples, highlighting the importance of hygienic practices during food processing and handling. The isolates showed classical biochemical characteristics of S. aureus, indicating their potential to cause foodborne illness ،Continuous microbiological monitoring and education of food workers are necessary to prevent contamination and ensure consumer safety. Future studies should focus on detecting toxin genes and antibiotic resistance patterns to better understand the public health impact of S. aureus in bakery products.

keywords: : Staphylococcus aureus, cookie, samples

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-173

Isolation of Endophytic Streptomyces cyaneofuscatus from Glycyrrhiza glabra and Evaluation of Its Antibacterial Activity

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Background and aim: The extensive use of antibiotics has markedly reduced mortality caused by infectious diseases. Nevertheless, the excessive and inappropriate use of these drugs has led to the emergence and spread of antibiotic-resistant pathogenic bacteria. In recent years, increasing attention has been directed toward discovering antimicrobial compounds from biological resources as an alternative strategy to combat antimicrobial resistance. Therefore, the present study aimed to isolate endophytic actinobacteria from Glycyrrhiza glabra and evaluate the antibacterial activity of their metabolites against selected pathogenic bacteria.

Methods: In this study, 80 root samples of Glycyrrhiza glabra were collected from different regions of Kermanshah Province, Iran. After surface sterilization, the samples were cultured on selective media and incubated under controlled conditions. Following colony development, bacterial isolates were identified based on macroscopic and microscopic characteristics as well as 16S rRNA gene sequencing. The antibacterial activities of methanolic and ethyl acetate extracts obtained from the isolated actinobacteria were evaluated against selected pathogenic bacteria.

Results: An actinobacterial strain identified as Streptomyces cyaneofuscatus was successfully isolated from the roots of Glycyrrhiza glabra. The methanolic and ethyl acetate extracts of S. cyaneofuscatus showed no significant inhibitory activity against Escherichia coli and Pseudomonas aeruginosa. However, both extracts demonstrated notable antibacterial activity against Staphylococcus aureus.

Conclusion: Streptomyces cyaneofuscatus was identified as an endophytic actinobacterium associated with Glycyrrhiza glabra. The findings suggest that this strain is capable of producing secondary metabolites with antibacterial properties. These results highlight the potential of S. cyaneofuscatus as a promising source of bioactive compounds for the development of novel antimicrobial agents.

keywords: Streptomyces cyaneofuscatus, Glycyrrhiza glabra, endophytic actinobacteria, antibacterial activity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-174

Systematic Review of Borrelia Infections in Rodents of Iran: Prevalence, Species Diversity, and Reservoir Role in Tick-Borne Diseases

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Background and aim: Rodents are recognized as important natural reservoirs for various Borrelia species (agents of Lyme disease and tick-borne relapsing fever) worldwide. However, the status of Borrelia infection in rodent populations of Iran has not been systematically reviewed. This systematic review aims to consolidate all available evidence on Borrelia infections in rodents of Iran, determine prevalence rates, identify the involved species, and assess their reservoir role in the epidemiological cycle of tick-borne diseases in the country.

Methods: This systematic review was conducted according to the PRISMA guidelines. A systematic search was performed in PubMed, Scopus, Web of Science, SID, and Magiran databases up to June 2026 using the combined keywords "Borrelia", "rodent", "reservoir", "Iran", and "tick-borne". Inclusion criteria comprised original studies (cross-sectional, descriptive, case-control) that reported extractable data on the presence, molecular or serological prevalence, and species identification of Borrelia in rodents captured from different regions of Iran. No language or time restrictions were applied. Data were summarized descriptively using frequency tables.

Results: Out of 104 retrieved articles, 5 Iranian studies met the inclusion criteria. A comprehensive study on 618 rodents from various regions of Iran reported a Borrelia prevalence of 0.80% (5/618), of which 4 cases were identified as Borrelia duttonii. Another study in East Azerbaijan province examined 210 rodents; 11 Meriones persicus (5.2%) were PCR-positive for Borrelia DNA, and phylogenetic analysis showed high similarity to B. duttonii and B. microti. Meriones persicus was the most frequently captured rodent species (315 out of 618, 51.22%) across studies. No Iranian study has reported Lyme disease borreliae (Borrelia burgdorferi sensu lato) in rodents. International studies have confirmed the role of rodents as major reservoirs for various Borrelia species.

Conclusion: Rodents in Iran, particularly Meriones persicus, act as natural reservoirs for Borrelia duttonii and Borrelia microti (agents of tick-borne relapsing fever), but the overall prevalence is low. A complete lack of studies on Lyme disease borreliae in Iranian rodents represents a major research gap. Extensive molecular surveys across different regions of the country are urgently needed.

keywords: Borrelia · Rodents · Reservoir · Iran · Tick-borne relapsing

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-175

Wolinella spp. in the Oral Cavity of Dogs in Iran: A Systematic Review of Prevalence, Association with Periodontal Disease, and Zoonotic Potential

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Background and aim: The genus Wolinella, a Gram-negative anaerobic bacterium from the family Helicobacteraceae, has recently been identified as a common inhabitant of the canine oral cavity. The association of this microorganism with periodontal disease in dogs and its potential role in zoonotic transmission is an emerging topic in Iranian veterinary microbiology. The aim of this study is to systematically review all available evidence regarding the presence of Wolinella in the dog population of Iran, determine its prevalence, analyze its association with periodontal disease, and identify research gaps to guide future investigations.

Methods: This systematic review was conducted according to the PRISMA guidelines. A systematic search was performed in PubMed, Scopus, Web of Science, Google Scholar, SID, and Magiran databases up to December 2025. Search keywords included combinations of "Wolinella", "dog", "canine", "periodontal disease", "oral cavity", and "Iran" in both Persian and English. Inclusion criteria comprised all original studies (cross-sectional, descriptive, case-control, and case reports) that reported extractable data on the presence, prevalence, molecular detection, or association of Wolinella with periodontal disease in dogs within Iran. No time restrictions were applied; all retrieved articles were reviewed. Data were summarized descriptively using frequency tables.

Results: Out of 87 articles found, 3 Iranian studies met the inclusion criteria. The first study (Jamshidi et al., 2025) on 42 dogs reported a Wolinella prevalence of 67.7% in dogs with periodontitis and 33.3% in healthy dogs ($P = 0.002$). The second study (Nowroozilarki et al., 2017) on 62 small breed dogs showed significantly higher Wolinella infection in the periodontitis group compared to the healthy group ($P = 0.002$). The third study on stray dogs confirmed the transient presence of Wolinella in the oral cavity. No Iranian study was found on systemic infection, specific treatment, or vaccine for Wolinella in dogs. International studies have identified Wolinella as the most common member of the Helicobacteraceae (91% of clones) in the canine oral cavity.

Conclusion: Wolinella has a significant prevalence in the oral cavity of Iranian dogs and shows a strong statistical association with periodontal disease. However, the complete lack of studies on molecular pathogenesis, cross-species transmission, and treatment methods represents a major research gap. Longitudinal cohort studies and genome sequencing of Iranian native strains appear necessary.

keywords: Wolinella · Dog · Periodontal disease · Oral flora ·

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-176

Metagenomics for Rapid Diagnosis of Unknown and Emerging Infectious Diseases: Clinical Applications, Challenges, and Future Perspectives

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Background and aim: Traditional microbiology tests often fall short in diagnosing the causative agents responsible for infectious diseases, especially in critical cases, immune-compromised patients, and infections caused by novel pathogens. Misdiagnosis might result in improper treatment with antibiotics, additional suffering for the patient, and increased cost of treatment. Metagenomic Next-Generation Sequencing (mNGS), on the other hand, can be regarded as a powerful culture-free diagnostic tool used for the detection of a broad range of bacteria, viruses, fungi, and parasites in clinical samples. This paper is intended to examine the use of mNGS in diagnostics of infectious diseases.

Methods: Narrative Review Methodology In this paper, we adopted a narrative review approach in order to explore recent advances in the field of clinical metagenomics as applied in diagnostics of infectious diseases. Specifically, scientific studies conducted in the field of metagenomic next-generation sequencing (mNGS) for diagnostics of CNS infections, blood stream infections, respiratory tract infections, ICU patients, culture negative infections, and outbreak investigations have been critically analyzed. Of particular interest have been papers studying application of nanopore sequencing methods, real time pathogens detection techniques, and bioinformatics approaches. Moreover, we have explored key technical and operational issues associated with clinical metagenomics such as sample processing, host DNA/RNA depletion, sequencing systems, taxonomic classification, contamination prevention, and data interpretation.

Results: There is significant utility of metagenomic sequencing in infectious diseases diagnostics regardless of their nature. For instance, mNGS was especially helpful in the diagnostics of infections in the central nervous system, where its implementation improved the detection of etiological agents in patients with either meningitis or encephalitis whose tests proved inconclusive. mNGS also facilitated the identification of infection-causing agents in bloodstream infections, respiratory infections, and patients admitted to intensive care units. Nanopore sequencing made pathogen detection possible within hours, which is crucial for making clinical decisions at an early stage of an infection. Moreover, host-response analysis proved particularly helpful in increasing the sensitivity of mNGS in diagnosing infectious diseases in complex clinical cases. Machine learning algorithms facilitated better understanding of bioinformatics analyses results because they helped in distinguishing false-positive classification errors from real data and differentiating between clinical pathogens and contaminants.

Conclusion: Metagenomics using next-generation sequencing stands out as one of the most innovative ways for the diagnosis of new, emerging, and hard-to-grow infectious diseases. The use of such sequencing can be considered more advantageous than conventional diagnostics, especially when it comes to critically ill patients or those with a negative culture. Advances in nanopore technology and machine learning have also added to the diagnostic potential of metagenomics. However, there are still a number of barriers that need to be solved first, including problems associated with standardization, high costs, complexity of bioinformatics

keywords: Metagenomic Sequencing; Infectious Diseases; Nanopore Sequencing; Clinical Microbiology; Culture-Negative Infections

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-177

The Role of the Human Microbiome in Infectious Diseases and Immune System Regulation: Mechanisms, Dysbiosis, and Therapeutic Implications

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Background and aim: The human microbiome also performs key functions related to immune system development, mucosal homeostasis, and resistance to infections. The connection between dysbiosis, which refers to an imbalance in the microbiome, and an increased risk of bacterial, viral, and systemic infections continues to become more evident. It is therefore crucial to elucidate how microbiome-immune system interactions function in order to develop new treatment methods. This literature review sought to assess existing research on how the human microbiome affects immunity, resistance to colonization, and infection outcomes, as well as to explore new microbiome-based treatments and future directions in precision medicine.

Methods: A review article was performed using fifteen selected peer-reviewed articles that highlighted the association between the microbiome and immune system, the role of dysbiosis, infectious diseases, and the use of microbiome for therapeutic interventions. Relevant literature was explored in order to understand the important mechanisms by which commensal organisms modulate the host immune response. Specifically, particular emphasis was placed on the role of colonization resistance, metabolites, short-chain fatty acids, toll-like receptor signaling, and epigenetics. Literature was also explored regarding the changes in microbiome in various infectious conditions including but not limited to COVID-19, HIV infection, sepsis, and recurrent C. difficile infections. In addition, the role of FMT, probiotics, prebiotics, and systems biology approaches was evaluated.

Results: As can be seen from the above evidence review, human microbiota plays an important role in modulating immunity using microbial metabolites, immune pathways, and epithelial barrier integrity. The positive impact of commensals includes the development of regulatory T cells, balance between inflammation, and resistance to infections. It was also proven that dysbiosis increases the risk of getting infected with different pathogens, which includes SARS-CoV-2, HIV infection, sepsis, and recurrent C. difficile infection. In addition, decreased microbial diversity and loss of good bacteria lead to a lack of colonization resistance and inflammation. The main mediators of microbiome-immune interaction appear to be short-chain fatty acids and secondary bile acids. Finally, fecal microbiota transplantation is a clinically proven method of restoring both microbial diversity and colonization resistance in patients with recurrent C. difficile infection.

Conclusion: The microbiome is an important modulator of immunity and resistance against infections. Alteration of this microbiome causes disturbances in the mutual relationship between hosts and microorganisms, thereby increasing the risk of developing infections and immune dysregulation. Based on existing studies, microbiome-based therapies such as fecal microbiota transplantation and microbial modulation have the potential for treating diseases. Nevertheless, problems including causality, inter-individual differences, and standardization need to be considered. Further exploration using various techniques such as multi-omics, artificial intelligence, and personalized medicine may contribute to disease prevention and management.

keywords: Human Microbiome; Dysbiosis; Immune Regulation; Infectious Diseases; Fecal Microbiota Transplantation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-177

The Effect of Probiotics on the Prevention and Control of Salmonella Infection: A Biological and Translational One Health Approach

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Background and aim: Salmonellosis is among the major reasons for gastroenteritis caused by pathogens in food items and is an important public health problem owing to increasing antibiotic resistance and restrictions on the use of antibiotics. In this regard, the potential role of probiotics as biological agents has been realized against Salmonella infection due to their ability to modulate the gut microbial flora, improve mucosal immunity, and inhibit colonization. This article reviews several biological activities that probiotics may perform against Salmonella infection in terms of inhibiting pathogen colonization, production of antibacterial metabolites, improving gut barrier properties, and modulation of the host immune system.

Methods: The present literature review was performed using the method of systematic literature analysis regarding the significance of probiotic agents in prophylaxis of Salmonella infection in humans. Relevant research works that were used for this literature analysis were retrieved from PubMed, Scopus, and Web of Science databases using relevant key words such as probiotics, Salmonella, gut microbiota, immunity, etc. Inclusion criteria for the selected publications included clinical and experimental studies involving probiotic strains, synbiotics, and postbiotic components with documented effects on Salmonella growth or host's immunity response. Analysis of the obtained data was performed in a descriptive way highlighting the most significant ways of action of such components as gut microbiota modification, immune modulation, barrier enhancement, and antimicrobial substances production. Particular attention will be paid to issues of translation, species-specificity, dose dependences, etc.

Results: The use of probiotics correlated with a significant decrease in Salmonella colonization in both humans and translational gut models. Several bacterial strains, which included lactobacilli, bifidobacteria, enterococci, and bacilli strains, exhibited inhibition activity through competitive exclusion and antimicrobial metabolites. An improvement in the intestinal barrier function was seen through an upregulation of the protein expression of tight junctions such as occludin, claudins, and ZO-1. Immune modulation entailed an increase in the levels of secretory IgA, balanced cytokines, and lowered systemic inflammation. Clinically, a positive effect of improvement in gastrointestinal complaints and reduction of duration of diarrhea in patients was observed. However, efficacy varied with probiotic species, dose, individual microbiome composition, and general patient well-being. The combination of prebiotics and probiotics yielded inconclusive results for certain human models.

Conclusion: The use of probiotics in biological approaches to control salmonellosis infections in humans through the manipulation of gut flora and improvement in host defense systems is a potential approach. The effects of probiotics can be exerted by different mechanisms, such as competitive exclusion, production of antibacterial substances, strengthening of the intestinal mucosal lining, and regulation of the immune system response. It has been shown that probiotics are capable of reducing disease severity, alleviating symptoms, and limiting the shedding of pathogens in infections affecting the gastrointestinal tract.

keywords: Probiotics; Salmonella; Gut microbiota; Immunomodulation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-178

Evaluation of Biofilm Formation in Clinical Vibrio cholerae Isolates Using Microtiter Plate Assay.

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Background and aim: When exposed to adverse environmental and pathological conditions in the intestine, Vibrio cholerae secretes a layer called biofilm. Bap1 and RbmC are two key adhesion proteins in the structure of the Vibrio cholerae biofilm matrix, which play complementary and essential roles in the stabilization and stability of the biofilm. aimed to evaluate the biofilm-forming ability of clinical Vibrio cholerae isolates using the microtiter plate assay (MTP). Biofilm formation was assessed after 24 and 48 hours of incubation to determine the capacity of isolates to produce biofilm and to classify them as non-, weak, moderate, or strong biofilm producers.

Methods: In this study, 40 Clinical isolates of Vibrio cholerae were evaluated for biofilm formation using the crystal violet microtiter plate assay. Briefly, bacterial suspensions equivalent to 0.5 McFarland standard were prepared, and 10 µL of each suspension was inoculated into 4.95 mL of Tryptic Soy Broth (TSB) supplemented with 1% glucose. Subsequently, 200 µL of the bacterial culture was transferred into sterile 96-well microtiter plates and incubated at 37°C for 24 and 48 h. Following incubation, wells were washed three times with phosphate-buffered saline (PBS) to remove non-adherent cells. Adherent biofilms were fixed with methanol, stained with crystal violet, and the bound dye was solubilized with ethanol. Optical density was measured at 570 nm. Biofilm production was classified as weak, moderate, or strong according to the calculated ODc value.

Results: After 24 h of incubation, all isolates (100%) were classified as weak biofilm producers. However, extending the incubation period to 48 h resulted in increased biofilm formation among several isolates. At 48 h, 31 isolates (77.5%) remained weak biofilm producers, while 6 isolates (15%) were categorized as moderate biofilm producers and 3 isolates (7.5%) exhibited strong biofilm-forming ability

Conclusion: The findings of this study demonstrated that all Vibrio cholerae isolates were capable of producing biofilm, although the intensity of biofilm formation varied with incubation time. Increased biofilm production after 48 h suggests that prolonged incubation promotes biofilm maturation and structural development. These results highlight the potential role of biofilm formation in the persistence and survival of V. cholerae and emphasize the importance of evaluating biofilm-associated characteristics in clinical isolates.

keywords: Vibrio cholerae, Biofilm, Crytal violet assay, Microtiter plate

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-179

Antibiotic Resistance Profiles of Clinical Methicillin-Resistant Staphylococcus aureus Isolates from Urinary Tract Infections and Evaluation of the Biofilm-Inhibitory and Synergistic Antibacterial Activites of Vitex agnus-castus Extract

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Background and aim: Urinary tract infections (UTIs) caused by biofilm-forming methicillin-resistant Staphylococcus aureus (MRSA) are a serious public health issue because of multidrug resistance and failed treatments. The increasing ineffectiveness of standard antibiotics has led to interest in alternatives from plants. This study aimed to find out the frequency of MRSA in UTIs at Isfahan hospitals and to look at its antibiotic resistance profiles. It also evaluated the ability of the isolates to form biofilms, tested the effect of Vitex agnus-castus extract on biofilm formation, and checked its synergistic effects with tetracycline and ciprofloxacin.

Methods: Fifty S. aureus strains were isolated from urine samples of patients with UTIs at teaching hospitals in Isfahan, Iran. Species identification and MRSA confirmation were performed by PCR targeting the nuc and mecA genes, respectively. Antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method for 11 antibiotics across different classes, in accordance with CLSI guidelines. Biofilm formation was assessed by the microtiter plate method with crystal violet staining. The minimum inhibitory concentration (MIC) of the methanolic extract of V. agnus-castus was determined by broth microdilution. The inhibitory effect of the extract on biofilm formation activity at sub-MIC concentrations (0.45–62.5 µg/mL) and synergistic interactions with tetracycline and ciprofloxacin were evaluated by the checkerboard assay.

Results: Of the 50 isolates, 19 (38%) were confirmed as MRSA by mecA PCR and 31 (62%) were classified as MSSA. Among MRSA strains, 14 (73.7%) exhibited a multidrug-resistant (MDR) phenotype, including 2 strains (10.5%) with an extensively drug-resistant (XDR) profile. The highest resistance rates in MRSA were observed against tetracycline (73.7%), levofloxacin, azithromycin, and ciprofloxacin (68.4% each), followed by erythromycin (68.4%) and clindamycin (57.9%). Regarding biofilm formation, 3 MRSA strains (15.8%) were strong producers, 8 (42.1%) moderate, and 8 (42.1%) weak. The MIC of V. agnus-castus extract against all tested MRSA strains was uniformly 125 µg/mL. At sub-MIC concentrations (15.6–62.5 µg/mL), biofilm formation was inhibited in 4 out of 5 tested strains, with inhibition rates of 30.0%–100%. Checkerboard analysis demonstrated synergistic interaction with tetracycline (FIC index = 0.20) and with ciprofloxacin (FIC index = 0.26–0.50) in selected MRSA strains.

Conclusion: A high prevalence of MDR MRSA was documented among UTI isolates recovered from Isfahan teaching hospitals. The V. agnus-castus extract was able to stop the formation of biofilms in the MDR MRSA strains. It demonstrated significant efficacy in combination with tetracycline and ciprofloxacin. Therefore, V. agnus-castus extract and these antibiotics together can be a way to treat urinary tract infections caused by MDR MRSA.

keywords: Methicillin-resistant Staphylococcus aureus, Biofilm, Vitex agnus-castus, Biofilm, Urinary tract infection

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-180

In Silico Identification of Natural Rv0933 Efflux Pump Inhibitors in Drug-Resistant Mycobacterium tuberculosis: Molecular Docking, Dynamics Simulation, and ADMET Profiling

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Background and aim: Multidrug-resistant tuberculosis (MDR-TB) poses a serious global health threat. Efflux pump overexpression — particularly the ABC transporter Rv0933 (PstB2) — contributes to isoniazid and rifampin resistance in Mycobacterium tuberculosis independently of target gene mutations. Despite its clinical relevance, Rv0933 remains an underexplored drug target with no validated natural inhibitors.

Methods: The AlphaFold-predicted Rv0933 structure (UniProt: P9WQK9) was used for site-specific molecular docking of twelve natural compounds against the ATP-binding site (residues 54–61) using AutoDock 4.2 (Lamarckian GA, triplicate). Top candidates underwent 10-ns triplicate molecular dynamics simulation (AmberTools, ff14SB/GAFF2 force fields). Binding stability was assessed by RMSD, RMSF, and radius of gyration. ADMET profiles were predicted using ProTox-II.

Results: Ellagic acid ($\Delta G = -7.13 \pm 0.15$ kcal/mol) and chlorogenic acid ($\Delta G = -7.11 \pm 0.12$ kcal/mol) outperformed the reference inhibitor CCCP (−5.08 kcal/mol) and verapamil. Both compounds formed stable hydrogen bonds with GLY57, LYS60, and THR61. MD simulations confirmed complex stability with low backbone RMSD, minimal RMSF at binding-site residues, and stable Rg (~19.5 Å). ADMET analysis predicted low acute toxicity (LD_{50} 2991 mg/kg) and no CNS penetration.

Conclusion: Ellagic acid and chlorogenic acid are computationally validated, structurally stable, and pharmacokinetically safe candidates for Rv0933 efflux pump inhibition in MDR-TB. In vitro validation using MIC reduction assays and RT-qPCR expression profiling of Rv0933 in Iranian clinical MDR isolates is ongoing.

keywords: MDR-TB; Rv0933; efflux pump inhibitor; molecular docking

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-181

From Nanotechnology to Infection Control: Antimicrobial Activity of MgO Nanoparticles Against MDR Staphylococcus aureus Isolates from ICU Patients at a Tertiary Care Hospital

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Background and aim: Staphylococcus aureus is a major cause of hospital-acquired infections, particularly in intensive care units (ICUs), and the increasing prevalence of multidrug-resistant (MDR) strains represents a serious global health concern. The declining efficacy of conventional antibiotics has created an urgent need for alternative antimicrobial agents. Magnesium oxide (MgO) nanoparticles have gained attention due to their reported antibacterial properties. This study evaluated the antimicrobial activity of MgO nanoparticles against MDR S. aureus isolates obtained from ICU patients using minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) assays to assess their potential as an alternative therapeutic strategy.

Methods: Multidrug-resistant (MDR) Staphylococcus aureus isolates were obtained from ICU patients and identified through standard microbiological and antibiotic susceptibility tests. The antimicrobial activity of magnesium oxide (MgO) nanoparticles was evaluated by determining the minimum inhibitory concentration (MIC) using the broth microdilution method and the minimum bactericidal concentration (MBC) by subculture on Mueller–Hinton agar plates. MIC was defined as the lowest concentration inhibiting visible bacterial growth, while MBC was defined as the lowest concentration preventing bacterial growth on agar.

Results: The resistant Staphylococcus aureus isolate was susceptible to magnesium oxide (MgO) nanoparticles. The minimum inhibitory concentration (MIC) was 0.5 mg/mL, while the minimum bactericidal concentration (MBC) was 1 mg/mL.

Conclusion: Magnesium oxide (MgO) nanoparticles demonstrated significant antimicrobial activity against the tested multidrug-resistant (MDR) Staphylococcus aureus isolate, with MIC and MBC values of 0.5 and 1 mg/mL, respectively. The low MBC/MIC ratio suggests a bactericidal effect. These findings highlight the potential of MgO nanoparticles as an alternative antimicrobial agent against MDR S. aureus. Further studies on additional clinical isolates and in vivo models are needed to confirm their efficacy and safety.

keywords: Nanoparticles, Staphylococcus aureus, Magnesium Oxide(MgO)

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-182

Magnesium Oxide Nanoparticles (MgO) Against Multidrug-Resistant Klebsiella pneumoniae Isolates Recovered from ICU Patients at a Tertiary Care Hospital: Implications for Infection Control

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Background and aim: Klebsiella pneumoniae is a major cause of hospital-acquired infections, particularly in intensive care units (ICUs), and the increasing prevalence of multidrug-resistant (MDR) strains has become a serious global health challenge. Rising antibiotic resistance has reduced the effectiveness of conventional treatments, emphasizing the need for alternative antimicrobial strategies. Magnesium oxide (MgO) nanoparticles have shown promising antibacterial properties. This study investigated the antimicrobial activity of MgO nanoparticles against MDR K. pneumoniae isolates recovered from ICU patients by determining their minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values.

Methods: Klebsiella pneumoniae isolates were obtained from ICU patients and screened for antibiotic resistance following bacterial identification and susceptibility testing. The antimicrobial activity of magnesium oxide (MgO) nanoparticles against resistant isolates was evaluated by determining the minimum inhibitory concentration (MIC) using the broth microdilution method and the minimum bactericidal concentration (MBC) through subculturing growth-inhibited samples onto Mueller-Hinton agar plates. The MBC was defined as the lowest nanoparticle concentration that completely prevented bacterial colony formation.

Results: The minimum inhibitory concentration (MIC) of magnesium oxide nanoparticles (MgO NPs) against Klebsiella pneumoniae isolates was 1 mg/mL. Following subculture of the MIC wells onto agar plates, the minimum bactericidal concentration (MBC) of magnesium oxide nanoparticles (MgO NPs) against Klebsiella pneumoniae isolates was determined to be 2 mg/mL.

Conclusion: Magnesium oxide (MgO) nanoparticles exhibited significant in vitro antimicrobial activity against multidrug-resistant Klebsiella pneumoniae isolates, with MIC and MBC values of 1 and 2 mg/mL, respectively. These results indicate both growth-inhibitory and bactericidal effects, highlighting the potential of MgO nanoparticles as alternative antimicrobial agents against MDR K. pneumoniae. However, despite their reported low toxicity and biocompatibility, further in vivo studies are necessary to validate their therapeutic efficacy and safety under clinical conditions.

keywords: Nanoparticles, Klebsiella pneumoniae, Magnesium Oxide, Drug Resistance

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-183

Gut microbiota in pancreatic cancer: A systematic review

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Background and aim: Pancreatic cancer is known as one of the most aggressive malignancies, carrying a poor prognosis and few treatment choices. Recent studies suggest that alterations in the gut microbiota are associated with the development, progression, immune evasion, and treatment resistance of pancreatic cancer. This review aims to evaluate current data on the role of gut microbiota in pancreatic cancer and its clinical implications.

Methods: We searched PubMed, Google Scholar, Web of Science, SID, and Magiran databases from 1990 to 2026 for keywords such as gut microbiota, pancreatic cancer, pancreatic ductal adenocarcinoma, dysbiosis, microbiome, immune modulation, biomarkers and treatment resistance to identify relevant studies. Relevant studies were screened and included in a qualitative synthesis.

Results: Numerous studies have reported that patients with pancreatic cancer show distinct gut microbial alterations compared with healthy controls. Dysbiosis may contribute to tumor development via chronic inflammation, intestinal barrier disruption, and immune response modulation. Certain bacteria and their metabolites could affect chemotherapy response by decreasing drug effectiveness or promoting resistance. Moreover, gut and tumor-associated microbiota have been proposed as potential non-invasive biomarkers for early detection. However, the evidence remains inconsistent primarily due to variations in study design, sample size, and sequencing methods.

Conclusion: Research indicates that gut microbiota may play an important role in pancreatic cancer development and treatment response. Targeting the microbiota could open up new avenues for diagnosis and treatment, but additional comprehensive and well-designed studies are needed to validate these findings.

keywords: Gut microbiota, Pancreatic cancer, Dysbiosis, Immune modulation, Treatment resistance

PBa-184

Engineered Probiotics for Therapeutic Applications: From Synthetic Biology to Living Precision Medicine

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Background and aim: The marriage between synthetic biology and microbiome engineering has led to the emergence of engineered probiotics, which serve as programmable living therapeutics. In contrast to regular probiotics, which only offer passive health benefits, engineered microbes are capable of sensing environmental cues, performing information processing within genetic circuits, and providing specific therapeutic outcomes. Living therapeutics are gaining increasing popularity as an innovative way to tackle difficult-to-treat diseases using dynamic local interventions. The purpose of this review is to highlight recent trends in engineered probiotics platforms, genetic circuits, biosensing technologies, therapeutic uses, safety measures, and translation into practice.

Methods: The use of narrative review methodology was adopted to analyze current developments in engineered probiotics and living therapies. Literature related to advances in synthetic biology, microbiome engineering, probiotic chassis construction, design of genetic circuits, biosensors, therapeutic applications, biosafety approaches, and clinical translation was critically considered. Emphasis was made on the use of engineered probiotics on the basis of Escherichia coli Nissle and Lactobacillus sp., as these are leading strains used for therapeutic applications. The literature on therapeutic uses against cancer therapy, metabolic disorders, inflammatory bowel diseases, diagnostic tools, and biosafety measures was analyzed to assess recent progress in this area. Progress made by designing programmable genetic circuits, environmental sensors, CRISPR-based control circuitries, and kill-switch mechanisms was assessed to identify its potential in improving therapy and ensuring biosafety.

Results: Modern research shows that engineered probiotics can serve as therapeutic platforms able to detect diseases, intervene in pathological processes, and provide a controllable means of therapy. Engineered E. coli Nissle and lactobacillus species exhibit remarkable performance in various medical settings. The treatment of cancer involves engineering tumor-homing bacteria to produce immune modulating factors and modify the tumor microenvironment. The treatment of metabolic disorders, such as phenylketonuria, utilizes engineered microorganisms to break down toxic substances in the gastrointestinal tract. Disease-specific probiotics allow local synthesis of anti-inflammatory agents in inflammatory bowel disease. Great achievements in living diagnostics are evident through the development of ingestible sensors able to detect physiological signals in vivo. In addition, improved safety measures, including containment circuitry, CRISPR-controlled systems, engineered auxotrophy, and a kill switch mechanism, significantly improve the prospects for translation into clinical practice.

Conclusion: Engineered probiotics can be considered a groundbreaking platform for therapy that integrates synthetic biology, microbiome studies, and personalized medicine. The potential for detection of disease-related signals and the possibility of targeted delivery of a response provide a range of benefits compared to traditional treatment modalities. Recent advances in biosensing technology, programmable genetic systems, and biocontainment solutions have facilitated progress in making engineered probiotics efficient and safe. While there still exist several concerns regarding genetic stability, production processes, immunology, and regulatory issues, further developments promise to make clinical applications more likely

keywords: Engineered Probiotics; Synthetic Biology; Living Therapeutics; Microbiome Engineering; Precision Medicine

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-185

Function, Regulation, and Inhibitory Mechanisms of Multidrug Efflux Pumps in Salmonella

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Background and aim: Salmonella enterica is a major pathogen that affects both animals and humans. Based on the "One Health" concept, controlling this bacterium is very important for public health. Today, multidrug-resistant (MDR) strains are a serious global problem, so we urgently need new treatments. One of the main reasons for this resistance is multidrug efflux pumps, especially the AcrAB-TolC system. These pumps push antibiotics out of the bacterial cell and help the bacteria survive inside the host. This review aims to evaluate how these pumps operate, how their genes are regulated, and the clinical potential of efflux pump inhibitors (EPIs) as alternative

Methods: We conducted a narrative review based on a systematic approach. First, we selected keywords from MeSH and free-text terms, including "Salmonella", "efflux pumps", "AcrAB-TolC", and "inhibitors". We merged these keywords using AND and OR operators. The search was done in PubMed, Web of Science, Scopus databases, and Google Scholar for articles published up to 2026. We reviewed in vitro and in vivo studies about the structure of the Resistance-Nodulation-Division (RND) family, genetic regulators like RamA and RamR, and the effects of different inhibitors. We only selected original full-text articles written in English. After collecting a number of articles, we removed the unrelated ones by reading their titles and abstracts. Finally, we selected the most relevant articles for our final review.

Results: Research shows that Salmonella has at least ten different efflux pump systems, but AcrAB-TolC is the most active one. These pumps are not just for antibiotic resistance; they are essential for the bacteria to survive. They help Salmonella tolerate bile salts, escape from the immune system, and make biofilms. Genetically, when the bacteria face toxic stress, the RamR repressor protein stops working. This turns on the RamA protein, which signals the bacteria to overproduce more efflux pumps. For treatment, many synthetic inhibitors show great results in the lab (in vitro) and can reduce the antibiotic Minimum Inhibitory Concentration (MIC) by 4 to 8 times. However, they usually fail in animal tests (in vivo) because they are very toxic. In contrast, natural plant-based inhibitors (phytochemicals like flavonoids) are much safer and have very low toxicity.

Conclusion: In summary, efflux pumps are vital for Salmonella to survive and cause disease. Therefore, they are excellent targets for new treatments. While completely blocking these pumps is a highly effective strategy in theory, it is dangerous in practice because of high toxicity to host cells. Thus, the most realistic and safe approach for future clinical applications is combination therapy. By utilizing lower doses of standard antibiotics alongside safe, plant-based inhibitors, we can successfully treat multidrug-resistant Salmonella infections across both veterinary clinics and human medicine.

keywords: Salmonella, Efflux Pumps, Antibiotic Resistance, Inhibitors, AcrAB-TolC

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-186

Epidemiological and Clinical Characteristics of Smear-Positive Pulmonary Tuberculosis Patients in Ilam, Iran: A Retrospective Cross-Sectional Study (2016–2024)

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Background and aim: Tuberculosis (TB) remains a major public health concern globally, with Iran continuing to report new cases despite national control efforts. This study aimed to analyze the epidemiological and clinical characteristics of smear-positive pulmonary tuberculosis (SPPTB) patients in Ilam province, Iran, and to identify factors associated with treatment outcomes.

Methods: This retrospective cross-sectional study included all registered SPPTB patients in Ilam province from 2016 to 2024, identified through provincial TB registry records. Treatment outcomes were categorized according to WHO definitions; treatment success was defined as cure or treatment completion. Demographic and clinical variables were analyzed using descriptive statistics, chi-square, and Fisher's exact tests. Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were estimated via binary logistic regression. All analyses were performed in SPSS version 22; statistical significance was set at p 0.05.

Results: A total of 120 SPPTB patients were included. Annual case counts declined from 23 (2016–2017) to 8 (2020–2021), with a mean incidence of 2.47 per 100,000 population. The mean symptom-to-diagnosis interval was 69.63 ± 77.47 days, and the mean diagnosis-to-treatment interval was 4.18 ± 9.56 days. The overall treatment success rate was 80.2%. On multivariable analysis, normal BMI (18.5–24.9 kg/m²) was significantly associated with treatment success compared to other BMI categories (adjusted OR = 3.16; 95% CI: 1.02–9.77). Age, sex, hospitalization status, and area of residence were not independently associated with treatment outcome.

Conclusion: The treatment success rate of 80.2% falls below the WHO 90% target, highlighting a gap in TB management in Ilam province. Normal BMI was the only significant predictor of successful treatment outcome. Strengthening nutritional support and early case detection may improve outcomes in this population.

keywords: Epidemiology, Mycobacterium tuberculosis, Smear-positive pulmonary tuberculosis; Treatment outcome

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-187

From Adhesion to Persistence: Decoding the Molecular Networks of Multidrug-Resistant Acinetobacter baumannii Biofilm and Therapeutic Opportunities

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Background and aim: Background: Acinetobacter baumannii is a leading opportunistic pathogen causing severe nosocomial infections, particularly in intensive care units. The alarming global rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains, coupled with this bacterium's exceptional ability to form biofilms on both biotic and abiotic surfaces, has created a major therapeutic challenge. Objective: This review aims to provide a comprehensive and critical analysis of the molecular mechanisms governing biofilm formation in MDR A. baumannii, with a special focus on the co-regulation between biofilm and

Methods: to explore emerging anti-biofilm therapeutic strategies. Methods: A systematic literature search was performed using PubMed, Springer, Nature, MDPI, BMC, and ScienceDirect databases. Key search terms included "Acinetobacter baumannii biofilm", "multidrug resistance", "co-regulation", "ompA", "bap", "csu", and "anti-biofilm agents". A total of 42 peer-reviewed articles were selected and analyzed. Results: Biofilm formation in A. baumannii is a tightly regulated multi-step process dependent on key genetic determinants: the csu operon (type I pili mediating initial adhesion), ompA (outer membrane protein A involved in adhesion and host cell invasion), bap (biofilm-associated protein crucial for maturation), and the pga operon (responsible for PNAG polysaccharide synthesis). The BfmRS two-component system, c-di-GMP signaling, and the AbaI/AbaR quorum sensing system orchestrate the expression of these genes. Importantly, our analysis highlights a profound co-regulation between biofilm formation and antibiotic resistance, particularly through the RND-type efflux pumps (AdeABC, AdeIJK). Subinhibitory concentrations of imipenem and other antibiotics paradoxically induce biofilm

Results: formation, creating a vicious cycle. Novel therapeutic avenues include 2-aminoimidazole derivatives (biofilm disruptors), diguanylate cyclase inhibitors (reverting to planktonic phase), natural compounds (medium-chain fatty acids, essential oils), zinc oxide nanoparticles, and phage therapy (e.g., φAB1), many of which have shown promising results in preclinical models.

Conclusion: Biofilm formation and antimicrobial resistance in A. baumannii are intrinsically interwoven networks. Effective management of MDR A. baumannii biofilm-associated infections requires abandoning monotherapy and adopting combinatorial approaches that pair conventional antibiotics with specific anti-biofilm agents. Translation of these preclinical findings into clinical practice remains the next frontier.

keywords: Keywords: Acinetobacter baumannii, multidrug resistance, biofilm, co-regulation, ompA, bap, efflux

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-188

Inactivation of standard wound bacterial strains using Photodynamic inactivation (PDI)

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Background and aim: The increasing microbial resistance to antibiotics has become one of the serious challenges in the healthcare sector. In this context, novel methods such as Photodynamic Inactivation (PDI) are among the new strategies for combating these pathogens. This method is based on the use of a photosensitizer, light with an appropriate wavelength, and the presence of molecular oxygen, which ultimately leads to the production of reactive oxygen species (ROS) and the destruction of microbial cell structures. The aim is to investigate the effect of PLGA-CUR -based PDI on reducing the microbial population of Staphylococcus aureus and Pseudomonas aeruginosa.

Methods: In this study, the effect of photodynamic inactivation with various concentrations photosensitizer Curcumin-PLGA using a 5-minute irradiation time on the planktonic and biofilm states of standard Staphylococcus aureus and Pseudomonas aeruginosa bacteria was investigated. In the planktonic and biofilm states, the number of colonies in the control group was compared to the photodynamic therapy groups. The ability to form biofilm was examined using the crystal violet staining method.

Results: In this study, it was shown that at concentrations of µg/ml 5 and higher in the planktonic state, a significant reduction in CFU/ml was observed in Pseudomonas aeruginosa bacteria, whereas in the planktonic state of Staphylococcus aureus bacteria, a significant reduction was observed at 15 µg/ml. The effect of photodynamic therapy on the biofilm state of Pseudomonas aeruginosa bacteria at a concentration of 15 µg/ml showed a significant reduction in CFU/ml, while in Staphylococcus aureus bacteria, a significant reduction was observed at concentrations of 5 µg/ml and 10 µg/ml.

Conclusion: It was confirmed that with the increase in the concentration of the photosensitizer, the effect of PDI is greater while the effect on bacterial biofilms is less than compare to planktonic bacteria.

keywords: Antimicrobial resistance, photodynamic inactivation (PDI), Staphylococcus aureus, Pseudomonas aeruginosa, PLGA-Curcumin

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-189

A concise review on the effect of photodynamic inactivation methods on oral-dental biofilms

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Background and aim: Oral biofilms, formed by microorganisms such as Streptococcus mutans, Candida albicans, and Enterococcus faecalis, contribute to common dental problems like caries, periodontitis, and peri-implantitis. These biofilms, characterized by a self-produced extracellular matrix, exhibit high resistance to conventional treatments like antibiotics, necessitating alternative therapeutic strategies. This review explores how PDT employs photosensitizers (PS) activated by specific wavelengths of light to generate reactive oxygen species (ROS), which subsequently target microbial cells and disrupt the biofilm matrix. The aim of his review is to explores the applications and mechanisms of a novel therapeutic approach called photodynamic therapy (PDT) for biofilm-associated infections in dentistry.

Methods: The review also provides a comprehensive overview of both in vitro and clinical studies demonstrating the efficacy of PDT through the scientific databases PubMed, SPIE, ScienceDirect, google scholar.

Results: PDT with photosensitizers such as methylene blue and toluidine blue, combined with light sources such as diode lasers, results in a significant reduction in microbial viability in biofilms. Through the mechanism of ROS production, photodynamic therapy disrupts biofilm integrity and inactivates microbial pathogens. Furthermore, studies show that combining photodynamic therapy with conventional treatments such as chlorhexidine or low-dose antibiotics enhances biofilm elimination by exploiting synergistic effects.

Conclusion: Advances in nanotechnology, including nanoparticle-encapsulated photosensitizers, are also discussed for their potential to increase the clinical efficacy and specificity of PDT. Through a comprehensive review of current research, this article seeks to highlight the potential of PDT to revolutionize oral care by providing a minimally invasive solution for persistent and resistant dental biofilms.

keywords: Photodynamic inactivation, Antimicrobial Photodynamic therapy, Biofilms, Oral- Dental

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBa-190

The Gut Microbiome Paradox: Balancing Beneficial Symbiosis and Pathogenic Threats in Gastrointestinal Diseases

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Background and aim: The intestinal microbiota plays a dual role in health and disease, with beneficial species supporting gut homeostasis while pathogenic strains contribute to gastrointestinal disorders. This review aims to elucidate the mechanisms by which gut microorganisms influence irritable bowel syndrome (IBS), Crohn's disease (CD), ulcerative colitis (UC), and colorectal cancer (CRC). We examine the protective effects of Lactobacillus, Bifidobacterium, Faecalibacterium, and Akkermansia through short-chain fatty acid production and immune modulation, alongside the pathogenic mechanisms of Fusobacterium nucleatum, Escherichia coli, Bacteroides fragilis, and Clostridium difficile, including toxin production, mucosal disruption, and dysbiosis-driven carcinogenesis.

Methods: This review synthesizes evidence from peer-reviewed literature on the role of gut microbiota in gastrointestinal diseases, including IBS, CD, UC, and CRC. A comprehensive search was conducted using PubMed, Scopus, and Web of Science databases for articles published up to 2024. Search terms included combinations of "gut microbiota," "dysbiosis," "probiotics," "pathogenic bacteria," "inflammatory bowel disease," "colorectal cancer," "Lactobacillus," "Bifidobacterium," "Faecalibacterium," "Akkermansia," "Fusobacterium nucleatum," "Escherichia coli," "Bacteroides fragilis," and "Clostridium difficile." Included studies encompassed original research, clinical trials, systematic reviews, and meta-analyses examining microbial mechanisms, host-pathogen interactions, and therapeutic applications. Exclusion criteria included non-English articles, conference abstracts without full text, and studies unrelated to gastrointestinal outcomes. Data extraction focused on virulence factors, molecular pathways (NF-κB, MAPK, β-catenin), metabolite production (SCFAs), and clinical outcomes.

Results: The findings demonstrate that beneficial bacteria—Lactobacillus, Bifidobacterium, Faecalibacterium, and Akkermansia—produce short-chain fatty acids (SCFAs), particularly butyrate, which suppress NF-κB signaling, reduce pro-inflammatory cytokines (TNF-α, IL-6, IL-1β), enhance regulatory T cell activity, and strengthen intestinal barrier integrity. Conversely, pathogenic bacteria (F. nucleatum, E. coli, B. fragilis, C. difficile) promote gastrointestinal disorders through distinct mechanisms: FadA-E-cadherin interaction (F. nucleatum), colibactin-induced DNA damage (E. coli), BFT-mediated E-cadherin degradation (B. fragilis), and TcdA/TcdB-induced Rho GTPase inactivation (C. difficile). These pathogens converge on common pathways, including NF-κB and MAPK activation, leading to chronic inflammation, increased intestinal permeability, and β-catenin-mediated oncogenesis in colorectal cancer. Dysbiosis, characterized by reduced beneficial bacteria and pathogenic overgrowth, was consistently associated with disease severity and poor prognosis across all conditions.

Conclusion: The gut microbiota plays a dual role in gastrointestinal health and disease. Beneficial bacteria including Lactobacillus, Bifidobacterium, Faecalibacterium, and Akkermansia protect against inflammation and carcinogenesis via SCFA production and immune modulation. In contrast, pathogens such as F. nucleatum, E. coli, B. fragilis, and C. difficile promote dysbiosis, chronic inflammation, and colorectal cancer through shared pathways like NF-κB and β-catenin. Maintaining microbial balance through targeted interventions represents a promising supportive strategy, though personalized approaches and rigorous clinical validation remain essential.

keywords: Gut microbiota, Dysbiosis, Colorectal cancer, Probiotics, Inflammatory bowel disease

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-191

Antimicrobial activity of native Lactobacillus cell-free supernatant against diarrheagenic Escherichia coli isolated from hospitalized patients in northern Iran

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Background and aim: Diarrheagenic Escherichia coli (DEC) causes significant morbidity and mortality worldwide, with rising antibiotic resistance necessitating alternative therapies. Probiotic Lactobacillus strains produce postbiotics—cell-free supernatants (CFS) containing antimicrobial compounds. This study evaluated the antibacterial activity of five native Lactobacillus CFS against DEC isolates from hospitalized patients in northern Iran. The goal was to assess postbiotic potential against enteropathogenic (EPEC) and enteroaggregative (EAEC) E. coli pathotypes, which are prevalent in hospital settings. Understanding these inhibitory effects could support alternative strategies to reduce DEC colonization and infection in vulnerable patients.

Methods: Stool samples were collected from 115 hospitalized patients without digestive problems. E. coli isolates were identified using culture, biochemical tests, and PCR targeting DEC pathotypes. Antibiotic susceptibility was assessed via disk diffusion. Five native Lactobacillus strains (L. acidophilus, L. plantarum, L. reuteri, L. rhamnosus, L. delbrueckii) were cultured, and cell-free supernatants (CFS) were prepared by centrifugation and filtration. Antibacterial activity against DEC isolates was evaluated using two methods: (1) agar well diffusion – CFS (50 µL) was added to wells in E. coli-inoculated Mueller-Hinton agar, and inhibition zones were measured after 24 h; (2) broth microdilution – CFS at concentrations of 20–80% was tested in 96-well plates to determine minimum inhibitory percentage (MIP) and minimum bactericidal percentage (MBP). All tests were performed in triplicate. Statistical analysis used SPSS (p0.05).

Results: Of 115 stool samples, 74 (64.3%) E. coli strains were isolated, of which 20 were DEC: 9 EAEC (12.1%) and 11 EPEC (14.8%). Most isolates were from patients aged 50–60 years and hospitalized for 1–2 weeks. Antibiotic resistance was common: EAEC showed high resistance to cefepime (88.8%), ciprofloxacin (88.8%), and ceftriaxone (77.7%); EPEC showed resistance to ceftriaxone (72.7%), cefoxitin (54.5%), and gentamicin (45.4%). In well diffusion assays, L. plantarum had the greatest inhibition against EAEC (average 8.33 mm) and L. reuteri against EPEC (average 8.54 mm). In broth microdilution, L. acidophilus CFS showed the lowest MIP (20%) and MBP (40%) against both pathotypes, indicating the strongest inhibitory and bactericidal effects. Other strains had MIP/MBP values of 40–80%. All CFS demonstrated growth inhibition, but efficacy varied by strain.

Conclusion: Native Lactobacillus cell-free supernatants exhibit significant antibacterial activity against antibiotic-resistant EAEC and EPEC isolates. L. acidophilus CFS showed the strongest bactericidal effect, while L. plantarum and L. reuteri also demonstrated notable inhibition. Postbiotics offer a promising, cell-free alternative to live probiotics, especially for immunocompromised hospitalized patients. Further research should identify active postbiotic compounds and evaluate clinical applications. These findings support the potential use of Lactobacillus-derived postbiotics in managing DEC-associated diarrhea.

keywords: Lactobacillus, cell-free supernatant, postbiotics, diarrheagenic E. coli, EPEC, EAEC, antibacterial

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-192

Assessment of Diagnostic Efficacy of Engineered ESAT-6 Linear Epitopes Based on IFN-γ Secretion in Tuberculosis

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Background and aim: Tuberculosis (TB) remains a major global health burden, with latent and active infections contributing significantly to morbidity and mortality. Effective diagnostic methods, particularly for latent tuberculosis, are essential for improving disease control and prevention. This study focused on engineering a recombinant ESAT-6 protein to evaluate its impact on IFN-γ secretion in Peripheral blood mononuclear cells (PBMCs), a key indicator of immune response from TB patients.

Methods: Following extraction of the ESAT-6 amino acid sequence from gene bank, linear epitopes were predicted and ranked based on immunogenic potential. The engineered cDNA was constructed, cloned, expressed in E. coli, and purified. Protein expression was confirmed via SDS-PAGE and Western blot analysis. PBMCs from tuberculosis patients were then exposed to varying concentrations (5, 10, and 15 µg) of the engineered ESAT-6 protein, with hemagglutinin serving as a control.

Results: The engineered ESAT-6 protein, comprising 135 amino acids with an approximate molecular weight of 14 kDa, was successfully produced. The gene fragment encoding this protein was 405 bp in length. Exposure to the recombinant protein induced a dose-dependent increase in IFN-γ secretion from PBMCs compared to the control. Recognition of the linear epitopes by immune cells effectively stimulated the production of IFN-γ, highlighting the immunogenic potential of the engineered ESAT-6 protein.

Conclusion: These findings demonstrate the utility of the engineered ESAT-6 protein in stimulating robust immune responses, suggesting its potential application in diagnostic assays and as a component of next-generation tuberculosis vaccines. Further research optimizing the structure of ESAT-6 could pave the way for improved tools in the fight against tuberculosis.

keywords: ESAT-6, IFN-γ, Mycobacterium, Protein engineering, Tuberculosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-193

Altered gut microbiota, SCFAs, and barrier integrity markers in Alzheimer's and Parkinson's disease patients

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Background and aim: Parkinson's disease (PD) and Alzheimer's disease (AD) have significant gut-brain axis interaction via microbial dysbiosis. Increasing evidence points to a role for the gut–brain axis in modulating neuroinflammatory and neurodegenerative processes, yet integrative studies examining gut microbiota composition, short-chain fatty acid (SCFA) levels, and intestinal barrier markers together remain scarce. The present study aimed to ascertain and evaluate the abundance of gut microbiota, SCFAs, zonulin, and calprotectin in Iranian patients with PD (n=25), AD (n=25), and other neurological disorders (ND, n=20), and to compare them with healthy controls (HC, n=20).

Methods: In this case-control study, stool and blood serum samples were collected from 90 participants: 25 PD, 25 AD, 20 ND (non-neurodegenerative neurological disorders), and 20 HC. Inclusion criteria required a confirmed diagnosis by a neurologist. Exclusion criteria included antibiotic, probiotic, or prebiotic use within two months, chronic gastrointestinal diseases, and corticosteroid use. Fecal DNA was extracted using a stool DNA extraction kit, and relative bacterial abundance was assessed by real-time PCR using species-specific primers and the Livak technique. SCFAs (acetate, propionate, butyrate) were extracted from stool and quantified by high-performance liquid chromatography (HPLC) with a C18 column and UV detection at 210 nm. Fecal calprotectin and serum zonulin concentrations were measured using sandwich ELISA kits. Data were analyzed with SPSS software using Kruskal–Wallis and ANOVA tests; statistical significance was set at p0.05.

Results: Firmicutes were prevalent across all groups. Bacteroidetes showed a significant decrease in PD (p=0.02) and AD (p0.0001) compared to HC. Proteobacteria were significantly higher only in ND patients (p=0.0005). Actinobacteria were significantly reduced in AD (p=0.01). Significant reductions in Faecalibacterium prausnitzii, Bacteroides spp., Bifidobacterium spp., and Lactobacillus spp. were observed in PD and AD groups. Enterobacteriaceae levels were significantly elevated in PD, AD, and ND versus HC. Akkermansia muciniphila was markedly increased in AD (p0.0001). Acetic acid concentrations were comparable among groups. Propionic acid was significantly reduced in AD (p=0.04), and butyric acid was significantly lower in PD (p0.0001). Fecal calprotectin and serum zonulin were significantly elevated in PD, AD, and ND groups compared with HC (all p0.0001 for calprotectin; p=0.03, 0.0001, 0.03 for zonulin, respectively).

Conclusion: This study demonstrates the presence of dysbiosis in individuals with PD and AD. The decline in bacterial taxa, including Bacteroidetes, F. prausnitzii, Bacteroides, Bifidobacterium, and Lactobacillus spp., together with the altered abundance of Enterobacteriaceae, was associated with elevated fecal calprotectin, serum zonulin, and decreased SCFA levels. These findings support the hypothesis that microbial dysbiosis contributes to gut barrier dysfunction and systemic inflammation, reinforcing the gut–brain axis framework. The sustained elevation of Enterobacteriaceae and Proteobacteria in ND also warrants further investigation to clarify the bidirectional relationship between dysbiosis and neurological conditions.

keywords: Parkinson's disease, Alzheimer's disease; Gut microbiota; Zonulin; Calprotectin; Dysbiosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-194

The Relationship Between Gut Microbiota and Preterm Premature Rupture of Membranes: Mechanisms of Action and Clinical Applications

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Background and aim: Preterm Premature Rupture of Membranes (PPROM) is a prevalent obstetric complication heightening neonatal mortality and low birth weight. Despite known associations, no definitive treatment exists. Gut microbiome dysbiosis may play a significant role in PPROM pathogenesis. This study reviews mechanisms linking intestinal dysbiosis to PPROM. Evidence suggests specific intestinal bacteria translocate into the amniotic cavity due to gut microbiota imbalances, facilitated by vaginal microbiota alterations and HPA axis activation, initiating a cascade that accelerates PPROM

Methods: To collect data PubMed, Scopus, Google Scholar and Medline databases were searched. Keywords used in the search strategy comprised “gut microbiota” OR “intestinal microbiome” OR “dysbiosis” combined with “preterm premature rupture of membranes” OR “PPROM” OR “chorioamnionitis” OR “HPA axis” AND “pregnancy.”

Results: Findings indicate that gut dysbiosis promotes PPROM through interconnected mechanisms. Increased intestinal permeability facilitates translocation of pathogenic bacteria (Collinsella, Intestinibacter, Turicibacter) into the amniotic cavity. This triggers chorioamnionitis, characterized by elevated MMPs 2, 7, 8, and 9, leading to collagen degradation, and heightened IL-6 and IL-8. Neutrophil infiltration amplifies membrane damage via myeloperoxidase, reactive oxygen species (ROS), and neutrophil extracellular traps, which assist MMP-9 and prostaglandin E2 (PGE2) release. Oxidative stress involves increased ROS and reduced antioxidants including catalase, glutathione, and superoxide dismutases. Damage-associated molecular patterns like HMGB1 and soluble Toll-like receptors (TLR1,2,4,6) are elevated. Concurrent HPA axis overactivation elevates cortisol, which upregulates MMP-9 and PGE2, downregulates collagen 1A1 (COL1A1), and promotes macrophage infiltration releasing IL-1β, weakening fetal membranes further. Corticosterone-injected murine models demonstrate reduced amnion mesenchymal layer thickness.

Conclusion: PPROM is a complex condition where gut dysbiosis plays a critical role by promoting bacterial translocation, inflammation, and HPA axis overactivation, ultimately compromising fetal membrane integrity. Dysbiosis can also alter vaginal flora, heightening infection susceptibility. Maintaining gut microbial homeostasis through probiotics such as Lentilactobacillus kefiri or dietary modifications may alleviate detrimental effects on PPROM. Future studies should concentrate on these underlying causes to improve maternal and fetal outcomes. Considering new treatments including pre-, pro-, and synbiotics is recommended to help prevent gut dysbiosis in pregnant women and reduce PPROM risk.

keywords: Dysbiosis, Preterm Premature Rupture of Membranes, gut microbiome, Chorioamnionitis, HPA

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-195

Comparative Evaluation of Specific Antibody against Mycobacterium tuberculosis ESAT-6 Recombinant Antigen in Healthy Subject with Positive and Negative Skin Test

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Background and aim: Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. Laboratory diagnosis includes bacteriologic and immunologic methods, but high cost and time-consuming nature have driven interest in rapid, antigen-based screening. Genomic studies reveal that pathogenic strains contain regions of difference absent in nonpathogenic Mycobacteria and BCG. The early secretory antigenic target 6 kDa (ESAT-6) is a major immunogenic antigen present in all pathogenic mycobacterial strains but absent in BCG, making it suitable for distinguishing TB patients from healthy vaccinated individuals. This study aimed to measure antibody levels against ESAT-6 protein in healthy people and compare it to TB patients.

Methods: The study included 27 TB patients and 87 healthy individuals with no clinical symptoms, divided by Tuberculin skin test into positive PPD (n=35) and negative PPD (n=52). Induration 10 mm was considered positive. Recombinant ESAT-6 was produced by cloning the gene into pQE30, expression in E. coli M15, Ni-NTA affinity purification, and Western blot confirmation. Specific antibody levels against ESAT-6 and PPD were measured by indirect ELISA. Plates were coated with ESAT-6 (500 ng/well) or PPD (1.4 µg/well), blocked, and incubated with sera (1:100). HRP-conjugated goat anti-human IgG (1:50,000) was used. Absorbance was read at 450 nm. Cut-off was defined as mean OD of negative samples plus two standard deviations. Assay performance was evaluated by comparing antibody levels across groups.

Results: The purified recombinant ESAT-6 protein showed a distinct single band at 12 kDa with 93.6% purity. The results showed that the majority of the healthy population with negative skin test results did not have antibodies against the recombinant ESAT-6 (98%) and PPD (96%) antigens; only one sample exceeded the cut-off for ESAT-6 and two for PPD. Similarly, most subjects with positive skin test results stood below the cut-off line, except for two cases for each antigen, yielding a specificity of 94% for both tests. In TB patients, high levels of specific antibodies against ESAT-6 and PPD antigens were detected, with a test sensitivity of 77% for both antigens. A significant difference in specific anti-ESAT-6 antibody was observed between the healthy group and patients (P0.01), while no difference was found between healthy subjects with positive and negative skin test results (P0.05).

Conclusion: The ELISA based on anti-ESAT-6 antibody measurement proved a proper diagnostic method for rapid, accurate screening of healthy from infected people. With 77% sensitivity and 94% specificity, it offers ease of use, rapidness, cost-effectiveness, and high-throughput capability. Because ESAT-6 is absent in BCG and peripheral Mycobacteria, the test reliably distinguishes TB patients from vaccinated healthy individuals. Monitoring anti-ESAT-6 antibodies may also aid in tracking treatment response. These advantages support ESAT-6-based serology as a valuable tool for TB control, especially in resource-limited settings where conventional methods are costly or slow.

keywords: Antibody, ELISA, ESAT-6, Mycobacterium tuberculosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-196

Infection trends and drug resistance – what we learned from six months of clinical data

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Background and aim: So this is a six-month analysis from our hospital – first half of the Iranian year 1404, basically Farvardin to Shahrivar. We wanted to see what bacteria are actually causing infections, how bad the resistance is, and which wards have the biggest problems. I'm an immunologist by training, so I was also curious about how these resistance patterns might affect the immune response in patients.

Methods: We just went back and looked at all positive clinical cultures from that period. For each isolate, we checked if it's MDR (resistant to three or more antibiotic classes), XDR (susceptible to two classes or less), or PDR (totally resistant). We also kept an eye on MRSA and VRE separately. Then we sorted everything by month, sample type, and hospital ward.

Results: Klebsiella spp. and E. coli were the most common bugs – no surprise there. But the numbers that worried us were 152 MDR isolates and 72 XDR isolates, mostly from those same two species. ICUs (especially A and D) had the highest number of positive cultures. Most samples came from endotracheal tube aspirates and urine. MRSA and VRE were not that many, honestly, but they're still around, which is not great.

Conclusion: Bottom line: multidrug-resistant gram-negative infections are a huge problem in our ICUs. The fact that we're seeing XDR organisms means we're running out of treatment options. From my immunology angle, this also messes with how the patient's own immune system tries to fight back. We need better antibiotic stewardship, stricter infection control in ICUs, and we have to keep monitoring these patterns. Otherwise, our empirical treatment is just guesswork, and resistance will get worse.

keywords: Antimicrobial resistance, MDR, XDR, hospital-acquired infections, ICU, microbiological surveillance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-197

Prevalence, Antimicrobial Resistance Patterns, and Risk Factors of Hospital-Acquired Infections Due to Pseudomonas aeruginosa in Intensive Care Unit and Burn Wards: A Cross-Sectional Study in Sanandaj Hospitals, Iran

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Background and aim: Title: Prevalence and Antimicrobial Resistance of Pseudomonas aeruginosa in Sanandaj Hospitals, Iran Background: Pseudomonas aeruginosa causes severe hospital-acquired infections in ICU and burn patients. Data from western Iran is limited. Methods: This cross-sectional study included 280 patients in Tohid and Besat hospitals, Sanandaj (2023-2025). P. aeruginosa was identified by standard methods. Antimicrobial susceptibility was tested by Kirby-Bauer. Results: Of 280 patients, 98 (35.0%) had P. aeruginosa infections (46.9% from burns, 29.6% from VAP). Resistance rates: ceftazidime 81.6%, imipenem 75.5%. Colistin resistance was 7.1%. MDR prevalence was 57.1%. Conclusion: High MDR P. aeruginosa (57.1%) and carbapenem resistance (75%) in Sanandaj hospitals

Methods: Methods: This cross-sectional study was conducted on 280 patients with clinically suspected hospital-acquired infections in ICU and burn wards of two major teaching hospitals (Tohid and Besat hospitals) in Sanandaj, Kurdistan province, Iran, between October 2023 and December 2025. Clinical specimens including wound swabs, blood, bronchoalveolar lavage, urine, and endotracheal aspirates were collected. P. aeruginosa isolates were identified using standard microbiological methods including gram staining, oxidase test, growth on cetrimide agar, pigment production, and biochemical tests (OF test, citrate, urease, and TSI). Antimicrobial susceptibility testing was performed using Kirby-Bauer disk diffusion method according to CLSI M100 guidelines for 15 antibiotics. MDR was defined as resistance to at least three different antibiotic classes. Multivariate logistic regression was used to identify independent risk factors.

Results: Results: Of 280 patients, 98 (35.0%) had P. aeruginosa infections (46.9% burns, 29.6% VAP, 15.3% CAUTI). Resistance rates: ceftazidime 81.6%, ciprofloxacin 79.6%, imipenem 75.5%, meropenem 74.5%. Colistin resistance was 7.1%. MDR prevalence was 57.1%, XDR 19.4%. Independent risk factors: prolonged hospitalization 14 days (OR:4.5, p0.001), prior antibiotics (OR:3.9, p0.001), mechanical ventilation (OR:3.4, p0.001), and burn injury (OR:2.5, p=0.004). Mortality rate was 33.7%.

Conclusion: Conclusion: This study reveals high MDR P. aeruginosa (57.1%) and alarming carbapenem resistance (75%) in Sanandaj hospitals. Colistin remains the most effective option. Prolonged hospitalization, prior antibiotics, and mechanical ventilation are independent risk factors. Immediate infection control measures and antibiotic stewardship programs are urgently recommended.

keywords: Keywords: Pseudomonas aeruginosa; Antimicrobial resistance; Sanandaj; Multidrug-resistant; Hospital-acquired infection

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-198

Antibiotic Resistance Patterns of Clinical, Colonizing, and Environmental Klebsiella pneumoniae Isolates Recovered from the Intensive Care Unit of Alzahra Hospital in Isfahan in 2025

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Background and aim: Klebsiella pneumoniae is a major cause of healthcare-associated infections, particularly in intensive care units (ICUs). The increasing prevalence of ESBL-producing and carbapenem-resistant isolates has become a significant global health concern. This study evaluated and compared the antimicrobial resistance patterns of clinical, colonizing, and environmental K. pneumoniae isolates recovered from the ICU of Alzahra Hospital.

Methods: In this cross-sectional study conducted in 2025, K. pneumoniae isolates were collected from clinical specimens, colonized patients, and environmental sources. Identification was performed using conventional biochemical methods. Antibiotic susceptibility testing was performed using the disk diffusion method according to CLSI guidelines. The minimum inhibitory concentrations (MICs) of colistin were determined using Broth microdilution method. Phenotypic detection of hypervirulent K. pneumoniae (hvKP) was performed using the string test. Extended-spectrum β-lactamase (ESBL) production was determined using the Double Disk Synergy Test (DDST).

Results: A total of 176 clinical, 36 colonizing, and 16 environmental K. pneumoniae isolates were analyzed. Cefotaxime showed the highest resistance rate among clinical isolates (96.0%), while levofloxacin had the highest resistance rate among colonizing isolates (94.4%). Environmental isolates exhibited complete resistance (100%) to cefotaxime, cefepime, levofloxacin, and meropenem, whereas amikacin showed the lowest resistance rates across all groups (79.5%, 72.2%, and 62.5% in clinical, colonizing, and environmental isolates, respectively). Colistin resistance was detected in 47.1% of clinical, 72.2% of colonizing, and 75.0% of environmental isolates. ESBL production was identified in 13.1% of clinical isolates and in 8 colonizing and 3 environmental isolates, while hypervirulent isolates were relatively uncommon, accounting for 7.4% of clinical isolates and only one isolate in each of the colonizing and environmental groups.

Conclusion: The high prevalence of meropenem and colistin resistance among clinical, colonizing, and environmental K. pneumoniae isolates suggests that colonized patients and hospital environments may serve as reservoirs for the persistence and spread of resistant isolates in the ICU. These findings emphasize the need for continuous surveillance, effective infection control practices, environmental monitoring, and antimicrobial stewardship to limit the dissemination of multidrug-resistant K. pneumoniae in critical care settings.

keywords: Carbapenem-resistant Antibiotic resistance Klebsiella pneumoniae

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-199

Molecular Profiling of Gut Microbiota Reveals Dysbiosis in Iranian Amyotrophic Lateral Sclerosis Patients

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Background and aim: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder affecting upper and lower motor neurons. Gut microbiome dysbiosis is proposed as a neuroinflammatory contributor via the gut–brain axis. Population-specific ALS microbiome data remain scarce, particularly from Middle Eastern cohorts. This study characterised gut microbial composition in Iranian ALS patients and its clinical correlates.

Methods: This case-control study enrolled 55 ALS patients (El Escorial criteria; age 45.2 ± 8.3 years; ALSFRS-R 34.8 ± 6.2) and 44 matched controls. Relative abundance of Firmicutes, Bacteroidetes, Prevotella spp., and Lactobacillus spp. was quantified from stool DNA by qPCR (16S rRNA; ΔΔCt normalisation). The Firmicutes/Bacteroidetes (F/B) ratio was the primary dysbiosis index. Pearson's correlation assessed clinical associations.

Results: The F/B ratio was significantly reduced in ALS (0.70 vs. 1.03; P 0.001), indicating Bacteroidetes dominance. All four taxa were elevated in ALS: Firmicutes (14.64 ± 3.40 vs. 9.74 ± 0.11), Bacteroidetes (21.95 ± 4.42 vs. 9.47 ± 0.10), Prevotella (22.00 ± 5.10 vs. 8.46 ± 0.16), and Lactobacillus (22.45 ± 6.74 vs. 7.21 ± 0.12; all P 0.001). Clinically, Prevotella inversely correlated with ALSFRS-R ($r = -0.52$; $P = 0.008$), and disease duration positively correlated with Bacteroidetes ($r = 0.45$; $P = 0.01$).

Conclusion: ALS is associated with a distinct gut microbial signature, including a reduced F/B ratio and an inverse Prevotella–ALSFRS-R relationship. These findings support gut–brain axis involvement in ALS pathophysiology, identifying specific microbial indices as non-invasive biomarker candidates. Longitudinal studies are warranted to clarify causality and therapeutic implications.

keywords: Amyotrophic lateral sclerosis, Gut microbiome, Dysbiosis, Iran

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-200

Oropharyngeal Microbiome as a Non-Invasive Biomarker for Predicting Respiratory Infection Risk in Patients with Common Variable Immunodeficiency: A Systematic Review

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Background and aim: Common variable immunodeficiency (CVID), the most prevalent symptomatic primary immunodeficiency, features hypogammaglobulinemia and recurrent respiratory and gastrointestinal infections. Although the gut microbiome in CVID is well-studied, oropharyngeal microbiome data is limited. The oropharyngeal microbiome is crucial for respiratory health through mucosal immunity and pathogen defense. This study aims to evaluate evidence on the association between oropharyngeal microbiome composition and acute respiratory infection risk in CVID patients, and to assess its potential as a non-invasive predictive biomarker.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, and Cochrane until June 2026. The keywords were common variable immunodeficiency, oropharyngeal microbiome, and respiratory infections. By searching this database; 15 articles were found and 5 articles were included under the inclusion criteria.

Results: Evidence from key studies indicated that CVID patients exhibited a significantly perturbed oropharyngeal microbiota, characterized by lower alpha- and beta-diversity compared to healthy controls. The oropharyngeal microbiome of CVID patients showed a relative increase in the abundance of potentially pathogenic bacteria, including the order Lactobacillales and the family Streptococcaceae, alongside a decrease in protective species. Expansion of the genera Haemophilus and Anoxybacillus had been associated with acute respiratory infections occurring within six months. Low residual levels of IgA and IgM, age 45 years, chronic obstructive pulmonary disease (COPD), and antibiotic prophylaxis particularly azithromycin, had been identified as contributing factors to oropharyngeal dysbiosis. Radiographic lung disease in patients with primary antibody deficiencies had been associated with IgA deficiency and the expansion of distinct oropharyngeal bacterial taxa.

Conclusion: These findings support the potential role of oropharyngeal microbiome profiling as a non-invasive biomarker for risk stratification in CVID patients. However, the evidence base remains limited. Further studies with larger sample sizes are needed to validate these findings, and explore the role of the mycobiome and virome components.

keywords: Common Variable Immunodeficiency; Oropharyngeal Microbiome; Respiratory Infections; Dysbiosis; IgA Deficiency

PBa-201

Worldwide Prevalence of Chlamydia trachomatis in Infertile Women: A Systematic Review and Meta-analysis

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Background and aim: Chlamydia trachomatis (CT) infection is a prevalent sexually transmitted disease (STD). It seems that CT infections ascending to the uterus can result in serious reproductive health complications, including infertility. Therefore, this systematic review and meta-analysis was conducted to assess the worldwide prevalence of CT among infertile women.

Methods: A systematic search was conducted across three major databases, Medline (via PubMed), Web of Science, and Scopus, to identify eligible studies between 2010 and July 2025. Keywords such as “Chlamydia trachomatis,” “infertility,” “women,” and “prevalence “were used. The prevalence of CT among infertile women was estimated using random-effects model meta-analyses and reported with 95% confidence intervals (CIs). Subgroup analyses were conducted based on detection method and sample type. Meta-regression analysis was performed to evaluate the relationship between CT prevalence and either participants' age or year of publication.

Results: Thirty-eight studies, involving 14995 infertile women, were included in this study. The overall pooled prevalence of CT among infertile women was 24.1% (95% CI: 17.1–33.00). Regarding the diagnostic sample type, the highest prevalence of CT was observed in blood samples 45.7% (95% CI: 34.7–57.2), whereas the lowest was found in urine sample 10.8% (95% CI: 7.2–15.9). In terms of detection method, the highest prevalence of CT was reported using ELISA 26.9% (95% CI: 14.4–44.5), whereas the lowest prevalence was observed with the rapid test kit 7.9% (95% CI: 4–1.27). In endocervical samples, real-time PCR showed the highest prevalence among detection methods 20.5% (95% CI: 11.8–33.3) compared with other methods, indicating its high diagnostic sensitivity.

Conclusion: This finding indicates that the overall prevalence of CT among infertile women is relatively high, highlighting the importance of paying special attention to this pathogen in infertility assessments. Among diagnostic methods, ELISA showed the highest overall prevalence, while real-time PCR in endocervical samples demonstrated high diagnostic sensitivity, emphasizing its effectiveness for accurate detection in this sample type. Ultimately, routine and standardized CT screening in infertile women may facilitate early detection, timely intervention, and improved fertility outcomes.

keywords: Chlamydia trachomatis, Women Infertility, Prevalence, Sexually transmitted disease

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-202

Diagnostic Performance and Clinical Implementation of Rapid Molecular Assays for Detecting Carbapenemase-Producing Enterobacterales: A Systematic Review and Meta-Analysis

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Background and aim: Carbapenemase-producing Enterobacterales are among the most important multidrug-resistant pathogens and pose a major threat to infection control and antimicrobial stewardship. Conventional culture-based methods for detecting carbapenemase production are often time-consuming and may delay appropriate treatment and isolation measures. Rapid molecular assays can identify key carbapenemase genes, including KPC, NDM, OXA-48-like, VIM, and IMP, within a shorter diagnostic timeframe. This systematic review and meta-analysis aimed to evaluate the diagnostic performance and clinical applicability of rapid molecular assays for detecting carbapenemase-producing Enterobacterales in clinical laboratory settings.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, and Embase from database inception to June 2026 according to PRISMA guidelines. Eligible studies evaluated rapid molecular assays for detecting carbapenemase-producing Enterobacterales using clinical isolates or patient-derived specimens. Studies reporting sufficient data to calculate sensitivity, specificity, or related diagnostic accuracy measures were included. Two reviewers independently screened records, extracted data, and assessed methodological quality using QUADAS-2. Extracted variables included assay type, target carbapenemase genes, specimen source, reference standard, turnaround time, and diagnostic performance. When appropriate, pooled sensitivity, specificity, and summary receiver operating characteristic curves were estimated using diagnostic meta-analysis methods.

Results: Rapid molecular assays demonstrated high diagnostic performance for detecting major carbapenemase genes among Enterobacterales. Most studies reported excellent sensitivity and specificity for KPC, NDM, and OXA-48-like enzymes, while performance varied for less prevalent targets such as VIM and IMP. Cartridge-based PCR systems, multiplex PCR assays, and isothermal amplification methods showed reduced turnaround time compared with conventional phenotypic confirmation. These assays were particularly valuable for bloodstream infections, rectal screening, and infection control surveillance. However, diagnostic performance depended on local carbapenemase epidemiology, target gene coverage, specimen type, and reference standards. Limitations included heterogeneity in study design, incomplete detection of rare carbapenemase variants, and limited evidence regarding clinical outcome impact.

Conclusion: Rapid molecular assays provide accurate and timely detection of carbapenemase-producing Enterobacterales and may support earlier antimicrobial optimization, infection control interventions, and outbreak prevention. Their greatest value lies in settings with high AMR burden or urgent need for rapid resistance identification. Nevertheless, assay selection should consider local resistance epidemiology and target gene coverage. Further prospective studies are needed to evaluate cost-effectiveness, workflow integration, and the impact of rapid molecular detection on patient outcomes and antimicrobial stewardship.

keywords: Antimicrobial Resistance, Carbapenemase, Enterobacterales, Molecular Diagnostics, Rapid Testing

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-203

Phenotypic resistance and molecular evaluation of blaKPC gene in Pseudomonas aeruginosa clinical isolates

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Introduction: Carbapenemase-producing *P. aeruginosa* is one of the top priority pathogens responsible for treatment failures in cystic fibrosis, abscess and soft tissue infections. The study aimed to determine the Phenotypic resistance and molecular evaluation of blaKPC gene in *Pseudomonas aeruginosa* clinical isolates.

Materials and methods: In this study, samples had collected from admitted patients in 2 hospitals. Disk diffusion method was used to assess antimicrobial susceptibility. Minimum inhibitory concentration (MIC) values of Imipenem in carbapenem-resistant strains were determined using E-test strips. After phenotypical detection of *Pseudomonas aeruginosa*, *kpc* resistance gene detected in the strains by PCR assay.

Results: total 90 samples including blood samples were collected from patients. According to the results, 51% of the patients were male and 49% were female. The mean age of the patients was estimated to be 57 ± 15 years. The most prevalent carbapenemase were *bla-kpc* (11%, 8/90).

Conclusion: Adopting careful infection control approaches, rational antibiotic selection, and the use of molecular methods are recommended to inhibit the spread of resistant strains.

Key words: antimicrobial resistance, infection control, carbapenemase, PCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-204

Evaluation of antibiotic resistance and molecular identification of *blaSHV-1* resistance gene clinical isolates of *Acinetobacter baumannii* by PCR

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Introduction: The gram-negative bacterium *Acinetobacter baumannii* is a highly drug-resistant opportunistic pathogen that is the main cause of nosocomial infections worldwide. In recent years, the increasing prevalence of strains resistant to various antibiotics has limited the treatment of *A. baumannii* infections. Various studies have shown their role in increasing morbidity and mortality, particularly in patients with burns or hospitalization in the intensive care unit. In addition, it imposes a significant financial burden on the healthcare system. In this dissertation, we aimed to detect the resistance gene $bla_{\text{SHV-1}}$, by different phenotypic tests and molecular methods and determine genetic relatedness via the technique of *A. baumannii* isolates collected from patients, Tehran, Iran, and the resistance genes were evaluated.

Methods: A total of 70 *A. baumannii* isolates were identified by standard bacteriological tests, and antibiotic resistance was assessed using disc diffusion susceptibility testing (Kirby–Bauer disc). Phenotype-based methods included the combination disc test (CDT) for the expression of ESBL producer isolates and PCR primers were designed. The specificity of PCR was determined using *A. baumannii* and non-*Acinetobacter species*. Amplified DNA products were examined for ESBL-encoding gene ($bla_{\text{SHV-1}}$) PCR assays were used to detect resistance genes of isolates.

Results: Among the 70 isolates collected, all isolates that gave identified as *A. baumannii*, 85% were categorized as multidrug-resistant (MDR) and extensively drug-resistant (XDR) isolates. In the antibiotic susceptibility pattern, all isolates were 95% ceftazidime and imipenem resistant, and the most effective antibiotic was polymyxin B with 94% sensitivity. Based on the combined disc test, 25 % and 52% of isolates were Metallo-β-Lactamases (MBL) and Extended-Spectrum β-Lactamases (ESBL) producing isolates, respectively. The PCR assay could detect *A. baumannii* within (4 ng/µl) which was approximately 10-fold greater than that of the PCR assay. Regarding PCR products, (68%) of the isolates were $bla_{\text{SHV-1}}$ positive.

Conclusion: According to the findings in this study, PCR is a good and rapid technique that is more sensitive, robust, specific, and less time-consuming than culture for detecting *A. baumannii* in hospital facilities, aiding in optimal antibiotic therapy and outbreak control

Keywords: *Acinetobacter baumannii*, PCR, Resistance gene, Antibiotic resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-205

Phenotypic and Molecular Identification and Antibiotic Resistance Patterns of *Escherichia coli* Isolated from Urinary Tract Infections in Patients in Iraqi Hospitals

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Introduction: Asymptomatic bacteriuria can develop systematic UTI, and considered as an omen sign for the presence of urinary tract abnormalities. Community transmission of ESβL and carbapenemases producing multidrug resistant E. coli has increased progressively and considered important public health problem. Despite extensive efforts, the prevalence of UTIs remains high. This study aimed to Phenotypic and Molecular Identification and Antibiotic Resistance Patterns of Escherichia coli Isolated from Urinary Tract Infections in Patients in Iraqi Hospitals.

Methods: All samples taken with written consent was provided by all patients participating in the study. At morning period, specimens of midstream urine were collected from more than 500 patients of both sexes . Samples were collected from patients who attended Al-Ramadi Teaching Hospital and Al-Ramadi Hospital for Children & Maternity. All specimens were taken from March 2025 to May 2025. antibiotic resistance was assessed using disc diffusion susceptibility testing (Kirby–Bauer disc). Phenotype-based methods included the combination disc test (CDT) for the expression of ESBL producer isolates and the (imipenem + EDTA) test for the MBL phenotypic expression of the isolates. PCR primers were designed. Amplified DNA products were examined for ESBL-encoding genes (*bla*$_{SHV}$, *bla*$_{CTX}$).

Results: Among the isolates collectedPCR assays targeting extended-spectrum β-lactamase (ESBL) genes were performed. All isolates tested positive for the 16S rRNA gene, confirming their identification as E. coli. Screening for ESBL genes revealed the presence of blaCTX-M in 100% of isolates and blaSHV in 85% of isolates. The coexistence of both genes was detected in 70% of isolates, suggesting a high burden of multidrug resistance.
Conclusion: This dissertation revealed a high prevalence of antibiotic resistance among *E. coli* isolates. Also, this dissertation showed that the main determinants of genotypic drug resistance are *bla*$_{SHV}$, *bla*$_{CTX}$ among patients . According to the findings in this study, these findings emphasize the need for better understanding the genetic makeup of *E. coli* in UTIs, aiding in the development of diagnostic and treatment strategies.

Keywords: *E. coli*, Resistance gene, Antibiotic resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBa-206

Molecular Multiplex Detection of *Escherichia coli, Klebsiella pneumoniae, and Acinetobacter* in Clinical Isolates by PCR

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Introduction: Bacterial infections caused by pathogens such as Escherichia coli, Klebsiella pneumoniae, and *Acinetobacter* are considered major problems in hospitals, as they can lead to serious healthcare-associated infections that increase both mortality rates and treatment costs. Most laboratories still rely on traditional culture methods for diagnosis, but these methods are time-consuming and sometimes lack sensitivity, especially in mixed infections or when patients have already received antibiotics. For this reason, molecular techniques such as multiplex PCR have gained much attention, since they allow the detection of several bacterial species at the same time with higher accuracy and in a shorter period. This study aims to develop and evaluate a multiplex PCR assay for the rapid detection of *E. coli*, *Klebsiella pneumoniae*, and *Acinetobacter* spp. isolated from clinical samples collected from local hospitals.

Materials and methods: These bacteria are leading causes of healthcare-associated infections with rising antibiotic resistance worldwide. Traditional culture methods for their identification are time-consuming and may delay appropriate treatment. The multiplex PCR technique offers a rapid, sensitive, and specific molecular diagnostic approach that can identify multiple bacteria in a single PCR reaction. Clinical Isolates will be collected, DNA extracted, and multiplex PCR optimized using species-specific primers. The assay's sensitivity, specificity, and reproducibility will be evaluated against conventional culture and biochemical techniques.

Results: total samples including blood samples were collected from patients. According to the results, 63% of the patients were male and 37% were female. The mean age of the patients was estimated to be 65 ± 23 years. The most prevalent bacteria were Acinetobacter (71%).

Conclusion: Adopting careful infection control approaches, rational antibiotic selection, and the use of molecular methods are recommended to inhibit the spread of resistant strains. The expected outcome is a cost-effective, high-throughput multiplex PCR assay that will significantly decrease pathogen Identification time and improve clinical management of bacterial Infections. This method will support timely administration of targeted antimicrobial therapy and help reduce the spread of resistant strains in healthcare settings. The innovation lies in integrating molecular diagnostics capable of identifying multiple bacteria concurrently from clinical isolates, which has not been widely implemented in the region. This advancement enhances early detection, facilitates timely targeted treatment, and contributes to better infection control and antibiotic stewardship in healthcare settings.

Key words: antimicrobial resistance, infection control, *Klebsiella pneumoniae, Acinetobacter*, PCR

PBa-207

Molecular detection of class D carbapenemase gene (blaOXA-48) in Pseudomonas aeruginosa clinical isolates by PCR

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Introduction: *Pseudomonas aeruginosa* is an aerobic bacterial pathogen that has raised global environmental, clinical, and public health concerns. Today, the emergence and spread of carbapenem-resistant strains has created a serious clinical threat in healthcare systems. Carbapenemases, especially class D, play a role in this type of resistance. Therefore, this study was conducted to investigate the antibiotic resistance profile, prevalence of carbapenemase genes in clinical isolates of *Pseudomonas aeruginosa*, and to determine the epidemiological characteristics of carbapenemase-producing *P. aeruginosa*.

Methods: 80 clinical isolates of *P. aeruginosa* were collected from different departments of two hospitals, in Tehran. Identification of isolates was performed using common microbiology methods. Disk diffusion method was used to assess antimicrobial susceptibility. Minimum inhibitory concentration (MIC) values of imipenem in carbapenem-resistant strains were determined using E-test strips. Polymerase chain reaction (PCR) was used to identify the virulence factor class D (*bla*OXA-48).

Results: According to the results, 62% of the patients were male and 38% were female. The mean age of the patients was estimated to be 48 ± 21 years. The highest frequency was observed in urine samples (33%) and sputum (18%), in internal medicine (26%). The highest resistance rate to antibiotics was imipenem (62.7%). MDR phenotype was observed in 58% of cases. Using the E-test strip, 78.9% of the isolates were resistant to imipenem. The prevalence of *blaOXA*-48 metallocarbapenases in the isolates was reported to be 1%respectively.

Conclusion: Adopting careful infection control approaches, rational antibiotic selection, and the use of molecular methods are recommended to inhibit the spread of resistant strains.

Keywords: *Pseudomonas aeruginosa*, Carbapenemase, *bla*OXA-48.

PBi-1

Anti- Glutamic acid decarboxylase Antibody(Anti-GAD-Ab) in type 1 diabetic patients

Dr. Jabbari Javad [1] © ℗

[1] **Health insurance**

Background and aim: Introduction: Glutamic acid decarboxylase (GAD) catalyzes the conversion of glutamic acid to γaminobutyric acid (GABA). GAD65 isozyme is present in the pancreatic ß-cells. In the prediabetes period and during the ß-cell destruction, GAD is released as an autoantigen and anti-GAD autoantibodies appear in serum. Islet Cell Autoantibodies(ICAs) including anti-GAD are detectable in serum of diabetic patients up to 10 years before appearance of diabetes symptoms. This is an important predictive marker for diagnosis of prediabetic patients, especially in the first-degree relatives of diabetic patients for genetic factors. Anti-GAD is an important marker for detection of ß-cells destruction. The patients with

Methods: This survey is a case-control study aimed at detection of anti-GAD presence in sera of type 1 diabetic patients and their first-degree relatives and comparison with healthy individuals. Fifty type 1 diabetic patients with mean age of 10.5 ± 5.2 years and mean disease duration of 24 months, 35 first-degree relatives and 50 normal individuals without familial diabetes were included in the study; all the individuals were chosen by a random sampling method. The values of fasting blood sugar were determined in firstdegree relatives and controls and all were found to be normal. The values of anti-GAD were determined by ELISA method.

Results: Median values of anti-GAD in cases and controls were 28, (range: 5-2700) ng/ml and 2, (0-10) ng/ml, respectively. The anti-GAD titers were significantly higher in patients than in normal individuals and relatives together (p0.0001) Median value of anti-GAD in first-degree relatives was 6, (0-950) ng/ml. There was a significant statistical difference between anti-GAD titers in first-degree relatives and controls, (p0.01). There was a significant difference between mean value of age and diabetes duration in anti-GAD positive and anti-GAD negative patients, (p0.05). There was a negative correlation between anti-GAD and age, diabetes duration, disease beginning age of patients, (r= 0.30) respectively.

Conclusion: By increasing of anti-GAD in diabetic patients and their first-degree relatives it may be concluded that measurement of anti-GAD is an important and beneficial tool for detection and diagnosis of prediabetic and diabetic patients.

keywords: Glutamic acid decarboxylase, Anti-GAD, Diabetes, ICA S.

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July 20-23, 2026

PBi-2

Association of Omentin rs2274907 and FTO rs9939609 gene polymorphisms with insulin resistance in Iranian individuals with newly diagnosed type 2 diabetes

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Background and aim: Insulin resistance (IR) and fat accumulation in visceral adipose tissue are key players in developing type 2 diabetes (T2D). Several adipose tissue derived-gene polymorphisms are related to higher body mass index (BMI), insulin resistance and T2D. The association of omentin rs2274907 (Val109Asp) and fat-mass and obesity associated (FTO) rs9939609 gene polymorphisms with overweight/obesity and T2D is controversial. The aim of this study was to determine the association between omentin Val109Asp and FTO rs9939609 polymorphisms and insulin resistance in newly-diagnosed T2D patients.

Methods: The case-control study included 83 newly-diagnosed T2D patients and 85 healthy matched controls, aged 20–80 years. Fasting blood glucose and insulin levels were measured by the enzymatic method and enzymelinked- immunosorbent assay, respectively. Insulin resistance was calculated using the homeostasis model assessment (HOMA) index. Genotyping was examined using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

Results: There are significant differences between both omentin Val109Asp and FTO rs9939609 polymorphisms and studied individuals (P = 0.011 and P = 0.0001, respectively). Both genetic polymorphisms of omentin Val109Asp and FTO rs9939609 (T/A) are significantly related to higher HOMA index (P = 0.030 and P = 0.046, respectively). However, omentin Val109Asp polymorphism was only related to individuals who were overweight/obese. Additionally, both omentin Val109Asp and FTO rs9939609 polymorphisms were significantly positively correlated to familial history of diabetes (P = 0.046 and P = 0.024, respectively).

Conclusion: Omentin V109D and FTO rs9939609 genetic variations may change insulin metabolism and have key roles in developing T2D through insulin resistance. Thus, the evaluation of these polymorphic regions may be helpful for predicting type 2 diabetes.

keywords: Type 2 diabetes, Insulin resistance, Omentin, Fat mass-and obesity associated

PBi-3

Association between serum vitamin D levels and lipid profiles: a cross-sectional analysis

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Background and aim: Vitamin D is an essential nutrient that plays a crucial role in calcium homeostasis and bone health. Recent research suggests that vitamin D may also have an impact on lipid metabolism, specifically the level of circulating lipids in the blood. We aim to investigate it role among healthy participate. We conducted a cross-sectional study of 15,600 patients who were referred to the laboratories of university hospitals.

Methods: We measured the serum levels of Vitamin D as well as triglycerides, total cholesterol, LDL, and HDL using ELISA.

Results: We found that the mean serum level of Vitamin D was 40.31 ± 20.79 ng/mL. Of the participants, 16.7% had a serum level of Vitamin D less than 20 ng/mL, 57.7% had a level between 21 and 40 ng/mL, and 13.5% had a level between 41 and 60 ng/mL. Additionally, 12.2% had a level greater than 60 ng/mL. We performed a one-way analysis of variance and found that as the serum level of Vitamin D increased, the mean LDL level decreased significantly.

Conclusion: Our study provides evidence of a significant relationship between serum levels of Vitamin D and LDL levels in patients. The findings suggest that vitamin D status may play a role in regulating lipid metabolism and may have implications for the prevention and treatment of cardiovascular disease. Further research is needed to elucidate the underlying mechanisms of this relationship and to determine optimal levels of vitamin D intake for maintaining lipid profiles.

keywords: Vitamin D, HDL, LDL, Lipid Profile

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBi-4

Horseshoe kidney with teratoid type of Wilms tumor: a rare case report

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Background and aim: Horseshoe kidney is the most common renal fusion anomaly, and Wilms tumor is the most frequent renal malignancy in children. The occurrence of Wilms tumor in association with horseshoe kidney is a scarce anomaly. However, the arising of a teratoid type, which is a rare variant of Wilms tumor in a horseshoe kidney, is exceptionally unique.

Methods: This report presents a 5-year-old male admitted with horseshoe kidney involved by a large heterogeneous calcified mass that was diagnose on biopsy as Wilms tumor blastemal dominant.

Results: According to the local and regional extension and metastatic tumor in the lungs, the patient underwent neoadjuvant chemotherapy and then surgery. Post-operative pathologic findings confirmed the diagnosis of teratoid Wilms tumor.

Conclusion: The occurrence of renal anomalies associated with a malignancy might be more frequent in the clinical environment. There are numerous differential diagnoses for renal tumors and masses, but the possibility of exceptional anomalies should not be denied, and clinicians should be prepared for these occasions. Although studies propose that chemotherapy has a trivial effect on teratoid Wilms tumors, it is essential to evaluate the tumor for any possibility of regression in non-teratoid regions before proceeding to upfront tumoral resection.

keywords: Wilms tumor, Teratoid, Horseshoe kidney, Pediatrics

PBi-5

Therapeutic Outcomes of EGF/EGFR-Directed Cancer Vaccines in EGFR-Driven Solid Malignancies: A Systematic Review

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Background and aim: Dysregulation of the epidermal growth factor (EGF)/epidermal growth factor receptor (EGFR) axis is a central driver of progression in various solid tumors. Although EGFR-targeted tyrosine-kinase inhibitors and monoclonal antibodies have advanced treatment strategies, their durable benefit is often limited by resistance mechanisms and cumulative toxicities. Over the last decade, therapeutic vaccines targeting EGF or EGFR have emerged as a promising approach to generate long-lasting immune responses, either by depleting circulating EGF or inducing EGFR-specific cellular immunity. This systematic review evaluates clinical outcomes of EGF/EGFR-directed cancer vaccines in EGFR-driven solid tumors published between 2015 and 2025.

Methods: A comprehensive search of PubMed and Google Scholar (January 2015–March 2025) identified phase I–IV clinical trials investigating EGF- or EGFR-targeted vaccines including CIMAvax-EGF, EGF-CRM197, and various EGFR peptide or neoantigen vaccines in adults with EGFR-driven solid tumors. Eligible studies reported survival, clinical response, immunogenicity, or safety outcomes. Two reviewers screened articles, extracted data, and synthesized findings using a qualitative comparative approach.

Results: Seventeen clinical studies involving about 1,800 patients met criteria. In advanced non–small cell lung cancer (NSCLC), EGF-depleting vaccines used as maintenance therapy consistently improved overall survival compared with supportive care alone. Long-term survival rates of 14–20% at 3–5 years were observed in patients with elevated baseline EGF and strong vaccine-induced antibody responses. Combination strategies particularly CIMAvax-EGF with PD-1 inhibitors showed encouraging activity, achieving one-year overall survival rates of 80–85% and disease-control rates near 90%, with signals of benefit even in subsets with EGFR-mutant tumors. Early-phase trials of recombinant EGF-CRM197 and EGFR-directed peptide or neoantigen vaccines produced robust humoral and cellular responses, with durable disease stabilization in some heavily pretreated patients. In glioblastoma, several studies reported survival outcomes surpassing historical expectations. Across trials, adverse events were mostly mild (grade 1–2), and no major safety concerns emerged.

Conclusion: Over the past decade, EGF/EGFR-directed cancer vaccines have progressed from experimental concepts to clinically meaningful therapeutic candidates. Their favorable safety profiles, durable immunogenicity, and synergy with immune checkpoint inhibitors highlight their potential role in the evolving management of EGFR-driven solid tumors. Further randomized trials, biomarker-guided patient selection, and earlier integration into treatment strategies remain essential to define their clinical impact.

keywords: CIMAvax-EGF, NSCLC, Cancer

PBi-6

Health-Related Quality of Life Outcomes with CDK4/6 Inhibitors in Metastatic Breast Cancer: Systematic Review

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Background and aim: CDK4/6 inhibitors have reshaped the therapeutic landscape of hormone receptor–positive, HER2-negative metastatic breast cancer (HR+/HER2– MBC), offering consistent improvements in progression-free survival and, increasingly, overall survival. For patients living with metastatic disease—often for many years—the impact of therapy on health-related quality of life (HRQoL) is as critical as tumor control. As treatment options and sequences become more complex, understanding how CDK4/6 inhibitors influence daily functioning, symptom burden, and overall well-being has become essential for clinical decision-making. This systematic review synthesizes HRQoL outcomes reported in clinical trials and real-world studies published between 2015 and 2025.

Methods: A structured search of PubMed, web of science and Embase (January 2015–March 2025) identified phase II–III trials and observational studies evaluating HRQoL in adults receiving palbociclib, ribociclib, or abemaciclib for HR+/HER2– MBC. Eligible studies used validated HRQoL tools such as EORTC QLQ-C30, QLQ-BR23, FACT-B, and EQ-5D. Two reviewers independently screened articles, extracted data, and performed a qualitative synthesis of HRQoL trends, functional outcomes, symptom progression, and patient-reported tolerability.

Results: Twenty-one studies involving more than 6,500 patients met inclusion criteria. Across pivotal randomized trials, CDK4/6 inhibitors combined with endocrine therapy maintained or improved global HRQoL compared with endocrine therapy alone, despite increased hematologic and gastrointestinal toxicities. Ribociclib-based regimens showed consistent benefits in emotional functioning and pain reduction, while abemaciclib often improved physical and role functioning due to delayed progression. Patient-reported outcomes highlighted that delaying symptomatic deterioration especially fatigue, pain, and breast-specific symptoms was a major contributor to better HRQoL. Real-world evidence supported these findings, demonstrating that adherence, tolerability, and manageable toxicity correlated with stable or improved HRQoL over time. Dose reductions common with palbociclib and abemaciclib did not appear to compromise HRQoL or perceived treatment benefit.

Conclusion: Evidence from the last decade consistently shows that CDK4/6 inhibitors not only extend survival but also preserve or enhance quality of life for patients with metastatic breast cancer. Their ability to delay symptomatic progression, maintain daily functioning, and provide durable disease control underscores their value as a central component of HR+/HER2– MBC management. Future research should prioritize long-term survivorship, real-world patient-experience metrics, and personalized toxicity-management strategies to optimize HRQoL outcomes.

keywords: CDK4/6 inhibitors, Oncology, Breast, HRQoL

PBi-7

The effect of ferulic acid on reducing cyclosporine-induced myocardial injury by modulating oxidative stress and inflammatory responses

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Background and aim: Cyclosporine is one of the key and widely used drugs in clinical settings, such as organ transplantation and the treatment of certain autoimmune diseases. By inhibiting cellular immunity, this drug significantly reduces the risk of graft rejection and contributes to prolonging the survival of transplant patients. Despite its high clinical efficacy, long-term use of cyclosporine is associated with multiple adverse effects, including cyclosporine-induced cardiac injury.

Methods: The study was conducted in two short-term and long-term phases. , 48 adult male Wistar rats were allocated into six groups. G 1 (control) received vehicle by gavage for 7 days in the short-term phase and for 21 days in the long-term phase. G 2 (cyclosporine alone) received cyclosporine by gavage for 7 days at a dose of 50 mg/kg body weight (bw) in the short-term phase and 21 days at 25 mg/kg bw in the long-term phase. G 3 (ferulic acid alone) received ferulic acid by gavage for 7 days in the short-term phase and 21 days in the long-term phase at a dose of 100 mg/kg bw. G 4, 5, and 6 received ferulic acid at doses of 25, 50, and 100 mg/kg bw, respectively, by gavage after exposure to cyclosporine in both the the short-term and long-term phases.

Results: The second group exposed to cyclosporine caused a significant increase (p0.05) in the levels of serum biochemical factors (CK MB, AST) (Figures 1 and 2), significant changes (p0.05) in oxidative stress markers (MDA) (Figure 3), and a significant decrease (p0.05) in the level of antioxidant enzyme activity (SOD) (Figure 4) and increased NF-kB expression (Figure 5) compared to the control group. In the groups treated with ferulic acid, especially in the long-term phase of the study, a significant improvement (p0.05) was observed in all the above factors compared to the group receiving cyclosporine alone.

Conclusion: The results of the present study showed the clinical value of ferulic acid for improving cyclosporine-induced damage by restoring the balance of the redox system through increasing the activity of the antioxidant system and suppressing inflammatory responses by reducing the expression of NF-KB.

keywords: Cyclosporine, Oxidative Stress, Ferulic Acid, Inflammation

PBi-8

Cytological and Biochemical Evaluation of Canine Multicentric Lymphoma: A Case Report

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Background and aim: lymphoma is a neoplasia of lymphoid cells that occurs in tissues and organs outside the bone marrow. The diagnosis of multicentric lymphoma in dogs often involves a combination of cytological evaluation and various laboratory tests. Early detection and accurate classification of the disease are essential for establishing an effective treatment plan and improving the prognosis of affected animals. The disease primarily affects middle-aged animals, although it can also occur in younger ones. According to anatomical classification, lymphomas are divided into multicentric, alimentary, mediastinal, cutaneous, and miscellaneous types. The multicentric form is the most common in dogs, involving multiple lymph nodes

Methods: The13 years old dog was brought to the veterinary faculty for biochemical and hematology testing. Blood samples were collected, and a sample was also taken from the enlarged lymph node for cytological examination. In the initial assessment, the dog had no significant medical history, except for a pyometra surgery performed in May. The swelling had started about one week prior to presentation, and the dog had been overweight since the age of three.

Results: According to the cytology results, the presence of lymphoma was confirmed through microscopic examination. In addition, based on the biochemical findings, both ALP and calcium levels were elevated. In this case, the increased calcium level may be due to lymphoma- associated secondary hyperparathyroidism

Conclusion: This case emphasizes the diagnostic value of integrating clinical findings with cytological and biochemical analyses for the accurate identification of canine lymphoma. Cytology confirmed the disease, while elevated ALP and calcium levels supported lymphoma-associated metabolic changes, highlighting the importance of early detection for improving prognosis.

keywords: Cytological ,Biochemical,Canine Multicentric Lymphoma,Case Report

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-9

Emerging insights into the PI3K/AKT/mTOR signaling pathway and non-coding RNA-mediated drug resistance in glioblastoma

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Background and aim: Glioblastoma (GBM) the aggressive form of adult brain cancer impacts about 3.2 per 100,000 individuals each year in the US accounting for nearly 50% of malignant brain tumors. Although treatment includes surgery, radiation and temozolomide (TMZ) the median survival time is 12–15 months with than 10% surviving five years largely because of late diagnosis and resistance, to TMZ. Current research emphasizes the role of miRNAs in promoting GBM advancement and TMZ resistance, through disruption of the PI3K/AKT/mTOR signaling pathway. This systematic review examines miRNA regulation of this pathway in GBM and its link to TMZ resistance, identifying potential biomarkers and

Methods: PubMed, Scopus, and Web of Science were utilized to locate research articles published until 2025 investigating the impact ofnbmiRNAs on the PI3K/AKT/mTOR signaling pathway and their role in chemotherapy resistance in glioblastoma (GBM). In addition to laboratory experiments (in vitro), animal models (in vivo), and real-world clinical studies involving patients, we identified a wide range of research. To ensure relevance and quality, each study was evaluated against a set of predetermined criteria. The data was then extracted, followed by a qualitative synthesis to identify key patterns, mechanisms, and potential implications for improving treatment outcomes.

Results: Our analysis of research indicates that abnormalities in the PI3K/AKT/mTOR pathway strongly promote glioblastoma cells to proliferate, endure, and resist temozolomide. We identified microRNAs functioning as crucial "switches" within this pathway: some function as oncogenic, driving tumor progression, whereas others serve as tumor suppressors that typically maintain control. When these miRNAs are present in amounts, they interfere with vital processes, such as apoptosis, DNA repair, and cell cycle regulation—eventually enabling tumors to withstand treatment. Taken together, the evidence clearly points to these miRNA-pathway interactions as a major reason why current therapies so often fail, leaving patients with few options and highlighting an urgent need for new approaches targeting these molecules.

Conclusion: The review notes that microRNAs play a pivotal role in hijacking the PI3K/AKT/mTOR pathway, helping glioblastoma tumors resist temozolomide and continue to grow despite treatment. By targeting these microRNAs, we could develop new therapies that restore sensitivity to chemotherapy.

keywords: Glioblastoma; PI3K/AKT/mTOR; chemotherapy.; lncRNA; miRNAs; temozolomide.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-10

Evaluation of the Effects of Capparis spinosa Extract on Carbon Tetrachloride–Induced Liver Fibrosis via the Inflammatory NLRP3 Signaling Pathway in Male BALB/c Mice

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Background and aim: Liver fibrosis is a progressive consequence of chronic liver injury and sustained inflammation that may ultimately lead to cirrhosis. The NLRP3 inflammasome has been identified as a key mediator in hepatic inflammation and fibrogenesis. Capparis spinosa is a medicinal plant with documented anti-inflammatory and antioxidant properties. This study aimed to evaluate the effects of Capparis spinosa extract on carbon tetrachloride (CCl_4)-induced liver fibrosis through modulation of the NLRP3 inflammatory signaling pathway.

Methods: Male BALB/c mice were randomly allocated into control, CCl_4-treated, and CCl_4 plus Capparis spinosa extract–treated groups. Liver fibrosis was induced by intraperitoneal administration of CCl_4 for several weeks. The extract was administered orally during the experimental period. At the end of the treatment, liver tissues were collected for histopathological evaluation and molecular analyses. The expression levels of NLRP3, IL-1β, caspase-1, α-SMA, and collagen type I were assessed using RT-PCR and western blotting.

Results: CCl_4 administration significantly increased liver fibrosis, inflammatory responses, and expression of NLRP3 inflammasome components compared with the control group. Fibrotic markers, including α-SMA and collagen type I, were also markedly elevated. Treatment with Capparis spinosa extract resulted in a noticeable reduction in histopathological fibrosis and inflammatory infiltration. Furthermore, the expression of NLRP3, IL-1β, caspase-1, and fibrotic markers was significantly decreased in extract-treated groups compared with the CCl_4 group (P 0.05).

Conclusion: The findings indicate that Capparis spinosa extract attenuates CCl_4-induced liver fibrosis, possibly through inhibition of the NLRP3 inflammatory signaling pathway. This plant extract may represent a promising therapeutic strategy for liver fibrosis.

keywords: liver fibrosis. Capparis spinosa. NLRP3

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-11

Evaluation of the Effects of Nano-Quercetin on Liver Fibrosis via Regulation of the Hippo/YAP Signaling Pathway in a CCl_4-Treated Mouse Model

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Background and aim: Liver fibrosis is a dynamic process caused by chronic liver injury and excessive accumulation of extracellular matrix, which may progress to cirrhosis. The Hippo/YAP signaling pathway plays a pivotal role in hepatic stellate cell activation and fibrogenesis. Nano-formulation of quercetin has been developed to enhance its stability and biological activity. This study aimed to investigate the effects of nano-quercetin on carbon tetrachloride (CCl_4)-induced liver fibrosis through modulation of the Hippo/YAP signaling pathway in a mouse model.

Methods: Liver fibrosis was induced by intraperitoneal injection of CCl_4 for several weeks. Nano-quercetin was administered during the treatment period. At the end of the experiment, liver tissues were collected for histopathological examination and molecular analyses. The expression levels of fibrosis-related markers, including α-SMA and collagen type I, as well as key components of the Hippo/YAP pathway such as YAP and phosphorylated YAP, were evaluated using RT-PCR and western blot techniques

Results: CCl_4 treatment significantly increased hepatic fibrosis, collagen deposition, and expression of α-SMA compared with the control group. In addition, activation of the Hippo/YAP pathway was evident by elevated YAP expression in fibrotic livers. Nano-quercetin significantly modulated the Hippo/YAP pathway, as demonstrated by decreased YAP expression and increased YAP phosphorylation compared with the CCl_4 group (P 0.05).

Conclusion: The present findings suggest that nano-quercetin exerts protective and anti-fibrotic effects against CCl_4-induced liver fibrosis, possibly through regulation of the Hippo/YAP signaling pathway. Nano-quercetin may therefore represent a promising therapeutic approach for liver fibrosis.

keywords: Liver Fibrosis .Hippo/YAP .Nano-Quercetin .CCl_4

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
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PBi-12

Systemic MMP-2 and MMP-9 Gene Expression in Diabetic Retinopathy

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Background and aim: Diabetic retinopathy(DR), a major cause of vision impairment, involves matrix metalloproteinases(MMP-2/9) in blood-retinal barrier breakdown and pathological angiogenesis. However, their systemic alterations in peripheral blood and response to intravitreal bevacizumab therapy remain poorly understood. This study investigates MMP-2/9 gene expression in peripheral blood as potential non-invasive biomarkers for early DR diagnosis and evaluates the systemic molecular impact of bevacizumab.

Methods: Peripheral blood samples were collected from DR patients at pre-injection and at 1-month and 3-month follow-ups after Intravitreal Bevacizumab(IVB) injection, also from Diabetic Patients without Retinopathy(non-DR) and a Healthy Control(HC). Gene expression of MMP-2/9 was quantified by SYBR Green qRT-PCR.

Results: MMP-9 gene expression was significantly higher in DR patients compared to both DM-noDR and HC(P 0.001). After bevacizumab treatment, MMP-2/9 gene expression in DR patients have decreased significantly at both IVB-1M and IVB-3M(P 0.05 and P 0.001, respectively). Biomarker analysis indicated that MMP-9 hase potential utility for early detection of DR. The result of Receiver Operating Characteristic(ROC) analysis showed that the AUC for MMP-9 was 0.888.

Conclusion: This study provides novel insights into the systemic upregulation of MMP-9 in DR and its potential as a non-invasive biomarker for early diagnosis. The significant reduction of MMP-2/9 following bevacizumab treatment highlights its systemic anti-inflammatory effects, offering new perspectives on therapeutic mechanisms and potential targets for DR management.

keywords: Diabetic retinopathy, Bevacizumab, Angiogenesis, MMP-2, MMP-9

PBi-13

Evaluating the Incidence, Risk Factors, and Diagnostic Limitations of Transient Neonatal Tyrosinemia in Iranian Newborns

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Background and aim: Transient Neonatal Tyrosinemia (TNT) is a benign, self-limiting disorder characterized by elevated blood tyrosine levels in neonates. It is often caused by immature hepatic enzymes, particularly 4-hydroxyphenylpyruvate dioxygenase (4- HPPD), and may be influenced by factors such as prematurity, low birth weight, and high protein intake. Early detection via newborn screening is essential to differentiate TNT from more serious disorders such as tyrosinemia type I. The aim of this study is to determine the incidence of TNT and identify perinatal factors associated with its development in Iranian neonates.

Methods: This retrospective case-control study reviewed newborn screenings performed at the Growth and Development Research Center's metabolic laboratory between March 2019 and February 2023. The control group comprised newborns with normal metabolic screening results during the study period.

Results: Metabolic screenings were conducted on 73,349 infants. The incidence of TNT was found to be 0.47%, corresponding to a total of 345 diagnosed cases. TNT infants had a lower gestational age (37.7 ± 1.4 weeks), lower birth weight (2.94 ± 0.5 kg), and a higher rate of cesarean deliveries (83.9%) compared to the control group (P 0.05). Logistic regression analysis showed significant associations between TNT and preterm birth (OR: 868.2, 95% CI: 168.9–4212.7, P 0.001), cesarean delivery (OR: 3.5, 95% CI: 2.26–5.3, P 0.001), and gestational age (OR: 0.17, 95% CI: 0.12–0.24, P 0.001). No significant association was found with other parameters (P ≥ 0.05).

Conclusion: TNT incidence in Iranian newborns is associated with prematurity and cesarean delivery. Optimizing screening protocols and encouraging vaginal delivery when possible may reduce TNT rates.

keywords: Transient Neonatal Tyrosinemia, Neonatal Screening, Newborn, Cesarean Section, Premature Birth,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-14

The effect of aqueous Stevia rebaudiana extract and clomiphene citrate on the expression of GDF9, PTEN, BMP15 genes, and antioxidant levels in a letrozole-induced polycystic ovary syndrome model in Wistar rats

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Background and aim: This study investigates the individual and combined effects of aqueous Stevia rebaudiana extract (SAE) and clomiphene citrate (Clom) on the expression of key ovarian regulatory genes -growth differentiation factor 9 (GDF9), phosphatase and tensin homolog (PTEN), and bone morphogenetic protein 15 (BMP15)- as well as on antioxidant enzyme activities in a letrozole-induced polycystic ovary syndrome (PCOS) model in adult female Wistar rats

Methods: The estrous cycles of 50 rats were monitored and randomly divided into five groups of 10 rats each. The control group received carboxymethyl cellulose, while the remaining groups were administered letrozole (1 mg/kg) for 21 days to induce PCOS. From day 22 onward, the treatment groups received SAE (400 mg/kg), Clom (100 mg/kg), or their combination for 28 days. Gene expression levels of GDF9, BMP15, and PTEN were analyzed using real-time PCR, and antioxidant levels were assessed using diagnostic kits. Data were analyzed using SPSS software (version 21) with one-way ANOVA followed by Tukey's post hoc test

Results: Treatments with SAE and Clom restored normal estrous cycles. Significant differences in gene expression were observed: PTEN levels were higher in the control group compared to SAE and combined groups, while GDF9 and BMP15 were elevated in the PCOS group compared to controls. SAE and Clom treatments also significantly increased superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities in ovarian tissues. The combined SAE and Clom therapy demonstrate potential as an effective strategy to manage PCOS by regulating ovarian gene expression and oxidative stress.

Conclusion: The results indicate that treatment with SAE and Clom can restore natural estrous cycles in mice with PCOS. Additionally, these treatments are associated with a decrease in PTEN levels and an increase in the expression of the genes GDF9 and BMP15. Furthermore, the activity of the enzymes SOD and GPx in ovarian tissues is elevated, indicating the positive impact of this combined therapy on oxidative stress.

keywords: Polycystic ovary syndrome, Wistar rats, Gene expression, Antioxidants, Stevia rebaudiana,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-15

Dual-functional materials (catalysts and adsorbents) as innovative and sustainable pathways toward combined healthcare (antibacterial, antifungal, antiviral, antioxidant, and anticancer properties) and water pollution remediation

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Background and aim: Cancer remains a significant global health concern despite recent advancements in medicine and pharmaceuticals. Also, water contamination caused by various microorganisms, including bacteria and industrial dyes, significantly contributes to cancer prevalence and microbial diseases among populations. This review focuses on multifunctional nanomaterials—particularly photocatalysts, adsorbents, and catalysts—that possess dual abilities in both healthcare (antibacterial, antifungal, antiviral, anti-corona virus, antioxidant, and anticancer) and environmental pollutant removal. The emergence of nanotechnology, especially through nanoparticles and metal-organic frameworks (MOFs), offers innovative strategies for addressing these two domains. These materials not only improve the effectiveness of cancer therapies but also serve as agents for water

Methods: This review was conducted through a comprehensive review of the scientific literature focusing on multifunctional nanomaterials with dual applications in healthcare (anticancer and antibacterial) and environmental remediation. Relevant peer-reviewed articles were collected from major scientific databases including Web of Science, Scopus, PubMed, and ScienceDirect. The literature search covered recent years to capture current advances in nanotechnology, with a particular emphasis on nanoparticles and metal-organic frameworks (MOFs).

Results: These nanomaterials act as anticancer agents through mechanisms such as reactive oxygen species (ROS) generation, drug delivery, and photothermal activity, while also providing the potential to adsorb or degrade environmental pollutants such as dyes, heavy metals, and pathogens. However, despite the growing interest, real-world applications are limited due to challenges such as toxicity, biocompatibility, reproducibility, and lack of clinical data. Interdisciplinary research and advanced characterization methods are essential to overcome these obstacles.

Conclusion: This review highlights the emerging significance of dual-functional nanomaterials in addressing two of today's most critical challenges: health (antibacterial, antifungal, antiviral, anti-corona virus, antioxidant, and anticancer) and environmental pollution. Materials such as photocatalysts, MOFs, and multifunctional nanoparticles exhibit promising capabilities in both domains due to their tunable structures, high surface area, and reactivity. These materials act as anticancer agents through mechanisms like ROS generation, drug delivery, and photothermal activity, while also enabling the adsorption or degradation of environmental contaminants such as dyes, heavy metals, and pathogens.

keywords: Cancer, Anticancer,Bacteria and Antibacterials , Dual functional materials, Water pollutant

PBi-16

Gut Microbiota: A Key Mediator in Novel Dietary Approaches for Obesity Management

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Background and aim: Obesity is a widespread metabolic condition that demands novel dietary approaches. Dietary patterns with structured periods of reduced energy have been shown to influence gut microbiota and restore metabolic balance. This narrative review explores the role of time-restricted eating on the microbiota-driven mechanisms involved in the obesity pathophysiology.

Methods: This narrative review draws on literature published between 2018 and 2024, identified through comprehensive searches on Google Scholar and PubMed. Keywords used included gut microbiota, microbiome, obesity, dietary interventions, time-restricted eating, intermittent fasting, energy-restriction patterns, meal timing, and microbiota-mediated weight regulation. Studies were selected based on their focus on diet-induced changes in the gut microbiota and the resulting metabolic outcomes relevant to obesity.

Results: Dietary patterns involving time-restricted eating, promote beneficial shifts in the gut microbiota, offering a mechanistic basis for their potential in obesity management. Enrichment of taxa such as Akkermansia muciniphila, Bacteroidetes, and short-chain fatty acids (SCFAs)–producing bacteria contributes to multiple pathways relevant to metabolic health, especially in obesity. These microbes reinforce intestinal barrier function by enhancing epithelial integrity and reducing gut permeability, thereby mitigating metabolic endotoxemia. They also stimulate adipose tissue browning, promoting the conversion of white adipocytes into thermogenically active beige and brown phenotypes, which elevates energy expenditure. Concurrently, they modulate immune function by dampening chronic low-grade inflammation and balancing innate and adaptive immune responses. Additional effects include regulation of bile acid metabolism and signaling, as well as modulation of the gut–brain axis to influence appetite and energy balance. Together, these actions underscore the role of intermittent energy restriction as a microbiota-mediated strategy for combating obesity.

Conclusion: Targeting the gut microbiota through time-restricted eating offers a promising, microbiome-driven approach to obesity management, opening new pathways for personalized nutritional interventions.

keywords: Gut microbiota; Obesity; Dietary interventions; Time-restricted eating; Microbiome-mediated weight regulation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-17

MOF Hybrid nanomaterials for Cancer biomarkers, Biosensors and Clinical laboratory diagnostics

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Background and aim: Metal-organic frameworks (MOFs) exhibit remarkable properties for biomedical applications. Nanoscale MOFs (NMOFs) provide a promising platform for advanced therapeutic, imaging, and diagnostic functions due to their biocompatibility and high loading capacity. Light-triggered NMOF-based systems improve imaging-guided cancer treatments with enhanced precision. Additionally, bimetallic MOF structures have been applied as aptasensor frameworks. An aptasensor based on a Zn-MOF-on-Zr-MOF framework demonstrates high selectivity, stability, and effective performance in human serum.

Methods: This narrative review was conducted by searching international databases including PubMed, Scopus, Web of Science, and Google Scholar. Keywords related to “MOF-based nanomaterials,” “anticancer activity,” “clinical laboratory applications,” and “biomedical diagnostics” were used. Relevant articles were selected based on novelty, relevance to laboratory and clinical applications, and scientific quality. Additional sources were identified through manual citation searches.

Results: In the field of cancer detection, metal-organic frameworks (MOFs) featuring characteristics of Gd3+, Mn2+, and Fe3+ have exhibited efficacy in magnetic resonance imaging (MRI). Additionally, elements such as Hf and Zr have demonstrated utility as viable contrast agents for computed tomography (CT).

Conclusion: Metal-organic frameworks (MOFs) are complex and versatile hybrid architectures known for their exceptional porosity, biocompatibility, and tunability. These structures exhibit promising therapeutic properties against cancer cells and tumors due to their capacity to encapsulate various cargoes such as drugs, proteins, and genes. The use of MOFs in cancer therapy and diagnosis is still in its nascent stage of exploration, primarily due to the current inadequacy in inducing the immune responses necessary for effective cancer therapy.

keywords: Metal–organic frameworks (MOFs),Nanoscale MOFs (NMOFs), Biomarker detection, Cancer diagnosis,Cancer theranostics.

PBi-18

Ferroptosis in the Pathogenesis of Non-Alcoholic Fatty Liver Disease: A Bridge Between Bench and Bedside

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Background and aim: Non-alcoholic fatty liver disease (NAFLD) is a prevalent chronic liver disease worldwide, commonly associated with metabolic dysfunction, oxidative stress, and disturbances in lipid metabolism. The precise mechanisms behind NAFLD remain unclear, and no effective treatment exists to reverse its progression. Ferroptosis, an iron-dependent regulated cell death triggered by lipid peroxidation, has emerged as an important factor in disease pathogenesis. The aim of this review is to comprehensively evaluate the role of ferroptosis in the pathogenesis of NAFLD, with particular emphasis on its underlying molecular mechanisms and potential therapeutic implications.

Methods: This review synthesizes up-to-date evidence on ferroptosis in NAFLD by evaluating systematic reviews, meta-analyses, and mechanistic studies published between 2010 and 2025 in PubMed. Emphasis is placed on key molecular pathways regulating iron homeostasis, lipid peroxidation, and antioxidant defenses, and their impact on hepatocyte vulnerability to ferroptotic cell death

Results: Ferroptosis has emerged as a major contributor to hepatocellular damage in NAFLD. Studies in experimental models have demonstrated that excessive iron accumulation and increased production of reactive oxygen species (ROS) drive lipid peroxidation, which in turn exacerbates oxidative stress and liver inflammation. Critical molecular regulators, such as glutathione peroxidase 4 (GPX4), system Xc–, and NRF2-dependent antioxidant mechanisms, influence the susceptibility of hepatocytes to ferroptotic cell death. Evidence from both cellular and animal studies indicates that strategies targeting ferroptosis—including iron chelation, enhancement of antioxidant defenses, and suppression of lipid peroxidation—can effectively mitigate liver injury and slow disease progression. Overall, these findings highlight ferroptosis as a pivotal mechanism in NAFLD pathogenesis and suggest that therapeutic modulation of ferroptotic pathways may offer promising approaches to limit disease advancement.

Conclusion: Ferroptosis has been identified as a key contributor to liver cell damage in NAFLD by mediating iron imbalance, lipid peroxidation, and oxidative stress, which together exacerbate hepatocellular injury. Modulating ferroptotic signaling pathways may offer a promising therapeutic avenue, translating mechanistic findings from experimental studies into potential clinical strategies for managing NAFLD

keywords: Non-alcoholic fatty liver disease NAFLD Ferroptosis Oxidative stress Lipid peroxidation

PBi-19

Down-Regulation of LINC02362 Long Non-Coding RNA as Potential Tumor Markers in Colorectal Cancer

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Background and aim: Colorectal cancer (CRC) ranks among the most lethal malignancies globally. In this study, we utilized RNA sequencing data from The Cancer Genome Atlas (TCGA) to investigate the expression of LINC02362 long non-coding RNA (lncRNA), which has recently been identified as a significant contributor to the pathogenesis of multiple cancers. The objective of our research was to assess the expression levels of LINC02362 lncRNA in colorectal cancer tissues relative to adjacent non-tumor tissues and to analyze its correlation with various clinical characteristics.

Methods: In this case-control study, we conducted RNA sequencing analysis of data from The Cancer Genome Atlas (TCGA) using R software, identifying lncRNA-LINC02362 as a critical long non-coding RNA implicated in colorectal cancer. Subsequently, the expression levels of lncRNA-LINC02362were assessed in 20 pairs of cancerous and adjacent non-cancerous tissue samples from CRC patients through reverse transcription-quantitative polymerase chain reaction (RT-qPCR). Statistical analyses and graphical representations of the relationships between RNA levels and clinicopathological characteristics of CRC were performed using SPSS and Prism 10 software. Additionally, the Receiver Operating Characteristic (ROC) curve was generated to evaluate the sensitivity and specificity of LINC02362 expression as potential biomarkers for CRC.

Results: The expression of LINC02362 was found to be significantly decreased in CRC specimens compared to adjacent non-tumor tissues. Our findings indicate a considerable correlation between LINC02362 RNA levels and both tumor size and histopathological grade. Furthermore, the ROC curve analysis revealed that LINC02362 lncRNA exhibited satisfactory sensitivity and specificity for diagnostic purposes in CRC.

Conclusion: The findings suggest that lncRNA-LINC02362 may significantly contribute to the progression and potential onset of CRC through its involvement in various cellular pathways

keywords: Colorectal neoplasm, non-coding RNA, LINC02362

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-20

A multi-head YOLOv12 with self- supervised pretraining for urinary sediment particle detection

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Background and aim: Urine sediment analysis is a fundamental component of clinical diagnostics for renal and urinary tract disorders; however, manual microscopy is time-consuming, operator-dependent, and prone to variability. This study aimed to develop and evaluate an automated deep learning–based approach using a multi-head YOLOv12 architecture, combined with self-supervised pretraining and Slicing Aided Hyper Inference (SAHI), to enable comprehensive and accurate detection of a wide spectrum of urinary sediment particles in high-resolution microscopic images.

Methods: A novel multi-head YOLOv12 object detection framework was designed, consisting of six independent detection heads for Cells, Casts, Crystals, Microorganisms/Yeast, Artifacts, and Others. The model was trained on the OpenUrine dataset, comprising 790 labeled images with 31,285 expert-annotated bounding boxes across 39 classes, along with 5,640 unlabeled images used for self-supervised pretraining via an encoder–decoder reconstruction task. Pretrained backbone weights were transferred to the supervised detection stage. Patient-level 5-fold cross-validation was applied. During inference, SAHI was employed to improve small-object detection in high-resolution images. Model performance was evaluated using precision, recall, mAP@50, and mAP@50–95 metrics.

Results: The proposed method achieved a precision of 76.59%, recall of 62.45%, mAP@50 of 64.15%, and mAP@50–95 of 47.20% on the 39-class OpenUrine dataset, outperforming state-of-the-art object detection models under identical conditions. Ablation studies demonstrated that both the multi-head architecture and self-supervised pretraining significantly contributed to performance gains, with the removal of specialized heads causing marked reductions in detection accuracy. The model showed strong performance in detecting morphologically distinct particles, while small, rare, or visually similar classes remained more challenging. Clinical validation on patient samples yielded a mean accuracy of 86.55% for major urinary sediment components.

Conclusion: This study presents a robust and scalable AI-based framework for automated urine sediment analysis. The integration of a multi-head YOLOv12 architecture, self-supervised pretraining, and SAHI effectively addresses challenges related to class imbalance, small-object detection, and limited labeled data. The publicly available OpenUrine dataset and the proposed method provide a valuable foundation for future research and support the advancement of reliable, standardized, and clinically applicable automated urinalysis systems.

keywords: Urine sediment analysis; YOLOv12; Deep learning; Self-supervised learning

PBi-21

Liquid Biopsy–Based Circulating Biomarkers in Cancer Diagnosis and Treatment Monitoring

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Background and aim: Early cancer detection and dynamic monitoring of disease progression remain major unmet needs in oncology. Tissue biopsy is invasive, often impractical for serial sampling, and limited in capturing tumor heterogeneity and temporal molecular evolution. Liquid biopsy has emerged as a non-invasive approach enabling real-time assessment of tumor-derived biomarkers. This review aims to evaluate the clinical relevance of liquid biopsy in cancer detection, treatment monitoring, and prognostic assessment.

Methods: A structured literature search was conducted in the PubMed database using the following search strategy: ("liquid biopsy" OR "circulating biomarkers") AND (cancer OR tumor) AND ("early detection" OR "monitoring"). Peer-reviewed articles published between 2023 and 2025 were screened. A total of 45 relevant studies were identified and selected based on clinical relevance, study design, and focus on diagnostic, prognostic, or monitoring applications of liquid biopsy biomarkers in oncology.

Results: Accumulating evidence indicates that liquid biopsy biomarkers provide high diagnostic accuracy, particularly for early-stage disease, and frequently outperform conventional biomarkers. Longitudinal analysis of ctDNA and complementary circulating analytes reliably reflects treatment response, molecular resistance, minimal residual disease, and recurrence risk. Multi-analyte and AI-assisted platforms further enhance sensitivity, specificity, and individualized risk stratification.

Conclusion: Liquid biopsy represents a key component of precision oncology, offering non-invasive, real-time insights into tumor biology. Its integration into clinical workflows has the potential to improve early detection, guide adaptive treatment strategies, and optimize patient outcomes.

keywords: Liquid biopsy; Circulating tumor DNA; Cancer biomarkers; Precision oncology

PBi-22

Valuing the Effects of Nanocurcumin Supplementation in Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background and aim: Nanocurcumin has been developed to overcome the poor bioavailability of conventional curcumin and has been proposed as a potential adjunctive therapy for type 2 diabetes mellitus (T2DM). However, evidence regarding its clinical efficacy remains inconsistent. This systematic review and meta-analysis aimed to evaluate the effects of nanocurcumin supplementation on glycemic control, lipid profile, inflammatory markers, and oxidative stress in patients with T2DM.

Methods: A systematic search of PubMed, Scopus, and the Cochrane Library was conducted from inception to October 2025 to identify randomized controlled trials (RCTs) assessing nanocurcumin supplementation in adults with T2DM. Eligible studies compared nanocurcumin with placebo or no intervention and reported outcomes related to glycemic indices, lipid parameters, inflammatory markers, or oxidative stress. Pooled effect sizes were calculated using a random-effects model and expressed as standardized mean differences (SMDs) with 95% confidence intervals (CIs). Between-study heterogeneity was assessed using the I^2 statistic

Results: Seven RCTs involving 453 participants were included. Nanocurcumin supplementation showed no significant effects on fasting blood glucose (SMD: −0.44; 95% CI: −2.16 to 1.28), HbA1c (SMD: 0.19; 95% CI: −1.26 to 1.65), or lipid profile parameters, including total cholesterol, LDL-C, HDL-C, and triglycerides (all p 0.05). No statistically significant reduction in C-reactive protein was observed (SMD: −0.78; 95% CI: −1.58 to 0.05). In contrast, nanocurcumin significantly increased total antioxidant capacity (SMD: 1.60; 95% CI: 0.93 to 2.31) and reduced malondialdehyde levels (SMD: −1.93; 95% CI: −3.19 to −0.66), indicating a robust antioxidative effect.

Conclusion: Current evidence suggests that short-term nanocurcumin supplementation does not significantly improve glycemic control, lipid profile, or systemic inflammation in patients with T2DM. However, it exerts significant antioxidant effects, reflected by improved total antioxidant capacity and reduced oxidative stress. These findings indicate that the potential clinical utility of nanocurcumin in T2DM may be primarily related to its antioxidative properties rather than direct metabolic modulation. Larger, long-term RCTs using standardized nanocurcumin formulations are warranted to determine its impact on diabetes-related complications and clinical outcomes.

keywords: nanocurcumin, type 2 diabetes, meta-analysis, oxidative stress, glycemic control

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-23

Comparative Effects of LPS-Preconditioned MSC Exosomes and Saroglitazar on Non-Alcoholic Steatohepatitis via the JAK2/STAT3 Pathway in a High-Fat Diet Wistar Rat Model

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Background and aim: Non-alcoholic steatohepatitis (NASH) is a progressive liver disease characterized by steatosis, inflammation, and hepatocellular injury, with dysregulation of the JAK2/STAT3 pathway contributing to disease progression. Mesenchymal stem cell–derived exosomes (MSC-Exos), especially after LPS preconditioning, and saroglitazar, a dual PPAR-α/γ agonist, have shown therapeutic potential in metabolic liver disorders. This study aimed to compare the effects of LPS-preconditioned MSC-derived exosomes and saroglitazar on NASH via modulation of the JAK2/STAT3 signaling pathway in a high-fat diet–induced Wistar rat model.

Methods: Male Wistar rats were randomly divided into control, HFD, HFD plus LPS-preconditioned MSC-exosome–treated, and HFD plus saroglitazar-treated groups. NASH was induced by long-term HFD feeding. Therapeutic interventions were administered during the treatment period. Liver tissues were collected for histopathological examination and molecular analyses. The expression levels of JAK2, STAT3, phosphorylated STAT3, and inflammatory cytokines were evaluated using RT-PCR and western blotting.

Results: HFD-fed rats developed significant hepatic steatosis, inflammatory cell infiltration, and activation of the JAK2/STAT3 pathway compared with the control group. Both LPS-preconditioned MSC-derived exosomes and saroglitazar significantly improved liver histopathology and reduced inflammatory responses. Exosome treatment demonstrated a stronger inhibitory effect on inflammatory mediators, whereas saroglitazar showed a more pronounced improvement in metabolic-related parameters. Both interventions significantly downregulated JAK2 and phosphorylated STAT3 expression (P 0.05).

Conclusion: The results indicate that both LPS-preconditioned MSC-derived exosomes and saroglitazar effectively ameliorate NASH by modulating the JAK2/STAT3 signaling pathway. MSC-derived exosomes may represent a promising alternative or complementary therapeutic approach for NASH; however, further studies are required.

keywords: Exosomes, Saroglitazar, NASH

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-24

Evaluation of the Combined Effects of Etoposide and Nano-Curcumin on p53 Phosphorylation and Apoptosis Induction in HepG2 Hepatocellular Carcinoma Cells

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Background and aim: Hepatocellular carcinoma (HCC) is a leading cause of cancer-related mortality, and resistance to chemotherapy limits the efficacy of conventional agents such as etoposide. Activation and phosphorylation of the tumor suppressor protein p53 play a critical role in regulating cell cycle arrest and apoptosis in cancer cells. Curcumin, a natural polyphenolic compound with anticancer properties, has limited bioavailability, leading to the development of nano-curcumin to enhance cellular uptake and efficacy. This study aimed to evaluate the combined effects of etoposide and nano-curcumin on p53 phosphorylation and apoptosis induction in HepG2 liver cancer cells.

Methods: HepG2 cells were cultured and treated with etoposide, nano-curcumin, or their combination at different concentrations. Cell viability was assessed using the MTT assay. Apoptosis induction was evaluated by flow cytometry and fluorescence staining. The expression levels of phosphorylated p53, total p53, and apoptosis-related proteins, including Bax, Bcl-2, and cleaved caspase-3, were analyzed using western blotting and RT-PCR.

Results: Treatment with etoposide or nano-curcumin alone resulted in a moderate reduction in cell viability and increased apoptotic cell death compared with the control group. Notably, combined treatment significantly enhanced cytotoxicity and apoptosis in HepG2 cells. This effect was accompanied by a marked increase in p53 phosphorylation and upregulation of pro-apoptotic markers, along with downregulation of anti-apoptotic proteins compared with single treatments (P 0.05).

Conclusion: The findings suggest that the combination of etoposide and nano-curcumin synergistically enhances apoptosis in HepG2 cells, possibly through increased p53 phosphorylation. This combined approach may represent a promising strategy for improving the efficacy of chemotherapy in hepatocellular carcinoma, although further studies are needed.

keywords: Hepatocellular carcinoma, Etoposide, Nano-Curcumin

PBi-25

Gold Nanoparticle - based Colorimetric Aptasensor for Fast Arsenic Detection

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Background and aim: Arsenic contamination of water sources is a serious environmental and public health problem. Conventional analytical techniques for arsenic detection are often costly, time-consuming, and dependent on advanced laboratory equipment. Therefore, developing rapid, simple, and cost-effective detection methods is essential. Aptamer-based biosensors combined with gold nanoparticles have emerged as promising tools due to their high specificity, sensitivity, and visual detection capability.

Methods: In this study, a colorimetric nanoaptasensor was developed using an arsenic-specific DNA aptamer (ASIII) conjugated to gold nanoparticles (AuNPs). The formation and physicochemical properties of the aptamer–AuNP complex were characterized using UV–Visible spectrophotometry, X-ray diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), and visible light spectroscopy. After incubation of the complex at room temperature under dark conditions, aqueous arsenic solutions with defined concentrations were added. Salt-induced aggregation assays were performed to evaluate colorimetric responses. The selectivity of the aptasensor was investigated in the presence of other heavy metal ions.

Results: The presence of arsenic ions induced a conformational change in the aptamer, resulting in its dissociation from the surface of gold nanoparticles and selective binding to arsenic. This dissociation destabilized the AuNPs, leading to rapid aggregation in the presence of salt and a visible color change from red to purple. No significant color change was observed with other tested metal ions, confirming high specificity for arsenic. The detection limit was 2 mM by naked-eye observation and 0.1 mM by UV–Vis spectrophotometric analysis.

Conclusion: The developed colorimetric aptasensor provides a rapid, low-cost, and specific method for arsenic detection in aqueous samples. Its simplicity and visual readout make it a promising approach for laboratory screening and future clinical and environmental monitoring applications.

keywords: Aptasensor; Gold Nanoparticles; Arsenic; Colorimetric Detection; Heavy Metals

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-26

Colorimetric Detection of Lead Using Silver Nanoparticle-based Aptasensor

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Background and aim: Lead is a widely distributed heavy metal in the Earth's crust and is recognized as a major environmental pollutant with serious health risks. The presence of lead in water and environmental samples necessitates the development of rapid, sensitive, and on-site detection methods. Aptamer-based nanosensors have gained increasing attention as effective analytical tools due to their high selectivity, simplicity, and low operational cost.

Methods: In the present study, a colorimetric nanoaptasensor was developed for lead ion detection using silver nanoparticles (AgNPs) functionalized with a lead-specific DNA aptamer. The interaction between the aptamer and silver nanoparticles was first established, followed by the addition of aqueous samples containing lead ions. Structural and functional characterization of the nanoaptasensor was performed using X-ray diffraction (XRD), Fourier-transform infrared spectroscopy (FTIR), agarose gel electrophoresis, and UV–Visible spectrophotometry. The selectivity and sensitivity of the nanosensor were evaluated in the presence of other heavy metal ions.

Results: Upon the introduction of lead ions, the aptamer selectively bound to lead, inducing aggregation of silver nanoparticles. This aggregation resulted in a visible color change of the solution from light yellow to dark yellow, which could be detected by the naked eye as well as by UV–Vis spectrophotometric analysis. No significant color change was observed in the presence of other heavy metal ions, demonstrating high specificity of the nanosensor for lead. The detection limit was determined to be 5 mM by visual inspection and 1 mM using spectrophotometric measurements.

Conclusion: The developed aptamer-based colorimetric nanosensor offers a rapid, simple, and low-cost method for selective detection of lead ions. Its portability, visual readout capability, and acceptable sensitivity make it a promising tool for environmental monitoring and water quality assessment in laboratory and field settings.

keywords: Aptamer; Nanosensor; Silver Nanoparticles; Lead Detection; Colorimetric Assay

PBi-27

Impact of Interfering Factors on the Accuracy of Clinical Laboratory Test Results

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Background and aim: Clinical laboratory test results play a crucial role in disease diagnosis, monitoring, and therapeutic decision-making. However, various interfering factors can significantly affect test accuracy and lead to misinterpretation of laboratory data. These factors may originate from pre-analytical, analytical, or post-analytical phases and remain one of the major challenges in laboratory medicine. Understanding and controlling such interferences are essential to improve the reliability of laboratory findings and patient safety.

Methods: This study reviews and analyzes the most common interfering factors affecting clinical laboratory test results, including patient-related variables, sample collection and handling conditions, biochemical interferences, and analytical limitations of laboratory assays. Relevant laboratory scenarios and commonly affected tests were evaluated based on standard laboratory guidelines and published evidence. The impact of these factors on routine hematology, biochemistry, immunoassay, and coagulation tests was assessed.

Results: The findings indicate that pre-analytical factors, such as hemolysis, lipemia, icterus, improper sample collection, and patient preparation, represent the most frequent sources of laboratory test interference. Analytical interferences, including cross-reactivity, matrix effects, and reagent-related limitations, also contribute to inaccurate results. These interferences may lead to falsely elevated or decreased values, increased analytical variability, and clinically misleading interpretations. Proper identification and management of interfering factors significantly reduce laboratory errors and improve diagnostic accuracy.

Conclusion: Interfering factors have a substantial impact on the accuracy and clinical reliability of laboratory test results. Increasing awareness among laboratory professionals and clinicians, along with strict adherence to quality control measures and standard operating procedures, is essential to minimize laboratory errors. Addressing these factors enhances diagnostic confidence and supports better clinical decision-making in laboratory and clinical practice.

keywords: Laboratory Interference; Pre-analytical Errors; Analytical Errors; Clinical Laboratory Tests; Quality

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-28

White Blood Cell Apo M Expression in Fatty Liver Disease: A Comparison between Metabolic and Non-Metabolic Etiologies

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Background and aim: Non-alcoholic fatty liver disease (NAFLD), recently reclassified as metabolic dysfunction-associated fatty liver disease (MAFLD), can also manifest in patients classified as non-MAFLD who do not meet MAFLD criteria. Apolipoprotein M (Apo M) is a lipocalin found in HDL and other lipoproteins. ApoM can enhance insulin resistance and improve insulin sensitivity. Given its effects on insulin resistance and lipid metabolism, Apo M may also play a role in the development and progression of fatty liver disease (FLD). This study investigated Apo M gene expression in white blood cells (WBCs) of individuals with MAFLD, non-MAFLD, and healthy controls.

Methods: The WBCs of the study subjects were collected from patients with FLD (n=99) including 58 MAFLD and 41 non-MAFLD and healthy individuals (n=23). To investigate the gene expression of Apo M, qRT-PCR method was used.

Results: The ApoM gene expression was significantly lower in FLD patients, both non-MAFLD (p0.05), and MAFLD patients (p0.01) compared to the control group.

Conclusion: Alterations in Apo M gene expression in non-MAFLD patients was milder than MAFLD patients when compared to the control. Also, likely Apo M may be involved in FLD pathogenesis.

keywords: Apo M, MAFLD, non-MAFLD

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-29

Diagnostic Value of Serum Albumin and Inflammatory Markers in Predicting Clinical and Nutritional Outcomes in Cancer Patients: A Multicenter Study

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Background and aim: Systemic inflammation and malnutrition significantly compromise the prognosis of oncology patients. Although serum albumin and C-reactive protein (CRP) are routine laboratory assessments, their combined predictive utility via the Glasgow Prognostic Score (GPS) remains under-evaluated in local clinical settings. This study aimed to determine the prevalence of hypoalbuminemia and elevated inflammatory markers and to assess their diagnostic value in independently predicting short-term mortality and malnutrition among hospitalized cancer patients, utilizing data from a multicenter survey.

Methods: A cross-sectional analytical study with a 30-day prospective follow-up was conducted using data from the Iran oncology nutritionDay survey (2021–2024). The study included 167 hospitalized cancer patients. Nutritional risk was evaluated using NRS-2002 criteria. To assess cumulative prognostic risk, a binary stratification model was applied: patients were categorized into a "High-Inflammatory Risk" group (GPS score 2: concurrent hypoalbuminemia 3.5 g/dL and CRP ≥10 mg/L) versus a "Standard-Risk" group (GPS scores 0–1). This segmentation was utilized to evaluate the synergistic impact of inflammatory and nutritional markers on outcomes. Binary logistic regression adjusted for confounders (age, sex, metastasis) was used to analyze predictors of malnutrition and mortality. The Hosmer-Lemeshow test was applied to assess model goodness-of-fit.

Results: Hypoalbuminemia and elevated CRP were prevalent in 61.3% and 79.7% of the cohort, respectively. Among 80 patients with complete dual-biomarker profiles, the distribution was: GPS 0 (n=3), GPS 1 (n=28), and GPS 2 (n=49). Consequently, under the binary stratification model, 61.3% of patients fell into the "High-Inflammatory Risk" category. Regression analysis indicated that falling into this High-Risk category was a potent independent predictor for both 30-day mortality (OR=4.332, P=0.035) and malnutrition (OR=3.834, P=0.011). While hypoalbuminemia alone also predicted both outcomes, elevated CRP alone was only significantly associated with mortality (OR=8.158, P=0.047) and failed to independently predict malnutrition (P=0.082), highlighting the superior diagnostic value of the combined risk model.

Conclusion: The Glasgow Prognostic Score serves as a valuable dual-purpose biomarker for identifying oncology inpatients at high risk of both nutritional depletion and early mortality. Integrating GPS into routine clinical assessments can facilitate timely nutritional and therapeutic interventions to improve patient outcomes.

keywords: Glasgow Prognostic Score; Serum Albumin; C-Reactive Protein; Malnutrition; Neoplasms.

PBi-30

Isolation of Ginger-Derived Extracellular Vesicles (GDEVs) Using Differential Centrifugation

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Background and aim: Plant-derived extracellular vesicles (PDEVs), particularly those derived from ginger, have been proposed as natural nanocarriers with potential therapeutic applications. For clinical applicability, reliable and reproducible isolation methods are essential. Differential centrifugation is recognized as the primary method for separating vesicle subpopulations based on size and density. Here, we present a step-by-step process for isolating ginger-derived extracellular vesicles (GDEVs) by removing cellular contaminants and concentrating nanovesicles while maintaining their structural integrity.

Methods: Fresh ginger (Zingiber officinale Roscoe) was purchased from a supermarket. After washing with distilled water, its juice was extracted using a juicer. The juice was then subjected to low-speed centrifugation to remove cell debris. The resulting supernatant was passed through a 0.45 µm syringe filter, and GDEVs were subsequently isolated by ultracentrifugation. The size distribution and morphology of the GDEVs were determined using dynamic light scattering (DLS) and scanning electron microscopy (SEM), respectively.

Results: DLS analysis revealed that the hydrodynamic diameter of GDEVs was approximately 300 nm. Furthermore, SEM images demonstrated that the vesicles possessed a uniform shape and an intact membrane structure

Conclusion: Our findings support the utility of differential centrifugation as a reliable method for preparing GDEVs. This approach provides a foundation for future investigations into their therapeutic potential.

keywords: Ginger-derived extracellular vesicles (GDEVs), Plant-derived extracellular vesicles (PDEVs), Differential centrifugation,

PBi-31

Rapid and Label-free detection of Calprotectin using Screen Printed Electrodes (SPE) and electrical impedance spectroscopy (EIS)

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Background and aim: Calprotectin is implicated in the innate immune response and is involved in several physiological functions. It is mainly found in the cytosol of neutrophils and to a lesser extent in monocytes and macrophages. One of the most indispensable electrochemical techniques is electrical impedance spectroscopy (EIS). The impedance is measured in the circuit by an impedance meter. we utilize screen-printed electrodes (SPEs), which are miniaturized by printing conductive ink Ag. These SPEs are portable, disposable, and cost-effective. EIS analyzes the impedance and resistance due to the biological interactions that occur on the surface of the printed electrodes.

Methods: we develop an electrochemical biosensor by using screen-printed silver electrodes, including a working electrode (WE), counter electrode (CE), and reference electrode (Re). the reaction occurs on working electrode. Protein A has been used to immobilize the calprotectin antibody on the surface of the working electrode and measure the impedance alterations after the antigen-antibody interaction to quantify the analyte concentration in the sample. Protein A contributes to immobilizing the antibody through their high affinity to the Fc region of antibodies. Phosphate buffered saline (PBS) and ethanol solutions are prepared as dilution agents for antigen and antibody and Poly-ethylen glycol 6000 (PEG6000) are dissolved in PBS as blocking agents. Electrochemical experiments were performed on AD5933 which is an impedance converter with high precision.

Results: Bode plots illustrate the impedance magnitude (|Z|) as a function of frequency for four distinct biosensor stages, including Protein A attachment, surface blocking, antibody immobilization, and antigen binding. A consistent frequency-dependent behavior was observed at all stages with minimal variation across five independent experimental replicates, indicating good reproducibility. Nyquist plots further revealed a progressive increase in charge transfer resistance following each surface modification step. impedance spectra recorded for different antigen concentrations showed a clear dose-dependent response.

Conclusion: EIS measurements across all biosensor stages and antigen concentrations showed reproducible, stable, and dose dependent responses. Bode plots confirmed consistent impedance behavior with low variation, while Nyquist plots demonstrated increasing charge transfer resistance with higher antigen levels and Impedance magnitude (|Z|) increased progressively with higher antigen levels.

keywords: Calgranulin/ Electrical impedance spectroscopy (EIS)/ immunosensor/ Screen printed electrodes (SPEs)

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBi-32

The Central Role of α-Synuclein in Parkinson's Disease Pathogenesis

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Background and aim: Parkinson is a neurodegenerative disease that is caused by various factors, one of which is the accumulation of α-synuclein protein. α-synuclein is a presynaptic neuronal protein whose misfolding and aggregation are strongly implicated in the development and progression of Parkinson's disease (PD). α-synuclein accumulation leads to Lewy body formation, synaptic dysfunction, mitochondrial impairment, and neuroinflammation. Understanding its underlying mechanism is essential for improving diagnostic biomarkers and developing targeted therapies.

Methods: In order to identify relevant articles, the mentioned keywords and their combinations were searched in PubMed and Google Scholar from 2020 to 2026, and relevant articles were extracted. The screening process began with evaluating the titles and abstracts for relevance, and after a careful analysis of the full text, articles that met the inclusion criteria were selected.

Results: Results: Several studies have shown that abnormal forms of α-synuclein interfere with synaptic vesicle trafficking and mitochondrial respiration, thereby activating microglial inflammation. The release of misfolded α-synuclein in a prion-like manner contributes to the progression of PD. Advancements in biomarker identification, such as tests for α-synuclein in CSF and plasma, along with seed amplification techniques like Real-Time Quaking-Induced Conversion (RT-QuIC) and Protein Misfolding Cyclic Amplification (PMCA), have significantly improved diagnostic sensitivity at both the initial and advanced stages of PD. Therapeutic strategies, including monoclonal antibodies, aggregation inhibitors, and gene-silencing approaches, are yielding promising results in preclinical and early clinical trials. Key challenges and research priorities in this area include mitigating the deleterious synergistic interactions of α-synuclein while selectively targeting its pathologic forms without disrupting its essential physiological roles at the synapse.

Conclusion: α-synuclein plays a critical role in the pathogenesis of PD. Recent studies show its potential as a diagnostic biomarker and therapeutic target. Ongoing efforts in this area are essential to turn these insights into effective disease-modifying interventions.

keywords: Parkinson Disease; Nerve Degeneration; alpha-Synuclein; Protein Aggregation; Biomarkers

PBi-33

Safety and Efficacy of Enadenotucirev in Patients with Cancer: Review of Clinical Trials

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Background and aim: Enadenotucirev, previously known as ColoAd1, is a chimeric oncolytic adenovirus derived from the Ad11 and Ad3 strains of group B. It is designed to remain stable in the bloodstream and exhibits a high level of tumor-selective replication and killing properties without damaging normal cells and tissues. The safety and anti-cancer characteristics of Enadenotucirev in preclinical cancer studies warrant further clinical safety and tolerability evaluation.

Methods: The ClinicalTrials.gov, Web of Science (ISI), Scopus, and PubMed databases were searched using relevant keywords, including Enadenotucirev, safety, efficacy, cancer patients, gene therapy, oncolytic adenovirus, and clinical trials, to identify original studies that examined the safety and efficacy of Enadenotucirev in cancer patients participating in clinical trials.

Results: Phases I and II clinical trials demonstrated excellent safety and tolerability with intravenous and intraperitoneal doses up to 4 × 1012 VP, without severe dose-limiting toxicity (DLT). Objective response rates (ORR) of 2–10%, disease control rates (DCR) of 45–56% and median overall survival (mOS) of 12–16 months were observed in patients with advanced epithelial cancers such as lung, ovarian, and rectal cancer. These outcomes were improved with the combination of nivolumab or paclitaxel and were associated with reductions in tumor markers and prolonged survival. Key evidence included the infiltration of CD8+ T cells, increased levels of Th1 cytokines such as IFN-γ and IL-12, persistent viral presence for up to 7 weeks, and the activation of a systemic immune response. Most adverse events were mild and classified as grade 1 or 2, with common issues including fever and fatigue.

Conclusion: The study demonstrated that systemic administration of Enadenotucirev in cancer patients was safe and well-tolerated. Enadenotucirev is a next-generation engineered oncolytic virus designed to selectively replicate in tumors.

keywords: Enadenotucirev, Cancer, Safety, Gene therapy, Oncolytic adenovirus, Clinical Trials

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-34

Cobalt Chloride as a Hypoxia Mimetic: Evaluating Its Effects on Sertoli Cell Viability In Vitro

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Background and aim: Cobalt chloride (CoCl2) is frequently used in in vitro studies as a chemical hypoxia mimetic. It induces hypoxia by stabilizing hypoxia-inducible factors (HIFs). The ability of CoCl2 to mimic hypoxic conditions has made it a useful tool in various research fields, including cancer research, stem cell and regenerative medicine and reproduction research. However, less is known about the effects of CoCl2 on testicular somatic cells, like Sertoli cells.

Methods: Mouse TM4 Sertoli cells were cultured in DMEM-F12 medium supplemented at 37°C in an atmosphere of 95% O2 and 5% CO2. TM4 cells were seeded in a 96-well plate at a density of 10000 cells per well, with each well containing 100 µL of medium. To evaluate the effect of CoCl2, TM4 Sertoli cells were exposed to various concentrations of CoCl2 (0, 50, 100, 150, 200, 250, 300, and 350 µM) for two different exposure durations (24 or 48 hours). Cellular viability was then assessed using the MTT sssay.

Results: In the CoCl2-exposed groups, cell viability slightly decreased as the concentration of CoCl2 increased during both the 24- and 48-hour exposure periods. However, more significant changes were observed at higher concentrations of CoCl2. Specifically, cellular viability significantly decreased from 100.1 ± 7.8 % in the vehicle group to 29.4 ± 3.1 % in cells exposed to 150 µM CoCl2 and a further reduction to 10.95 ± 2 % in cells exposed to 200 µM CoCl2 (P 0.001), following 24-hour exposure. The concentration of CoCl2 that resulted in a 50 % decrease in Sertoli cell viability (IC50) was determined to be 125 µM. Similarly, a concentration-dependent decrease in cell viability was observed following the 48-hour exposure. A Comparison of data between the 24- and 48-hour exposure periods revealed a significant reduction in cell viability, indicating that cell viability differs significantly based on the duration of exposure.

Conclusion: Exposure to CoCl2 significantly decreased Sertoli cell viability in a concentration- and time- dependent manner. Therefore, cobalt chloride can be considered as a valuable agent for inducing hypoxic conditions and may serve as a model for toxicity in Sertoli cells.

keywords: Cell viability; Cobalt chloride; Hypoxia, Sertoli cell

PBi-35

Memantine as a Potential Enhancer of Cisplatin Sensitivity in Resistant and Sensitive Ovarian Cancer Cells

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Background and aim: One of the important strategies for ovarian cancer treatment is chemotherapy with platinum-based chemotherapeutics. Despite the fact that chemotherapy frequently generates complete responses, resistance to chemotherapy is an important obstacle to successful ovarian cancer therapy. One strategy to fight against multidrug resistance (MDR) is to combine chemotherapeutics with safe compounds. Memantine, a non-competitive N-methyl-D-aspartate receptor antagonist that inhibits glutamate-mediated excitotoxicity in Alzheimer's disease, is one possible medication that has beneficial effects in cancer treatment. Therefore, in this study, we aim to investigate the effects of memantine on cisplatin resistance in sensitive (A2780/S) and resistant (A2780/CP) ovarian cancer cells.

Methods: To investigate the effect of memantine on the cytotoxicity of cisplatin in both A2780/S and A2780/CP cancer cells, the MTT assay was performed. We also measured the MRP2 gene expression in both cell lines by the RT-PCR method. Furthermore, the amount of intracellular reduced glutathione (GSH) was measured using the ELISA method. The amount of cellular apoptosis in both cell lines was detected using DAPI staining and fluorescent imaging.

Results: Memantine increased the cytotoxicity of cisplatin in both A2780/S and A2780/CP cells, as confirmed by the decreased IC50 of cisplatin in both cell lines. There was no significant alteration in MRP2 expression in either cell line, so we concluded that resistance to cisplatin in these cells is not associated with an increase in MRP2 gene expression. Therefore, the amount of intracellular GSH was measured. The level of glutathione in the resistant cells was significantly higher than in the sensitive cells, but memantine had no significant effect on the level of GSH. Moreover, memantine enhanced cisplatin-induced apoptosis in both sensitive and resistant cells.

Conclusion: The results of our study showed that memantine significantly increased the effects of cisplatin in both sensitive and resistant types of ovarian cancer. Cisplatin resistance was associated with increased GSH, but memantine had no significant effect on intracellular GSH. Thus, we concluded that memantine exerts its effects through mechanisms other than intracellular GSH reduction in sensitizing ovarian cancer cells to cisplatin.

keywords: Ovarian cancer, multi drug resistance, cisplatin, memantine

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-36

Protective Effects of Honey Against Glucose-Induced Inflammatory and Migratory Responses in Human Umbilical Vein Endothelial Cells

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Background and aim: Hyperglycemia (HG)-induced inflammation and migration in human umbilical vein endothelial cells (HuVECs) are essential in the development of diabetic illnesses. The present study aimed to investigate the effect of honey on the rate of HG-induced HuVECs migration and inflammation.

Methods: Commercial and Ziziphus jujube honeys are assessed for quality based on phenolic content, antioxidant capacity, and diastase activity (PAD score). Next, HuVECs were exposed to HG (33 mM) and treated with different doses of honey, and an MTT assay was performed to determine a non-toxic dose. Then, real-time PCR was performed to assess the effects of honey on the expression of inflammatory genes.

Results: Based on PAD scores, honey samples were classified into low-score honey (LH; commercial honey) and high-score honey (HH; Ziziphus jujube honey). The highest non-cytotoxic concentration of honey was 12.5 mg/mL. Treatment with honey significantly suppressed the expression of pro-inflammatory cytokines, including IL-1β, IL-6, IL-8, and TNF-α, in HG-stimulated HUVECs (P 0.05).

Conclusion: This study demonstrates that honey treatment significantly attenuates hyperglycemia-induced inflammation and migration in HUVECs. These findings suggest that honey may modulate HG-mediated endothelial injury and exert protective effects against diabetic vascular complications.

keywords: Human Umbilical Vein Endothelial Cells; Hyperglycemia; PAD Score; Pro-Inflammatory

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-37

The effect of Fluorouracil-based combination therapy on metabolic enzyme activity, expression of glucose metabolism-related genes, and ROS levels in colorectal cancer cell line (HT-29) using a Drug Repositioning approach

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Background and aim: Drug resistance in colorectal cancer (CRC) limits the efficacy of 5-fluorouracil (5-FU). Since metabolic alterations, especially dependence on aerobic glycolysis, are considered one of the pillars of drug resistance and cancer cell survival, this study, with a drug repositioning approach, sought to identify a potential co-treatment and evaluate its effects on glycolytic metabolism pathways in the HT-29 cell line. In in silico screening, medroxyprogesterone acetate (MPA) was selected as the final candidate with the greatest overlap on glycolysis and hypoxia pathways and accessibility criteria.

Methods: Cell viability was measured by the MTT assay after 72-hour treatment with 5-FU (50–250 µM), MPA (0.5–8 mM) and the combination 5-FU (0.5 µM) + MPA (2–16 mM). Expression of genes related to glucose metabolism/transport HK2, GLUT1, MCT1/4 and LDH-A was assessed by qPCR, levels of reactive oxygen species (ROS) by flow cytometry (24 hours), and metabolic indices of medium glucose consumption and lysate LDH were evaluated at 24/48/72 hours.

Results: 5-FU significantly reduced HT-29 cell viability, whereas MPA alone showed no clear cytotoxicity. In combination, increasing MPA doses attenuated 5-FU–induced cytotoxicity, though viability remained below control levels (P0.05). At 72 hours, genes involved in glucose uptake and anaerobic glycolysis (GLUT1, HK2, LDH-A, MCT1/4) were upregulated, most prominently with the combination treatment. ROS levels decreased at 24 hours in both single treatments, with the greatest reduction in the 5-FU+MPA group. Metabolic measures showed a biphasic response, with reduced glucose consumption and LDH at 24–48 hours followed by increased levels at 72 hours compared to control (P0.05).

Conclusion: Our findings reveal a paradox: although MPA—selected by in silico predictions—induces transcriptomic changes in glycolytic pathways, these changes do not necessarily produce a cytotoxic phenotype and may instead create transient metabolic adaptations that activate survival mechanisms and ultimately antagonize 5-FU. This underscores the complexity of metabolic regulation in cancer and the need for further studies to precisely optimize dose–timing and integratively assess energy and oxidative-stress signaling before proposing MPA as an adjuvant therapy for colorectal cancer.

keywords: colorectal cancer, 5-fluorouracil, medroxyprogesterone acetate, Drug Repositioning, cellular metabolism

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-38

Preconcentration of morphine in urine sample using a green and solvent-free microextraction method

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Background and aim: The ability of extraction and preconcentration of small amounts of substances from biological samples is very important in medical toxicology. On the other hand, minimal use of organic solvents is an important issue to prevent environmental damage. In the present study, we developed a new solid phase microextraction fiber using plant extracts as sorbent for extraction and preconcentration of morphine in urine sample.

Methods: For this purpose, raw carbon nanotubes (CNTs) were functionalized with tobacco extracts. Functionalization was confirmed by Fourier transform infrared (FTIR) and Raman spectroscopy in addition to scanning electron microscope (SEM) images. The functionalized CNTs were coated on polypropylene hollow fiber.

Results: The results of HPLC analysis showed that the produced fiber could preconcentrate a very low concentration of morphine (0.25 ng/ml) in small volume of urine samples. Limit of detection (LOD) and limit of quantification (LOQ) for the produced fiber were determined 0.25 ng/ml and 0.825 ng/ml, respectively, and recovery of the fiber was determined 89% at LOQ.

Conclusion: Findings of the current study suggested that the provided method could improve the efficiency of morphine detection. In addition, the described method is a green analytical method with the lowest use of chemical solution in which a biodegradable fiber could be used for several times with no significant loss in concentrating capacity.

keywords: HPLC, Plant, Green chemistry, Morphine

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-39

The Role of Trace Elements in Alzheimer's Disease

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Background and aim: Alzheimer's disease (AD) is the leading cause of dementia and represents a chronic, progressive neurodegenerative condition marked by the deposition of amyloid-β (Aβ) plaques and the -related formation of tau neurofibrillary tangles. Growing evidence indicates that disturbances in micronutrient balance play a substantial role in both the development and progression of AD by modulating protein aggregation, oxidative damage, and intracellular signaling mechanisms.

Methods: We searched PubMed, Google Scholar, Clinical Trials and other Databases. We also reviewed these articles and collected the necessary information. Search terms included combinations of "Alzheimer's disease," "metals," and "trace elements."

Results: Excessive accumulation of metals such as aluminum, iron, and copper has been associated with enhanced neuroinflammatory responses, increased amyloid-β deposition, and tau hyperphosphorylation, through with oxidative stress, mitochondrial impairment, and microglial activation. Zinc exhibits a bidirectional effect, whereby insufficient levels disrupt synaptic integrity, while elevated concentrations promote Aβ aggregation and tau pathology. In addition, selenium deficiency compromises antioxidant capacity and promotes ferroptotic cell death through diminished activity of glutathione peroxidase 4 (GPX4)(5). Exposure to toxic heavy metals, including cadmium, lead, mercury, and arsenic, further contributes to neurodegeneration by inducing oxidative stress, disrupting calcium homeostasis, and triggering apoptotic pathways. These pathogenic effects are mediated predominantly through signaling cascades such as NF-κB, NLRP3 inflammasome activation, calcium-dependent pathways, PI3K/Akt/mTOR signaling, and glycogen synthase kinase-3β (GSK-3β).

Conclusion: Overall, dysregulation of trace elements represents a significant contributor to neuronal injury in AD and constitutes a promising target for therapeutic intervention. Elucidating the molecular mechanisms influenced by metal imbalance may facilitate the development of strategies aimed at restoring metal homeostasis, mitigating oxidative and inflammatory damage, limiting tau pathology, and ultimately slowing disease progression.

keywords: Alzheimer's disease, AD, Metals, and Trace elements

PBi-40

Prognostic Value of ANA in Autoimmune Thyroid Diseases: A Systematic Review

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Background and aim: Autoimmune thyroid diseases (AITDs), primarily Hashimoto's thyroiditis (HT) and Graves' disease (GD), are among the most prevalent organ-specific autoimmune disorders and are increasingly recognized as part of a broader spectrum of systemic immune dysregulation. Anti-nuclear antibodies (ANA), traditionally associated with systemic autoimmune diseases, are frequently detected in patients with AITDs, yet their clinical and prognostic relevance remains controversial. This systematic review aimed to evaluate the prevalence of ANA in AITDs and to clarify its potential role as a biomarker for disease severity, progression, and risk stratification.

Methods: This systematic review followed PRISMA 2020 guidelines and included studies published between January 2022 and December 2025. A comprehensive search of major databases, including PubMed and Google Scholar, identified thirteen eligible studies on adult patients with clinically confirmed HT or GD. Despite methodological heterogeneity, consistent trends emerged regarding the immunological and clinical implications of ANA positivity in AITDs.

Results: Across the reviewed literature, ANA prevalence ranged from approximately 20–55% in patients with Hashimoto's thyroiditis and 10–47% in those with Graves' disease, indicating that ANA positivity is a common and clinically meaningful finding rather than an incidental laboratory abnormality. Elevated ANA titers were repeatedly associated with enhanced immune activation, as demonstrated by higher levels of thyroid-specific autoantibodies, including thyroid peroxidase antibodies (TPOAb) and thyroglobulin antibodies (TgAb), as well as increased lymphocytic infiltration of thyroid tissue. Clinically, ANA-positive individuals often exhibited more aggressive disease phenotypes. In HT, ANA positivity was linked to faster progression toward overt hypothyroidism and increased levothyroxine requirements. In GD, it was associated with a higher risk of extrathyroidal manifestations, particularly Graves' ophthalmopathy. Several studies further highlighted the prognostic relevance of specific ANA immunofluorescence patterns, such as homogeneous and speckled staining, which appeared to correlate with disease severity and immune burden.

Conclusion: ANA positivity is a meaningful indicator of disease activity and progression risk in autoimmune thyroid diseases. Integrating ANA testing with conventional thyroid function and autoantibody assessments may enhance clinical monitoring and risk stratification. Large-scale, standardized longitudinal studies are needed to validate these observations and to establish clear clinical guidelines for ANA use in AITDs.

keywords: ANA, Autoimmune thyroid diseases, Hashimoto, Graves

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-41

Mercury and Lead Levels in Common Soaps from Local Markets in Mashhad, Iran

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Background and aim: The potential toxicity of human exposure was investigated to heavy metals from diverse sources but few or none was on Iranian soaps. Hence, we aimed to determine the presence of lead and mercury in selected soaps commonly used in Mashhad, northeastern Iran.

Methods: Different common brands of cosmetic, hygiene and contraband soaps were purchased from retail market of Mashhad. Levels of these metals were determined using atomic absorption spectroscopy technique.

Results: All samples had the mercury and lead levels but did not exceed the maximum acceptable level (1 µg/g for mercury and 20 µg/g for lead) recommended by FDA. The mean levels of mercury were 0.02, 0.08 and 0.23 µg/g, respectively in cosmetic, hygiene and contraband soaps. These levels for lead were 0.10, 0.19 and 0.13 µg/g.

Conclusion: The content of mercury and lead in common soaps is currently not a concern in this city. However, as human body may be exposed to several toxic metals from different care products simultaneously, cumulative toxic effects of these metals must be considered important.

keywords: Atomic Absorption Spectroscopy, Iran, Lead, Mercury, Soap

PBi-42

Investigation of the relationship between vitamin D levels and serum hemoglobin, iron, and ferritin levels in patients visiting the specialized and subspecialized polyclinic laboratory Shahrood University of Medical Sciences

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Background and aim: : Vitamin D functions as an autocrine/paracrine hormone playing a major role in multiple biological processes. Evidence contributes to hematopoiesis and iron metabolism. This study was conducted to examine the association between vitamin D levels and hematologic parameters including hemoglobin, hematocrit, serum iron, and ferritin in Iranian population.

Methods: Vitamin D and ferritin levels were measured by ELISA, serum iron was assessed by biochemical autoanalyzer, and hemoglobin along with other blood indices by automatic cell counter CBC device. Participants were classified into three groups based on vitamin D status: deficiency, insufficiency, and sufficiency. ANCOVA was used to compare means between groups, and multiple regression was performed to assess the independent association of vitamin D with blood indices. A significance level of P 0.05 was set.

Results: Although regression analysis in the overall population did not show significant associations with hematological indices, a significant correlation between serum vitamin D levels and serum iron, hematocrit, and hemoglobin was observed in the vitamin D-deficient group. In ANCOVA analysis, after adjusting for confounding factors, serum ferritin levels were higher in the vitamin D-deficient group compared to other groups, suggesting disturbed iron metabolism and potential subclinical inflammation.

Conclusion: The results suggest that vitamin D is likely involved in iron homeostasis and erythropoiesis. The findings of the present study highlight the importance of addressing vitamin D deficiency as a possible contributor to anemia, particularly in deficient individuals.

keywords: Vitamin D-ferritin-serum iron-hemoglobin

PBi-43

Thymoquinone-Based Combination Therapy in Breast Cancer: A Systematic Review

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Background and aim: Breast cancer is one of the most common malignancies worldwide and remains a leading cause of cancer-related morbidity and mortality among women. Although advances in diagnosis and treatment have improved patient outcomes, therapeutic resistance and treatment-related toxicity remain major challenges. These limitations have increased interest in combination therapeutic strategies. Thymoquinone, the main bioactive compound of Nigella sativa, has shown anticancer, antioxidant, and anti-inflammatory properties in experimental studies and may enhance the efficacy of conventional therapies while reducing adverse effects.This systematic review aims to assess the anticancer potential of combined thymoquinone treatment in breast cancer.

Methods: The study conducted an exhaustive search of published literature in databases including Proquest, PubMed, Scopus, Google Scholar, and Web of Science up to January 2, 2023, focusing on combination therapy with thymoquinone for breast cancer treatment. Subsequently, the identified articles were screened for their relevance to the research objectives, examining treatment modalities and research outcomes.

Results: Initially, 1,397 articles were retrieved, and after stringent screening and adherence to study criteria, 22 studies were selected for in-depth analysis. These studies encompassed 13 in vitro investigations, nine in vivo studies, and one combining both approaches. The most prevalent combination studied was tamoxifen/thymoquinone.

Conclusion: The adoption of combination therapy with thymoquinone presents a promising strategy for breast cancer treatment. This approach exhibits favorable outcomes, including enhanced treatment responses, mitigation of drug resistance, protection of cardiac and healthy cells, reduction of chemotherapy-related side effects, and radiosensitization to radiotherapy.

keywords: Thymoquinone; Breast Cancer; Combination Therapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-44

Association Between Serum Erythropoietin Levels and Red Blood Cell Indices in Adults

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Background and aim: Erythropoietin (EPO) is a glycoprotein hormone primarily synthesized by the kidneys and, to a lesser extent, by erythroid progenitor cells. It regulates erythropoiesis by stimulating red blood cell (RBC) production and promoting erythrocyte survival. Through these actions, EPO maintains hemoglobin concentration and overall red blood cell mass, influencing hematologic indices such as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). This study aimed to investigate the associations between naturally occurring differences in serum EPO concentrations and detailed hematological parameters in a clinical population.

Methods: A total of 43 adult participants were enrolled and categorized into three groups based on serum EPO levels: low, normal, and high. Serum EPO was quantitatively measured by chemiluminescence to ensure accurate group classification. Participants with hemoglobin levels exceeding 18.5 g/dL in males and 17.5 g/dL in females were excluded to avoid potential bias from erythrocytosis. Hematological parameters—including hemoglobin, RBC count, MCV, MCH, and MCHC—were determined using standard automated laboratory techniques. Age was recorded for demographic comparison.

Results: Hemoglobin levels varied across erythropoietin (EPO) categories, with a lower mean hemoglobin in the high EPO group (9.37 ± 1.00 g/dL) compared with the normal (14.36 ± 3.36 g/dL) and low (14.74 ± 2.55 g/dL) EPO groups. Mean corpuscular hemoglobin concentration (MCHC) was also reduced in the high EPO group (31.30 ± 1.65 g/dL) relative to the normal (33.25 ± 0.69 g/dL) and low (33.24 ± 0.86 g/dL) groups. In contrast, red blood cell count, mean corpuscular volume, mean corpuscular hemoglobin, and age were broadly similar across EPO categories and are reported without emphasis on between-group differences

Conclusion: Serum EPO levels were significantly associated with hemoglobin concentration ($P = 0.025$) and MCHC ($P = 0.001$), indicating that EPO status is more closely related to hemoglobinization and erythrocyte functional quality than to cell number or size. No statistically significant differences were detected across EPO groups for red blood cell count ($P = 0.066$), mean corpuscular volume ($P = 0.769$), mean corpuscular hemoglobin ($P = 0.391$), or age ($P = 0.577$), suggesting these parameters are less sensitive to variation in endogenous EPO within this cohort.

keywords: Erythropoietin, Hemoglobin

PBi-45

Oral administration of crocin significantly alleviated anxiety, and depressive-like behavior following ethanol and nicotine abstinence in adolescent male rats

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Background and aim: The co-abuse of nicotine (Nic) and ethanol (Eth) is a significant concern, particularly among adolescents, due to its detrimental effects on mental health. The present study investigates the effects of crocin, a constituent of saffron, on anxiety and depressive-like behavior caused by Nic-Eth abstinence in adolescent male rats.

Methods: Seventy adolescent male rats were divided into seven groups, including a vehicle group, a Nic-Eth group, and groups treated with crocin at different doses. The animals were subjected to various behavioral tests, including the elevated plus maze, open field, and forced swimming test, to assess anxiety and depressive-like behavior. The study also measured various biochemical parameters, including malondialdehyde (MDA) levels, thiol content, catalase and superoxide dismutase (SOD) activity, and levels of inflammatory and anti-inflammatory factors such as TNF-α and IL-10. These measurements were made using various assays, including ELISA kits and spectrophotometric methods.

Results: The results showed that crocin, especially at doses of 20 and 30 mg/kg, attenuated anxiety and depressive-like behavior in the Nic-Eth group. Crocin also improved anxiety-like behaviors in the open field test and elevated plus maze test, and decreased depression-like behavior in the forced swimming test. Biochemical analysis revealed that crocin improved oxidative/anti-oxidative imbalance and inflammatory/anti-inflammatory mediator imbalance induced by Nic-Eth abstinence. Crocin decreased malondialdehyde (MDA) levels, increased thiol content, and enhanced superoxide dismutase (SOD) and catalase (CAT) activity. Additionally, crocin improved IL-10 levels and decreased TNF-α levels, indicating its anti-inflammatory effects. The study also found that crocin increased serotonin levels and decreased monoamine oxidase (MAO) activity, which may contribute to its anxiolytic and antidepressant effects. Brain-derived neurotrophic factor (BDNF) levels were also increased in the Nic-Eth group treated with crocin, suggesting its potential role in neural plasticity and learning-memory processes.

Conclusion: The study suggests that crocin has potential anxiolytic and anti-depressant effects with minimal side effects, making it a potential treatment for abstinence symptoms following Nic or Eth consumption. However, further investigation is required to elucidate the mechanisms of action and to explore the long-term effects of crocin.

keywords: Crocin, Anxiety, Depression, Abstinence, Nicotine, Ethanol

PBi-46

Betaine improves hormonal abnormalities and oxidative stress in rats with letrozole-induced polycystic ovarian syndrome

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Background and aim: Polycystic ovarian syndrome (PCOS) is a common metabolic disorder in women that is frequently associated with infertility and reduced quality of life. This study investigated the potential ameliorative effects of betaine on PCOS-related abnormalities in rats by evaluating hormonal changes and antioxidant biomarker levels.

Methods: Adult female rats with normal estrous cyclicity were assigned to the control, betaine (100 mg/kg), PCOS, PCOS + betaine (50 mg/kg), and PCOS + betaine (100 mg/kg) groups (n = 6). To induce PCOS, rats were administered oral letrozole (1 mg/kg/day) for 21 days and treated with betaine for 14 days. To confirm PCOS development, estrous cyclicity was checked, and rats with irregular estrous cycles were enrolled in this study.

Results: Rats with PCOS exhibited hormonal abnormalities, as manifested by a significant increase in testosterone and luteinizing hormone (LH) levels and a considerable decrease in follicle-stimulating hormone (FSH) levels. Moreover, catalase and glutathione peroxidase activities were significantly lower in the PCOS group than in the control group. Treatment of PCOS rats with betaine significantly reduced the concentrations of testosterone and LH and increased the levels of FSH compared to those in untreated PCOS rats. Additionally, betaine-treated PCOS rats exhibited higher ovarian catalase and glutathione peroxidase activities than untreated PCOS rats. Interestingly, the expression of nuclear factor erythroid 2-related factor 2 (Nrf2) was increased in betaine-treated PCOS rats compared to that in untreated PCOS rats.

Conclusion: The results of this study showed that betaine may ameliorate PCOS-induced hormonal abnormalities and oxidative stress in rats, highlighting its potential for further investigation in clinical settings. Improvements in antioxidant enzyme activities and hormonal balance indicate that the alleviative effects of betaine may be mediated by the modulation of oxidative stress and endocrine function, supporting future translational research.

keywords: Polycystic ovarian syndrome; betaine; oxidative stress

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-47

Curcumin Attenuates Loud Noise–Induced Stress in Rats: The Mediating Role of Circulating Oxidative Stress Reduction

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Background and aim: Exposure to loud auditory stimuli is a potent environmental stressor that can induce systemic oxidative stress through activation of neuroendocrine and inflammatory pathways. Noise-induced stress has been associated with increased production of reactive oxygen species (ROS) and impairment of antioxidant defense mechanisms in the blood. Curcumin, a bioactive polyphenolic compound derived from Curcuma longa, has demonstrated strong antioxidant properties and the ability to modulate redox-sensitive signaling pathways. The present experimental study aimed to investigate whether the stress-attenuating effects of curcumin in rats exposed to loud auditory stimulation are mediated through the reduction of oxidative stress markers in blood.

Methods: Adult male rats were randomly divided into four groups: control, noise-exposed, curcumin-treated, and noise-exposed plus curcumin-treated. Auditory stress was induced by exposure to high-intensity noise (100–110 dB) for 2 hours per day over a 14-day period. Curcumin was administered orally at a standardized dose throughout the experimental period. Blood samples were collected at the end of the protocol to assess oxidative stress parameters, including malondialdehyde (MDA) levels, total antioxidant capacity (TAC), and activities of antioxidant enzymes such as superoxide dismutase (SOD) and catalase. Serum corticosterone levels were also measured to evaluate stress response.

Results: Rats exposed to loud noise exhibited a significant increase in blood MDA levels and corticosterone concentrations, along with a marked reduction in TAC, SOD, and catalase activity compared to controls (P 0.05). Curcumin administration significantly reversed these alterations in noise-exposed rats, evidenced by decreased lipid peroxidation and enhanced antioxidant enzyme activity (P 0.05). Mediation analysis indicated that improvement in blood oxidative stress markers partially mediated the effect of curcumin on reducing stress hormone levels.

Conclusion: The findings suggest that curcumin mitigates loud noise–induced stress in rats primarily through modulation of oxidative stress pathways in the blood. Reduction of systemic oxidative damage appears to be a key mediator in the protective effects of curcumin against auditory stress. These results highlight the potential role of curcumin as a therapeutic agent targeting oxidative stress–related mechanisms in stress-associated conditions.

keywords: Curcumin, Noise, Oxidative stress, Circulation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-48

Protective Effects of Curcumin Against Glioma Cells

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Background and aim: Glioma is of the most aggressive and common primary brain tumors, characterized by rapid proliferation, invasiveness, resistance to conventional therapies, and poor prognosis. Despite advances in surgery, radiotherapy, and chemotherapy, effective treatment options remain limited, highlighting the need for novel therapeutic agents. Curcumin, a natural polyphenolic compound derived from Curcuma longa, has gained considerable attention due to its antioxidant, anti-inflammatory, and anticancer properties. Increasing evidence suggests that curcumin may exert protective and therapeutic effects against various cancers, including glioma. This study aimed to investigate the protective effects of curcumin against glioma and to explore its underlying cellular and molecular mechanisms

Methods: In this experimental research study, glioma cells were treated with different concentrations of curcumin for defined time periods. Cell viability and proliferation were assessed using standard assays. Apoptosis was evaluated through morphological analysis and measurement of apoptotic markers. In addition, oxidative stress parameters and inflammatory mediators were analyzed. Expression levels of key signaling molecules involved in cell survival, apoptosis, and tumor progression were examined using molecular and biochemical techniques.

Results: Curcumin treatment significantly reduced glioma cell viability and proliferation in a dose- and time-dependent manner (P 0.05). Treated cells showed increased apoptotic activity, accompanied by upregulation of pro-apoptotic markers and downregulation of anti-apoptotic proteins. Moreover, curcumin markedly decreased oxidative stress levels and suppressed inflammatory mediators associated with glioma progression. Modulation of critical signaling pathways involved in cell cycle regulation and tumor growth was also observed following curcumin exposure.

Conclusion: The findings of this study demonstrate that curcumin exerts significant protective and anticancer effects against glioma by inhibiting tumor cell proliferation, inducing apoptosis, and reducing oxidative and inflammatory stress. These results suggest that curcumin may serve as a promising adjunct or alternative therapeutic agent for glioma management. Further in vivo and clinical studies are warranted to confirm its efficacy and translational potential.

keywords: Glioma, Curcumin, tumor proliferation, Oxidative stress

PBi-49

Serum Brain-Derived Neurotrophic Factor (BDNF) Levels in Elderly Individuals with Cognitive Impairment

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Background and aim: Age-related cognitive impairment and mild cognitive decline are major public health concerns among older adults and are considered potential precursors to dementia. In recent years, biological markers associated with neuroplasticity have received increasing attention. One such marker is Brain-Derived Neurotrophic Factor (BDNF), a neurotrophin that plays a critical role in neuronal survival, synaptic plasticity, learning, and memory processes. Reduced levels of BDNF have been linked to cognitive dysfunction and neurodegenerative disorders. The present study aimed to investigate serum BDNF levels in elderly individuals with cognitive impairment and compare them with cognitively healthy older adults.

Methods: This descriptive-analytical cross-sectional study was conducted on 80 elderly participants aged 60 years and older. Participants were divided into two groups: individuals with mild cognitive impairment and cognitively healthy controls. Cognitive status was assessed using standardized cognitive assessment tools. Peripheral blood samples were collected from all participants, and serum BDNF levels were measured using the enzyme-linked immunosorbent assay (ELISA) method. Statistical analyses were performed using independent t-tests and Pearson correlation coefficients to evaluate group differences and associations between variables.

Results: The findings demonstrated that mean serum BDNF levels were significantly lower in elderly individuals with cognitive impairment compared to the healthy control group (P 0.05). Additionally, a significant positive correlation was observed between cognitive test scores and serum BDNF levels, indicating that lower BDNF concentrations were associated with poorer cognitive performance.

Conclusion: The results of this study suggest that reduced serum BDNF levels are associated with cognitive impairment in older adults. BDNF may serve as a potential biological marker for the early identification of individuals at risk for cognitive decline. Further longitudinal studies with larger sample sizes are recommended to clarify the predictive value of BDNF and its role in the progression of age-related cognitive disorders.

keywords: Cognition, Brain-Derived Neurotrophic Factor, Biomarker, Memory

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-50

High-Resolution Melting–Based Analysis of Manganese Superoxide Dismutase (MnSOD Val-9Ala) Gene Polymorphism in Patients with Gastric Cancer

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Background and aim: Gastric cancer is a multifactorial malignancy with complex carcinogenic and immunopathological mechanisms, remaining a major cause of cancer-related mortality in Asia. Reactive oxygen species (ROS) have a significant role in gastric carcinogenesis. Manganese superoxide dismutase (MnSOD), a mitochondrial antioxidant enzyme, protects against oxidative stress by converting superoxide radicals into hydrogen peroxide and oxygen. A T-to-C substitution at nucleotide 47, resulting in the Val-9Ala polymorphism, may alter the mitochondrial targeting sequence of MnSOD and influence susceptibility to gastric cancer. This study aimed to analyze MnSOD single nucleotide polymorphisms (SNPs) in gastric cancer patients using high-resolution melting (HRM) analysis.

Methods: Genomic DNA was extracted from 30 formalin-fixed paraffin-embedded tissue samples obtained from patients with gastric cancer and from 30 healthy control individuals. The MnSOD Val-9Ala (T/C) polymorphism was evaluated using high-resolution melting analysis based on differences in melting temperature (Tm) profiles. Selected samples were subsequently validated by DNA sequencing.

Results: HRM analysis successfully discriminated MnSOD genotypes in both study groups. In the control group, the frequencies of Ala/Ala, Ala/Val, and Val/Val genotypes were 23.3%, 63.3%, and 13.3%, respectively, whereas the corresponding frequencies in the gastric cancer group were 16.6%, 53.3%, and 30%. The Ala allele frequency was 54% in healthy individuals and 43% in patients with gastric cancer, while the Val allele frequency was 56% and 44% in the control and case groups, respectively. The sensitivity and specificity of HRM for identifying MnSOD SNPs were both calculated to be 100%, as confirmed by sequencing.

Conclusion: The findings of this preliminary study suggest a potential association between MnSOD Val-9Ala polymorphism and gastric cancer. High-resolution melting analysis appears to be a reliable and efficient method for SNP analysis. Further large-scale and interdisciplinary studies are warranted to clarify the clinical relevance of MnSOD polymorphisms in gastric cancer.

keywords: Gastric cancer, Gene polymorphisms, High-Resolution Melting, Manganese Superoxide Dismutase.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-51

MicroRNA-146a gene polymorphism (rs2910164) association with risk of β-thalassemia major: A case-control study

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Background and aim: β-thalassemia major is a severe inherited hemoglobinopathy characterized by chronic anemia, transfusion dependence, and systemic complications. MicroRNA-146a (miR-146a) plays a critical role in modulating inflammatory responses, and its functional polymorphism rs2910164 has been implicated in various inflammatory and hematological disorders. This study aimed to investigate the association between the miR-146a rs2910164 C/G polymorphism and the risk of β-thalassemia major.

Methods: A case-control study was conducted involving 150 β-thalassemia major patients and 150 age- and gender-matched healthy controls. Demographic, clinical, and laboratory data were collected, including complete blood counts, inflammatory markers (hs-CRP, ESR), iron overload indicators, and complication profiles. Genotyping of the rs2910164 polymorphism was performed using tetra-primer ARMS-PCR. Statistical analyses included Hardy–Weinberg equilibrium testing, calculation of odds ratios (ORs) with 95% confidence intervals (CIs) under multiple genetic models, and adjustment for potential confounders such as BMI.

Results: The patient group exhibited a distinct clinical phenotype, including significantly lower BMI (p 0.001), severe anemia (Hb: 6.9 ± 0.8 g/dL), elevated HbF (18.5%), high serum ferritin (median 3200 ng/mL), and increased inflammatory markers (p 0.001). Genotype distributions in controls were in Hardy–Weinberg equilibrium (p = 0.082), whereas patients showed significant deviation (p 0.001). The homozygous GG genotype was associated with a significantly increased risk of β-thalassemia major under codominant (GG vs. CC: OR = 2.21, 95% CI: 1.18–4.09, p = 0.021) and recessive models (GG vs. CC+CG: OR = 2.35, 95% CI: 1.31–4.22, p = 0.009). The G allele frequency was higher in patients (40.3% vs. 32.0%, OR = 1.50, 95% CI: 1.11–2.10, p = 0.039).

Conclusion: The miR-146a rs2910164 GG genotype is significantly associated with an increased risk of β-thalassemia major, suggesting a potential role of miR-146a-mediated inflammatory dysregulation in disease susceptibility. These findings highlight the relevance of genetic markers in understanding disease mechanisms and support further investigation into personalized approaches for risk stratification and management in β-thalassemia major.

keywords: miR-146a, β-thalassemia major, Polymorphism

PBi-52

Single-Cell Analysis in Oral Squamous Cell Carcinoma: Unraveling Heterogeneity and Driving Biomarker Discovery

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Background and aim: Oral squamous cell carcinoma (OSCC) is among the most common malignant tumors in the head and neck region. This cancer is recognized with substantial intratumoral heterogeneity that contributes to treatment resistance, metastasis, and poor prognosis. Traditional bulk sequencing techniques cannot capture cellular diversity, whereas single-cell analysis enables detailed profiling of individual cells within the tumor microenvironment (TME).

Methods: In this study, we searched the Google Scholar, PubMed, and Scopus databases and included original articles, systematic reviews, and meta-analyses related to single-cell analysis in OSCC.

Results: Single-cell analysis has demonstrated significant potential in OSCC biology, including tumor cell subpopulations with distinct oncogenic mechanisms during progression from normal oral mucosa to oral potentially malignant disorders and invasive OSCC. For example, single-cell analysis identified upregulated pathways in cancer-associated fibroblasts that were associated with invasion and metastasis. In addition, multiregional transcriptomics in HPV-negative OSCC highlighted spatial heterogeneity, associating specific immune cell infiltrates with treatment responses. The analyses after chemotherapy demonstrated alterations in the TME, including altered immune cell composition and enhanced cisplatin resistance via PI3K/AKT signaling in resistant cells. Additionally, integrated single-cell and bulk RNA-seq approaches identified differentially expressed genes in tumor-infiltrating lymphocytes, linking them to prognosis and to the efficacy of neoadjuvant immunotherapy. These results show that single-cell approaches have identified potential biomarkers, such as specific genes and signaling pathways, that are not accessible to bulk analyses.

Conclusion: Single-cell analysis provides a comprehensive understanding of OSCC heterogeneity and offers good opportunities to identify novel biomarkers, stratify patients, and design personalized therapies.

keywords: Single-cell analysis, Oral squamous cell carcinoma, Tumor heterogeneity, Biomarkers

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-53

The association between rs2287499 and rs1042522 variants and expression and folding of TP53 is involved in polycystic ovary syndrome pathogenesis: in-silico analysis

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Background and aim: Polycystic ovary syndrome (PCOS) is a multifactorial endocrinopathy characterized by various reproductive and metabolic abnormalities. The tumor suppressor p53 (TP53) plays a crucial role in cellular stress responses. Alterations in its structure or expression can influence PCOS pathogenesis. We aim to use in-silico analyses to predict the effects of the rs2287499 and rs1042522 genetic variants on the expression and structural stability of the TP53 protein.

Methods: This study investigates the association of two genetic variants, rs2287499 and rs1042522, with the expression levels and folding stability of TP53 protein through in-silico analyses. Utilizing bioinformatics tools (VMD, WebLogo and PROMO), we examined the potential impacts of these single nucleotide polymorphisms (SNPs) on TP53 transcriptional activity, protein structure, and functional integrity.

Results: Our findings indicate that the rs2287499 variant significantly influences TP53 expression levels, while rs1042522 is associated with altered protein folding dynamics. These changes may disrupt TP53's normal regulatory functions, contributing to PCOS etiology. Furthermore, our study establishes a framework for integrating genetic variants into the understanding of TP53-mediated mechanisms in PCOS, which could pave the way for developing targeted therapeutic strategies.

Conclusion: These results underscore the importance of genetic variants in PCOS hormonal and metabolic dysregulation.

keywords: TP53, PCOS, Bioinformatics, rs1042522, rs2287499

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-54

Targeted Hyperthermia at the Laboratory–Clinic Interface: Biochemical Mechanisms, Biomarkers, and Therapeutic Sensitization in Cancer

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Background and aim: Targeted hyperthermia has re-emerged as an adjunct modality in cancer therapy, yet its clinical application remains largely empirical and insufficiently guided by laboratory biomarkers. From a clinical biochemistry perspective, hyperthermia induces measurable proteotoxic, metabolic, and immunogenic stress responses that influence tumor sensitivity to chemotherapy, radiotherapy, and immunotherapy. The aim of this review is to synthesize current evidence on the biochemical mechanisms of targeted hyperthermia and to highlight laboratory-measurable biomarkers that may enable biomarker-guided, laboratory-to-clinic integration of hyperthermia in personalized oncology.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. A comprehensive literature search was performed in PubMed, Scopus, and Web of Science for studies published between 2019 and 2024 using predefined keywords related to targeted hyperthermia, clinical biochemistry, proteotoxic stress, biomarkers, and cancer therapy. Original research articles, translational studies, and clinical trials reporting biochemical, molecular, or immunological outcomes were included. Data were extracted focusing on laboratory-measurable mechanisms, pharmacodynamic biomarkers, and clinical relevance. Study selection and data synthesis were performed independently to ensure methodological rigor.

Results: The review showed that targeted hyperthermia induces measurable biochemical changes in tumors, including proteotoxic stress via heat shock protein saturation, impaired DNA repair, and metabolic alterations such as glycolytic stress and ROS generation. Hyperthermia also triggered immunogenic cell death, evidenced by ATP, HMGB1, and calreticulin release, enhancing dendritic cell activation. Translational and clinical studies reported improved drug delivery, favorable pharmacokinetics, and synergistic effects when combined with chemotherapy, radiotherapy, or immune-based therapies, highlighting its potential as a laboratory-guided adjunct in cancer treatment.

Conclusion: Targeted hyperthermia functions as a potent biochemical modulator that enhances therapeutic sensitivity through measurable proteotoxic, metabolic, and immunogenic mechanisms. Evidence supports its role in disrupting tumor homeostasis, improving drug delivery, and promoting immunogenic cell death when integrated with standard and immune-based therapies. Transitioning hyperthermia from an empirically applied modality to a biomarker-guided, laboratory-driven intervention may optimize its clinical efficacy and support personalized cancer treatment strategies.

keywords: Hyperthermia, Clinical Biochemistry, Proteotoxic Stress, Immunogenic Cell Death

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-55

Antioxidant and anti-inflammatory effects of chrysin niosomes

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Background and aim: Previous experiments have reported that chrysin niosomes has potential antioxidant effects. Hence, in this experiment, we evaluated the antioxidant effects of this niosomes in the high-fat diet (HFD) rats.

Methods: In this experiment, Wistar rats were randomly divided into 3 groups, including 1- healthy animals, 2: high-fat diet (HFD) group, and 3: HFD + chrysin niosomes. In the end of the experiment, the biochemical factors such as urea and creatinine were determined. Oxidative stress markers, including malondialdehyde (MDA), total antioxidant activity (TAC), total oxidative status (TOS) were measured. Furthermore, morphological changes in the kidney were evaluated by using hematoxylin and eosin (H & E). The results were analyzed using SPSS as mean ± SEM by ANOVA followed by Tukey as a post-hoc test.

Results: The levels of urea and creatinine significantly increased by HFD, while treatment with chrysin niosomes normalized these factors. HFD also increased the malondialdehyde (MDA), total oxidative status (TOS) and reduced antioxidant activity (TAC). While treatment with cerium oxide nanoparticles normalized these factors. chrysin niosomes nanoparticles also alleviated morphological changes of kidney.

Conclusion: Our results showed that chrysin niosomes reduce oxidative stress in HFD model and can be a propose as a potential treatment of hyperlipidemia.

keywords: high-fat diet (HFD), rats, malondialdehyde

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-56

Pre-Analytical Phase as the Major Source of Laboratory Errors: A Systematic Review of Frequency and Preventive Interventions

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Background and aim: Pre-analytical errors (PAEs) are the most common laboratory errors, occurring before the analytical phase and mainly resulting from inappropriate test requests, inadequate patient preparation, and improper specimen collection, labeling, handling, or transport. According to ISO 15189:2012, the pre-analytical phase encompasses all steps from test ordering to sample receipt for analysis. PAEs account for approximately 70% of laboratory errors and represent a major threat to diagnostic accuracy and patient safety. This systematic review evaluates the frequency, types, and distribution of PAEs, with particular emphasis on blood sample quality, human factors, and variations across laboratory sections and clinical settings.

Methods: This systematic review was conducted in accordance with PRISMA guidelines. PubMed, Scopus, and Web of Science were searched for articles published between 2015 and 2025 using keywords including “pre-analytical errors,” “specimen quality,” “hemolysis,” and “laboratory errors.” Eligible studies included original research, observational studies, randomized controlled trials, and relevant case reports addressing pre-analytical errors or their impact on laboratory test accuracy. Reviews, editorials, abstracts, animal studies, and non-relevant articles were excluded. Titles and abstracts were independently screened, followed by full-text assessment, and duplicates were removed using reference management software.

Results: A total of 3,137 rejected or repeated test orders (0.09%) were identified among 3,346,199 test requests, of which 2,104 cases (67.1%) were attributed to pre-analytical errors, corresponding to a PAE rate of 0.063% (95% CI: 0.060–0.066%). The most frequent causes of specimen rejection were clotted samples (32%) and insufficient sample volume (31%). Hematology accounted for the highest proportion of PAEs (48.4%), followed by clinical chemistry (26.2%). Inpatient units exhibited the highest error rates (47.3%), with most errors occurring during the morning shift (58.2%). Poor blood sample quality, particularly hemolysis, was identified as the leading contributor to PAEs, and human error accounted for 82.6% of all errors. Case reports highlighted critical instances in which improper sampling or collection from central lines resulted in conflicting laboratory findings, emphasizing the importance of standardized procedures and careful specimen handling.

Conclusion: Pre-analytical errors remain the leading and largely preventable source of laboratory inaccuracies, predominantly resulting from poor specimen quality and human-related factors. The implementation of standardized procedures, continuous staff training, automation, and improved clinician–laboratory communication is essential to reduce PAEs, enhance diagnostic reliability, and improve patient safety, particularly in high-risk clinical settings.

keywords: pre-analytical errors, specimen quality, hemolysis, laboratory errors

PBi-57

Endometrial Regeneration and the Role of the Extracellular Matrix: Mechanisms, Challenges, and Future Perspectives

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[1] دانشگاه علوم پزشکی اسدآباد

Background and aim: Endometrial regeneration is a cornerstone of reproductive health, with the extracellular matrix (ECM) playing a pivotal role in tissue repair, regeneration, and fertility restoration. Dysregulated ECM remodeling is at the heart of many debilitating conditions, including infertility, endometriosis, Asherman's syndrome, and uterine fibroids, all of which disrupt the delicate balance necessary for effective endometrial regeneration.This review presents a cutting-edge analysis of ECM dynamics, emphasizing its central role in the endometrial regeneration process and highlighting novel ECM-targeted therapies that hold transformative potential for addressing these complex disorders. We focus on emerging strategies such as stem cell-based therapies, growth factor modulation, matrix

Methods: Relevant literature was identified by a PubMed search, and Google Scholar (2010-2025) of English language papers using the terms " Platelet Activation ", " Endothelial Dysfunction ", " Platelet ", " Leukocyte ", "Clinical Practice" and " , "Therapy". mediators are released and affect endothelial cells (ECs) and lead to endothelial dysfunction (ED).

Results: Revolutionary technological advancements, including 3D bioprinting, biocompatible ECM scaffolds, and organoid models, are providing new avenues for personalized therapeutic approaches aimed at optimizing ECM interaction and enhancing regenerative outcomes for individual patients. Despite these promising developments, significant challenges remain in evaluating the long-term safety and efficacy of ECM-targeted treatments. This review also identifies critical knowledge gaps, particularly in understanding the molecular mechanisms governing ECM remodeling in the endometrial context, urging further exploration to unlock the full therapeutic potential of ECM-based regeneration strategies.

Conclusion: Through precise modulation of ECM dynamics, this research sets the stage for innovative treatments that could revolutionize the management of uterine dysfunction and significantly enhance fertility restoration.

keywords: Endometrial Regeneration, Extracellular Matrix, Infertility, Personalized Medicine.

PBi-58

Quality Control Analysis of Platelet Apheresis Products from the Terumo BCT Reveos System: Evaluating pH, Platelet Count, and Swirling Effect During 7-Day Storage

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Background and aim: Platelet transfusion is critical for thrombocytopenic patients, and ensuring product quality during storage is essential. While traditional devices like Fresenius COM.TEC and Haemonetics MCS+ have been studied, newer systems like Terumo BCT Reveos require evaluation. This study assesses the quality of platelet apheresis products from the Reveos system by measuring pH, platelet count (PLT), and swirling effect over a 7-day storage period.

Methods: This experimental study collected 30 platelet apheresis products from healthy male donors at the Tehran Blood Transfusion Center using the Terumo BCT Reveos system. Samples were tested on days 1, 3, 5, and 7 of storage. pH was measured using a pH meter, platelet counts were obtained with an automated hematology analyzer, and swirling effect was assessed visually and scored (0: no swirl, 3: excellent swirl). Statistical analysis was performed using repeated-measures ANOVA in R software, with p0.05 considered significant.

Results: pH values showed a gradual decline from 7.2±0.1 on day 1 to 6.9±0.2 on day 7 (p0.001). Platelet counts remained stable throughout storage (Day 1: 1.1×10^{11}±0.2, Day 7: 1.0×10^{11}±0.3, p=0.12). Swirling scores decreased significantly, with 100% of units scoring 3 on day 1, but only 40% scoring ≥2 on day 7 (p0.0001). A strong negative correlation was observed between pH decrease and swirling score reduction (r=-0.85, p0.01).

Conclusion: The Terumo BCT Reveos system produces platelet products that maintain acceptable platelet counts over 7 days, but pH and swirling quality decline significantly after day 5. For optimal transfusion efficacy, use within 5 days of storage is recommended.

keywords: Platelet storage, Terumo BCT Reveos, Quality control, pH, Swirling effect

PBi-59

Cell and Molecular Mechanisms of the Tumor Microenvironment in Testicular Germ Cell Tumors: Role in Growth, Metastasis, and Therapeutic Response

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Background and aim: Testicular germ cell tumors (TGCTs) are the most common malignancies in young adult men. While cisplatin-based chemotherapy achieves high cure rates, a subset of patients develops chemoresistance and relapse. Accumulating evidence highlights the tumor microenvironment (TME) comprising immune, stromal, and vascular components as a critical regulator of tumor progression, metastasis, and therapy response.

Methods: We performed a comprehensive review of literature focusing on the cellular and molecular mechanisms shaping the TGCT TME, including tumor-associated macrophages, neutrophils, myeloid-derived suppressor cells, dendritic cells, NK and T cells, cancer-associated fibroblasts, and endothelial cells. Key processes analyzed included immune evasion, metabolic and epigenetic reprogramming, extracellular matrix remodeling, angiogenesis, and paracrine signaling.

Results: TGCTs exploit the immune-privileged testicular niche to promote immunosuppressive phenotypes: M2 macrophages, N2 neutrophils, tolerogenic dendritic cells, exhausted T cells, and hypofunctional NK cells create a highly suppressive immune landscape. Stromal cells remodel ECM, secrete paracrine survival factors, and enhance angiogenesis, fostering proliferation, invasion, and chemoresistance. Hypoxia, cytokines (TGF-β, IL-10, IL-6), and metabolic adaptation synergize with epigenetic modifications to stabilize these protumorigenic states. Subtype-specific differences exist: seminomas retain partial immune activation (“inflamed but regulated”), whereas non-seminomatous tumors display immune exclusion and higher therapy resistance.

Conclusion: The TGCT microenvironment orchestrates tumor growth, metastasis, and therapeutic response through intricate immune-stromal-vascular interactions. Targeting immunosuppressive circuits, metabolic adaptation, and stromal signaling offers a promising avenue to overcome chemoresistance. Detailed understanding of TGCT TME dynamics provides a framework for the development of TME-directed and combinatorial therapeutic strategies.

keywords: Tumor Microenvironment, Testicular Germ Cell Tumors, Molecular Mechanisms

PBi-60

The Role of STAT3 in the Pathogenesis and Progression of Colorectal Cancer: A Systematic Review

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Background and aim: Colorectal cancer (CRC) is one of the most important public health issues in the world, and the role of molecular factors such as the STAT3 protein in its progression has attracted much attention. Persistent activation of STAT3 can promote the growth of cancer cells, and therefore, STAT3 has been identified as a potential target for CRC treatment. Given the importance of this issue, the present study analyzes the evidence published since 2016 on the role of STAT3 in colorectal cancer as a systematic review.

Methods: We searched across databases like PubMed, Scopus, and Google Scholar, employing the keywords "STAT3" AND "Colorectal cancer," for publications published from 2016 to 2026. Inclusion criteria encompassed in vitro, in vivo, and clinical research examining the roles of STAT3 in colorectal cancer. The data extracted concern molecular mechanisms, signaling pathways, and therapeutic implications of STAT3 in CRC.

Results: A total of approximately 1332 studies were initially retrieved. Numerous studies demonstrated that STAT3 is frequently overexpressed or aberrantly activated in colorectal cancer tissues and cell lines. STAT3 activation was associated with increased tumor cell proliferation, suppression of apoptosis, immune evasion, and chemoresistance. Emerging therapeutic strategies targeting STAT3, including small-molecule inhibitors and nanoparticle-based drug delivery systems, have shown promising preclinical outcomes.

Conclusion: Evidence published after 2016 shows that STAT3 plays an essential role in CRC development, progression, and treatment resistance. STAT3 may also act as a potential diagnostic biomarker and a promising target for therapy.

keywords: Colorectal cancer; Signal transducer and activator of transcription 3; systematic

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-61

Nanocarrier-Based Chemotherapy: Capecitabine Encapsulation in Polycaprolactone-polyethylene glycol for Colorectal Cancer cells

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Background and aim: Colorectal cancer causes many deaths despite many treatment options. Capecitabine (CAP) uses as the standard chemotherapy regimen for colorectal cancer. However, after a period of administration, the free drug does not induce effective apoptosis due to rapid metabolism. This work aims to encapsulate CAP and evaluates cytotoxic and apoptotic effects on HCT-119 colorectal cancer cells, and human umbilical vein endothelial cells (HUVECs).

Methods: CAP nano-formulation was prepared by (PCL-PEG-PCL) biodegradable copolymer to improve drugs' bioavailability as an anticancer agent. The nanoparticles were prepared with the Ultrasonic homogenization method. The physicochemical characteristics of nanoparticles were evaluated using FTIR, DLS, and FESEM techniques. The zeta potential, entrapment efficiency, drug release, and storage stability were studied. Also, cell viability and apoptosis were examined by using MTT and acridine orange (AO) and propidium iodide (PI), respectively.

Results: The smaller hydrodynamic size (291.1 nm), polydispersity index (0.203), and zeta potential (-20.8 mV) were observed in nanoparticles. Nanoparticles revealed good formulation and storage stability at 25◦C in 90 days. Despite the increase in IC50 of nanoparticles compared to the free drug, the cytotoxic effect was observed with a slow release of the drug. (p-value 0.05). In (AO/PI) staining, the percentage of apoptotic cells in the CAP- loaded (PCL-PEG-PCL) in HUVEC and HCT-116 were calculated as 54% and 51.22%, respectively.

Conclusion: Developed micelles formulation was able to sustain the drug release and entrap the CAP to more apoptosis of cancer cells. The CAP-loaded (PCL-PEG-PCL) nanoparticles in this research could be an effective strategy for targeted colorectal cancer therapy.

keywords: Colorectal cancer; Capecitabine; (PCL-PEG-PCL); Apoptosis

PBi-62

Anti-CD133-grafted single-walled carbon nanotubes as doxorubicin carrier

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Background and aim: Advances in nanomedicine have spurred interest in antibody-conjugated carbon nanotubes for targeted cancer therapy. CD133, a marker enriched in chemoresistant cancer stem cells, presents a strategic target for precision drug delivery. This study explores functionalized single-walled carbon nanotubes (SWCNTs) as dual-action platforms for enhanced doxorubicin (DXR) delivery and CD133-specific targeting.

Methods: Two nano formulations-SWCNT-Ab/DXR (antibody-functionalized) and SWCNT-PEG-Ab/DXR (pegylated antibody-functionalized)-were engineered to encapsulate DXR. Release profiles, cytotoxicity, and apoptosis were assessed in CD133+ HT-29 colorectal cancer cells and CD133− CHO control cells. Computational modeling included DFT-D structural optimization, Monte Carlo adsorption simulations for DXR binding analysis, and molecular docking to evaluate carrier-receptor interactions.

Results: PEGylation markedly enhanced colloidal stability and drug-loading capacity, with SWCNT-PEG-Ab/DXR achieving 92% DXR encapsulation vs. 78% for non-PEGylated counterparts. In vitro, the PEGylated system showed amplified cytotoxicity (IC50: 2.1 µM vs. 3.8 µM for SWCNT-Ab/DXR) and 1.7-fold higher apoptosis induction in HT-29 cells. Computational data aligned with experimental findings: DXR adsorption energy was strongest on PEG-NH2- modified SWCNTs (− 32.6 kcal/mol) versus carboxylated variants (− 24.8 kcal/mol), confirming PEG's role in stabilizing drug-carrier interactions

Conclusion: By integrating PEG-mediated stealth properties, charge-modified surfaces, and antibody targeting, SWCNT-PEG-Ab/DXR emerges as a multifunctional nanoplatform with enhanced tumor selectivity and therapeutic payload delivery. This dual experimental-computational approach underscores the potential of rationally engineered nanotubes to overcome limitations in conventional chemotherapy.

keywords: SWCNTs, CD133Ab, Doxorubicin, Polyethylenglycol, Cytotoxicity, Monte carlo locator module

PBi-63

Methylene Blue Attenuates Ovarian Oxidative Stress and Follicular Dysfunction in a Mouse Model of Polycystic Ovary Syndrome

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Background and aim: Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder characterized by impaired follicular development and ovulatory dysfunction, in which oxidative stress plays a critical pathogenic role. Increasing evidence suggests that excessive oxidative damage in ovarian granulosa cells contributes to follicular atresia and disrupted ovarian function. Methylene blue (MB) has recently gained attention for its potent antioxidant and cytoprotective properties. In the present study, a letrozole-induced PCOS mouse model was employed to evaluate the effects of MB on ovarian oxidative stress and histopathological alterations in the ovaries of PCOS-induced mice by letrozole.

Methods: Thirty female mice were randomly assigned into three groups (n = 10 per group): control, PCOS, and MB-treated PCOS. PCOS was induced via oral administration of letrozole. Mice in the MB-treated group received daily intraperitoneal injections of MB at a dose of 0.5 mg/kg for two weeks. Ovarian total antioxidant capacity (TAC) was measured to evaluate oxidative stress. Histological examinations were conducted to assess follicular morphology, the number of atretic follicles, and overall ovarian structure. Additionally, quantitative real-time PCR was used to determine the expression levels of Nrf2 and FoxO3a, key regulators of antioxidant defense and cell survival.

Results: Letrozole-induced PCOS significantly reduced ovarian TAC levels and increased the number of atretic follicles compared with control mice. Treatment with MB effectively restored antioxidant capacity and improved ovarian histology by preserving follicular morphology, reducing atresia follicles, and maintaining the organization of granulosa cells. Furthermore, MB administration significantly upregulated Nrf2 and FoxO3a expression, indicating activation of key antioxidative and cytoprotective pathways. No adverse effects were observed in MB-treated mice.

Conclusion: These findings demonstrate that methylene blue mitigates oxidative stress and protects ovarian follicular structures in a PCOS mouse model. The activation of Nrf2 and FoxO3a genes may underlie these beneficial effects. Overall, MB shows promise as a potential therapeutic agent for alleviating ovarian dysfunction in PCOS, warranting further preclinical and clinical investigations.

keywords: Polycystic ovary syndrome; Methylene blue; Oxidative stress

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PBi-64

SR-B1 and LDLR Receptors expression in the malignant and benign Endometrial tumors

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Background and aim: Objective: Among gynecological malignancies, endometrial cancer (EC) ranks 2nd among worldwide. This study examined the expression and concentration of HDL (SR-B1) and LDL (LDLR) receptors, HDL- C and LDL-C concentrations in the malignant endometrial tissues.

Methods:Paired tumor and adjacent normal endometrial tissues were collected from treatment-naïve patients and SRB1 and LDLR mRNA and protein levels were quantified by qRT–PCR (normalized to B2M) and ELISA, respectively. Lipid content was measured using spectrophotometer. Findings were validated using paired TCGA-UCEC RNA-seq data (DESeq2; $|\log_2 FC|$ 1.5, p 0.05). KEGG pathway enrichment and differential expression visualization were performed in R. Data are presented as mean ± SEM; group comparisons used Mann–Whitney U test (p 0.05).

Results: Results: The expressions and concentrations SR-B1 (P = 0.008, P = 0.0004), LDLR (P = 0.004, P= 0.007), HDL-C (P 0.0001), and LDL-C (P 0.0001) in the malignant tumors were significantly higher than those of normal tissues. ROC curves for SR-B1, LDLR and lipoprotein expression and concentration were significant.

Conclusion: Conclusions: The mechanisms may be related to the lipoprotein metabolism and concentration via increasing receptor levels.

keywords: Endometrial cancer, HDL-C, LDL-C, SR-B1, LDLR, ELISA, qRT-PCR.

PBi-65

Extracellular Vesicles as Mechanistic Mediators and Next-Generation Biomarkers in Reproductive Medicine

صبا صفدرپور [1] © Ⓟ

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Background and aim: Extracellular vesicles (EVs) are nano-sized, membrane-bound particles secreted by somatic and germ cells, carrying proteins, lipids, and nucleic acids, including microRNAs. Emerging evidence indicates that EVs play critical mechanistic roles in gamete maturation, fertilization, and early embryogenesis by mediating intercellular communication within follicular fluid, seminal plasma, and embryo culture media. Their molecular cargo modulates key signaling pathways such as PI3K/AKT, MAPK, and Wnt, influencing oocyte competence, sperm functionality, and embryo developmental potential. These properties position EVs as promising non-invasive biomarkers for predicting and optimizing assisted reproductive technology (ART) outcomes.

Methods: A systematic literature review was conducted using PubMed, Scopus, and Web of Science databases up to 2025. Studies analyzing EVs in reproductive fluids with functional assessments of their cargo, signaling pathways, and correlations with ART success were included. Both mechanistic in vitro studies and clinical observational data were considered.

Results: EVs carry distinct molecular signatures, including miRNAs (e.g., miR-21, miR-146a) and proteins (e.g., HSP70, integrins), which regulate oocyte maturation, sperm capacitation, and embryo implantation via autocrine and paracrine signaling. High-throughput EV profiling reveals correlations between specific cargo patterns and gamete/embryo quality. Mechanistic studies demonstrate that EV-mediated modulation of PI3K/AKT and MAPK pathways enhances oocyte competence, while EV-derived miRNAs regulate apoptosis and oxidative stress in sperm and embryos. Clinically, EV signatures in follicular fluid and seminal plasma can non-invasively predict IVF outcomes, potentially reducing invasive assessments.

Conclusion: Extracellular vesicles function as mechanistic mediators and innovative biomarkers in reproductive medicine. Integrating EV profiling into ART protocols could enable personalized, non-invasive prediction of gamete and embryo quality, optimize treatment strategies, and improve success rates. Future studies should focus on standardizing EV isolation, validating molecular signatures, and elucidating mechanistic pathways to translate these findings into clinical practice.

keywords: Extracellular vesicles, Reproductive medicine, ART, Embryo quality, MicroRNA

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-66

Comparative Prognostic Utility of C-reactive Protein-to-Albumin Ratio (CAR) versus Platelet-to-Albumin Ratio (PAR) in Cardiovascular Diseases: A Systematic Review and Meta-Analysis

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Background and aim: Systemic inflammation and nutritional status are crucial to the prognosis of cardiovascular disease. The C-reactive protein-to-albumin ratio (CAR) and platelet-to-albumin ratio (PAR) are simple, accessible biomarkers derived from routine blood tests, offering a pragmatic reflection of these interconnected pathways. While promising for risk stratification, the evidence for their prognostic utility remains heterogeneous and fragmented. This systematic review, therefore, aims to synthesize and indirectly compare the predictive value of CAR versus PAR for predicting major adverse cardiovascular outcomes, assessing their potential for integration into clinical practice

Methods: A systematic literature search was performed in accordance with PRISMA guidelines. The electronic databases Scopus, PubMed, and Google Scholar were queried from January 2020 to March 2026. The search strategy combined terms related to the biomarkers ("C-reactive protein-to-albumin ratio," "CAR," "platelet-to-albumin ratio," "PAR") and cardiovascular outcomes. Two independent reviewers screened all identified records by title, abstract, and full text against predefined eligibility criteria. Studies were included if they were observational (cohort or case-control) and investigated the prognostic value of CAR and/or PAR for adverse cardiovascular outcomes (e.g., mortality, MACE) in adult human populations. Reviews, editorials, animal studies, and non-English publications were excluded. Disagreements during the screening and data extraction process were resolved through discussion or consultation with a third reviewer. Data from eligible studies were extracted into a standardized form, capturing study characteristics, population, biomarker details, outcomes, and key results.

Results: A systematic search of Scopus and PubMed identified 446 records. Following the removal of 253 duplicates, the titles and abstracts of 193 studies were screened, resulting in the final inclusion of 45 eligible studies. Of these, 39 studies investigated the CAR ratio and 6 examined the PAR ratio, with some studies assessing both indices. The synthesized evidence strongly supports the prognostic association of both biomarkers with adverse cardiovascular outcomes. The vast majority of CAR studies identified it as an independent predictor of mortality (all-cause and cardiovascular), MACE, coronary disease severity, and complications following procedures like PCI and TAVR. However, a small number of studies, primarily in general or elderly populations, found no clear superiority of CAR over CRP alone. Regarding PAR, most studies confirmed its significant association with mortality, particularly in critically ill and dialysis-dependent patients and MACE. Direct head-to-head comparative studies of CAR versus PAR were scarce.

Conclusion: This systematic review of 45 studies highlights the prognostic value of two composite biomarkers CAR and PAR in cardiovascular disease. Both show independent associations with mortality and MACE. CAR is more extensively validated across various cardiac conditions, while PAR, though less studied, has strong predictive power in high-risk groups such as those with critical illness or renal dysfunction A key clinical advantage is their high accessibility and low cost, as they are derived from routine blood tests. Incorporating CAR and PAR into existing risk-stratification panels provides a practical and cost-effective

keywords: C-reactive protein-to-albumin ratio, Platelet-to-albumin ratio, Cardiovascular disease prognosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-67

The synergistic effect of vitamin C and vitamin E supplementation on carbonyl protein and heat shock protein 70 in Alzheimer's brain tissue in a rat model.

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Background and aim: Background: Alzheimer's disease is one of the most common types of dementia, characterized by increased oxidative stress and decreased cellular protective mechanisms. Although the role of antioxidant supplements in the health of Alzheimer's patients has been reported, the differences between them are not yet well understood. Therefore, the aim of the present study was to investigate the effect of eight weeks of vitamin C (VC) and vitamin E (VE) supplementation on carbonyl protein (CP) and heat shock protein 70 (HSP70) in the brain tissue of rats with Alzheimer's disease induced by trimethyltin (TMT).

Methods: Methods: For this purpose, in this experimental study, 28 rats with Alzheimer's disease induced by injection of 10 mg/kg TMT were divided into the following groups: (1) patient control, (2) sham (VE solvent), (3) vitamin C, and (4) vitamin E (VE). Subsequently, the vitamin C group received 4 mg/kg/day of vitamin C, and the vitamin E group received 30 mg/kg/day of vitamin E dissolved in dextrose and food flavoring orally for eight weeks. For data analysis, Shapiro-Wilk test, one-way analysis of variance (ANOVA), and Tukey's post hoc test were used.

Results: Results: The results of the present study showed that carbonyl protein levels in the vitamin C and vitamin E groups were significantly lower, and HSP70 levels in the vitamin C and E groups were significantly higher than in the patient control group ($P \leq 0.05$). However, no significant difference was observed between the vitamin C and vitamin E supplement groups (P 0.05).

Conclusion: Conclusion: Based on the results, it seems that both vitamin C and vitamin E have antioxidant and cytoprotective effects, and no significant difference was observed between the administered doses of these two vitamins.

keywords: Keywords: Vitamin C, Vitamin E, Oxidative stress, HSP70, Alzheimer's disease

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-68

The protective effects of fish oil on gastric ulcer induced by ethanol and the expression of NFkB and P53 genes

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Background and aim: Background:Gastric ulcer is a benign lesion of the mucous epithelium caused by the exposure of the stomach to excessive acid and the aggressive activity of pepsin. The aim of this study was to investigate the effect of fish oil on gastric ulcer caused by ethanol in rats. Fish oil derived from Scomberoides commersonianus has significantly reduced the severity of injury in aspirin-induced, cold restraint stress (CRS), alcohol-induced, and pylorus ligation gastric ulcer models. One study has demonstrated the potential of fish oil in preserving gastric mucosal integrity due to its effect on aggressive and defensive mucosal factors. Fish oil significantly

Methods: Methods: In this study, 42 male rats were used in 7 groups (n=6). The first group (sham): sunflower oil as a drug carrier is gavage for 14 days and no gastric ulcer induction. The second group: fish oil (FO) at a dose of 5 mg/kg for 14 days and no gastric ulcer induction. The third group: FO with a dose of 10 mg/kg for 14 days and no gastric ulcer induction. The fourth group (control): sunflower oil for 14 days and gastric ulcer induction with ethanol 1 ml per 200 grams of body weight. The fifth group (positive control): Omeprazole with a dose of 20 mg/bw for 14 days and gastric ulcer induction. Sixth group: FO with a dose of 5 mg/kg for 14 days and gastric ulcer induction. Seventh group: FO with a dose of 10 mg/kg for 14 days and gastric ulcer induction. The results were analyzed using

Results: The average number of wounds in the fifth and sixth groups was significantly less than the fourth group (P0.05). Also, a significant difference was observed in the mean number of wounds between the sixth and seventh groups (P0.05). Fish oil in both doses used could reduce the number of stomach ulcers. Also, a dose of 10 mg/kg of fish oil showed better effects than omeprazole with a dose of 20 mg/bw.

Conclusion: It is worth mentioning that both doses of fish oil could decrease the expression of NFkB and P53 genes in stomach tissue (P0.05). The results showed that pretreatment with fish oil can reduce the damage caused by ethanol by reducing the expression of NFkB and P53 genes. Therefore, these molecules and pathways demonstrated a protective role against ethanol-induced gastric ulcers and other harmful substances. Additionally, ROS/RNS increases oxidative stress-induced apoptosis in gastric mucosal cells.

keywords: : NFkB, P53, Oxidative stress, Gastric ulcer , fish oil

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-69

The effect of four weeks of aerobic exercise along with beetroot supplementation on some kidney injury indices in elderly diabetic rats.

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Background and aim: Background: Alzheimer's disease is one of the most common types of dementia, characterized by increased oxidative stress and decreased cellular protective mechanisms. Although the role of antioxidant supplements in the health of Alzheimer's patients has been reported, the differences between them are not yet well understood. Disruption of cellular redox balance, increased oxidant attack on structural proteins, is accompanied by elevated levels of carbonylated protein and malondialdehyde, as well as decreased levels of protective proteins such as HSP70. Therefore, the aim of the present study was to investigate the effect of eight weeks of vitamin C (VC) and vitamin E

Methods: Methods: Thirty-two rats with diabetes induced by injection of 55 mg/kg streptozotocin were divided into the following groups: (1) control, (2) continuous exercise, (3) beetroot supplement consumption, (4) continuous exercise and beetroot supplement consumption. Additionally, 8 healthy rats were considered as the healthy control group to investigate the effect of diabetes induction on the research variables. Subsequently, groups 2 and 4 exercised for four weeks at a speed of 9 to 15 meters per minute, equivalent to 55-60% of maximum speed. Rats in groups 3 and 4 consumed 10 ml per kg of body weight of red beetroot (beetroot) juice daily for four weeks, dissolved in drinking water.

Results: Results: The results of the present study showed that carbonyl protein levels in the vitamin C and vitamin E groups were significantly lower, and HSP70 levels in the vitamin C and E groups were significantly higher than in the patient control group ($P \leq 0.05$). However, no significant difference was observed between the vitamin C and vitamin E supplement groups (P 0.05). The present study showed that carbonyl protein levels in the vitamin C and vitamin E groups were significantly lower, and HSP70 levels in the vitamin C and E groups were significantly higher than in the patient control group. However, no significant difference was observed between the vitamin C and E supplement groups.

Conclusion: Conclusion: Based on the results, it seems that both vitamin C and vitamin E have antioxidant and cytoprotective effects, and no significant difference was observed between the administered doses of these two vitamins. Therefore, the conducted research indicates the antioxidant effects and neuronal protective role of vitamin C and vitamin E. However, previous studies have either individually investigated the effect of one supplement or examined the effect of consuming both vitamins simultaneously; yet, few studies had compared their effects with each other.

keywords: Keywords: Aerobic exercise, Beetroot, Kidney, Diabetes

PBi-70

Carbon monoxide poisoning, clinical symptoms, laboratory findings, and treatment outcome in children

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Background and aim: Carbon monoxide (CO), a colorless, odorless gas, could develop during the incomplete combustion of organic materials. CO has high affinity to hemoglobin, making it lethal even in low doses. CO poisoning in children has been less studied overall. This study aimed to investigate the demographic, clinical, and laboratory findings, and the outcomes, of CO poisoning in pediatric patients.

Methods: This cross-sectional study was conducted in 2023 on all pediatric patients admitted to a tertiary referral pediatrics hospital and two tertiary referral hospital for poisoning, diagnosed with acute CO poisoning between 2011 and 2024. The required data was obtained from hospitalization medical records.

Results: : In this study, 110 patients with acute CO poisoning were enrolled. Average age of the patients was 8.5±5.4 years old with a range of 7m to 18 years. 50 (45.5%) of the patients were male and 100 (90.9%) of them had been poisoned in their homes. While 48 (43.6%) were alone at the time of CO poisoning, 62 (56.4%) had at least one other person be poisoned along them. Patients showed metabolic acidosis, high lactate, BUN, CPK and low HCO3, all of whom were significantly trending towards normal after 6 hours of hospitalization. Treatments used were compared with disease outcome as well. We found no significant correlation between intubation, O2 therapy, and fluid therapy with disease outcome. However, patients who received O2 therapy were significantly more likely to survive (p0.05), even if they had significantly higher rate of complications

Conclusion: CO poisoning in pediatric patients could manifest with a variety of symptoms and needs to be addressed quickly as to not leave sequelae

keywords: poisoning, Carbon monoxide, Toxicity, Emergency, Laboratory data

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-71

Emerging Trends in Targeting Breast Cancer Using Curcumin-Loaded Niosomes

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Background and aim: Breast cancer is the most common cancer among women, accounting for approximately 12 % of newly diagnosed cancer cases annually. Breast cancer cells can develop resistance to conventional therapies, necessitating the discovery of new antitumor compounds. Curcumin (CUR) have been identified as an anticancer agent in breast cancer treatment due to its antioxidant and anti-inflammatory properties. However, its application is limited by factors such as low water solubility, rapid metabolism, low oral bioavailability, and low cellular absorption. To overcome the stated barriers and enhance CUR's anticancer activity, niosomes, an effective delivery system, are proposed to improve CUR's physicochemical properties

Methods: We searched the PubMed, Scopus, and Web of Science (ISI) databases using appropriate keywords, including “breast cancer”, “curcumin”, “noisome”, and “targeted therapy”, up to November 2025 to identify the latest original articles that examined the role of niosomal nanocarriers in enhancing and targeting the delivery of curcumin in breast cancer cells.

Results: Niosomes effectively enhance the bioavailability and cellular uptake of CUR in breast cancer cell lines by increasing its solubility and stability in physiological environments. Compared to free CUR, CUR-loaded niosomes selectively enhance cytotoxicity in cancer cells, reduce the IC_{50} of curcumin, increase cell apoptosis, induce cell cycle arrest, and inhibit cellular migration and invasion. Moreover, noisome provides co-delivery of therapeutic agents besides CUR, leading to higher antitumor activities compared with monotherapy.

Conclusion: Niosomes selectively target breast cancer cells, making them a promising carrier candidate for breast cancer treatment.

keywords: Breast cancer, Curcumin, Targeted delivery, Niosome

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-72

Maximum performance of the aptamer-based ELISA system immobilized on the streptavidin-coated platform for detection of human D-dimer protein

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Background and aim: Background: This study aimed to investigate the maximum performance achieved by the aptamer-based ELISA system on a streptavidin-coated platform when optimizing major parameters. Methods: Key experimental parameters, including the temperature of the aptamers-incubation time, sample buffer type and pH, aptamer concentration and time of incubation were tested. The assay's sensitivity and specificity were then evaluated using D-dimer standards and plasma-interfering proteins, such as albumin and fibrinogen. Results: The maximum performance of the aptamer-based ELISA system immobilized on the streptavidin-coated platform attained at 37 ◦C, Tris-HCl: pH ~ 7.5 sampling buffer, 1.5-h incubation time, and 50 µg/mL the concentrations of aptamer.

Methods: Key experimental parameters, including the temperature of the aptamers-incubation time, sample buffer type and pH, aptamer concentration and time of incubation were tested. The assay's sensitivity and specificity were then evaluated using D-dimer standards and plasma-interfering proteins, such as albumin and fibrinogen.

Results: The maximum performance of the aptamer-based ELISA system immobilized on the streptavidin-coated platform attained at 37 °C, Tris-HCl: pH ~ 7.5 sampling buffer, 1.5-h incubation time, and 50 µg/mL the concentrations of aptamer. Mentioned conditions enhanced detection accuracy and comparable sensitivity to antibody-based ELISA, and achieved a linear standard curve.

Conclusion: The results of this approach by using the ELISA system based on a streptavidin-coated platform not only can confirm that aptamer-based ELISA sensitivity is comparable to traditional antibody-based ELISA but also can reduce the time of production and thereby costs required for conducting the assay. Future researches are suggested to explore the potential of modified aptamers for the detection of biomarkers and applying this system to electrochemical-based biosensors.

keywords: DNA aptamer D-dimer ELISA Streptavidin-coated platform

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-73

MT1-MMP as a Master Regulator of Breast Cancer Progression: Signaling, Trafficking, and Clinical Targeting

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Background and aim: Breast cancer mortality is largely driven by invasion, metastasis, and resistance to therapy, processes strongly influenced by extracellular matrix remodeling. Matrix metalloproteinase-14 (MMP-14/MT1-MMP) is a key regulator of these events through its roles in collagen degradation, invadopodia formation, angiogenesis, epithelial-mesenchymal transition, and survival signaling. Increasing evidence also supports MMP-14 as a clinically relevant biomarker and therapeutic target. This review aimed to evaluate the molecular and clinical significance of MMP-14 in breast cancer, with particular emphasis on its translational and biomarker potential.

Methods: A comprehensive literature search was conducted across major scientific databases, screening peer-reviewed articles published between 2012 and 2025. A total of 350 articles were initially identified using predefined keywords related to MMP-14, breast cancer, invasion, metastasis, biomarkers, imaging, and therapy. After applying inclusion and exclusion criteria focusing on mechanistic relevance, clinical data, biomarker validation, and translational applicability, 95 articles were selected for detailed qualitative analysis.

Results: The reviewed evidence consistently demonstrates that MMP-14 is a pivotal regulator of breast cancer invasiveness and metastatic dissemination through coordinated control of extracellular matrix degradation, angiogenesis, lymph angiogenesis, EMT, and survival signaling. Clinically, elevated tissue and circulating levels of MMP-14 correlate with larger tumor size, lymph node involvement, vascular invasion, poor prognosis, and resistance to chemotherapy and radiotherapy, particularly in triple-negative breast cancer. Importantly, MMP-14 has emerged as a measurable biomarker in serum and tumor tissue, as well as a functional imaging target using activatable probes, MRI-correlated signatures, and theranostic antibodies. Preclinical and early translational studies further support MMP-14–directed antibodies and inhibitors as promising strategies to suppress invasion, enhance treatment sensitivity, and remodel the tumor microenvironment.

Conclusion: MMP-14 represents a critical molecular nexus linking tumor biology with clinically actionable outcomes in breast cancer. Its dual role as a driver of aggressive disease behavior and as a detectable biomarker positions it as a valuable target for laboratory diagnostics, prognostic stratification, and precision therapeutics. Integrating MMP-14 based biomarkers and targeted interventions into clinical workflows may substantially improve risk assessment, treatment monitoring, and therapeutic response, particularly in invasive and treatment-resistant breast cancer subtypes.

keywords: Breast cancer, MT1-MMP, Extracellular matrix remodeling, Cancer invasion, Tumor microenvironment

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBi-74

Comparison of pregnancy outcomes between the fourth and fifth day after embryo transfer: A retrospective study

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Background and aim: Abstract: The majority of embryo transfers (ETs) to date have been performed on day 3 to reduce the potential risk of fetal growth arrest. Transfer on day 5 provides higher clinical pregnancy outcomes with reduced risks of multiple pregnancies. The aim of this study was to evaluate the pregnancy outcome between day 5 embryo transfer and day 4 fresh embryo transfer in patients undergoing intracytoplasmic sperm injection (ICSI).

Methods: Materials and Methods: This study was conducted at the Infertility Research Center of Sarem Hospital, Tehran, in 1402 on 921 infertile women who had referred for ICSI. These patients were assigned to receive fresh embryo transfer (n=163) and blastocyst stage transfer (n=758). Statistical analyses were performed using SPSS software.

Results: Conclusion: There was no significant difference between the two groups in terms of mean age and pregnancy rate. The pregnancy rate on the fourth day (31.29%) was similar to that on the fifth day (28.50%). (Pv 50.0). However, there was a significant difference between the two groups in terms of embryo quality. (Pv0.05)

Conclusion: Discussion: Embryos at the blastocyst stage can produce a higher pregnancy success rate compared to other stages of embryonic cell division. Day 5 embryos can be embryos with a higher probability of implantation and a better strategy for identification and selection of groups. Despite all these descriptions, day 5 transfer at the blastocyst stage still has potential risks, cycle cancellation due to growth arrest and reduced embryo quality in vitro, even with the most advanced sequential culture medium. Therefore, day 4 embryos can be a useful option in busy IVF

keywords: Keywords: Pregnancy outcome, embryo transfer, in vitro fertilization, Embryonic grading,

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July 20-23, 2026

PBi-75

The Exploration of Key Regulatory Network Targets of miR-135b-5p to Overcome Carboplatin Resistance in Ovarian Cancer: A Bioinformatics Approach

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Background and aim: Ovarian cancer (OV) remains one of the leading causes of mortality among gynecological malignancies. Carboplatin is commonly used as a first-line chemotherapeutic agent for OV; however, the majority of patients eventually develop resistance to this treatment, resulting in therapeutic failure. MicroRNA-135b-5p, a member of the endogenous non-coding RNAs, plays a regulatory role in post-transcriptional gene expression and has been implicated in various neoplastic diseases. Depending on the cellular context, it can function either as a tumor suppressor or an oncogene. This study aims to analyze the regulatory interactions of microRNA-135b-5p to identify key molecular targets and provide insights into overcoming

Methods: Putative targets of miR-135b-5p were predicted using miRTarBase v9.0 and miRWalk (score 0.9), and the overlapping genes between the two databases were considered as the predicted targets. Functional enrichment analysis was performed using DAVID . PPI network was constructed via STRING 12.0 and analyzed in Cytoscape 3.10.3 using CytoHubba to identify hub genes. Expression profiling, survival analysis, and ROC evaluation of hub genes were conducted using GEPIA , KMplotter , and ROCplot , respectively.

Results: A total of 2,987 and 2,147 potential target genes of miR-135b-5p were identified from miRWalk and miRTarBase v9.0, respectively, with 444 overlapping genes between them. Gene enrichment analysis revealed significant involvement of these genes in the negative regulation of cell growth for biological processes and methylation-dependent protein binding for molecular functions. KEGG analysis further highlighted the Wnt signaling pathway as a key enriched pathway. The constructed PPI network consisted of 367 nodes and 1,495 edges. Topological analysis identified six key hub genes: KRAS, SRSF1, MDM2, HNRNPA1, RPS6, and DDX3X. Among them, RPS6 showed significantly reduced expression in tumor tissues compared to normal tissues, and its higher expression was positively associated with overall and progression-free survival (HR 1, p-value 0.05). ROC analysis showed that RPS6 could predict the chemotherapy response of ovarian cancer patients to carboplatin. Furthermore, RPS6 expression significantly differentiated platinum responders from non-responders based on 6- and

Conclusion: According to the findings of this study, miR-135b-5p may regulate key genes involved in carboplatin resistance in ovarian cancer. Among the identified target genes, RPS6, as a hub gene, could be a potential biomarker or therapeutic target due to its distinct expression pattern, prognostic significance, and ability to differentiate between platinum responders and non-responders. Overall, these results highlight the therapeutic and diagnostic potential of targeting the miR-135b-5p regulatory network to overcome chemoresistance in ovarian cancer.

keywords: Bioinformatics; Carboplatin resistance; MicroRNA; Ovarian Neoplasms; Protein-protein Interaction Network

PBi-76

Clinical Impact and Diagnostic Challenges of Syndromic Multiplex PCR Panels: A Systematic Review–Based Evidence Synthesis

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Background and aim: Syndromic multiplex PCR panels are increasingly implemented in clinical laboratories to enable rapid and simultaneous detection of multiple infectious pathogens. While their analytical advantages are well recognized, their real-world clinical impact and implementation challenges remain subjects of ongoing debate. This abstract summarizes evidence derived from published systematic reviews and meta-analyses, focusing on the translational pathway from laboratory diagnostics to clinical practice.

Methods: A structured literature search was conducted by reviewing published systematic reviews and meta-analyses evaluating syndromic multiplex PCR panels. Electronic databases including PubMed/MEDLINE, Scopus, Web of Science, and the Cochrane Library were searched for studies published between January 2018 and March 2024. Search strategies combined controlled vocabulary and free-text terms related to syndromic testing, multiplex PCR, rapid molecular diagnostics, and clinical outcomes. Reviews focusing on respiratory, gastrointestinal, and bloodstream infection panels were eligible. Data extracted from the included reviews comprised the number of primary studies, total patient populations, diagnostic accuracy metrics, turnaround time, clinical outcomes (antibiotic use, length of stay, infection control), and reported implementation challenges. Overall, evidence from 12 systematic reviews and meta-analyses, encompassing more than 450 primary studies, was narratively synthesized.

Results: Across the included systematic reviews, syndromic PCR panels demonstrated consistently high sensitivity and specificity compared with conventional microbiological methods, with a substantial reduction in diagnostic turnaround time. Several reviews reported improvements in early clinical decision-making and infection control practices. Meta-analytic evidence suggested a reduction in inappropriate empirical antibiotic use, particularly when test results were integrated into antimicrobial stewardship programs. Nonetheless, recurrent challenges were identified, including difficulty in differentiating colonization from active infection, interpretation of multiple simultaneous pathogen detections, absence of antimicrobial susceptibility data, and heterogeneity in clinical response to test results. Economic constraints and variability in local implementation protocols were also highlighted.

Conclusion: Evidence synthesized from recent systematic reviews supports the potential of syndromic multiplex PCR panels to enhance diagnostic efficiency and patient management. Addressing methodological, interpretative, and implementation challenges is critical to translating laboratory innovation into sustainable clinical impact.

keywords: Syndromic Multiplex PCR, Clinical Impact, molecular Diagnostic Techniques

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PBi-77

The impact of MicroRNAs on Breast cancer

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Background and aim: Breast cancer is one of the most prevalent malignancies among women worldwide and remains a leading cause of cancer-related mortality. Early diagnosis and precise prognostic evaluation are essential for improving patient survival and treatment outcomes. MicroRNAs (miRNAs) are small non-coding RNA molecules that regulate gene expression at the post-transcriptional level. Increasing evidence indicates that dysregulation of miRNAs contributes to breast cancer initiation, progression, invasion, metastasis, and therapeutic response. Due to their stability and disease-specific expression patterns, miRNAs have attracted attention as promising diagnostic and prognostic biomarkers. This review focuses on the biological and clinical significance of microRNAs in breast cancer.

Methods: In this narrative review, relevant studies published between 2019 and 2024 were identified through comprehensive searches of the PubMed and Google Scholar databases. The search strategy included combinations of keywords such as microRNA, breast cancer, biomarkers, diagnosis, and prognosis. Original research articles, narrative reviews, and systematic reviews written in English were considered eligible. Titles and abstracts were initially screened for relevance, followed by full-text evaluation of selected articles. Studies focusing on the biological roles, clinical significance, and diagnostic or prognostic applications of microRNAs in breast cancer were included. The collected data were qualitatively analyzed and synthesized to summarize current evidence.

Results: Based on the reviewed studies, several microRNAs were found to be significantly dysregulated in breast cancer. Oncogenic microRNAs such as miR-21 and miR-155 were consistently overexpressed, contributing to increased cell proliferation, invasion, and resistance to apoptosis. In contrast, tumor suppressor microRNAs including miR-34a and members of the miR-200 family were commonly downregulated and associated with enhanced metastatic potential. In addition, circulating microRNAs detected in serum or plasma demonstrated high stability and diagnostic accuracy, indicating their potential as non-invasive biomarkers for early detection and disease monitoring. Significant associations were also reported between microRNA expression profiles and tumor stage, lymph node involvement, and patient survival.

Conclusion: MicroRNAs have a substantial impact on the pathogenesis and clinical behavior of breast cancer by regulating key molecular pathways involved in tumor development and progression. They represent promising molecular biomarkers for diagnosis, prognosis, and therapeutic decision-making. Recent advances in molecular diagnostic techniques have increased the feasibility of microRNA analysis in routine clinical laboratory settings. However, further large-scale, standardized, and multicenter studies are required to confirm their clinical validity, optimize detection methods, and support their integration into personalized breast cancer management.

keywords: microRNA, breast cancer, biomarkers, diagnosis,prognosis.

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PBi-78

Serum Zinc Deficiency as a Potential Prognostic Marker in Diabetic Patients: A Systematic Review

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Background and aim: Zinc is a vital trace element that contributes to multiple physiological functions, including insulin production, storage, and release. Disruption of zinc balance has been linked to the development and progression of diabetes mellitus, particularly type 2 diabetes, characterized by insulin resistance and impaired pancreatic beta-cell function. Evidence indicates that lower serum zinc levels are frequently observed in diabetic patients and may be associated with suboptimal glycemic control and increased risk of microvascular complications. Recognizing zinc deficiency as a potential prognostic biomarker could help in risk assessment and inform targeted intervention strategies.

Methods: This systematic review evaluated studies reporting quantitative serum zinc measurements in individuals with diabetes and analyzed their relationship with clinical outcomes. Included studies examined associations between serum zinc and glycemic parameters (such as HbA1c and fasting glucose), as well as microvascular complications, including neuropathy, nephropathy, and retinopathy. Data extraction emphasized participant demographics, study design, serum zinc concentrations, and correlations with prognostic indicators. Studies that lacked quantitative zinc data or did not assess clinical relevance were excluded. The review integrated findings from observational, cross-sectional, and cohort studies to provide a comprehensive overview of the potential prognostic role of zinc deficiency in diabetes.

Results: Across studies, diabetic patients consistently exhibited lower serum zinc levels compared to non-diabetic controls. Reduced zinc concentrations were associated with higher HbA1c and poorer overall glycemic management, suggesting a link to disease progression. Several studies also reported correlations between zinc deficiency and the presence and severity of microvascular complications such as nephropathy, neuropathy, and retinopathy. Cohort studies indicated that baseline zinc deficiency may predict the development or worsening of certain diabetic complications over time, implying a potential role as an independent prognostic marker. Variability among studies regarding measurement methods, population characteristics, and control for confounding factors was noted. Nonetheless, the cumulative evidence supports a meaningful association between low serum zinc and adverse outcomes in diabetes.

Conclusion: The current evidence supports the consideration of serum zinc deficiency as a potential prognostic marker in diabetic patients, particularly for predicting poor glycemic control and risk of microvascular complications. Routine monitoring of zinc levels may help identify high-risk patients and inform targeted nutritional or therapeutic interventions. However, as most evidence derives from observational studies, causal relationships remain uncertain. Further prospective and interventional studies are required to clarify the prognostic value of zinc and to explore whether zinc supplementation could improve clinical outcomes in diabetes.

keywords: Zinc; Diabetes Mellitus; Prognosis; Microvascular Complications; Biomarkers

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July 20-23, 2026

PBi-79

The Correlation between Neonatal Hyponatremia and Neurodevelopmental Problems in Preterm Infants During the First Year of Life: A Prospective Case-Control Study

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Background and aim: Hyponatremia, a significant electrolyte imbalance, is frequently encountered in hospitalized neonates, especially preterm infants, due to renal immaturity. A sudden drop in serum sodium concentrations can lead to severe neurological sequelae, including seizures. Despite the known risks of hyponatremia and the increasing prevalence of neurodevelopmental disorders, literature exploring the direct correlation between neonatal hyponatremia and long-term neurodevelopmental outcomes is limited. This study aims to investigate this relationship in preterm infants during their first year of life.

Methods: This prospective case-control study was conducted on 120 preterm infants (Gestational Age: 32–36 weeks) in Iran (2022–2023). The population consisted of a Hyponatremia Group (n=60; Na+ 135 mEq/L) and a healthy Control Group (n=60). Neurodevelopmental outcomes were assessed periodically over the first year of life (at 2, 4, and 6 months) using the validated Ages and Stages Questionnaire (ASQ), which evaluates five developmental domains. Statistical analysis included ANCOVA and Chi-square tests.

Results: The hyponatremia group exhibited significantly lower gestational age, lower birth weight, and longer NICU stays compared to the control group (p0.001). Although sodium levels normalized by therapeutic interventions (Days 5-10, p0.05), the hyponatremia group achieved significantly lower mean ASQ scores across all five developmental domains at 2, 4, and 6 months (p0.05 for all). Furthermore, the prevalence of developmental delays (ASQ 35) was significantly higher in the hyponatremia group (p0.001). A history of hyponatremia increased the risk of developmental delay in the Personal-Social domain by 3.33 times (95% CI: 1.60-6.93).

Conclusion: Neonatal hyponatremia is significantly associated with an increased risk and prevalence of developmental delays across all domains during the first year of life. This strong association, even after controlling for major confounding factors, suggests that transient electrolyte imbalance can adversely affect the developing neonatal brain. Since hyponatremia is a highly treatable and preventable condition, these findings underscore the critical necessity of aggressive electrolyte monitoring and timely management in preterm infants. Early correction is essential for improving long-term neurodevelopmental prognosis.

keywords: Hyponatremia, Infant, Premature, Neurodevelopmental Disorders

PBi-80

Diagnostic Accuracy of Late-Night Salivary Cortisol and Serum Free Cortisol in the Diagnosis of Cushing's Syndrome: A Systematic Review and Appraisal

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Background and aim: Introduction: The biochemical diagnosis of endogenous Cushing's syndrome (CS) remains a significant clinical challenge, requiring tests with high diagnostic accuracy. Among the available tools, late-night salivary cortisol (LNSC) and serum free cortisol measurements are central to establishing hypercortisolism. A systematic review and synthesis of the available evidence on the sensitivity and diagnostic specificity of late-night salivary cortisol and serum free cortisol measurements for the diagnosis of Cushing's syndrome.

Methods: Methods: A systematic literature search was conducted for studies and meta-analyses published up to 2025 that had evaluated these tests in patients with confirmed CS compared with reference populations (e.g., healthy subjects, patients with Cushingoid-like states). Studies were assessed for quality, and data on test performance, including sensitivity, specificity, and factors affecting accuracy (e.g., assay method, patient characteristics, disease severity), were extracted and critically appraised.

Results: Results: Both LNSC and serum free cortisol measurements demonstrate high sensitivity for overt CS. However, their specificity is more variable and can be significantly limited in conditions such as pregnancy, psychiatric disorders, and alcoholism (Cushingoid-like states). Recent findings confirm that LNSC, which indicates loss of circadian rhythm, is a robust and useful first-line screening test with high diagnostic accuracy when performed with reliable immunoassay or liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods. Serum free cortisol assays, including those performed during dynamic tests, provide valuable quantitative data, but their performance is affected by assay specificity and interference from binding proteins. The overall diagnostic accuracy of both tests is influenced by individual patient factors, stage of disease, and laboratory techniques used.

Conclusion: Conclusion: Late-night salivary cortisol measurement and serum free cortisol are essential tests for the diagnosis of CS. While both demonstrate high sensitivity, achieving optimal diagnostic specificity requires careful interpretation in the clinical context, awareness of preanalytical variables, and the use of highly specific analytical methods. An integrated testing strategy, taking into account patient-specific factors and potential complications, is essential to maximize diagnostic accuracy and prevent misdiagnosis.

keywords: Keywords: Cushing's syndrome, diagnostic accuracy, late-night salivary cortisol, sensitivity and

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July 20-23, 2026

PBi-81

P-SMAD2/3 protein as regulators of MII oocytes in polycystic ovarian syndrome

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Background and aim: Background: Smad2/3 proteins are key mediators in oocyte maturation, yet their role in granulosa cells (GCs) surrounding oocytes in polycystic ovary syndrome (PCOS) remains unclear. Many oocytes in PCOS patients fail to progress beyond the germinal vesicle (GV) stage despite ovarian stimulation. Aim: To investigate the expression and activation of Smad2/3 in GCs surrounding MII and GV oocytes in women with PCOS.

Methods: Materials and Methods: GCs from MII and GV oocytes were collected from 38 women with PCOS. Smad2/3 and phosphorylated Smad2/3 (P-Smad2/3) protein levels were measured via Western blotting. e

Results: Results: P-Smad2/3 was lower in GCs surrounding GV oocytes relative to MII oocytes (p 0.001), highlighting reduced Smad2/3 signaling in immature oocytes.

Conclusion: Conclusion: Smad2/3 phosphorylation plays a crucial role in oocyte maturation. Downregulation of P-Smad2/3 is associated with impaired GV-to-MII progression in PCOS.

keywords: Polycystic ovary, Oocytes, Granulosa cell

PBi-82

Evaluating the effect of glucose oxidase in Zeolitic Imidazole Framework-8 on breast cancer cells

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Background and aim: This study develops zeolitic imidazolate framework-8 (ZIF-8) nanoparticles, a biocompatible pH-responsive metal-organic framework (MOF), to encapsulate and achieve controlled release of glucose oxidase (GOx) within acidic tumor microenvironments, thereby inducing glycolysis-dependent starvation therapy in estrogen receptor-positive MCF-7 breast cancer cells, which exhibit pronounced vulnerability owing to their glycolytic dependency.

Methods: MCF-7 cells were cultured in DMEM supplemented with 10% FBS and treated with GOx@ZIF-8 (0.6–10 μg mL^{-1}). Efficacy was assessed via MTT assays (metabolic activity, 24 h post-incubation) and colony formation assays (proliferative capacity, 7 days).

Results: Bare ZIF-8 exhibited no cytotoxicity in MCF-7 cells (MTT assay, 24 h). In contrast, GOx@ZIF-8 induced 80% cell death, achieving 93% cytotoxicity at 10 μg mL^{-1} (p 0.0001 vs. controls), with an IC_{50} of 2 μg mL^{-1} (24 h, calculated via Compusyn software). Colony formation assays confirmed complete inhibition of proliferation, with no colonies detected and minimal single-cell survival relative to controls.

Conclusion: GOx@ZIF-8 demonstrates potent in vitro starvation against ER-positive MCF-7 cells, positioning it as a promising enzyme-MOF platform for breast cancer therapy development.

keywords: Starvation therapy, Glucose oxidase, ZIF-8, MCF-7, Colony Formation Assay

PBi-83

Induction of Oxidative and Nitrosative Stress in MCF-7 Cells by GOx@ZIF-8 Nanozymes at Inhibitory Concentrations

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Background and aim: : The integration of natural enzymes into metal-organic frameworks (MOFs) has led to highly efficient "nanozymes" for targeted cancer therapy. Glucose oxidase encapsulated within Zeolitic Imidazol Framework (GOx@ZIF-8) functions as a catalytic nanozyme that triggers intracellular glucose depletion and oxidative damage. This study investigates the ability of GOx@ZIF-8 to induce oxidative and nitrosative stress in the human breast cancer cell line MCF-7 at specific inhibitory thresholds.

Methods: MCF-7 cells were treated with GOx@ZIF-8 at concentrations of 0.5, 1, and 2 µg/mL. These concentrations represent the half-maximal inhibitory concentration (IC50 = 2 µg/mL) and a lower inhibitory concentration (1/2IC50 = 1 µg/mL). Oxidative stress was quantified using the DCFH-DA fluorescence assay, with measurements recorded at minute 0 and minute 30. Nitrosative stress was concurrently assessed by measuring nitric oxide (NO) production using the Griess reagent assay. Statistical analysis was performed using GraphPad Prism, with significance defined as (p 0.05).

Results: GOx@ZIF-8 treatment resulted in an elevation of cellular stress markers. Statistical significance in ROS generation (DCF fluorescence) was achieved at 1 and 2 µg/mL within the 30-minute window (p 0.05). This rapid oxidative surge was closely mirrored by a significant increase in nitric oxide levels at all concentrations (p 0.05). The data suggest that the nanozyme initiates a rapid biochemical cascade through the simultaneous accumulation of reactive oxygen and nitrogen species, effectively overwhelming the antioxidant capacity of MCF-7 cells .

Conclusion: This study confirms that GOx@ZIF-8 nanozymes are potent inductors of dual oxidative and nitrosative stress in MCF-7 cells. The significant stress response observed at inhibitory concentrations highlights the high catalytic efficiency of the ZIF-8 platform.

keywords: Glucose Oxidase, Zeolitic Imidazol framework-8 , Nitrosative Stress, MCF-7, Oxidative

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-84

Associations of serum 1,3-β-D-glucan levels with sleep architecture alterations in chronic insomnia disorder

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Background and aim: Background: Chronic insomnia disorder (CID) is a widespread sleep disorder linked to increased risks of various chronic diseases and often precedes neurodegenerative conditions such as Parkinson's and Alzheimer's disease. Emerging evidence suggests that gut microbiome disturbances contribute to CID through the gut-brain axis, involving microbial metabolites and neuroactive proteins. This study explored the relationships between serum 1,3-β-D-glucan (a marker of intestinal permeability and microbial translocation) and sleep architecture in chronic insomnia individuals compared to healthy controls.

Methods: Methods: Blood samples were taken from 15 people who had been diagnosed with CID, based on their results from the Pittsburgh Sleep Quality Index (PSQI) and video-polysomnography tests. For comparison, blood was also collected from 15 healthy volunteers, whose sleep quality was assessed using the PSQI. Serum concentrations of 1,3-β-D-glucan was measured using enzyme-linked immunosorbent assay (ELISA). To evaluate the discriminative ability of serum β-glucan levels between people with chronic insomnia and healthy controls, ROC curve analysis was applied.

Results: Results: The findings showed significantly elevated serum 1,3-β-D-glucan (p 0.0001) levels in the CID group. Moreover, we found that the serum levels 1,3-β-D-glucan had high positive correlation with PSQI scores (correlation coefficient 0.477, p 0.05) in CID group. The optimal cutoff value of serum β-glucan was 20.5 pg/mL for predicting sleep quality (AUC: 0/9267; 95% confidence interval (CI): 0/8327 to 1/000; p 0/0001).

Conclusion: Conclusions: These results indicate that serum β-glucan levels are associated with insomnia severity. Thus, serum levels of this molecules could have potential utility as sensitive and specific tools for estimating insomnia severity, likely reflecting gut microbiome imbalance, and may assist in early diagnosis of neurodegenerative diseases.

keywords: Chronic insomnia; 1,3-β-D-Glucan; Gut-brain axis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-85

Microbiota-Driven Enhancement of GLP-1 Therapy in Metabolic PCOS: A Systematic Review

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Background and aim: Polycystic Ovarian Syndrome (PCOS) is known to be the most prevalent endocrine disorder among women during their reproductive years, and it is marked by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries, frequently associated with obesity, insulin resistance, and cardiovascular factors. Recent studies have identified alterations in gut microbiota to play a role in PCOS and include insulin signaling, androgen metabolism, and inflammation. The GLP-1 receptor agonists show significant improvement in symptoms. This article reviews the potential of microbiota-driven enhancement of GLP-1 therapy as a novel, mechanism-based strategy to optimize therapeutic outcomes in metabolic PCOS.

Methods: This review article was conducted using articles published in PubMed, ScienceDirect, Google Scholar, and Web of Science until November 2025. The keywords were Glucagon-Like Peptide 1, Microbiota, Gastrointestinal Microbiome, and Polycystic Ovary Syndrome. By searching these databases, 70 articles were found. After reading titles and abstracts, 43 of them were removed, and 27 articles were selected under the inclusion criteria. All articles were chosen from English-language sources.

Results: A total of 27 studies have been systematically reviewed regarding the effects of GLP-1 receptor agonists on gut microbiota and their effectiveness in managing both metabolic and reproductive aspects of metabolic polycystic ovary syndrome (Met-PCOS). The use of liraglutide and semaglutide has resulted in significant weight loss, decreased adiposity, improved insulin sensitivity, and demonstrated greater efficacy than metformin in managing Met-PCOS caused by obesity. In addition, liraglutide and semaglutide have improved gut microbiota composition by increasing the diversity of gut microbiota species in women with Met-PCOS. Furthermore, liraglutide and semaglutide have positively influenced hormonal reproduction by reducing the LH/FSH ratio, decreasing symptoms of hyperandrogenism, and regularizing menstrual cycles without uterotrophic effects. In the long term, liraglutide and semaglutide continue to produce sustained weight loss and improved glycemic and lipid profiles with only transient mild gastrointestinal side effects.

Conclusion: A microbiota-informed optimization strategy using GLP-1 appears to offer a theoretically rational method to optimize both metabolic and reproductive phenotypes within Metabolic PCOS. Although there is considerable success with this method, there is still a need to understand microbiota dysbiosis to better optimize this therapeutic approach.

keywords: Glucagon-Like Peptide 1; Microbiota; Gastrointestinal Microbiome; Polycystic Ovary Syndrome

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-86

Role of Filamin A and β-arrestin2 in Dopamine-Agonist Resistance Prolactinoma: A Systematic Review

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Background and aim: Prolactinoma is a benign pituitary tumor that increased release of the hormone prolactin. Prolactinomas are a common type of pituitary tumors.Patients usually present with visual complaints,irregularities in menstruation,galactorrhea and also male and female infertility.Most patients receive first-line treatment with one of the dopamine agonists (DAs),but some of them have proved to be DA-resistant.deficiencies in regulatory mechanisms pertaining to the dopamine D2 receptor (D2R) might underlie this antitreatment effect in a subset of such patients.This includes changes in the cytoskeleton protein Filamin A(FLA) and the scaffold protein β-arrestin2.This review will cover the role of FLNA and β-arrestin2 in DA resistance Prolactinoma.

Methods: This review article was conducted using articles published in PubMed, Google Scholar, and ScienceDirect between 2015 and 2025. The keywords were "β-arrestin2 AND Filamin A OR FLNA AND Prolactinoma AND Dopamine-Agonist Resistance." A search of these databases resulted in 45 articles being found, 32 of which were excluded based on titles and abstracts. A total of 13 articles were selected according to the inclusion criteria.

Results: Finally, 13 articles were included in the study. FLNA bound D2R at the cell membrane and stabilized its expression, prevented degradation while promoted recycling to sustain dopamine signaling. The later reduction of FLNA expression resulted in surface D2R being less available for inhibition of the dopamine-induced prolactinoma cells. FLNA silencing in DA-sensitive cells led to a significant decrease in D2R expression and abolished DA-induced inhibition of prolactin secretion and antiproliferative signaling. Conversely, overexpression of FLNA in DA-resistant prolactinomas partially restored D2R expression and dopamine responsiveness. β-arrestin2 is a multifunctional scaffold protein recruited to activated D2R that mediates receptor desensitization, internalization, and forms signaling complexes, including those that inhibit proliferative pathways such as AKT phosphorylation. Loss or reduced expression of β-arrestin2 disrupted these downstream pathways, blocking dopamine-induced inhibition of tumor growth, and was associated with dopamine agonist resistance.

Conclusion: Diminished expression of FLA and β-arrestin2 disrupts signaling for dopamine D2 receptor expression, a step that leads to the mechanism of dopamine agonist resistance in prolactinomas. Antagonizing these proteins may lead to new therapeutic strategies to fight resistance in affected patients. However, further research needs to be done in this field.

keywords: β-arrestin2-Filamin A- Prolactinoma- FLNA- Dopamine-Agonist Resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-87

Methylation Profiling of Plasma Cell-Free DNA for Ovarian Cancer Risk and Prognosis Assessment

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Background and aim: Ovarian cancer is an aggressive malignancy of the female reproductive tract, with approximately 75% of cases diagnosed at advanced stages due to the lack of effective diagnostic and monitoring biomarkers, resulting in a five-year survival rate of about 50%. In Iran, the incidence is estimated at 4 cases per 100,000 women annually. Tumor-derived cell-free DNA (cfDNA) carries cancer-specific DNA methylation alterations, representing a promising noninvasive biomarker for the diagnosis and prognosis of ovarian cancer.

Methods: A narrative review of the literature on ovarian cancer was conducted, focusing on the potential role of cell-free DNA (cfDNA) methylation in diagnosis, prognosis, and treatment monitoring. Scientific databases including PubMed, Scopus, Web of Science, and Google Scholar were explored to identify relevant studies, reviews, and expert opinions. The review emphasized molecular biology advances, epigenetic profiling techniques, and emerging diagnostic strategies, highlighting their clinical implications. Throughout the study, attention was given to key concepts such as “ovarian cancer”, “cfDNA”, “DNA methylation”, “early detection”, “prognosis”, “biomarker”, “molecular diagnostics”, and “epigenetics” to structure the narrative synthesis.

Results: Recent studies highlight liquid biopsy as a minimally invasive tool with great promise for the detection and management of malignant tumors. Among these, cfDNA-based assays have demonstrated the ability to capture tumor diversity and reveal molecular alterations, offering a dynamic picture of tumor evolution and recurrence risk. DNA methylation, a key epigenetic modification, is often disrupted in early cancer stages, affecting numerous cellular processes. Assessing cfDNA methylation profiles provides a non-invasive means to trace the tissue of origin and characterize tumor biology. In ovarian cancer, this approach shows potential for early identification, monitoring disease progression, and predicting treatment outcomes. By integrating cfDNA methylation analysis into clinical workflows, clinicians may improve individualized patient care, enabling timely interventions and better prognostic assessments. Overall, cfDNA methylation profiling represents a promising biomarker strategy that bridges molecular research and practical oncology applications.

Conclusion: This narrative review highlights the emerging role of cell-free DNA methylation as a non-invasive biomarker for ovarian cancer. Recent studies demonstrate its potential in early detection, monitoring disease progression, and evaluating treatment efficacy. Despite promising results, challenges remain in standardizing assays and integrating them into routine clinical practice. Continued research and validation are essential to fully harness cfDNA methylation for personalized patient care. Overall, this approach represents a significant step toward more precise and effective diagnosis and management of ovarian cancer.

keywords: DNA methylation, cell-free DNA, diagnosis, ovarian cancer, prognosis surveillance

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-88

Association of Interleukin 1β, 10, and 12 levels in Type 2 Diabetes Patients and Controls

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Background and aim: Due to lifestyle changes and rising obesity, type 2 diabetes is increasing worldwide. Environmental and genetic factors contribute to its development. Inflammatory factors are among these contributors, though the mechanisms triggering inflammation in diabetes are not fully understood. Inflammation appears to play a key role in insulin resistance. Based on this, we aimed to measure and compare levels of inflammatory cytokines, including interleukin 1β, 10, and 12, in patients with type 2 diabetes and healthy controls in this study.

Methods: This case-control study included 48 patients with diabetes and 48 healthy individuals who were free of metabolic disease. We used the ELISA (Enzyme-linked immunosorbent assay) kit from ZellBio company to measure the concentration of interleukins. The concentration of interleukins was calculated in pg/ml. SPSS.16 software was used for statistical analysis and the P value of 5% was considered statistically significant.

Results: In this study, the comparison of the results obtained from two groups of patients and healthy controls showed that the concentration of IL-1β, and 12 in the patient group was higher than in the healthy group and it was statistically significant, but comparing the two groups, the amount of interleukin 10 in the patient group was higher than the healthy group, but it was not statistically significant. The table below shows the concentration of inflammatory factors in two groups.

Conclusion: In the current study, we clarified associations between interleukins and type 2 diabetes as there was a significant increase in levels of interleukins in diabetes mellitus patients compared with healthy controls. Taken together, inflammatory factors in subjects with different genotypes could be a potential biomarker for determining the severity and prognosis of type 2 diabetes. However, more studies are needed to reveal its clinical values.

keywords: Type 2 diabetes ; inflammatory factors; interleukin

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-89

Extracellular Vesicle Biomarkers in Esophageal Squamous Cell Carcinoma: A Systematic Review of Their Functional Roles and Predictive Potential for Therapy Response

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Background and aim: Extracellular vesicles (EVs) are key mediators of tumor progression and therapy resistance in esophageal squamous cell carcinoma (ESCC), yet their role as predictive biomarkers for neoadjuvant chemoradiotherapy (nCRT) remains unclear. This systematic review synthesizes evidence on EV-derived molecules in ESCC, with a focus on their biological functions and clinical utility in predicting treatment outcomes.

Methods: Following PRISMA guidelines, we systematically searched Web of Science, PubMed, and Embase for original studies on EVs in human ESCC. Included studies reported on EV cargo with defined biological or clinical relevance. Data on EV isolation methods, molecular species (miRNAs, proteins), functional pathways, and associations with clinical endpoints were extracted and assessed for quality.

Results: Of 1,256 screened records, 112 studies met inclusion criteria. EV-derived miRNAs dominated the literature (86 studies), with miR-21-5p most frequently implicated in promoting angiogenesis, immune evasion, and therapy resistance via PTEN/AKT/STAT pathways. A subset of 37 studies linked EV cargo (e.g., miR-143-3p, miR-191-5p) directly to radio/chemo-resistance mechanisms. Diagnostic EV signatures showed high accuracy (AUC 0.89–0.98). However, only 8 studies prospectively evaluated EVs for predicting nCRT response, identifying miR-25-3p, miR-148a-3p, and CD82 as preliminary predictive markers. Heterogeneous EV isolation methods and limited validation cohorts were consistent limitations.

Conclusion: EVs play a central role in ESCC pathogenesis and resistance, primarily through miRNA-mediated signaling. While promising for diagnosis, their use in predicting nCRT response is critically underdeveloped. Future research must prioritize standardized EV protocols and prospective validation of multi-analyte EV signatures to enable personalized treatment strategies in ESCC.

keywords: Esophageal squamous cell carcinoma, Exosomes, MicroRNAs, Neoadjuvant therapy, Systematic review.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-90

Clinical Utility of Metabolomics in Metabolic Diseases and Cancer: A Systematic Review and Meta-Analysis

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Background and aim: Metabolic diseases and cancer are complex disorders characterized by heterogeneous molecular alterations that limit the diagnostic accuracy of conventional laboratory tests. Metabolomics, as a high-throughput analytical approach, provides a comprehensive snapshot of metabolic changes associated with disease onset and progression. Over the past decade, numerous studies have investigated metabolomic signatures for diagnostic and prognostic purposes; however, reported results vary across platforms, populations, and disease types. This systematic review and meta-analysis aimed to evaluate the clinical utility and diagnostic performance of metabolomics-based biomarkers in metabolic diseases and cancer.

Methods: A systematic search was conducted in PubMed, Scopus, and Web of Science for studies published between 2010 and 2025. Eligible studies applied metabolomics techniques to human samples for the diagnosis of metabolic diseases or cancer and reported diagnostic accuracy metrics. Study quality was assessed using established diagnostic study appraisal tools. Reported area under the receiver operating characteristic curve (AUC-ROC) values were synthesized using a random-effects model. Subgroup analyses were performed according to disease category, analytical platform, and sample type.

Results: A total of 68 studies were included in the systematic review, of which 34 provided sufficient data for quantitative synthesis. Metabolomics-based diagnostic models demonstrated good to excellent diagnostic accuracy across both disease groups. In metabolic diseases, pooled AUC values reported in the literature generally ranged from approximately 0.82 to 0.91, particularly in studies focusing on diabetes, non-alcoholic fatty liver disease, and inborn metabolic disorders. In cancer studies, metabolomic signatures achieved AUC values commonly between 0.78 and 0.95, with higher performance reported for colorectal, breast, and hepatocellular cancers. Liquid chromatography–mass spectrometry (LC-MS)–based platforms and serum or plasma samples showed the most consistent performance. Moderate heterogeneity was observed across studies.

Conclusion: Metabolomics demonstrates substantial clinical utility for the diagnosis of metabolic diseases and cancer. When integrated with clinical and laboratory data, metabolomics-based biomarkers have the potential to enhance diagnostic accuracy and support precision medicine approaches in routine clinical practice.

keywords: Metabolomics; Metabolic diseases; Cancer; Biomarkers; Meta-analysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-91

Identifying important variables (features) for setting up a clinical decision support system for cancer screening

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Background and aim: Colorectal cancer is the most common human cancer.This cancer type has different risk factors. The investigation on risk factors for early detection of this cancer type is crucial. The purpose of this study is designing system for early detection and common measurement of physicians for colorectal cancer.

Methods: The current research is descriptive and applied in which risk factors were identified by reviewing the articles. The two-stage Delphi method is used to identify the primary and then the final elements. The results obtained from the evaluation of questionnaires from drug experts were obtained through SPSS descriptive statistics software.

Results: After performing Delphi in two stages from a total of 135 primary data elements, finally 107 data elements were finalized in the form of nine information classes for use in clinical decision support systems.

Conclusion: The proposed data elements, as one of the most important prerequisites for the design of clinical decision support systems, can be the basis for improving the quality of system performance and reducing diagnostic errors.

keywords: decision support system, colorectal cancer, risk factor, minimum data set

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-92

Impact of Hysterectomy on Ovarian Function and Sex Hormones

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Background and aim: Hysterectomy is one of the most common surgical procedures in women, which is performed for various indications such as uncontrolled bleeding, benign and malignant tumors. Although ovarian hormonal function continues in cases where the ovaries are not removed, evidence indicates that hysterectomy can still influence circulating the levels of sex hormones. Sex hormones such as estradiol, progesterone, and testosterone play an essential role in regulating the menstrual cycle, maintaining bone health, cardiovascular health, and quality of life in women. After hysterectomy, changes in the secretion of these hormones lead to symptoms similar to premature menopause, reduced libido, and various metabolic

Methods: This study was conducted as a systematic review. To identify relevant studies, a comprehensive search was performed in the PubMed and Google Scholar databases for articles published between 2010 and 2025.The keywords used included combinations of “hysterectomy and ovarian functions”,”hysterectomy and LH or FSH or AMH”and “hysterectomy and sexual function” The initial search retrieved 10 records from PubMed and 18 from Google Scholar. After removing duplicates and studies without available full texts, 18 articles met the inclusion criteria and were included in the review.

Results: Studies indicate that Hysterectomy is associated with significant changes in female hormonal profile. Changes include decreased Anti-Mullerian hormone (AMH), inhibin B, and estradiol (E2) and increased Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH)after hysterectomy, which indicate decreased ovarian reserve and dysfunction, which ultimately accelerating menopause. This surgery may be associated with complications such as lymphatic disorders, edema, urinary dysfynction, anxiety and depression, sexual dysfunction, labial numbness, and dyspareunia Because estrogen levels decrease after surgery, problems such as vasomotor, osteoporosis, and coronary artery disease can be prevented by appropriate treatment . Failure to use hormone therapy also carries a risk of diabetes, severe depression, and Parkinson’s disease. The consequences of a hysterectomy depend on the patient’s age and the type of surgery.

Conclusion: The consequences of this surgery include decrease in Anti-Mullerin hormone (AMH), inhibin B, and estradiol (E2) along with an increase in FSH and LH after hysterectomy, which indicates reduced ovarian reserve and dysfunction, and accelerated menopause. Other consequences of this surgery include osteoporosis, depression, cardiovascular disease, and Parkinson's disease, all of which are due to decreased sex hormones. . Attention to hormone replacement therapy and selection of the type of surgery based on the patient's condition are essential to reduce complications.

keywords: hysterectomy and ovarian functions”,”hysterectomy and LH or FSH or AMH”and

PBi-93

Aging-Related Proteins Klotho and Sirtuins in Lung Cancer

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Background and aim: Lung cancer is one of the most common and important types of cancer. Although there are many risk factors for the development and progression of this disease, aging is one of the most important and has been shown to influence both disease progression and clinical manifestations. Increased oxidative stress and metabolic changes contribute to tumor progression, and aging-related molecules such as Klotho and sirtuins have emerged as key regulators. However, their clinical relevance in lung cancer remains unclear. The aim of this study was to investigate Klotho and sirtuins in lung cancer and to correlate laboratory findings with clinical outcomes.

Methods: A PubMed search was performed using the terms “Klotho”, “sirtuins” “lung cancer”. Articles published between 2015 and 2026 were reviewed more than 30 relevant studies were included.

Results: Results: Several studies have shown that reduced Klotho levels in lung cancer tissue are associated with progressive disease and poorer outcomes, but measuring Klotho and sirtuins in the blood does not seem to be completely useful and definitive in diagnosing the disease. The results of this review suggest that the function of sirtuins may vary depending on the biological context. Sirtuins are often associated with increased tumor growth, metastasis, and resistance to standard and targeted therapies. In contrast, SIRT3 is usually associated with protective effects, mainly by maintaining mitochondrial function and redox balance. Studies show that Klotho and sirtuins interact through key metabolic and stress response pathways, such as AMPK/mTOR signaling and FOXO-dependent transcription, which in turn affect autophagy, cellular senescence, and response to therapy. Regulation of these pathways in in vitro models appears to be beneficial in response to therapy.

Conclusion: The present study suggests that senescence-associated proteins may play an important role in lung cancer progression and resistance to treatment. Focusing on metabolic pathways as well as stress response pathways and even inflammation, with a focus on Klotho and sirtuins, could provide new insights for biomarker discovery, treatment, treatment monitoring, and metastasis of this disease.

keywords: Klotho Protein; Sirtuins; Lung Neoplasms; Aging; SignalTransduction

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-94

Insulin Resistance and Alzheimer's Disease: A Narrative Review

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Background and aim: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by amyloid-beta (Aβ) plaques, tau hyperphosphorylation, synaptic loss, and cognitive decline, affecting over 50 million people. Emerging evidence strongly links AD to metabolic disorders such as type 2 diabetes mellitus (T2DM), with insulin resistance (IR), which disrupts glucose metabolism and exacerbates neurodegeneration. This overlap has led to the conceptualization of AD as "type 3 diabetes," a brain-specific form of IR. This narrative review synthesizes the shared pathophysiological pathways, genetic and metabolomic biomarkers, and therapeutic implications between IR disorders and AD, highlighting the need for integrated approaches to mitigate cognitive impairment.

Methods: A comprehensive literature search was conducted across databases, including PubMed, Google Scholar, and Web of Science, using keywords such as "insulin resistance," "Alzheimer's disease," "type 3 diabetes," "brain insulin signaling," "metabolomics," and "genetics in AD and T2DM." The search spanned publications from 2020 to 2025 to incorporate foundational studies and recent advances. Five key review articles were selected. Inclusion criteria focused on English-language reviews emphasizing mechanistic overlaps, genetic factors, metabolomic profiles, and therapeutic interventions. Exclusion criteria eliminated studies on unrelated pathologies or non-human models without translational relevance.

Results: IR disrupts brain glucose metabolism, causing energy deficits, synaptic loss, and impaired neuronal plasticity. It promotes Aβ accumulation by competing for the insulin-degrading enzyme and drives tau hyperphosphorylation via GSK-3β activation. Shared risk factors include the APOE ε4 allele, which impairs lipid transport and insulin signaling, and metabolomic changes in lipids, amino acids, AGEs, and neurotransmitters (e.g., dopamine, GABA). Neuroinflammation (e.g., TNF-α-driven) worsens oxidative stress and mitochondrial dysfunction, accelerating neuronal death. the triglyceride-glucose index predicts rapid cognitive decline in early AD, quadrupling risk. Recent studies highlight insulin's role in brain health, identifying new therapeutic targets for diabetes-AD comorbidity. Clinical trials demonstrate that a diabetes drug combined with nasal insulin improved memory, brain blood flow, and health in early AD. GLP-1 agonists like liraglutide (2024 AAIC data) protect against dementia by reducing IR and inflammation. Lifestyle interventions, including diet and exercise, alongside insulin-sensitizers like metformin, enhance sensitivity and attenuate pathology.

Conclusion: This review summarizes the shared mechanisms and therapeutic targets linking insulin resistance and Alzheimer's disease. IR serves as a critical bridge between AD and metabolic disorders, substantiating the "type 3 diabetes" hypothesis. By targeting shared pathways such as inflammation, oxidative stress, and genetic-metabolomic overlaps, novel interventions like nasal insulin and GLP-1 drugs offer promising avenues for prevention and treatment. Recent trials underscore their potential to preserve cognitive function, urging integrated screening and therapies. Future research should prioritize longitudinal studies and personalized medicine to combat this growing epidemic.

keywords: Alziemer's Disease; Insulin Resistance; Amyloid β; Diabetes

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-95

Evaluation of Hesperidin's Antioxidant Effects on Liver Tissue of Mice Poisoned by Malathion

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Background and aim: Malathion is a widely used neurotoxic organophosphate pesticide, particularly in agricultural regions such as Iran. Its extensive and uncontrolled application leads to serious poisoning and damage to organs such as the liver. Malathion exerts its toxic effects through cholinesterase inhibition and induction of oxidative stress. Hesperidin, a flavonoid with antioxidant, anti-inflammatory, and hepatoprotective properties, may mitigate such damage. This study aimed to evaluate the protective effects of hesperidin against subacute malathion-induced hepatic injury in female mice.

Methods: In this experimental study, 32 female Syrian mice (20 ± 2 g) were randomly divided into four groups (n=8): negative control, malathion control, hesperidin control, and treatment (malathion + hesperidin). Malathion was administered intraperitoneally(IP) at a dose of 3 mg/kg/day, and hesperidin was administered at 20 mg/kg/day for 35 consecutive days. At the end of the experiment, animals were anesthetized with ketamine and xylazine, followed by cardiac blood sampling and liver tissue collection. Data were analyzed using SPSS version 24, and statistical significance was set at (p 0.05).

Results: Serum levels of liver enzymes (ALT, AST, ALP, total bilirubin, and direct bilirubin) and histopathological scores were significantly higher in the malathion control group and significantly reduced in the treatment group compared to malathion control (p 0.05). Tissue total antioxidant capacity (TAC) significantly decreased in the malathion group and increased in the hesperidin and treatment groups. Malondialdehyde (MDA) levels were significantly elevated in the malathion group and reduced in the treatment and hesperidin groups (p 0.05).

Conclusion: Although malathion caused significant hepatic histopathological changes and enzymatic disruptions, hesperidin administration effectively mitigated these adverse effects. These findings suggest that hesperidin may serve as a protective agent against malathion-induced hepatic toxicity.

keywords: Malathion, Hesperidin, Hepatic injury, Oxidative stress

PBi-96

Evaluation of Serum Vitamin D Levels in Patients with Esophageal Cancer: An Original Case-Control Study

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Background and aim: Esophageal cancer, a significant gastrointestinal malignancy, is influenced by immune dysfunction, chronic esophageal inflammation, and micronutrient imbalances. Vitamin D, a crucial micronutrient, regulates cell growth, differentiation, and apoptosis, potentially affecting cancer-related processes. Vitamin D levels in esophageal cancer patients remains controversial. This study aims to evaluate serum vitamin D levels in esophageal cancer patients compared to a control group

Methods: In this study, serum vitamin D levels were measured using the enzyme-linked immunosorbent assay (ELISA) method in a population of 50 individuals, including 25 healthy controls and 25 patients diagnosed with esophageal cancer.

Results: Esophageal cancer patients had significantly higher mean serum 25(OH) D levels than healthy individuals (p 0.05).

Conclusion: This unexpected finding suggests a complex role for Vitamin D in this malignancy, necessitating further research to understand its clinical implications and mechanism of action.

keywords: Esophageal cancer Vitamin D 25-hydroxyvitamin D [25(OH)D]

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-97

Major Depressive Disorder (MDD) as a Risk Factor for Alzheimer Disease (AD)

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Background and aim: Major depressive disorder (MDD) and Alzheimer's disease (AD) affect millions of people globally and both associated with significant morbidity and mortality. Despite clinical distinctions, MDD is frequently associated with memory dysfunction, while AD is commonly accompanied by depressive symptoms. Recent epidemiological studies and biomarkers indicate that MDD acts as an independent risk factor that increases the likelihood of developing AD. The aim of this narrative review is to summarize the current evidence supporting the role of MDD as a risk factor for AD.

Methods: This narrative review was conducted by searching for indexed articles in PubMed, Scopus, Web of Science, and Google Scholar. The keywords used included major depressive disorder, Alzheimer's disease, risk factors, biomarkers, and anxiety. Published studies in English from 2020 to 2025 were considered, focusing on epidemiological research, long-term cohorts, and biomarker analyses related to the relationship between depression and Alzheimer's disease.

Results: Recent epidemiological studies published between 2020 and 2025 consistently report that MDD is associated with a 1.5 to 2-fold increased risk of AD. This risk appears to be more pronounced in individuals with recurrent or chronic depressive episodes. Biomarker research indicates increased inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), amyloid-β deposition and tau hyperphosphorylation, elevated cortisol levels indicating overactivity of the hypothalamic-pituitary-adrenal (HPA) axis and decreased levels of brain-derived neurotrophic factor (BDNF). These changes are also seen in AD pathology, specially including amyloid-β deposition and tau hyperphosphorylation. Evidence regarding the impact of antidepressant treatments on cognitive decline remains varied; some studies suggest protective effects, while others report no significant benefits. Overall, findings from long-term cohorts and biomarker analyses reinforce the position of MDD as an important risk factor for AD, although further research is needed to clarify the underlying mechanisms and therapeutic implications.

Conclusion: MDD has been consistently associated with systemic inflammation, HPA axis dysregulation, amyloid-β deposition, tau hyperphosphorylation, and reduced BDNF and neuroplasticity. These changes reflect mechanisms involved in AD, including amyloid-β and tau pathology and synaptic dysfunction. Recent evidence reinforces the biological link between MDD and AD, with alterations in MDD occurring in parallel with neuronal changes seen in Alzheimer's pathobiology. Overall, although MDD is an independent risk factor for AD, converging pathways reveal substantial biological overlap and highlight the need for further investigation into their shared mechanisms and therapeutic targets.

keywords: Major Depressive Disorder, Alzheimer Disease, Risk Factors, Inflammation, Hypothalamo-Hypophyseal System

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-98

Bioactive Properties of Persian Gulf Algae: A Systematic Review of Antioxidant and Antitumor Activities

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Background and aim: Marine algae have gained increasing attention in recent years due to their diverse and potent bioactive compounds. The Persian Gulf, renowned for its rich marine biodiversity, is home to a diverse array of algal species. Given this richness, the current study aims to explore the antioxidant and antitumor properties of algae native to this region

Methods: A comprehensive literature search was conducted in four major scientific databases: PubMed, Web of Science, Scopus, and Google Scholar, covering studies published from inception to 2024. A combination of MeSH and Emtree terms was used to identify relevant studies. Articles reporting the antioxidant and/or antitumor effects of Persian Gulf algae were included. Extracted data included the scientific names of the algae, the bioactive compounds identified, solvents used for extraction, types of bioassays conducted, and the effectiveness of the extracted compounds.

Results: A total of 96 studies were included in this review. The majority focused on brown algae, among which several species showed notably high antioxidant activity. Extracts derived using organic solvents, especially methanol and ethanol, were most effective in isolating antioxidant agents. Regarding antitumor properties, organic solvents such as n-hexane, ethyl acetate, and dichloromethane generally performed better than aqueous solvents. Algal extracts have demonstrated significant cytotoxic activity against cancer cell lines, indicating their potential as promising candidates for the development of anticancer drugs

Conclusion: Algae from the Persian Gulf represent a promising and underexplored source of bioactive compounds with both antioxidant and antitumor properties. These findings support further research aimed at optimizing extraction techniques, identifying active molecules, and validating their therapeutic applications in preclinical and clinical settings.

keywords: Persian Gulf, marine algae, antioxidant activity, antitumor effect, bioactive compounds

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-99

Systemic Inflammation in Hashimoto's Thyroiditis: Evidence Supporting the CRP-to-Albumin Ratio

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Background and aim: Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disorder, characterised by chronic lymphocytic infiltration and progressive immune-mediated destruction of the thyroid gland, often resulting in hypothyroidism. Anti-thyroid peroxidase antibodies (anti-TPO) represent a hallmark of thyroid autoimmunity, while high-sensitivity C-reactive protein (hs-CRP) reflects systemic inflammatory activity; however, each marker has limitations in fully capturing the inflammatory burden of HT. Composite inflammatory indices integrating positive and negative acute-phase reactants provide a more stable and comprehensive assessment. This study aimed to evaluate the C-reactive protein to albumin ratio (CAR) in patients with Hashimoto's thyroiditis and to compare it to that of healthy

Methods: We conducted a systematic search of the PubMed, Scopus, and Google Scholar databases to identify relevant studies published between 2020 and 2025. The search strategy included the keywords Hashimoto's thyroiditis, C-reactive protein–to–albumin ratio (CAR), anti-thyroid peroxidase antibodies (anti-TPO), and their related synonyms. Duplicate records were removed using EndNote software (version 20). The methodological quality of the included studies was assessed using the GBI tool, and no language restrictions were applied.

Results: Following the search, 1142 articles were retrieved,1131 papers were excluded due to duplication or irrelevance and 11 articles were retained. In all included studies, serum hs-CRP levels were significantly elevated in the HT group compared to controls, with substantial heterogeneity across studies (I^2 75%). In contrast, serum albumin levels did not show a significant difference between groups with moderate heterogeneity. The pooled analysis showed a significantly higher CRP-to-Albumin Ratio (CAR) in HT patients, with low-to-moderate heterogeneity, suggesting a consistent association across available studies.

Conclusion: This systematic review highlights the role of systemic inflammation in Hashimoto's thyroiditis. While hs-CRP levels were consistently elevated, substantial heterogeneity suggests influence from population characteristics, comorbidities, and methodological variability. Serum albumin showed no significant difference, limiting its standalone value. In contrast, the CRP-to-albumin ratio demonstrated a consistent increase with lower heterogeneity, indicating superior performance as a composite inflammatory marker. By integrating positive and negative acute-phase reactants, CAR may better reflect inflammatory burden in HT, warranting confirmation in prospective studies.

keywords: Hashimoto's thyroiditis; CRP-to-albumin ratio; Autoimmune inflammation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-100

Fatal methadone poisoning: a ten-year analysis of clinical and laboratory characteristics in an Iranian toxicology center

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Background and aim: Methadone poisoning is a major cause of mortality, especially in patients with opioid use disorder. Its long half-life and unpredictable dose-response relationship led to severe complications, especially respiratory depression. This study describes the characteristics of methadone poisoning deaths in a toxicology center in Iran.

Methods: This cross-sectional study reviewed the medical records of 140 patients who died of methadone poisoning at Khorshid Hospital in Isfahan between 2015 and 2024. Data on demographic characteristics, cause of poisoning, history of substance use, clinical manifestations, laboratory findings, and cause of death were collected and analyzed using SPSS version 26 software.

Results: Most of the deceased were male (85.7%) with a mean age of 60 ± 13.2 years. The main causes of poisoning were abuse (41.4%) and suicide (40%). A history of substance abuse was present in 62.1% of cases. Classic clinical manifestations of opioid poisoning were common (decreased level of consciousness (90.7%), miosis (72.9%) and apnea (34.3%)). The most common laboratory finding was respiratory acidosis (mean pH = 7.30). Other paraclinical tests were normal or slightly increased. The most common cause of death was respiratory failure (60.7%), followed by cardiac arrhythmia (14.3%). A significant relationship was observed between the level of education, the presence of a history of drug abuse, the type of drug used in people with a history of addiction, and the presence of miosis with the time interval from poisoning to death.

Conclusion: Fatal methadone poisoning mainly affected older men; substance abuse (overdose) and suicide were the predominant causes. The clinical course was characterized by classic symptoms of opioid poisoning, leading to respiratory failure and death. These findings emphasize the need to implement safe methadone delivery methods for individuals seeking treatment, provide psychosocial support to high-risk patients, and provide long-term medical monitoring to prevent mortality in these patients.

keywords: poisoning, mortality, substance abuse, respiratory failure

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PBi-101

Context-Dependent Effects of Metformin on Amyloid-Beta Aggregation

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Background and aim: Alzheimer's disease (AD) is a multifactorial neurodegenerative disorder characterized by progressive cognitive impairment, with amyloid-beta (Aβ) accumulation as a central pathological hallmark. Increasing evidence links metabolic dysfunction and insulin resistance to AD pathogenesis, prompting interest in antidiabetic agents as potential modulators of amyloid pathology. Metformin, a first-line therapy for type 2 diabetes, has shown both neuroprotective and paradoxical pro-amyloid effects under specific conditions, particularly during prolonged high-dose exposure in insulin-resistant states. This narrative review critically examines the dual and context-dependent effects of metformin on amyloid-beta metabolism.

Methods: A narrative review of the literature was conducted using experimental, preclinical, and clinical studies that investigated the effects of metformin on amyloid-beta production, aggregation, and clearance. The analysis focused on key molecular and cellular pathways involved in amyloid homeostasis, including AMP-activated protein kinase (AMPK) signaling, insulin signaling pathways, mitochondrial function, autophagy regulation, oxidative stress, and neuroinflammation. Both beneficial and detrimental outcomes associated with metformin exposure were considered to provide a balanced and integrative perspective.

Results: Multiple studies demonstrate that metformin can reduce amyloid-beta accumulation through activation of AMPK, enhancement of autophagy-mediated clearance, improvement of insulin sensitivity, and attenuation of neuroinflammatory responses. These mechanisms may contribute to decreased Aβ production and increased clearance, particularly in metabolically impaired or insulin-resistant conditions. In contrast, evidence also suggests that metformin may increase amyloid-beta levels under certain circumstances, particularly in insulin-resistant individuals receiving prolonged high-dose treatment, as well as in conditions of altered neuronal energy metabolism or disrupted insulin signaling. Some studies report that AMPK activation by metformin may upregulate β-secretase (BACE1) expression or activity, thereby promoting amyloidogenic processing of amyloid precursor protein. Additionally, factors such as vitamin B12 deficiency, mitochondrial stress, and differences between diabetic and non-diabetic states appear to influence the direction of metformin's effects on amyloid pathology. Collectively, these findings highlight a complex and condition-dependent role for metformin in regulating amyloid-beta dynamics.

Conclusion: Metformin exerts dual and sometimes opposing effects on amyloid-beta metabolism, acting as a context-dependent modulator rather than a uniformly protective agent. These effects are particularly pronounced in insulin-resistant individuals receiving prolonged high-dose therapy. Its impact on Alzheimer's disease-related amyloid pathology appears to be influenced by dosage, duration of exposure, metabolic status, and underlying cellular conditions. A clearer mechanistic understanding of these variables is essential before metformin can be reliably considered as a preventive or therapeutic strategy targeting amyloid-beta pathology in Alzheimer's disease.

keywords: Metformin, Amyloid-beta, Alzheimer's disease, Context-dependent effects, Insulin resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-102

Trend of glycosylated hemoglobin (Hba1c) and fasting blood sugar (FBS) in Hafiz Diabetes Clinic in Sabzevar during 2017-2021

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Background and aim: The prevalence of diabetes is rising in the world. Glycemic control to reduce DM complications is one of the most important goals of diabetes management; thus we aimed to evaluate the trends of glycemic parameters in patients of Hafiz Diabetes Clinic in Sabzevar.

Methods: In this cross-sectional study, 140 patients with diabetes who were under treating at Sabzevar Diabetes Clinic were randomly selected. Demographic information, fasting blood sugar and hemoglobin A1c were extracted over a one-year period, and their trends were analyzed.

Results: Women were the majority of patients registered in the center (67.14%). The mean age of the patients was 59.22 ± 11.96 years, and the mean BMI was 28.93±4.53 kg / m2. The trends of FBS changes was decreasing (P = 0.059) but the trends of postprandial- glucose and HbA1C did not changed significantly. At the last patient visit, HbA1C≤7 was achieved in only 25% of cases.

Conclusion: Women refer to medical centers much more than men.the results showed that the control of glucose profile is achieved in a quarter of the patients in this center.

keywords: Control, Diabetes, Fasting sugar, HbA1C

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-103

Trastuzumab-Based Combination Chemotherapy in HER2-Positive Breast Cancer: A Meta-Analysis of Randomized Trials from 2020 Onwards

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Background and aim: HER2-positive breast cancer represents ~15-20% of breast cancer cases and historically carries worse prognosis. The addition of trastuzumab to chemotherapy significantly improved survival outcomes compared with chemotherapy alone. However, evolving combinations — especially trastuzumab-based regimens combined with pertuzumab and newer antibody-drug conjugates like trastuzumab deruxtecan (T-DXd) — have shifted first-line therapy, warranting a systematic review of randomized evidence from 2020 onwards. To systematically review and meta-analyze randomized controlled trials (RCTs) published from 2020 onwards that compared trastuzumab-based combination chemotherapy regimens with standard chemotherapy ± trastuzumab or other comparators in patients with HER2-positive breast cancer.

Methods: Electronic databases (PubMed, Science direct , google schoolar and proquest) were searched from 01 Jan 2020 to present. Eligible studies were RCTs involving adult HER2-positive breast cancer patients comparing trastuzumab-based combination chemotherapy regimens vs control regimens (chemotherapy alone, trastuzumab monotherapy, or other targeted combinations). Primary efficacy outcomes were progression-free survival (PFS) and overall survival (OS). Secondary outcomes included objective response rate (ORR), duration of response (DOR), and Grade ≥3 adverse events (AEs). Hazard ratios (HRs) and pooled risk ratios (RRs) were calculated using random-effects models.

Results: A total of X RCTs involving Y HER2-positive patients met inclusion criteria, including the DESTINY-Breast09 trial comparing T-DXd + pertuzumab vs THP. *Preliminary results demonstrated significantly longer PFS with T-DXd combinations (HR ~0.56; improved median PFS ~40.7 vs ~26.9 months). Other trials assessing trastuzumab + chemotherapy combinations showed improved ORR and survival outcomes relative to control arms. Safety profiles were consistent with known cardiac and hematologic toxicities associated with HER2-targeted therapy.

Conclusion: evidence supports that trastuzumab-based combination chemotherapy regimens improve key clinical outcomes (PFS, ORR) in patients with HER2-positive breast cancer.

keywords: HER2 , trastuzumab , combination therapy, breast cancer, meta analysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-104

Consolidating Clinical Insights and Uncovering Novel Regulatory Mechanisms of Exosomal microRNAs in Obesity and Non-Alcoholic Fatty Liver Disease: A Systematic Review and Bioinformatics Analysis

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Background and aim: Overweight and obesity, marked by excess adipose tissue, are major risk factors for metabolic disorders such as type 2 diabetes mellitus (T2DM), hypertension, and non-alcoholic fatty liver disease (NAFLD) [1,2]. Once common mainly in high-income countries, their prevalence is now rising in low- and middle-income regions. NAFLD, characterized by hepatic lipid accumulation without significant alcohol intake, affects nearly 30% of the global population [3–5]. Although some obese individuals remain metabolically healthy, differences in insulin resistance, adipose tissue function, and fat distribution influence disease risk [6]. Circulating microRNAs (miRNAs), especially those carried by exosomes, regulate inflammation and lipid metabolism, linking obesity

Methods: In accordance with PRISMA 2020 guidelines, a systematic search was performed on August 25, 2024, across MEDLINE, Embase, and ISI Web of Science. Both MeSH and non-MeSH terms were used to identify studies on exosomal miRNAs in obesity and NAFLD. Duplicates were removed using EndNote, and the protocol was registered in PROSPERO (CRD420251017335). The inclusion criteria encompassed human studies investigating (i) exosomal miRNAs altered by obesity, (ii) the impact of NAFLD on exosomal miRNAs, and (iii) changes in miRNAs linking obesity to NAFLD. Studies were excluded if they were in vitro, non-English, review articles, or lacked separate NAFLD-specific data (https://www.crd.york.ac.uk/prospero/; PROSPERO ID: CRD420251017335).

Results: A total of 20 studies from 2015 to 2024 were included, examining exosomal miRNAs in obesity and NAFLD. In obesity-related studies, miRNAs such as miR-33a-3p, miR-223-5p, miR-34a, and miR-126 were associated with insulin resistance, inflammation, and angiogenesis. NAFLD-focused studies reported miR-122-5p, miR-34a-5p, miR-192-5p, and let-7b as biomarkers linked to liver injury and fibrosis. Bioinformatics analyses identified let-7b and miR-335-5p as overlapping miRNAs in both conditions, targeting genes involved in metabolism, inflammation, and Wnt signaling. Enrichment analysis revealed involvement of critical pathways such as steroid biosynthesis, AMPK, and JAK-STAT. miRNA–mRNA network analysis highlighted hsa-miR-6085 and ADIPOQ as major regulatory hubs.

Conclusion: This study integrates systematic review and bioinformatics to explore miRNA regulation in obesity and NAFLD. Literature confirms only let-7b and miR-335-5p, while in silico predictions reveal 40,000 potential candidates, indicating vast regulatory complexity. Enriched pathways (AMPK, Wnt, JAK-STAT) link metabolism and inflammation. ADIPOQ, a key target of both confirmed miRNAs, emerges as a central node influencing insulin sensitivity and lipid metabolism. Combining empirical and computational approaches effectively generates hypotheses and identifies promising therapeutic targets for these interconnected conditions.

keywords: Obesity, Nonalcoholic Fatty Liver Disease, Computational Biology, Systematic Review,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-105

Investigating the relationship between opioid addiction and ischemic stroke risk factors: Based on Sabzevar cohort study data

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Background and aim: Ischemic stroke occurs due to a blockage in one of the arteries supplying blood to the brain. It is the second leading cause of death worldwide. Various risk factors, including age, gender, health, and lifestyle, contribute to the onset of ischemic stroke, and one modifiable risk factor whose role is still not fully understood is opioid dependence. No studies have been conducted so far to examine the relationship between these factors and addiction in the Sabzevar population, and this study was designed to investigate the relationship between opioid addiction and the risk factors for ischemic stroke.

Methods: This study was conducted through a cross-sectional survey on patients visiting the Persian Cohort Center in Sabzevar from 2017 to 2020, using a completed questionnaire. Blood samples from the participants were collected according to the Cohort Center protocol, and serum was separated. Biochemical markers were measured using an auto-analyzer. LDL was measured using the Friedewald method with the following equation: LDL C=TC-(HDL C+TG/5) For data analysis, the latest version of GraphPad and SPSS software was used. Data regarding all variables were collected, and T-test, Chi-square, and regression analyses were employed to compare and assess relationships between variables. A p-value of less than 0.05 was considered significant.

Results: This cross-sectional study involved 4,199 individuals with a minimum age of 37 years, a maximum age of 76 years, and a mean age of 52.24 years Out of 4,199 individuals studied in this study, 2,331 (55.5%) were male and 1,868 (44.5%) were female (P0.001). Regarding the use of blood pressure and heart disease medications, 3,440 patients had a history of use, and 759 patients did not have a history of using blood pressure and heart medications. Regarding the family history of strokes, 3,177 patients reported a family history of strokes, and 1,022 patients reported a family history of heart attacks. 3,198 patients had no family history of heart attacks, and 1,001 patients had a family history of heart attacks. The number of consumers, categorized by gender, was 562 among 1870 men and 79 among 2326 women. (P0.001)

Conclusion: According to this study, there was no statistically significant difference in blood lipid profile and blood glucose between the opioid-using and non-opioid-using groups (P=0.584). However, systolic and diastolic blood pressure were higher in the opioid-using group, and BMI was lower in this group (P0.001). The results of this study indicated that opioid use increased the risk of stroke and heart attack among users. This increase was statistically significant for heart attack and myocardial infarction (MI) (P0.001), but not for stroke (P=0.059).

keywords: opioids, stroke, addiction.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-106

Electromagnetic Radiation Exposure and Reproductive Function: A Systematic Review

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Background and aim: Background: The rapid expansion of wireless technologies has raised public concern regarding the potential health effects of electromagnetic radiation (EMR), particularly from Wi-Fi and other radiofrequency sources. Fertility, especially male reproductive health, has emerged as a significant issue in this context. This systematic review aims to evaluate existing research on the potential effects of EMR exposure on fertility.

Methods: Materials and Methods: A comprehensive literature search was conducted using the PubMed, Scopus, and Web of Science databases. The search was performed using the keywords “electromagnetic radiation (EMR), fertility, reproductive health, and impact.” After screening and eligibility assessment, twelve relevant articles were included in the review.

Results: Results: Unlike ionizing radiation, EMR does not possess sufficient energy to directly damage DNA. However, several biological mechanisms have been proposed through which EMR may affect fertility. EMR exposure may increase the production of reactive oxygen species (ROS), leading to oxidative stress and subsequent cellular damage in reproductive tissues. Prolonged exposure may also result in localized tissue heating, potentially impairing semen quality. Multiple studies have reported adverse effects of EMR exposure on sperm motility, viability, and concentration. Additionally, some evidence suggests that EMR exposure may alter hormonal regulation involved in reproduction. Oxidative stress appears to be the most strongly supported mechanism affecting sperm function and integrity. Most available studies have focused on male fertility, while data regarding female reproductive health remain limited. Consequently, current evidence is insufficient to draw definitive conclusions about the effects of EMR on female fertility.

Conclusion: Conclusion: Concerns regarding the impact of EMR on fertility, particularly male reproductive health, are supported by experimental evidence indicating potential adverse effects mediated primarily through oxidative stress. Nevertheless, the existing literature is characterized by inconsistent findings and a lack of robust human studies. At present, there is no conclusive evidence that typical environmental EMR exposure poses a significant risk to fertility. Further well-designed experimental and epidemiological studies are required, especially in light of the ongoing advancement of wireless technologies.

keywords: Keywords: Electromagnetic radiation; Fertility; Infertility; Reproductive health

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-107

Biphasic Effects of Aqueous Red Beetroot (Beta vulgaris) Extract on the Viability of MCF-7 Breast Cancer Cells

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Background and aim: Natural plant-derived compounds have gained increasing attention for their potential anticancer properties. Red beetroot (Beta vulgaris) is rich in betalains, particularly betanin, which exhibit antioxidant and anticancer activities in various experimental models. However, the effects of aqueous beetroot extracts on breast cancer cell viability remain insufficiently characterized. This study aimed to evaluate the cytotoxic and proliferative effects of an aqueous red beetroot extract on MCF-7 breast cancer cells.

Methods: Fresh red beetroot was homogenized and extracted in deionized water adjusted to pH 4. The mixture was incubated at 49 °C for 9 hours under constant shaking, followed by centrifugation and sequential filtration through 0.4 µm and 0.2 µm filters. MCF-7 cells were seeded in 96-well plates and treated with increasing concentrations of the extract (10–90% v/v) for 48 hours. Cell viability was assessed using the MTT assay, and absorbance values were normalized to untreated control cells.

Results: Treatment with high concentrations of red beetroot extract produced a moderate cytotoxic effect on MCF-7 cells. At the highest concentration tested (90% v/v), approximately 30% reduction in cell viability was observed compared to control cells. In contrast, low to moderate concentrations of the extract (10-60% v/v) significantly increased metabolic activity compared to untreated cells. Overall, the extract showed a concentration-dependent biphasic (hormetic) response, with no IC50 values achieved in the range of concentrations tested but an IC30 at the highest concentration tested (90% v/v).

Conclusion: Red beetroot aqueous extract showed a biphasic effect on MCF-7 breast cancer cells, with moderate cytotoxicity at high concentrations and increased cell viability at lower doses. These findings suggest that although beetroot aqueous extract can reduce breast cancer cell viability at high concentrations, its anticancer effect is limited under the tested conditions and may be influenced by other factors.

keywords: Red beetroot; Beta vulgaris; MCF-7; MTT assay

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-108

Investigating The Protective Effects Of Curcumin On Proliferation Of PC12 Cells Under Cigarette Smoke-Induced Neuronal Damage and Environmental Pollution

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Background and aim: Cigarette smoke contains numerous toxic compounds, including carbon monoxide, hydrogen cyanide, benzene, and formaldehyde. Exposure induces severe oxidative stress, a key process implicated in the pathophysiology of neurodegenerative disorders through neuronal damage. This study investigates the neurotoxic impact of cigarette smoke extract (CSE) on PC12 cells—a validated neuronal model—and evaluates the potential protective effect of curcumin, as a well-characterized natural antioxidant.

Methods: To prepare the cigarette smoke extract (CSE), the smoke produced from a single cigarette was collected and dissolved in 10 mL of PBS. PC12 cell line were exposed to the cigarette extract in 10 different concentrations ranging from 1.5µM to 30µM (also 3, 6,9, 12, 15, 18, 22.5 and 27µM), also co-treated with curcumin solution in two concentrations, 2.5µM and 5µM at 37 °C and 5% CO2. After 24 h, the cell viability was tested by MTT assay in PC12 cells.

Results: The MTT assay revealed a concentration-dependent decrease in PC12 cell viability in response to cigarette smoke extract (CSE), with viability dropping to as low as 26% at the highest concentration tested (30 µM). A significant reduction was observed at concentrations of 22.5 µM and higher but not in a monotonic pattern. Interestingly, a low concentration of CSE (3 µM) alone, slightly increased viability compared to the control. Moreover, curcumin pretreatment demonstrated a protective effect against CSE-induced toxicity at 2.5 µM. However, this protection was not observed at 5 µM curcumin concentration, which instead further reduced cell viability compared to CSE alone. This protective effect attenuated in higher than 22.5 µM concentrations of CSE.

Conclusion: Cell death was significantly activated by CSE, particularly at higher concentrations. Curcumin demonstrated a dual role; at lower concentrations, it showed protective effects to some extent, whereas at elevated concentrations, it increased cellular death. These opposing effects underscore the context-dependent activity of curcumin in this model. Future studies should explore the effects of doses below 2.5 µM and employ genetic assays to elucidate the precise pathways involved.

keywords: PC12 cells; curcumin; neuroprotective; Tobacco Products

PBi-109

Association of Paraoxonase1(PON1) Activity and Genotypes in Patients with Rheumatoid Arthritis

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Background and aim: Rheumatoid Arthritis (RA) is pathophysiologically an autoimmune disease caused by various unknown factors that mainly affects the joints. In recent years, due to medical advances, significant progress has been made in the diagnosis, identification and treatment of this disease. Among the factors that play a role in the development of Rheumatoid Arthritis, we can mention oxidants that cause the development and progression of the disease, so in this study we decided to measure the total amount of oxidant and antioxidant activity and the polymorphism of paraoxonase1 enzyme.

Methods: We measure the levels of PON1, TAC (total antioxidant capacity) and TOS (total oxidant status) with ELISA (Enzyme-linked immunosorbent assay) and spectrophotometric method for their activities. We also investigated polymorphisms of the PON1 (L55M and Q192R) by PCR-RFLP assays.

Results: Paraoxonase and arylesterase activity of PON1 as well as their concentrations were lower in patients with RA compared with control group, but from the view of the specific activity, it was not significant between two groups. In the compare of TAC, TOS, and OSI, the TOS and OSI were higher in the patients than controls, while patients had lower levels of TAC compared with controls. Serum PON1 concentrations and activities were higher in LL (comparison with LM and MM) and RR (comparison with QR and QQ) genotypes while we did not observe any significant differences in arylesterase levels among mentioned polymorphisms.

Conclusion: In the current study, we clarified associations between (PON1) polymorphisms (55, 192) and enzyme activities in RA as there was a significant reduction in PON1 levels in RA patients compared with healthy. Taken together, paraoxonase1 enzyme in subjects with different genotypes could be a potential biomarker for determining the severity and prognosis of RA. On the other hand, our study revealed that TOS and OSI were higher in the patients than controls, while TAC level in RA patients was low. However, more studies are needed to clarify its clinical values.

keywords: Rheumatoid arthritis; paraoxonase1; Polymorphism; Oxidative Stress

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-110

Enhancement of the Role of Non-Enzymatic Antioxidants by the Drug Largazole in Mesenchymal Stem Cells from Human Adipose Tissue Under Oxidative Stress Conditions by Epigenetic Mechanisms.

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Background and aim: While mesenchymal stem cells (MSCs) offer potential for use in regenerative medicine, their therapeutic potential is hindered by oxidative stress that is present in the pathogenic microenvironments. The role of epigenetic regulation of non-enzymatic systems for antioxidants (e.g., glutathione and thioredoxin based systems) has not been thoroughly investigated; we aim to determine if the histone deacetylase (HDAC) inhibitor Largazole will induce transcriptional upregulation of the important genes within those systems, enhancing MSCs' ability to endure oxidative stress.

Methods: The study used human adipose-derived MSCs which were cultured in vitro and divided into one of four groups representing the four experimental conditions (1) Control, (2) Oxidative stress induced by H_2O_2, (3) Largazole pre-treatment prior to exposure to H_2O_2, and (4) Largazole only. Analysis of gene expression was conducted exclusively by quantitative real-time PCR (qRT-PCR). Genes of interest included the rate limiting enzymes involved in the synthesis of glutathione (GCLC, GCLM), glutathione reductase (GSR), glutathione peroxidase 4 (GPX4), and the core components of the thioredoxin system (TXN, TXNRD1, TXNRD2, PRDX3) as well as the transcription factor Nrf2 and its negative regulator KEAP1. All expression data was normalized to the expression of the Housekeeping Genes and analyzed using the ΔΔCt method.

Results: The findings of this study demonstrate that pre-treatment of cells with Largazole significantly reduces the extent of disruption of antioxidant gene expression by H2O2. Largazole caused the up-regulation of four of the most important genes involved in antioxidant defence (GCLC, GCLM, GSR, and TXN), as well as the up-regulation of several Nrf2-targeted antioxidant genes. In comparison, cells exposed to H2O2 in the absence of Largazole did not up-regulate or down-regulate the expression of these redox-related genes as effectively as cells that were pre-treated with Largazole. Additionally, Largazole alone caused a modest increase in expression of many antioxidant proteins, even when cells were not being subjected to acute oxidative stress.

Conclusion: Overall, our results provide strong support for the idea that Largazole enhances the transcriptional activation of non-enzymatic antioxidant defence systems in MSCs (e.g., glutathione and thioredoxin pathways). We conclude that by reinforcing the redox networks of MSCs, Largazole has great potential to induce the survival and functional enhancement of MSCs when exposed to oxidative stress, which may greatly enhance their therapeutic potential in treating patients suffering from diabetic wounds, ischaemic diseases, and neurodegenerative disorders.

keywords: Largazole, Oxidative stress, Glutathione pathway

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-111

Neuroendocrine and Epigenetic Impacts of Vinyl Chloride, PVC, and Synthetic Phytoestrogens on Fetal Brain Sexual Differentiation

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Background and aim: Sexual differentiation of the fetal brain is a highly sensitive process regulated by hormonal signaling, gene expression, and epigenetic programming. Prenatal exposure to endocrine-disrupting chemicals (EDCs), including vinyl chloride (VC), polyvinyl chloride (PVC), and synthetic phytoestrogens, may disrupt neurodevelopment and sex-specific brain organization. This study aims to systematically review and synthesize current evidence on the neuroendocrine, molecular, and epigenetic effects of these compounds on fetal brain sexual differentiation. Furthermore, it seeks to identify potential mechanisms and risks associated with prenatal exposure, providing insight for preventive strategies to protect fetal neurodevelopment.

Methods: A systematic literature search was performed in PubMed, Scopus, Web of Science, and EMBASE for studies published between 2005 and July 2025. Original in vitro, in vivo, and human studies investigating prenatal or perinatal exposure to vinyl chloride (VC), polyvinyl chloride (PVC), or synthetic phytoestrogens and their effects on fetal brain development and sexual differentiation were included. Study selection and data extraction followed PRISMA guidelines. The methodological quality of human studies was assessed using the ROBINS-I tool, while animal studies were evaluated with the SYRCLE risk-of-bias tool. Data synthesis focused on neuroendocrine, molecular, and epigenetic outcomes, highlighting mechanisms by which these compounds may disrupt sex-specific brain development and identifying gaps in current knowledge to guide future research.

Results: Prenatal exposure to vinyl chloride (VC) increased oxidative stress, altered histone modifications, reduced hypothalamic aromatase expression, and disrupted migration of gonadotropin-releasing hormone neurons, impairing brain masculinization. PVC-related effects were mainly due to phthalate leaching, especially DEHP, leading to suppressed testosterone production, PPARγ activation, dopaminergic neuron disruption, and increased apoptosis in sexually dimorphic regions. Synthetic phytoestrogens, such as genistein and diethylstilbestrol, acted via estrogen receptor α/β signaling, inducing feminized brain phenotypes and sex-specific epigenetic changes, including ESR1 promoter hypermethylation. These findings highlight key molecular, neuroendocrine, and epigenetic mechanisms through which prenatal exposure to VC, PVC, and phytoestrogens disrupt fetal brain sexual differentiation.

Conclusion: VC, PVC, and synthetic phytoestrogens disrupt fetal brain sexual differentiation via overlapping neuroendocrine and epigenetic mechanisms. Male fetuses are especially vulnerable during critical androgen-dependent developmental periods. These findings emphasize the importance of minimizing prenatal exposure to endocrine-disrupting chemicals and the need for further longitudinal and sex-specific epigenetic studies to clarify long-term effects on neurodevelopment, brain sexual differentiation, and behavior. Understanding these mechanisms can guide preventive strategies and public health policies aimed at protecting fetal brain development from environmental and chemical insults.

keywords: Vinyl Chloride; PVC; Endocrine Disruptors; Brain Sexual Differentiation; Epigenetics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-112

Complete Situs Inversus with Levocardia and Congenitally Corrected Transposition of the Great Arteries

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Background and aim: Complex congenital heart diseases (CHD) with discordant atrioventricular and ventriculoarterial connections are exceptionally rare, particularly when combined with anomalous systemic and pulmonary venous drainage. Double inversion—defined by atrial situs inversus concurrent with l-transposition of the great arteries (l-TGA)—represents a profound disruption of embryonic laterality. Survival into adulthood in such cases is uncommon and typically contingent upon compensatory shunting pathways that maintain adequate systemic oxygenation and pulmonary blood flow. We aimed to describe an extraordinary case of double inversion accompanied by multiple coexisting anomalies—including an unreported intracardiac shunt between the right atrium and left ventricle—and to highlight the pivotal role of

Methods: A 35-year-old woman with a history of childhood open-heart surgery underwent comprehensive cardiovascular evaluation. Diagnostic modalities included transthoracic and transesophageal echocardiography, electrocardiography, contrast-enhanced ECG-gated cardiac computed tomography angiography (128-slice). Right heart catheterization was performed to quantify pulmonary artery pressures and vascular resistance. Imaging datasets were jointly interpreted by a multidisciplinary team comprising a congenital cardiologist, a cardiothoracic radiologist, and a cardiac surgeon. Anatomical descriptions adhered to the segmental nomenclature endorsed by the International Society for Nomenclature of Paediatric and Congenital Heart Disease. Written informed consent was obtained for publication of anonymized clinical and imaging data.

Results: Imaging confirmed atrial situs inversus with systemic venous return (SVC and IVC) draining into the morphologic left atrium and pulmonary veins emptying into the morphologic right atrium. Ventriculoarterial discordance consistent with l-TGA was present: the aorta arose from the morphologic right ventricle, and the pulmonary artery from the morphologic left ventricle. Additional findings included a large perimembranous ventricular septal defect (VSD), a patent ductus arteriosus (PDA), severe pulmonary arterial hypertension (mean PAP: 62 mmHg), a right-sided aortic arch, and an aberrant right pulmonary artery coursing posterior to the ascending aorta. Most notably, a direct intracardiac communication between the right atrium and left ventricle was identified—a previously unreported shunt pathway in this anatomical context. This constellation of anomalies likely enabled long-term survival through balanced bidirectional shunting that preserved both pulmonary perfusion and systemic oxygen delivery.

Conclusion: This case illustrates an exceptionally rare form of complex CHD characterized by double inversion and a novel intracardiac shunt, underscoring how synergistic anatomical adaptations can permit survival into adulthood despite profound structural derangements. It also emphasizes the indispensable value of advanced cross-sectional imaging in uncovering subtle yet critical anatomical details in adults with repaired or undiagnosed congenital heart disease. Accurate anatomical delineation is essential not only for diagnosis but also for guiding potential future interventions and prognostication in such patients.

keywords: situs inversus, levocardia, congenitally corrected transposition of great arteries, CCTGA,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-113

Evaluating the serum levels of interleukin-8 and soluble interleukin-6 receptor in stage I multiple myeloma patients

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Background and aim: Multiple Myeloma (MM) accounts for 10 percent of hematologic malignancies worldwide and poses major challenges in oncology. Previous studies have revealed the potential role of cytokines and their receptors in the pathogenesis of MM. Therefore, this study aimed to investigate the effect of interleukin-8 (IL-8) and soluble interleukin-6 receptor (sIL -6R) in patients with stage I of MM.

Methods: Thirty stage I of MM patients (13 males and 17 females) and thirty healthy participants (13 males and 17 females) were included in this case-control study. The participants were matched in age and sex. The patients with advanced MM, those receiving therapy and the control participants with any underlying diseases were excluded from the study. The levels of IL-8, sIL -6R, albumin, and β2-microglobulin were assessed in the serum samples.

Results: A significant increase in the serum levels of IL-8 (12.46 ± 2.70 vs 9.02 ± 2.94 ng/ml), and sIL -6R (5.39 ± 1.38 vs 4.10 ± 1.14 ng/ml) as well as a significant decrease in the albumin levels (3.9 ±0.52 vs 5 ± 0.35 g/dL) were observed in the MM patients in comparison with the control group (P0.05). Although β2-microglobulin levels exhibited an increase in the patients as compared with control group (1.72 ¬±¬ 0.66 vs 1.58 ± 0.49 mg/L), the results were not statistically significant (P0.05).

Conclusion: These results imply the possible involvement of IL-8 and sIL -6R in stage I of MM, pointing out the role of cytokines and their receptors in the disease pathogenesis especially in the early stages.

keywords: Multiple Myeloma, Interleukin-8, Soluble Interleukin-6 receptor

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-114

Evidence for Hesperidin as an Effective Factor in Initiating the Intrinsic Pathway of Apoptosis in KG1a Leukemia Cells

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Background and aim: Acute myeloid leukemia (AML) is the most common subtype of leukemia, accounting for 62% of all leukemia fatalities. As a polyphenol glycoside, hesperidin triggers the apoptotic pathway, which might positively affect combating cancer cells.

Methods: The MTT assay was used to determine the IC50 of hesperidin in KG1a cell lines. For the apoptotic cell morphology study, we used Hoechst 33 258 staining. Activation of the caspase-3 enzyme was evaluated by the caspase-3 assay and spectrophotometry. Cell cycle distribution was analyzed by propidium iodide staining and flow cytometry. Moreover, p21, survivin, Bax, and Bcl2 gene expression was investigated by real time PCR.

Results: Hesperidin decreased the viability of KG1a leukemic cell4s, but not that of HFF2, a non-cancer cell line. Apoptotic cell morphological alterations and increase in caspase-3 activity were observed after hesperidin treatment. Our results revealed that the expression of anti-apoptotic genes survivin and Bcl2 significantly decreased with hesperidin treatment, and pro-apoptotic gene Bax and cell cycle regulator p21 increased compared to the control group

Conclusion: These findings revealed that hesperidin may be an effective factor in initiating the intrinsic pathway of apoptosis and may be good candidate for the treatment of AML.

keywords: Acute myeloid leukemia, Hesperidin, Apoptosis, Cell cycle

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-115

Neuroprotection through adiponectin receptor agonist: an updated meta-analysis of preclinical Alzheimer's disease studies

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Background and aim: Alzheimer's disease (AD) is a leading cause of dementia, imposing a substantial burden on individuals and society. While existing therapies can reduce the symptoms of AD, they do not offer genuine therapeutic effectiveness. Adiponectin Receptor Agonist (ADN-R Ag) has been proposed as a novel therapeutic agent for AD. This study aims to evaluate its efficacy in treating AD model mice.

Methods: A systematic search of PubMed, Scopus, Cochrane Library, and Web of Science was conducted up to May 3, 2025. Research investigating the impact of ADN-R Ag on cognitive performance and associated molecular pathways in Alzheimer's disease models, specifically APP/PS1, P301S, and 5XFAD mice, was incorporated. The Alzheimer's disease models in the study were male and ranged in age from 5.5 to 8 months. Studies evaluating the effect of ADN-R Ag on AD model mice through cognitive function tests and related molecular mechanisms were included. Methodological quality assessment was performed using the CAMARADES tool for animal studies. The meta-analysis was performed following Cochrane guidelines

Results: Six articles were included for the review. ADN-R Ag significantly improved cognitive function in the metaanalysis. The weighted mean difference of ADN-R Ag was 21.75 (95% CI: 16.61–26.88; p 0.001) for alternation rate percentage in the Y-maze, 20.46 (95% CI: 11.41–29.51, p 0.001) for novel object exploration time percentage in the novel object recognition (NOR) test, -15.83 (95% CI: -23.33 to -8.32, p 0.001) for escape latency in the Morris water maze (MWM), and 13.89 (95% CI: 8.84–18.94; p 0.001) for target quadrant time in the probe test. Additionally, ADN-R Ag was reported to mitigate AD pathology by reducing Aβ depositions through inhibition of GSK3β/BACE1/NF-κB pathway, suppressing neuronal inflammation by suppressing microglial and astrocytes activity and reducing and IL1β and TNFα levels, enhancing autophagy, and improving mitochondrial function with significant involvement of the AMPK pathway.

Conclusion: Based on the current study, ADN-R Ag has therapeutic effects on AD. However, considering the complex underlying molecular mechanisms and limited prior studies, further research is needed.

keywords: Adiponectin receptor agonist, Alzheimer, Neuroprotection, Meta-analysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-116

NF_kB regulates the migration of Vascular smooth muscle cells after heparin and betulinic acid treatments

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Background and aim: The aim of the study was to examine the effect of Heparin in the migration and proliferation of vascular smooth muscle cells (VSMCs) and its association with the expression levels of NF-kB and collagen 3. Additionally, the incorporation of Heparin in VSMC cultures containing betulinic acid was studied.

Methods: 8 cell groups were cultivated and administered with the Heparin, Betulinic acid based on the viability and toxicity in 24-h and 48-h periods. The gene and protein expression levels were assessed by RT-qPCR and western blotting techniques. The VSMC migration was assessed by scratch test.

Results: Heparin (30 IU) significantly boosted (P 0.05) NF-kB gene and protein expression levels, as well as VSMC migration over the exposure period.Heparin (5 IU and 15 IU) raised collagen 3 gene expression levels during both times. Incorporating Heparin into cells with Betulinic acid impacted collagen 3 expression levels.

Conclusion: The data showed that Heparin doses (5 IU and 15 IU) were proper for vascular smooth muscle cells based on NF-kB and collagen 3 expression levels.

keywords: NF_kB Collagen3 Betulinic acid Heparin

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-117

Downregulation of POU6F2-as1 as a Biomarker in Colorectal Adenocarcinoma Tissues

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Background and aim: Colorectal cancer is one of the most fatal cancers in the gastrointestinal tract and remains the third most common and fourth leading cause of cancer-related death worldwide, despite overall improvements in treatment. Recent studies have highlighted the role of long non-coding RNAs (lncRNAs) in cancer biology. POU6F2-as1 is an antisense lncRNA that acts on the POU6F2 gene (a key factor in neural development and stem cells) and plays roles in various cancers. This study aimed to investigate the expression changes of POU6F2-as1 in tumor and adjacent normal tissues from patients with colorectal adenocarcinoma.

Methods: The expression level of POU6F2-as1 in normal and tumor tissues of 50 colorectal cancer patients (stages I–III), aged 24–74 years, was measured using Real-time PCR with SYBR Green. The correlation between POU6F2-as1 expression and demographic and pathological data was analyzed. Statistical analyses were performed using independent t-test and ANOVA

Results: The results showed a significant decrease (P 0.001) in POU6F2-as1 expression in tumor tissues compared to adjacent normal tissues. A significant association was found between POU6F2-as1 expression and smoking (P = 0.023). According to pathological data, the lowest expression was observed in stage 3 patients (P = 0.019). Furthermore, the expression of POU6F2-as1 was most significantly reduced in patients with metastasis, and this was statistically significant (P = 0.005).The results showed a significant decrease (P 0.001) in POU6F2-as1 expression in tumor tissues compared to adjacent normal tissues. A significant association was found between POU6F2-as1 expression and smoking (P = 0.023). According to pathological data, the lowest expression was observed in stage 3 patients (P = 0.019). Furthermore, the expression of POU6F2-as1 was most significantly reduced in patients with metastasis, and this was statistically significant (P = 0.005).

Conclusion: The significant downregulation of POU6F2-as1 in colorectal adenocarcinoma tissues suggests its potential role as a tumor suppressor. These findings identify POU6F2-as1 as a promising target for diagnosis, prognosis, and ultimately treatment of colorectal adenocarcinoma.

keywords: Colorectal cancer, POU6F2-as1, Real-time PCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-118

Association Between Serum Vitamin D Levels and Liver Function Index (FIB-4)in Women Over 50 Years Old

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Background and aim: Elderly women are known as a vulnerable population for progression of liver disease due to hormonal changes, physical inactivity and abdominal obesity. Recent studies have shown that vitamin D deficiency, as a serious public health concern, may play a role in the pathogenesis of chronic liver diseases. Despite limited evidence of the association between vitamin D and liver function, necessary information is still unavailable in post-menopause women. Therefore, the aim of this study was to investigate the relationship between serum vitamin D levels and non-invasive liver function index (FIB - 4) in women over 50 years of age.

Methods: The present study employed a cross-sectional design. The study population includes 560 women over 50 years old who referred to the laboratory of the Specialized and Subspecialized Polyclinic of Shahroud University of Medical Sciences between March 2020 and March 2021. Required information was obtained from the hospital information system (HIS) and clinical history of patients registered in the laboratory. The fibrosis-4 (FIB-4) index is a score based on readily available blood tests that are routinely measured which calculate as [age (year) × AST (IU/L)]/[platelets count (×109/L) × √ALT (IU/L)]

Results: The study population consisted of 3 groups: 1) vitamin D deficient group, 2) vitamin D insufficient group, and 3) vitamin D sufficient group. ANOVA analysis showed that the mean of FIB - 4 index was significantly different between three groups, so that the group with vitamin D deficiency showed maximum in FIB – 4 index (1.40±0.54 in group 1, 1.21±0.64 in group 2, and 1.18±0.62 in group 3). The linear regression analysis also revealed a significant negative correlation between serum vitamin D levels and mean FIB - 4 index after adjusting for age, the history of diabetes and vitamin D consumption.

Conclusion: In summary , the results of this study showed that the increase of vitamin d levels can reduce the mean of hepatic fibrosis index (Fib-4) in women over 50 years old. Thus , supplementation of vitamin D in these individuals may reduce the progression of liver disorders .

keywords: postmenomause women, liver disease, Fib-4

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-119

Downregulation of miR-494 in Colorectal Cancer: A Potential Tumor Suppressor miRNA

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Background and aim: In this case-control study, 50 patients with colorectal cancer aged 30–70 years were enrolled as the study group. After recording demographic and pathological data, tumor and adjacent normal tissue samples were collected from each patient and stored in RNA Later solution. Total RNA was extracted using an RNA extraction kit. Subsequently, cDNA was synthesized from the extracted miRNA using the BONmiR High Sensitivity MicroRNA 1st Strand cDNA Synthesis kit. Relative expression of miR-494 was determined by qRT-PCR using Green SYBR dye. Data were analyzed statistically using SPSS software, version 23.

Methods: The results of this study showed a significant increase in miR-494 expression in tumor tissue compared to adjacent normal tissue (P = 0.001). miR-494 expression was significantly higher in women than in men (P = 0.029). Moreover, miR-494 expression was most elevated in patients with lymph node metastasis, and this difference was statistically significant (P = 0.036).

Results: Colorectal cancer is the third most common cancer and the second leading cause of cancer-related deaths worldwide. MicroRNAs are a class of non-coding RNAs that play a crucial role in regulating gene expression at the post-transcriptional level. Studies have shown that miR-494 acts as a downstream regulator, and its expression level is reduced in cancers. The aim of this study is to investigate the expression level of miR-494 in colorectal cancer.

Conclusion: Our results indicate that miR-494 may function as a tumor suppressor miRNA in colorectal cancer. Therefore, further studies are needed to identify the molecular mechanisms underlying colorectal carcinogenesis

keywords: Colorectal Neoplasm, miR-494, Real-Time PCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-120

Study the effect of nettle extract (Urtica Dioica) on iron deficiency anemia induced in female rats

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Background and aim: Iron deficiency anemia is characterized by decreased hemoglobin synthesis, resulting in the production of hypochromic and microcytic red blood cells.Various side effects of pills available on the market, such as nausea, and on the other hand, the incomplete effectiveness of the pills available on the market in improving iron deficiency anemia in patients, or the increase in iron load resulting from the use of pills available on the market, which causes damage to the liver.So in this study examining the levels of iron,TIBC,CBC and Transferrin Saturation in a statistical manner and comparing it with the effect of ferrous sulfate.

Methods: Initially, 56 female Wistar rats were divided into seven groups of eight rats. The groups were as follows: the control group (hereinafter referred to as group 1) did not undergo any intervention until the end of the study. The deferasirox group (hereinafter referred to as group 2) received only deferasirox. The nettle group (hereinafter referred to as group 3) received only nettle extract. The ferrous sulfate group (hereinafter referred to as group 4) received only ferrous sulfate. The nettle + ferrous sulfate group (hereinafter referred to as group 5) received both nettle and ferrous sulfate. The deferasirox + nettle group (hereinafter referred to as group 6) initially received deferasirox and then nettle. The deferasirox + ferrous sulfate group (hereinafter referred to as group 7) initially received deferasirox and then ferrous sulfate.

Results: No statistically significant difference (p0.05) was observed in other groups. As a result, the effect of nettle extract with ferrous sulfate and the combination of nettle extract and ferrous sulfate on improving anemia in rats modeled with iron deficiency anemia was similar and almost similar through increasing hemoglobin and MCH levels, and the group that received nettle extract had high Transferrin Saturation.

Conclusion: Finally, the ability of nettle extract to modulate serum iron levels was shown, which in addition to improving iron deficiency anemia by increasing serum iron levels, also prevents iron overload, which can cause liver damage

keywords: female rats , iron deficiency anemia ,Urtica Dioica

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-121

Circulating microRNAs as Diagnostic and Pathophysiological Biomarkers in Polycystic Ovary Syndrome: A Systematic Review

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Background and aim: Polycystic Ovary Syndrome (PCOS) affects 6–15% of women of reproductive age and Polycystic Ovary Syndrome (PCOS) affects 6–15% of women of reproductive age and is characterized by hyperandrogenism, ovulatory dysfunction, and insulin resistance [1,2]. Chronic inflammation and metabolic disturbances play key roles in its pathophysiology [3]. MicroRNAs (miRNAs) are small non-coding RNAs that regulate gene expression post-transcriptionally and remain stable in serum and plasma [4,5]. Circulating miRNAs have recently emerged as promising non-invasive biomarkers for diagnosing and monitoring endocrine and metabolic disorders, including PCOS [6,7]. Their stability and regulatory functions make them potential tools for early detection.

Methods: This systematic review followed PRISMA 2020 guidelines [8]. Searches were conducted in PubMed, Scopus, and Web of Science (2010–2025). Human case–control or cohort studies assessing circulating (serum, plasma, or exosomal) miRNAs in PCOS women were included. Reviews, animal studies, and tissue-only analyses were excluded. Data on study characteristics, profiling methods, dysregulated miRNAs, and diagnostic performance were extracted and synthesized narratively [9,10].

Results: Over 30 studies were included. miR-93 and miR-223 were linked to insulin resistance [11,12]. miR-21 and miR-146a correlated with inflammatory pathways [13,14]. miR-27a and miR-122 associated with metabolic dysfunction [15,16]. Hyperandrogenism and ovarian dysfunction correlated with miR-222, miR-132, and miR-320 [17,18]. Diagnostic performance ranged from moderate to high, with AUCs 0.75–0.88; combined miRNA panels improved accuracy [19]. Therapeutic Potential: Circulating miRNAs have been proposed as potential therapeutic targets in PCOS. Altered miRNA expression may modulate pathways involved in hormonal imbalance, insulin signaling, and metabolic dysfunction. miRNAs regulating ovarian follicle development and metabolism could provide a novel therapeutic approach, although clinical interventions remain preliminary [20,21]. Large-scale studies are needed to validate therapeutic applications.

Conclusion: Current evidence supports circulating miRNAs as biomarkers reflecting insulin signaling, inflammation, and steroidogenesis. Variability in ethnicity, sample size, normalization strategies, and laboratory protocols limits comparability. Standardized multicenter studies are required before clinical implementation.

keywords: Polycystic ovary syndrome, miRNA, Ferroptosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-122

An Investigation into the Effects of Moderate-Dose Atorvastatin on Furin levels in the Bloodstream of Patients Diagnosed with Type 2 Diabetes Mellitus: A Randomized Clinical Trial

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Background and aim: Atorvastatin is a drug from the statin family that is widely used to prevent microvascular and macrovascular complications in patients with type 2 diabetes mellitus (T2DM). Atorvastatin exerts its primary cholesterol-lowering effect by blocking 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, thereby attenuating cholesterol synthesis. In addition, atorvastatin has pleiotropic effects beyond decrease the cholesterol levels. Given that furin is a potential factor for inducing atherosclerosis and renal and retinal damage, the aim of this study was to investigate the effects of atorvastatin therapy on blood furin levels in T2DM patients.

Methods: This study was a randomized controlled trial (RCT) conducted on 30 patients with T2DM. Patients received moderate-dose atorvastatin (40 mg/day) for three months. Serum furin levels were measured using a sandwich enzyme-linked immunosorbent assay (ELISA) test before and after atorvastatin treatment. Paired t-test was used to evaluate furin changes before and after treatment. The Iranian Registry of Clinical Trial (IRCT) code was IRCT20250320065133N1.

Results: Treatment with atorvastatin significantly enhanced furin levels in T2DM patients compared to before treatment (P 0.05).

Conclusion: According to studies, atorvastatin is a lipophilic compound that easily enters hepatic and non-hepatic cells and exerts its antioxidant and anti-inflammatory effects. Furin is a proprotein convertase that promotes microvascular and macrovascular complications by stimulating proinflammatory responses. So, considering the anti-inflammatory effects of atorvastatin, this study showed inconsistent effects of this drug in preventing T2DM complications.

keywords: Atorvastatin, T2DM, Furin, Cholesterol, RCT

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-123

Molecular Docking Analysis of Germacrone as a Potential Inhibitor of Hepatitis B X-Interacting Protein (HBxIP)

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Background and aim: Hepatitis B X-Interacting Protein (HBxIP) is a human cellular protein that was initially identified as a binding partner of the hepatitis B virus X protein (HBx). There are indications that HBxIP plays a major role in the control of apoptosis and cell survival, thus presenting a good target for cancer therapy. Germacrone is a bioactive compound of natural origin that is found in various Zingiberaceae plant families with pharmacological activities. The present study aims to evaluate the inhibitory potential of germacrone and its derivatives on HBxIP with the goal of assessing its therapeutic significance using molecular docking methods

Methods: The 3D structure of HBxIP was obtained from the Protein Data Bank (PDB ID: 3MSH) in PDB format. Germacrone known potential HBxIP inhibitor (PubChem CID: 6436348) along with its 20 analogs from the PubChem database, were selected in SDF format. The active site residues of HBxIP were identified prior to docking. Protein and ligand preparation involved removing the ligand from the protein structure, energy minimization, and adding charges and hydrogen atoms. Molegro Virtual Docker v. 6 was employed for molecular docking, and the best interaction with the lowest binding energy was analyzed using Molegro Molecular Viewer software. The pharmacokinetic properties of the ligand were then evaluated using the SwissADME server

Results: Among the ligands investigated, (E)-6-methyldodec-5-en-2-one (PubChem CID: 5355126) (molecular weight: 196.33 g/mol) demonstrated the most energetically favorable binding (ΔGbind = -72.2264 Kcal/mol) to the target protein HBxIP. This ligand formed 1 hydrogen bonds with HBxIP residue Thr (12), and engaged in 1 steric interaction (Leu 5). The ligand exhibited a Log S score of -3.33 and a Log P score of -3.94. It also possessed 0 hydrogen bond donors and 1 acceptors, with a polarity index (TPSA) of 17.07 $Å^2$.

Conclusion: In conclusion, (E)-6-methyldodec-5-en-2-one (PubChem CID: 5355126) showed potential inhibitory effects against HBxIP. However, further in vitro and in vivo investigations of germacrone-based compounds need to confirm this anticancer properties.

keywords: Germacrone, LAMTOR5 protein (HBxIP), Molecular Docking

PBi-124

Integrating NGMS and NGS: The Future of Precision Newborn Metabolic Screening

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Background and aim: Integrative Application of Next-Generation Metabolic Screening(NGMS) and Next-Generation Sequencing in Newborn Screening(NGS) for Inborn Errors of Metabolism Background Newborn screening (NBS) programs are designed to identify inborn errors of metabolism (IEMs) at a presymptomatic stage to enable early therapeutic intervention and prevent irreversible complications. Over the past two decades, next-generation metabolic screening (NGMS), mainly based on tandem mass spectrometry (MS/MS), has significantly expanded the scope of neonatal metabolic screening by allowing simultaneous detection of multiple metabolites from dried blood spot samples. Despite its high throughput and sensitivity, metabolite-based screening may be affected by physiological variability, transient metabolic changes, and biochemical

Methods: This review synthesizes evidence from recent studies investigating the combined use of NGMS and NGS in neonatal metabolic screening. NGMS platforms, including flow-injection tandem mass spectrometry (FIA-MS/MS) and liquid chromatography–tandem mass spectrometry (LC-MS/MS), are used for the quantitative profiling of amino acids, acylcarnitines, and other diagnostic metabolites in dried blood spot specimens. In parallel, NGS-based approaches—such as targeted gene panels, whole-exome sequencing (WES), and whole-genome sequencing (WGS)—enable high-resolution detection of disease-associated variants in genes involved in metabolic pathways. The analytical workflows, data processing pipelines, diagnostic performance metrics, and operational limitations of both technologies were evaluated based on current literature.

Results: Evidence suggests that NGMS remains highly effective for initial high-throughput biochemical screening, while NGS provides improved diagnostic specificity through direct identification of genetic etiologies. Integrating these approaches may reduce false-positive results associated with metabolite fluctuations and facilitate the interpretation of variants of uncertain significance by correlating genomic findings with biochemical phenotypes. Moreover, multi-omics integration enables a more comprehensive understanding of metabolic pathway disruptions and supports precision diagnosis in neonatal metabolic disorders. However, challenges remain, including increased analytical complexity, bioinformatic requirements, cost considerations, and ethical concerns related to genomic data interpretation and incidental findings.

Conclusion: The integration of NGMS and NGS represents a promising multi-omics framework for enhancing the sensitivity, specificity, and clinical utility of newborn screening for inborn errors of metabolism. By combining rapid biochemical detection with precise molecular diagnosis, this approach may improve early disease identification and optimize clinical management. Future implementation will require standardized workflows, robust bioinformatic infrastructures, and ethical guidelines to ensure responsible use of genomic information in population-based screening programs.

keywords: Newborn Screening, NGMS, NGS, Inborn Errors of Metabolism, Precision Medicine,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-125

Delivery Strategies of Therapeutic Oligonucleotides in Solid Tumors: A Systematic Review of Smart Nanocarrier Systems and Emerging Clinical Applications

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Background and aim: Solid tumors are still one of the main reasons for fatalities across the globe. But targeted oligonucleotides are an optimistic approach to gene specificity. The main drawback to their use in clinical settings is their delivery, which faces various issues such as fast biodegradability, poor diffusion in tumors, and the tumor microenvironment. This question has been solved by smart nanocarriers, which are targeted and sensitive to signals for delivering oligonucleotides to solid tumors to overcome effectiveness. This systematic literature review will cover the discussion on oligonucleotide delivery, specifically on smart nanocarriers and their developing use for solid tumors.

Methods: This review article was conducted by searching for relevant publications on PubMed, Science Direct, Google Scholar, and Web of Science up to January 2025. The search terms used were Nanoparticles, Drug Delivery System, Oligonucleotides, Antisense, and solid Neoplasms. A total of 65 articles were initially identified, with 45 articles excluded based on title and abstract review. Ultimately, 20 articles meeting the inclusion criteria were selected, all of which were in English.

Results: In this review, 20 articles were concluded, which showed that smart nanocarriers like stimuli-responsive lipid nanoparticles, polymeric micelles, gold nanoparticles, mesoporous silica, and DNA/RNA nanoassemblies effectively protected oligonucleotides from degradation, accumulated in tumor sites via the enhanced permeability and retention effect (EPR), facilitated active targeting via ligands like aptamers and antibodies, and released oligonucleotides in response to pH, redox, and enzymatic triggers in the tumor environment. Preclinical results from all these nanocarriers demonstrated enhanced uptake, escape from endosomes, gene silencing, and antitumor activity in various models of solid tumors like breast, lung, liver cancer, etc. Several nanocarriers entered early-stage clinical trials.

Conclusion: Smart nanocarrier systems are found to be highly promising with regard to overcoming the challenges of delivering therapeutic oligonucleotides to tumors, with some of them already showing promise in early-phase clinical trials. However, more studies are strongly recommended to address the challenges in tumor penetration, heterogeneity, and safety for successful translation.

keywords: Nanoparticles; Drug Delivery System; Oligonucleotides; Antisense; Solid Neoplasms; Target therapy.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-126

The Application of Patient-Derived Organoids (PDOs) in Predicting Clinical Response to Targeted Therapies in Solid Tumors: A Systematic Review

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Background and aim: Solid tumors exhibit significantly varied responses to targeted therapies due to their genetic and biological heterogeneity. Traditional models, such as xenografts and animal models, fail to fully reflect these complexities. Patient-derived organoids (PDOs), due to their high similarity to the original tissue, provide a platform for testing therapies in an environment resembling the human body. This personalized approach aids in improving clinical response predictions and selecting better treatment options. This systematic review aims to evaluate the existing evidence regarding the predictive capacity of PDOs in targeted therapy responses.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, and Web of Science until February 2026. The keywords were Organoids, Tumor Microenvironment, Personalized Medicine, Targeted Therapy,and Neoplasms. By searching this database; 52 articles were found, 37 of them by Reading titles and abstracts were removed. 15 articles were selected under the inclusion criteria. All articles were chosen from English articles.

Results: Results: In this review, ultimately, 15 articles were concluded. The results indicated that PDOs effectively predicted patient responses to targeted therapies. These biomedical models preserved the genetic and phenotypic characteristics of the original tumors. Furthermore, comparisons between laboratory results and clinical data demonstrated that PDOs served as a reliable tool for selecting the best treatment methods and developing personalized drugs. These findings confirmed that PDOs played a significant role in enhancing the prediction of responses to targeted therapies in solid tumors.

Conclusion: Taken together, the findings indicate that PDOs can effectively predict responses to targeted therapies in solid tumors. However, further research is needed to standardize culture and drug evaluation methods. Additionally, long-term studies examining the relationship between PDOs and actual clinical responses in patients are essential.

keywords: Organoids; Tumor Microenvironment; Personalized Medicine; Targeted Therapy; Neoplasms

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-127

Amyloid-β Biogenesis and Processing: A Narrative Review of Molecular Pathways Central to Alzheimer's Pathogenesis

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Background and aim: Alzheimer's disease (AD), the most common type of dementia worldwide, is pathologically defined by presence of amyloid-β (Aβ) plaques and neurofibrillary tangles. This review narrates the current knowledge on Aβ production, emphasizing the proteolytic cleavage of amyloid precursor protein (APP) at the molecular and genetic level to aid us comprehend the underlying machinery of plaque formation and the consecutive pathogenesis of AD.

Methods: Articles published between January 2020 and April 2025 were searched on databases, most notably PubMed, focusing on original and review literatures of the field. Many keywords and Mesh terms were used to screen applicable articles including "Amyloid Beta-Protein Precursor", "Alzheimer Disease", "Amyloid Precursor Protein Secretases" and "Neurogenesis". Also, the reference lists of included articles were reviewed to identify additional relevant studies.

Results: Our research indicates that APP undergoes sequential processing via two pathways: the non-amyloidogenic route, arbitrated by α-secretase and the amyloidogenic pathway, driven by β-secretase (BACE1/2). Depending on the type of β-secretase by which the amyloidogenic pathway is initiated, the final products can differ. Notably, Aβ42, with its enhanced aggregation potential, is pivotal in AD pathogenesis. The structural complexity of APP, including its isoforms and pathogenic mutations (e.g., Val717Ile), influences Aβ generation and tau pathology. Key byproducts of APP processing, such as soluble APP fragments (sAPPα, sAPPβ) and C-terminal fragments (CTFs), contribute to synaptic dysfunction, mitochondrial impairment, and oxidative stress. Remarkably, the non-amyloidogenic P3 peptide (Aβ17-40/42) exhibits amyloidogenic potential, challenging conventional therapeutic strategies. The amyloid precursor protein intracellular domain (AICD), a transcription factor derived from γ-secretase cleavage, regulates neurogenesis, synaptic function, and apoptosis, with elevated levels observed in AD models.

Conclusion: The review highlights the multifaceted nature of Aβ synthesis and its cascading effects, advocating for therapies targeting Aβ aggregation, CTF accumulation, and AICD-mediated pathways to address AD's intricate pathophysiology, hoping for simplifying and clarifying this complexity.

keywords: Amyloid beta-Protein Precursor; Alzheimer Disease; Neurogenesis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-128

Betaine Mitigates Paclitaxel-Induced Hepatotoxicity in Rats by Regulating Oxidative Stress, Inflammation, Apoptosis, and Autophagy

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Background and aim: Paclitaxel (PTL) is widely used in chemotherapy; however, its efficacy is compromised by the risk of liver toxicity. This is the first study to investigate the protective effect of betaine (BTN) against PTL-induced liver injury.

Methods: Rats were randomly divided into five experimental groups (n = 7 per group): control (saline), BTN (100 mg/kg/day), PTL (2 mg/kg/day), PTL + BTN (2 and 50 mg/kg/day), and PTL + BTN (2 and 100 mg/kg/day). After the rats received 2 mg/kg body weight PTL intraperitoneally for the first five consecutive days, BTN was administered orally for 10 days.

Results: Our results indicate that BTN restores liver antioxidant levels (SOD, FRAP, and GSH), improves liver function by lowering AST and ALT levels, and attenuates PTL-induced lipid peroxidation. In the livers of PTL-treated rats, BTN significantly decreased the levels of NF-κB and TNF-α proteins and the ratio of caspase-3/pro-caspase-3, whereas it increased the levels of Nrf2, LC3-II/LC3-I, and Bcl-2.

Conclusion: In summary, the results of this study suggest that BTN may ameliorate PTL-induced liver injury by regulating oxidative stress, inflammation, apoptosis, and autophagy.

keywords: Paclitaxel, betaine, Oxidative Stress, Apoptosis, Autophagy

PBi-129

Implications of miRNA-590 dysregulation in digestive tract malignancies: mechanistic aspects and clinical significance

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Background and aim: Digestive tract cancers are among the most prevalent health problems worldwide. Recent studies have demonstrated that dysregulation of miRNA-590 plays an important role in the development and progression of digestive tract malignancies. Changes in miRNA-590 expression have been associated with tumor grade, metastasis, recurrence, response to adjuvant therapy, patient prognosis, and overall survival, suggesting its potential as a diagnostic and prognostic biomarker as well as a therapeutic target.

Methods: This review examines and summarizes the current evidence regarding the biological functions of miRNA-590 in digestive tract cancers, including its molecular mechanisms, upstream regulators, downstream targets, and clinical significance in diagnosis, prognosis, and treatment.

Results: The reviewed studies indicate that miRNA-590 can function either as a tumor suppressor or as an oncogene depending on the cancer type and cellular context. It influences multiple cancer-related processes, including tumor growth, invasion, angiogenesis, metastasis, and resistance to chemotherapy. Furthermore, various upstream regulators and downstream signaling pathways of miRNA-590 have been identified, highlighting its complex role in tumor biology. Evidence also supports its value as a potential diagnostic and prognostic biomarker.

Conclusion: miRNA-590 plays a critical and context-dependent role in digestive tract cancers. Due to its involvement in tumor progression, treatment response, and patient outcomes, miRNA-590 represents a promising biomarker for diagnosis and prognosis and may serve as a potential therapeutic target for future cancer treatments.

keywords: miRNA-590, Digestive tract cancers, Biomarker, Prognosis, Diagnosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-130

Detection of caudal type homeobox 1 (CDX1) gene methylated DNA, as a stool-based diagnostic biomarker in colorectal cancer

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Background and aim: Colorectal cancer (CRC) is known to develop due to the accumulation of both genetic and epigenetic alterations, resulting in the conversion of intestinal epithelial cells to malignant adenocarcinoma cells. Caudal type homeobox 1 (CDX1) gene is a homeobox transcription factor and a selective tumor suppressor gene that is an important factor for the development of intestinal cells. This gene plays a role in the differentiation of intestinal epithelial cells, and its expression decreases in a number of cell lines derived from CRC, which suggests that a lack of CDX1 expression is a risk factor for the development of colorectal carcinoma.

Methods: In the present study, the methylation of CDX1 gene promoter region was assessed in stool samples of 50 CRC patients and 50 healthy individuals by MethyLight PCR using two primers and a Taq Man probe, which was completely specifically designed for fully methylated DNA of the gene promoter region. The percentage of methylated reference (PMR) of the studied gene in all samples was calculated similarly to previous studies. Statistical analysis was performed using SPSS 16.

Results: The PMR medians were 3.25 (95% CI:0.1–100) and 0.1 (95% CI: 0.07–1) in the stool samples of CRC patients and healthy individuals, respectively. The results showed a significant difference in CDX1 gene PMR between stool samples of CRC patients and controls (P-value\0.001).

Conclusion: According to the results of this study, it can be argued that measurement of CDX1 gene DNA in stool samples using the MethyLight PCR has acceptable sensitivity and specificity, and is adequately potential to be used as a noninvasive complementary method for the diagnosis of CRC, along with colonoscopy as the gold standard to this end. This study is the first report on CDX1 methylation in stool samples of CRC patients. Therefore, further research should be carried out with a larger sample size to evaluate its efficacy as a diagnostic

keywords: CDX1 gene; Colorectal Cancer; DNA methylation; Epigenetic; MethyLight PCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-131

Physalis polysaccharide-sericin nanocarriers for controlled alpha-lipoic acid delivery and improved human sperm cryopreservation

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Background and aim: The development of delivery systems that deliver ALA as a cryoprotectant to sperm in a controlled manner could provide a promising strategy to minimize the toxicity associated with direct use of alpha-lipoic acid (ALA) during cryopreservation. Therefore, the aim of this study was to design and evaluate a nanocarrier based on sericin (SER) and a polysaccharide extracted from Physalis alkekengi for ALA encapsulation in a way that minimizes the toxicity resulting from direct use of ALA by controlling the release

Methods: To find the optimal ratio of SER and polysaccharide (pro/poly), a polysaccharide-SER-based nanocarrier (Ph-SER-NC) was synthesized using different ratios of pro/poly. Then, based on the optimization results, Ph-SER-NC was synthesized by the nanoprecipitation method, and ALA was loaded into the nanocarriers by direct system of dissolution into the aqueous phase (ALA-Ph-SER-NC). Its physicochemical characteristics were determined by the dynamic light scattering (DLS) technique. Furthermore, Fourier transform infrared spectroscopy (FTIR) was used to characterize the chemical composition, molecular properties, and surface adsorption of functional groups of the ALA-Ph-SER-NC. Then, the effects of ALA-Ph-SER-NC on biological properties after cryopreservation were investigated.

Results: The results showed that the optimal ratio of pro/poly for Ph-SER-NC synthesis was 1:2, and the resulting Ph-SER-NC had a Z-average and PDI of 109 nm and 0.21, respectively. After ALA loading, the physicochemical properties of the ALA-Ph-SER-NC, including Z-average, PDI, and zeta potential of 186.9 nm, 0.456, and -11.8 mV, were determined, respectively. The encapsulation efficiency for ALA was determined to be 93.7%. Biological evaluation showed that at concentrations of 0.02 and 0.05 mmol/mL, the ALA-Ph-SER-NC group significantly improved sperm parameters, including increases of approximately 26% in total motility, 24% in morphology, and 12% in viability, along with a 28% reduction in DNA fragmentation index (DFI).

Conclusion: The results indicated that ALA-Ph-SER-NC, through controlled release of ALA, preserved key biological properties of sperm. Thus, the synthesized ALA-Ph-SER-NC offers a novel and effective approach to preserve sperm quality during cryopreservation in men at risk of reduced fertility.

keywords: Physalis Polysaccharide, Sericin, Polysaccharide-Protein Based, Cryoprotectant, Sperm Cryopreservation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-132

Diagnostic Accuracy of Rapid Molecular Tests vs. Conventional Culture for Carbapenemase-Producing Enterobacterales (CPE) in Rectal Surveillance: A Systematic Review and Meta-Analysis

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Background and aim: Carbapenemase-producing Enterobacterales (CPE) pose a serious threat in healthcare settings. Rectal surveillance of high-risk patients is crucial for infection control. Conventional culture, the gold standard, requires 24–72 hours, delaying isolation and treatment. Rapid molecular tests (e.g., Xpert Carba-R, BioFire) can detect CPE within 1–2 hours, but their diagnostic accuracy compared to culture remains unclear. This systematic review and meta-analysis aimed to estimate the pooled sensitivity and specificity of rapid molecular tests for CPE detection in rectal swabs, using conventional culture as the reference standard.

Methods: We systematically searched PubMed, Scopus, Embase, and Web of Science (January 2015 – April 2026). Inclusion criteria: (i) prospective or retrospective studies evaluating rapid molecular tests on rectal swabs/stool; (ii) conventional culture (with/without enrichment) as reference; (iii) data sufficient to calculate sensitivity, specificity, or predictive values. Two reviewers extracted data and assessed quality using QUADAS-2. A bivariate random-effects model was used to pool sensitivity and specificity. Heterogeneity was explored by subgroup analysis (test type, carbapenemase gene family, and prevalence setting).

Results: Of 983 screened records, 27 studies (n=12,468 samples) met inclusion criteria. Pooled sensitivity of rapid molecular tests was 95.2% (95% CI: 92.1–97.4%) and pooled specificity was 98.3% (95% CI: 97.0–99.1%). Subgroup analysis by test type: Xpert Carba-R (14 studies) showed sensitivity 96.1% (93.4–98.0%) and specificity 98.9% (97.5–99.5%); BioFire FilmArray (6 studies): sensitivity 93.8% (88.2–97.1%), specificity 97.5% (95.0–98.9%); in-house PCR (7 studies): sensitivity 94.5% (89.0–97.6%), specificity 96.8% (94.1–98.4%). Sensitivity was highest for KPC (98.2%) and OXA-48 (96.7%), lower for NDM (90.5%, p=0.02). Positive predictive value was 95% in high-prevalence settings (10%) but dropped to 72% in low-prevalence (2%). Turnaround time reduced from median 48 hours (culture) to 2 hours (molecular). False-negative rate was 4.8% (mainly low bacterial load), false-positive rate 1.7% (mainly non-viable DNA after decolonization).

Conclusion: Rapid molecular tests provide excellent sensitivity (95%) and specificity (98%) for CPE rectal surveillance, reducing turnaround time by 24 hours. They enable earlier isolation and targeted therapy. In low-prevalence settings, positive results should be confirmed by culture. A strategy of molecular screening first followed by culture confirmation is cost-effective for infection control, especially in endemic regions or outbreaks.

keywords: Carbapenemase; Enterobacterales; Rectal screening; Molecular diagnostics; Meta-analysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-133

Development of Novel Improved Aptamer Sequences for CA125 Tumor Marker Detection Using In Silico Maturation Based on Genetic Algorithm

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Background and aim: Cancer antigen 125 (CA125) is one of the most important biomarkers for early diagnosis and monitoring of Ovarian cancer. Although antibody-based assays are widely used for CA125 detection, limitations such as high production costs, environmental instability, and demanding storage conditions have encouraged the development of alternative recognition elements. Aptamers are synthetic single-stranded oligonucleotides capable of binding targets with high affinity and specificity and represent a promising substitute for antibodies. However, conventional SELEX procedures may not fully explore the sequence of candidate aptamers. In silico maturation (ISM), a post-SELEX optimization strategy based on genetic algorithms (GA), offers a powerful approach for

Methods: Twenty-five previously reported single-stranded DNA aptamers against CA125 were collected to establish the initial library. Secondary structures were predicted using Mfold, and three-dimensional structures were generated through a validated computational pipeline involving RNAComposer, Chimera, and MOE (v2019.0102 x64). The three-dimensional structure of CA125 was modeled using the I-TASSER server. Molecular docking analyses were performed using PatchDock and ZDOCK platforms to evaluate aptamer–target interactions. High-scoring aptamers were selected as parent sequences and subjected to four iterative rounds of ISM based on GA operators, including selection, crossover, and mutation. Candidate sequences were ranked according to docking score, free energy (ΔG), sequence length, total intermolecular interactions, and hydrogen bond formation. Selected aptamers were experimentally validated using salt-induced gold nanoparticle aggregation spectroscopy, and dissociation constants (Kd) were determined by nonlinear regression analysis.

Results: A total of 142 novel candidate aptamers were generated through four generations of GA optimization. Molecular docking results demonstrated a progressive increase in average docking scores across successive generations, indicating successful enhancement of binding affinity. Conserved interaction regions within the SEA9 and SEA11 domains of CA125 were identified as major binding sites. Among all generated sequences, aptamer sin15-g4 exhibited the highest docking score and favorable structural characteristics, including a stable hairpin-loop motif. Experimental validation confirmed the computational predictions, with selected optimized aptamers displaying stronger binding affinity than the commonly used control aptamer (Apt23). The Kd values of optimized aptamers ranged from 1.796 to 4.319 nM, compared with 5.968 nM for the control aptamer. Aptamer sin15-g4 demonstrated the strongest affinity, showing a 3.32-fold improvement over the control sequence. Furthermore, approximately 80% agreement was observed between computational and experimental affinity assessments.

Conclusion: The integration of ISM based on GA with computational screening techniques successfully generated novel CA125-specific aptamers with significantly enhanced binding affinity. The identified aptamers, particularly sin15-g4, demonstrated superior performance compared with previously reported sequences and may serve as promising molecular recognition elements for future CA125 biosensors and diagnostic assays. These findings support the utility of computational evolutionary approaches as efficient tools for aptamer engineering and biomarker detection.

keywords: CA125; Aptamer; In Silico Maturation; Genetic Algorithm; Ovarian Cancer; Molecular

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-134

Design of Enhanced Novel Aptamer Sequences for CA125 Detection Through Truncation-Based In Silico Maturation

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Background and aim: CA125 is an important clinical tumor marker for the early detection of Ovarian cancer, while conventional antibody-based CA125 assays are limited by high production cost, environmental sensitivity, and difficult storage requirements. Aptamers are promising alternatives because of their low cost, structural stability, and high affinity for biological targets, and truncation-based in silico maturation (ISM) has been proposed as an effective strategy to improve aptamer binding performance by reducing unnecessary sequence regions.

Methods: Previously reported single-stranded DNA aptamers against CA125 were collected to build an initial library, and their secondary and three-dimensional structures were predicted using a computational pipeline including Mfold, RNAcomposer, Chimera, and MOE (v2019.0102 x64). The three-dimensional structure of CA125 was modeled using the threading approach in I-TASSER, and aptamer-target interactions were assessed by molecular docking with PatchDock and ZDOCK, followed by interaction analysis in BIOVIA Discovery Studio (v21.1.0.20298). High-scoring parental aptamers were then subjected to truncation-based ISM through iterative library generation and screening, and selected candidates were further validated experimentally by salt-induced gold nanoparticle aggregation spectrophotometry and Kd estimation using nonlinear regression in GraphPad Prism 8.0.

Results: A total of 25 anti-CA125 ssDNA aptamers were collected from previous studies to form the initial library, and successive truncation rounds generated 29, 35, 28, and 26 new candidates in the Tru1 to Tru4 libraries, respectively. Docking analysis of the 118 truncation-derived aptamers showed an overall improvement in docking performance across generations. Among them, Dou1-g3-4 showed the highest docking score, had a 50-nucleotide sequence with three hairpin loops, and bound to the SEA9, SEA10, and SEA11 regions of CA125. Experimental affinity testing showed that all selected Tru-library aptamers except Apt2-10 had lower Kd values than the control aptamer Apt23, and Dou1-g3-4 demonstrated about 1.7-fold improved affinity over the control. The agreement between experimental and in silico affinity ranking was about 60%, supporting the utility of the computational truncation strategy for aptamer optimization.

Conclusion: Truncation-based ISM successfully generated improved CA125-binding aptamers from previously reported parental sequences and enhanced binding performance at both computational and experimental levels. These findings support the use of truncation-driven ISM as a practical approach for developing shorter and more efficient aptamers for CA125 detection and future aptamer-based biosensor design in ovarian cancer diagnostics.

keywords: CA125; Aptamer; In Silico Maturation; Truncation; Molecular Docking.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-135

Ferroptosis in the Pathogenesis of Non-Alcoholic Fatty Liver Disease: A Bridge Between Bench and Bedside

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Background and aim: Non-alcoholic fatty liver disease (NAFLD) is a prevalent chronic liver disease worldwide, commonly associated with metabolic dysfunction, oxidative stress, and disturbances in lipid metabolism. The precise mechanisms behind NAFLD remain unclear, and no effective treatment exists to reverse its progression. Ferroptosis, an iron-dependent regulated cell death triggered by lipid peroxidation, has emerged as an important factor in disease pathogenesis.(1, 2)

Methods: This review synthesizes up-to-date evidence on ferroptosis in NAFLD by evaluating systematic reviews, meta-analyses, and mechanistic studies published between 2010 and 2025 in PubMed. Emphasis is placed on key molecular pathways regulating iron homeostasis, lipid peroxidation, and antioxidant defenses, and their impact on hepatocyte vulnerability to ferroptotic cell death.(1, 3) This review critically evaluates the current understanding of ferroptosis in NAFLD by surveying systematic reviews, meta-analyses, mechanistic studies, and relevant experimental research published between 2010 and 2025 in PubMed. To achieve comprehensive coverage, additional articles from Web of Science and Scopus were screened. The selected studies explored molecular pathways regulating iron homeostasis, lipid peroxidation, and antioxidant defense systems, as well as their influence on hepatocyte vulnerability to ferroptotic cell death. Studies that did not directly address ferroptosis in NAFLD or lacked mechanistic detail were excluded. Extracted information included study design, key molecular regulators such as GPX4 and system Xc–, and

Results: Ferroptosis contributes to hepatocellular injury in NAFLD by promoting iron overload, enhancing reactive oxygen species (ROS) production, and disrupting lipid metabolism, collectively intensifying oxidative stress and inflammation. Critical regulators, including glutathione peroxidase 4 (GPX4), system Xc–, and NRF2-mediated antioxidant pathways, modulate cellular susceptibility to ferroptosis. Experimental evidence suggests that interventions targeting ferroptosis—through iron modulation or strengthening antioxidant defenses—can attenuate disease progression and liver damage.(1, 4) Ferroptosis has emerged as a major contributor to hepatocellular damage in NAFLD. Studies in experimental models have demonstrated that excessive iron accumulation and increased production of reactive oxygen species (ROS) drive lipid peroxidation, which in turn exacerbates oxidative stress and liver inflammation. Critical molecular regulators, such as glutathione peroxidase 4 (GPX4), system Xc–, and NRF2-dependent antioxidant mechanisms, influence the susceptibility of hepatocytes to ferroptotic cell death. Evidence from both cellular and animal studies indicates that strategies targeting ferroptosis—including iron chelation, enhancement of antioxidant defenses, and

Conclusion: Ferroptosis has been identified as a key contributor to liver cell damage in NAFLD by mediating iron imbalance, lipid peroxidation, and oxidative stress, which together exacerbate hepatocellular injury. Modulating ferroptotic signaling pathways may offer a promising therapeutic avenue, translating mechanistic findings from experimental studies into potential clinical strategies for managing NAFLD.(2, 3)

keywords: Ferroptosis, Non-alcoholic fatty liver disease (NAFLD), Lipid peroxidation, Iron overload,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-136

The role of hydrogel scaffolds for drug delivery in wound healing: A review article

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Background and aim: Introduction and Objective: Hydrogels are specific types of drug delivery systems that have been used in many branches of medicine, including cardiology, oncology, immunology, wound healing, and pain management. Hydrogel networks have the ability to provide temporal and spatial control of the release of various therapeutic agents such as small molecule drugs, macromolecule drugs, and cells. Due to their tunable physical properties, controllable degradability, and ability to protect unstable drugs from degradation, hydrogels can be used as a platform in which they can control their release by creating various physical and chemical interactions with encapsulated drugs. The aim of the

Methods: To find relevant data, the Elsevier, Springer, Pubmed, Google Scholar databases, as well as the internal databases Iranmedex, Magiran, Medlib, Jihad Daneshgah, and the list of theses available in the National Library were studied. The entry criteria for the study were that the objectives of the articles studied were consistent with the objectives of the article in question. The articles were also examined for non-duplicate title, type of study, and variables of the information

Results: In the search for the reviewed databases, 60 English articles and 10 Persian articles were selected for writing the study. The documents that were studied were from the period of 2000 to 2026

Conclusion: The review of studies shows that the new generation of hydrogel scaffolds, by integrating drug delivery capabilities, have changed wound treatment from traditional dressings to "active and intelligent repair". The potential of these systems in temporal and spatial drug release reduces inflammatory responses and increases the proliferation of regenerative cells. Also, many studies have shown that hydrogel scaffolds, by integrating drug delivery capabilities, are effective on fibroblast cell proliferation and migration, angiogenesis, cell survival, modulation of inflammatory parameters, as well as modulation of growth and apoptosis during the wound healing

keywords: Hydrogel scaffold, drug delivery, wound healing

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-137

The role of hydrogel scaffolds for drug delivery in peripheral nerve repair: A review article

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Background and aim: Peripheral nerve injury is one of the complex challenges in regenerative medicine that leads to loss of motor and sensory function. Despite the advances made, complete reconstruction of nerve pathways and guidance of axonal fibers to the target remains difficult. In the meantime, hydrogel scaffolds are known as ideal substrates for nerve repair due to their high biocompatibility, three-dimensional structure similar to neural tissue, and surface modification capabilities. However, the main challenge in current therapies is the precise time and location management of the therapeutic factors. This review article examines the strategic role of hydrogel scaffolds in drug delivery systems.

Methods: To find relevant data, the databases Elsevier, Springer, Pubmed, Google Scholar, as well as the internal databases Iranmedex, Magiran, Medlib, Jihad Daneshgah, and the list of theses available in the National Library were studied. The inclusion criteria for the study were that the objectives of the articles studied were consistent with the objectives of the article in question. The articles were also examined for the lack of duplication of title, type of study, and variables of information studied

Results: In searching for the databases to be studied, 60 English articles and 10 Persian articles were selected from the articles that were searched for. The documents that were studied were from the period of 2000 to 2026

Conclusion: The study review shows that the synergy between hydrogel scaffolds and drug delivery systems not only optimizes the microscopic environment for nerve growth, but also has a high potential to become new standards in nerve injury repair

keywords: Hydrogel scaffold, drug delivery, peripheral nerve repair

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-138

Quality of Life and Short-Term Postoperative Outcomes in Women Undergoing Total Laparoscopic Hysterectomy versus Total Abdominal Hysterectomy for Benign Uterine Pathology

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Background and aim: Hysterectomy remains the most frequently performed major gynaecological surgery worldwide for benign uterine pathology. Although total abdominal hysterectomy (TAH) has long been the standard, total laparoscopic hysterectomy (TLH) has emerged as a minimally invasive alternative with potential advantages in postoperative recovery and quality of life (QoL). The present study was undertaken to compare short-term postoperative outcomes and QoL between TLH and TAH in women operated for benign uterine pathology.

Methods: A prospective comparative observational study was conducted over one year in the Department of Obstetrics and Gynaecology at a tertiary care teaching hospital. Sixty women aged 35–60 years scheduled for hysterectomy for benign uterine indications were recruited and allocated into two groups of 30 each: Group A underwent TLH and Group B underwent TAH. Intraoperative parameters, postoperative pain (Visual Analogue Scale), analgesic requirement, hospital stay, return to routine activities, complications and QoL (assessed by SF-36 at baseline and six weeks postoperatively) were recorded. Statistical analysis was performed using SPSS v25; p 0.05 was considered significant.

Results: Mean operative time was significantly longer in the TLH group (112.4 ± 18.6 min vs 84.7 ± 15.2 min; p 0.001), but intraoperative blood loss (146.3 ± 42.1 mL vs 285.7 ± 68.4 mL; p 0.001), VAS pain at 24 h (3.2 ± 0.9 vs 5.6 ± 1.1; p 0.001), analgesic consumption, hospital stay (3.1 ± 0.7 vs 5.4 ± 1.0 days; p 0.001) and time to resume routine activities (10.6 ± 2.4 vs 21.8 ± 3.7 days; p 0.001) were significantly lower in the TLH group. Wound-related complications were higher with TAH (16.7 % vs 0 %; p = 0.020). At six weeks, all eight SF-36 domains showed significantly higher scores in the TLH group.

Conclusion: Total laparoscopic hysterectomy offered superior short-term postoperative recovery and quality-of-life outcomes compared with total abdominal hysterectomy for benign uterine pathology, despite a longer operative time, supporting its preferential use when expertise and infrastructure permit.

keywords: Total laparoscopic hysterectomy; Total abdominal hysterectomy; Benign uterine pathology; Quality

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-139

Intranasal AdipoRon Mitigated Anxiety and Depression-Like Behaviors in 6-OHDA-Induced Parkinson 's Disease Rat Model: Going Beyond Motor Symptoms

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Background and aim: Depression and anxiety are common non-motor symptoms of Parkinson's disease (PD) that may emerge before motor manifestations and significantly affect patients' quality of life. Current dopaminergic therapies, including levodopa, have limited efficacy in improving mood-related symptoms, highlighting the need for novel therapeutic approaches. AdipoRon, an adiponectin receptor agonist, has shown neuroprotective and anti-inflammatory properties through modulation of the AMPK/Sirt-1 signaling pathway. Therefore, this study aimed to investigate the potential anxiolytic and antidepressant effects of intranasal AdipoRon and to explore its underlying molecular mechanisms in a 6-hydroxydopamine (6-OHDA)-induced rat model of Parkinson's disease.

Methods: Sixty adult male Wistar rats were randomly assigned to control or Parkinson's disease (PD) groups. PD was induced by unilateral injection of 6-hydroxydopamine (6-OHDA, 10 µg) into the medial forebrain bundle (MFB), and successful lesioning was confirmed using the apomorphine-induced rotation test. One week after PD induction, animals received intranasal AdipoRon (0.1, 1, or 10 µg/rat), oral levodopa (10 mg/kg), or vehicle for 21 days. Anxiety- and depression-like behaviors were evaluated using the Open Field Test (OFT), Elevated Plus Maze (EPM), Forced Swimming Test (FST), and Sucrose Splash Test (SST). Following behavioral assessments, serum corticosterone levels were measured by ELISA. Protein expression of Sirt-1, NLRP3, caspase-1, and IL-1β in the prefrontal cortex was determined by Western blotting. Data were analyzed using one-way ANOVA followed by Tukey's post-hoc test, with p 0.05 considered statistically significant.

Results: Unilateral 6-OHDA injection successfully induced Parkinsonian features, as confirmed by a significant increase in apomorphine-induced contralateral rotations. Behavioral assessments demonstrated that PD rats exhibited anxiety-like behaviors, reduced locomotor activity, and depressive-like symptoms compared with sham animals. Intranasal AdipoRon (1 and 10 µg/rat) significantly improved anxiety-related parameters in the Open Field and Elevated Plus Maze tests, enhanced locomotor activity, reduced immobility time in the Forced Swimming Test, and increased grooming time in the Sucrose Splash Test. Furthermore, AdipoRon significantly decreased serum corticosterone levels in PD rats. Molecular analyses revealed that AdipoRon downregulated the expression of NLRP3 inflammasome components, including NLRP3, caspase-1, and IL-1β, while increasing Sirt-1 protein expression in the prefrontal cortex. These effects were dose-dependent and were most pronounced at 10 µg/rat.

Conclusion: Intranasal AdipoRon effectively alleviated anxiety- and depression-like behaviors in a 6-OHDA-induced rat model of Parkinson's disease. These behavioral improvements were accompanied by reduced serum corticosterone levels, suppression of NLRP3 inflammasome-related proteins, and increased Sirt-1 expression in the prefrontal cortex. The findings suggest that AdipoRon may represent a promising therapeutic strategy for managing neuropsychiatric symptoms associated with Parkinson's disease through modulation of neuroinflammatory and Sirt-1–related signaling pathways.

keywords: Anxiety and depression · Parkinson's disease · 6-OHDA · AdipoRon

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-140

Sialic Acid Modulates Cholesterol Homeostasis in Astrocytes by Regulating HMGCR, ABCA1, and CYP46A1 Protein Expression

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Background and aim: Cholesterol metabolism in the central nervous system is vital for neuronal function and synaptic integrity. Astrocytes play a central role in maintaining brain cholesterol homeostasis. Sialic acid, a key component of cell membranes and signaling molecules, has been implicated in various neurobiological processes. This study aimed to investigate the effects of sialic acid on the expression of key proteins involved in cholesterol synthesis (HMGCR), efflux (ABCA1), and elimination (CYP46A1) in astrocyte cells.

Methods: Astrocytes were isolated from newborn C57BL/6 mice and cultured and treated with sialic acid at concentrations of 100 and 500 µM for 24 hours. Protein expression levels of HMGCR, ABCA1, and CYP46A1 were quantified using western blotting. GAPDH was employed as an internal loading control. Densitometric analysis was conducted, and data were normalized to the untreated control group.

Results: Sialic acid induced a dose-dependent reduction in ABCA1 expression, declining to 70.2% ± 4.1% of control at 500 µM. HMGCR expression increased significantly at 100 µM (139.7% ± 6.3% of control, p0.05) but normalized to baseline at 500 µM. Notably, CYP46A1 expression was markedly upregulated at 500 µM, reaching 165.4% ± 5.8% of control (p0.01).

Conclusion: Sialic acid exerts concentration-specific modulatory effects on astrocytic cholesterol metabolism. Low-dose sialic acid transiently enhances cholesterol synthesis, whereas high-dose treatment suppresses ABCA1-mediated efflux and preferentially activates CYP46A1-dependent elimination. This metabolic shift suggests a potential neuroprotective mechanism, favoring cholesterol clearance via the CYP46A1 pathway, with possible therapeutic implications for disorders of brain cholesterol dysregulation.

keywords: Sialic acid; Cholesterol metabolism; HMGCR; ABCA1; CYP46A1

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-141

Synergistic Effects of Metformin and Naringenin on the IRS-1/GLUT4 Axis in a Rat Model of Diet-Induced Insulin Resistance

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Background and aim: Insulin resistance (IR) is a central feature of fructose-induced metabolic disorders. This study aimed to investigate the combined effect of metformin and naringenin on two key genes in the insulin signaling pathway-IRS-1 (insulin receptor substrate-1) and GLUT4 (glucose transporter type 4)- in the soleus muscle of fructose-induced insulin-resistant rats.

Methods: Insulin resistance was induced in 25 Wistar rats by administering 10% fructose solution for 8 weeks. The rats were randomly divided into five groups: normal control, fructose-fed (F), fructose+metformin (200 mg/kg), fructose+naringenin (50 mg/kg), and fructose+combination (metformin + naringenin). At the end of the treatment, gene expression levels of IRS-1 and GLUT4 in the soleus muscle were measured, along with serum glucose and insulin indices (HOMA-IR, G/I ratio).

Results: Combined treatment with metformin and naringenin significantly upregulated the expression of IRS-1 and GLUT4 compared to the untreated fructose-fed group. This upregulation was associated with marked improvements in HOMA-IR and the G/I ratio, indicating reduced insulin resistance. The combination therapy showed a significantly greater effect on increasing IRS-1 and GLUT4 expression than either metformin or naringenin alone.

Conclusion: The metformin-naringenin combination effectively attenuates fructose-induced insulin resistance by enhancing the expression of IRS-1 and GLUT4 in skeletal muscle. These findings demonstrate a synergistic interaction between pharmacological and phytochemical agents in improving insulin signaling and glucose uptake.

keywords: : Insulin resistance; Naringenin; IRS-1; GLUT4; Insulin signaling pathway

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-142

Cumulus Cell IRS1 Transcript Levels as a Non-Invasive Biomarker of Oocyte Developmental Competence

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Background and aim: Post ovulatory aging compromises oocyte developmental competence, and cumulus cells are thought to mediate this effect through insulin/PI3K/AKT signaling. Insulin receptor substrate 1 (IRS1) is the critical upstream adaptor of this pathway, yet its expression dynamics during cumulus cell aging remain incompletely characterized. To evaluate IRS1 gene expression changes in mouse cumulus cells after in vivo and in vitro post ovulatory aging and to assess whether IRS1 can serve as a non invasive biomarker of oocyte quality.

Methods: Cumulus–oocyte complexes were recovered from hormonally stimulated mice and subjected to 6 h of post ovulatory aging either in vivo or in vitro. Total RNA was isolated from cumulus cells, and IRS1 transcript levels were measured by quantitative real time PCR using the $2^{-}\Delta\Delta Ct$ method with β actin as the reference gene. Differences were analyzed by Kruskal–Wallis followed by Dunn's multiple comparison test (P 0.05).

Results: IRS1 expression was dramatically upregulated in both aging conditions. Compared with fresh controls, the in vivo aged group showed a 23.54 fold increase, and the in vitro aged group exhibited a 93.25 fold increase (P 0.05). The substantially greater rise in vitro indicates that culture conditions intensify aging related stress in cumulus cells, leading to accumulation of IRS1 transcripts without corresponding downstream pathway activation.

Conclusion: Overexpression of IRS1 is a hallmark of post ovulatory cumulus cell aging and indicates uncoupling of upstream insulin signaling from downstream effectors. IRS1 expression profiling could provide a non invasive biomarker for oocyte developmental competence and guide the refinement of IVF timing, culture media, and oocyte selection strategies in assisted reproductive technologies.

keywords: IRS1, Insulin signaling, Cumulus cells, Post ovulatory aging, Oocyte developmental

PBi-143

Effects of Mobile Phone Electromagnetic Radiation on Fertility and Reproductive Outcomes: A Systematic Review

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Background and aim: با افزایش استفاده از تلفن‌های همراه، نگرانی‌ها درباره اثرات احتمالی تابش (RF-EMF) و میدان‌های الکترومغناطیسی با فرکانس رادیویی (EMR) الکترومغناطیسی بر سلامت انسان افزایش یافته است. برخی مطالعات نشان داده‌اند که این تابش‌ها می‌توانند بر فرایندهای تولیدمثلی مانند کیفیت گامت‌ها، رشد جنین و عملکرد هورمونی تأثیر بگذارند. با توجه به اهمیت باروری و افزایش شیوع ناباروری در سبک زندگی مدرن، بررسی نظام‌مند شواهد موجود درباره اثرات تابش تلفن همراه بر سیستم تولیدمثل ضروری است.

Methods: در این مطالعه مرور سیستماتیک، سه پژوهش مرتبط با اثر تابش تلفن همراه یا RF-EMF بر پیامدهای تولیدمثلی بررسی شد. این مطالعات شامل تحقیقات آزمایشگاهی روی حیوانات و یک پروتکل مرور سیستماتیک در انسان بودند. داده‌ها از نظر اثرات تابش بر رشد جنین، فرایند اووژنز، فولیکولوژنز، هورمون‌های تخمدانی و کیفیت سلولی تحلیل و مقایسه شدند. یافته‌ها به صورت توصیفی خلاصه و الگوهای مشترک میان مطالعات استخراج گردید.

Results: نتایج مطالعات نشان داد که قرارگیری در معرض تابش الکترومغناطیسی تلفن همراه می‌تواند اثرات منفی با فرکانس ۹۰۰–۱۸۰۰ EMR قابل توجهی بر سیستم تولیدمثل داشته باشد. در مطالعه‌ای روی جنین موش، تابش مگاهرتز باعث تأخیر در تقسیمات سلولی جنین، افزایش الگوهای غیرطبیعی تقسیم سلولی، افزایش قطعه‌قطعه شدن جنین و کاهش زنده‌مانی سلولی بلاستوسیست شد. در مطالعه دیگری روی موش‌های باردار، قرارگیری در معرض تابش تلفن همراه منجر به کاهش معنی‌دار سطح هورمون‌های استروژن و پروژسترون، کاهش تعداد فولیکول‌های اولیه و افزایش آپوپتوز فولیکول‌های اولیه گردید؛ این اثرات در مواجهه طولانی‌تر شدیدتر بود. همچنین پروتکل مرور سیستماتیک سازمان جهانی بهداشت نشان می‌دهد که شواهد موجود در مطالعات انسانی در حال جمع‌آوری و ارزیابی هستند تا ارتباط احتمالی RF-EMF با ناباروری مردان، تغییرات اسپرم و پیامدهای بارداری مانند سقط، زایمان زودرس و ناهنجاری‌های مادرزادی مشخص شود.

Conclusion: بر اساس شواهد موجود، تابش الکترومغناطیسی ناشی از تلفن همراه می‌تواند اثرات منفی بالقوه‌ای بر عملکرد تولیدمثلی، رشد جنینی و فرایندهای تخمدانی داشته باشد، به‌ویژه در مدل‌های حیوانی. با این حال، برای تعیین دقیق اثرات در انسان به مطالعات مشاهده‌ای بیشتر و مرورهای سیستماتیک جامع نیاز است. کاهش مدت و شدت مواجهه با تابش تلفن همراه ممکن است به عنوان یک اقدام احتیاطی در نظر گرفته شود.

keywords: تابش الکترومغناطیسی، تلفن همراه، باروری، پیامدهای تولیدمثلی، رشد جنینی

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-144

Mitochondrial Transplantation Attenuates CCl_4 Induced Hepatic Fibrosis Through Activation of the AMPK/LKB1/SIRT3 Signaling Axis

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Background and aim: Hepatic fibrosis is a progressive liver disorder characterized by excessive extracellular matrix accumulation and distortion of normal hepatic architecture. Growing evidence indicates that mitochondrial dysfunction and oxidative stress play central roles in fibrogenesis. Therefore, approaches that restore mitochondrial integrity and function may offer therapeutic benefits in liver fibrosis.

Methods: Liver fibrosis was induced in male C57BL/6J mice through intraperitoneal injections of carbon tetrachloride (CCl_4) for five weeks. Functional mitochondria were freshly isolated and administered via tail vein injection. Liver injury and fibrosis were assessed using serum biochemical parameters (ALT, AST, and ALP), histological analyses (H&E, Masson's trichrome, and Sirius Red staining), and hepatic hydroxyproline content. Oxidative stress was evaluated by measuring malondialdehyde (MDA), glutathione (GSH), and superoxide dismutase (SOD). Changes in fibrosis-related genes and proteins, including components of the AMPK/LKB1/SIRT3 pathway, were examined by qRT-PCR and Western blotting.

Results: Mitochondrial transplantation ameliorated CCl_4-induced liver damage, reflected by lower serum ALT, AST, and ALP levels compared with untreated fibrotic mice . Histological evaluation revealed improved hepatic structure, reduced inflammatory cell infiltration, and diminished collagen accumulation. These findings were further supported by a reduction in hepatic hydroxyproline content. In addition, mitochondrial transplantation alleviated oxidative stress by decreasing MDA levels while restoring GSH content and SOD activity. Mechanistically, treatment enhanced the expression of AMPK, LKB1, and SIRT3 and was accompanied by downregulation of key profibrotic markers, including TGF-β1, α-SMA, and collagen I.

Conclusion: Mitochondrial transplantation effectively attenuated liver injury, oxidative stress, and fibrotic remodeling in CCl_4-induced hepatic fibrosis. The protective effects were associated, at least in part, with activation of the AMPK/LKB1/SIRT3 signaling axis. These findings support mitochondrial transplantation as a potential organelle-based therapeutic approach for the management of liver fibrosis.

keywords: Mitochondrial transplantation; Liver fibrosis; CCl_4-induced hepatic injury; Oxidative stress; AMPK/LKB1/SIRT3

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-145

Beyond the Oncogene Dogma: Significant Downregulation of a Specific Linear PVT1 Isoform in Gastric Carcinoma and Its Molecular Implications.

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Background and aim: The long non-coding RNA PVT1 is predominantly recognized as an oncogene in gastric cancer (GC) (1). However, the PVT1 genomic locus exhibits extreme transcriptional complexity, producing multiple linear and circular isoforms with potentially opposing biological roles (2). This study aimed to investigate the expression dynamics of linear PVT1 transcript variant 1 across the entire spectrum of gastric carcinogenesis (Normal → Atrophy → Cancer) and to determine whether its downregulation follows a progressive trend during disease progression.

Methods: In this case-control study, PVT1 expression was evaluated in 60 human gastric tissue samples, comprising 20 normal, 20 atrophic gastritis, and 20 gastric cancer specimens. Following RNA extraction and cDNA synthesis, gene expression was quantified using RT-qPCR (SYBR Green method). Bioinformatic validation (NCBI BLAST) confirmed that the primers exclusively target linear PVT1 transcript variant 1 (RefSeq: NR_003367). Data were normalized against GAPDH, and fold changes were calculated using the 2^(-ΔΔCt) method. While pairwise comparisons were performed using the Mann-Whitney U test, the Jonckheere-Terpstra trend test was employed to evaluate the progressive expression changes across the three-stage carcinogenesis model.

Results: Contrary to the general consensus of PVT1 upregulation in GC, our findings revealed a striking paradox. Pairwise comparisons showed that linear PVT1 variant 1 was significantly downregulated in gastric cancer tissues compared to both normal controls and atrophic tissues ($p = 0.003$). Notably, the difference between atrophy and normal groups did not reach statistical significance ($p = 0.103$). However, and most importantly, the Jonckheere-Terpstra trend test revealed a highly significant progressive downregulation of PVT1 variant 1 across the entire carcinogenesis spectrum (p 0.0001), indicating that the depletion of this specific linear isoform is a gradual, stepwise event that begins in the premalignant atrophic stage and culminates in full-blown carcinoma.

Conclusion: Our study demonstrates, for the first time, that linear PVT1 variant 1 undergoes a progressive, stepwise downregulation throughout gastric carcinogenesis. This phenomenon may be driven by isoform switching (depletion of linear transcripts to fuel oncogenic circPVT1 biogenesis) or reflect a distinct tumor-suppressive role of this specific variant that is progressively lost during disease progression. These findings underscore the critical necessity of isoform-specific and longitudinal analysis in lncRNA research and open new avenues for understanding the molecular intricacies of gastric cancer progression.

keywords: long non-coding RNA PVT1, gastric cancer, Atrophy, Cancer

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-146

Improvement of metabolic indices and restoration of AKT and GSK-3β expression by metformin and naringenin combination in a high-fructose diet-induced insulin resistance model

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Background and aim: Insulin resistance (IR) plays a critical role in diet induced metabolic disorders. However, the combined effects of conventional antidiabetic agents (e.g., metformin) and bioactive flavonoids (e.g., naringenin) on the insulin signaling pathway, particularly on the expression of GSK 3β and Akt, remain poorly understood. This study aimed to investigate the combined effect of metformin and naringenin on glucose metabolism and the Akt/GSK 3β axis in a rat model of fructose induced insulin resistance.

Methods: Twenty five male Wistar rats were randomly assigned to five groups: normal control, fructose fed (F), fructose + metformin (200 mg/kg), fructose + naringenin (50 mg/kg), and a combination of both. IR was induced by administering 10% fructose solution for eight weeks. Serum glucose and insulin levels were measured to calculate HOMA IR, ISI, FIRI, and G/I indices. Gene expression of key insulin signaling components, including Akt and GSK 3β, was assessed in soleus muscle tissue.

Results: Combined treatment significantly improved HOMA IR, FIRI, and G/I ratio, and reduced ISI compared to untreated fructose fed rats. At the molecular level, the metformin/naringenin combination upregulated Akt expression and downregulated GSK 3β expression more effectively than either agent alone.

Conclusion: The combination of metformin and naringenin effectively ameliorated fructose induced insulin resistance and restored key elements of the insulin signaling pathway in soleus muscle, particularly through modulation of the Akt/GSK 3β axis. These findings highlight a synergistic interaction between a pharmacological agent (metformin) and a phytochemical (naringenin) in counteracting metabolic dysfunction.

keywords: Insulin resistance; Naringenin; High fructose diet; Akt pathway; Glucose metabolism

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-147

Curcumin-Loaded PVA-Alginate-SiO_2 Hydrogel Nanocarriers Induce Ferroptosis in Cancer Cells

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Background and aim: Ferroptosis, an iron-dependent form of regulated cell death driven by lipid peroxidation and oxidative stress, has recently attracted considerable attention as a promising therapeutic strategy in cancer treatment. Curcumin possesses significant anticancer, antioxidant, and anti-inflammatory properties; however, its clinical efficacy is limited by poor solubility, low bioavailability, and rapid degradation under physiological conditions. Hydrogel-based nanocarriers composed of polyvinyl alcohol (PVA), alginate, and silicon dioxide (SiO_2) have emerged as promising drug delivery systems capable of enhancing curcumin stability and targeted delivery.

Methods: A comprehensive narrative review of published literature was conducted using electronic databases including PubMed, Scopus, Web of Science, and Google Scholar. Relevant studies published in English focusing on ferroptosis, curcumin nanoformulations, hydrogel nanocarriers, PVA–alginate composites, SiO_2 nanoparticles, and cancer therapy were analyzed and synthesized. Emphasis was placed on molecular mechanisms associated with ferroptosis regulation, including GPX4 inhibition, SLC7A11 suppression, glutathione depletion, reactive oxygen species accumulation, and lipid peroxidation.

Results: The reviewed evidence suggests that curcumin-loaded PVA–alginate–SiO_2 hydrogel nanocarriers may significantly improve curcumin bioavailability, cellular uptake, sustained release behavior, and anticancer activity. These multifunctional nanoplatforms appear to enhance ferroptotic responses in tumor cells through modulation of oxidative stress pathways, iron metabolism, and ferroptosis-related genes and proteins. Furthermore, the physicochemical characteristics of PVA–alginate–SiO_2 hydrogels, including biocompatibility, swelling capacity, mechanical stability, and high drug-loading efficiency, support their suitability for targeted cancer therapy. Several in vitro and in vivo studies demonstrated enhanced cytotoxicity against cancer cells with reduced systemic toxicity compared to free curcumin.

Conclusion: Curcumin-loaded PVA–alginate–SiO_2 hydrogel nanocarriers represent a promising therapeutic platform for ferroptosis-mediated cancer treatment. By improving curcumin delivery and potentiating ferroptotic signaling pathways, these nanocarriers may overcome important limitations of conventional anticancer therapies. Nevertheless, further preclinical investigations and clinical studies are required to validate their safety, efficacy, and translational potential in oncology.

keywords: Curcumin; Ferroptosis; Hydrogel nanocarrier; PVA; Alginate; Silicon dioxide nanoparticles; Cancer

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-148

Dapagliflozin attenuates carbon tetrachloride induced-liver fibrosis through modulation of the YAP/TAZ signaling pathway

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Background and aim: Background: Liver fibrosis is a progressive pathological process characterized by excessive extracellular matrix deposition, hepatic stellate cell activation, and tissue remodeling. The Hippo pathway effectors Yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ) have emerged as key regulators of hepatic fibrogenesis. Dapagliflozin, a sodiumglucose cotransporter 2 (SGLT2) inhibitor, has demonstrated anti-inflammatory and anti-fibrotic effects in several organs; however, its role in liver fibrosis and its relationship with YAP/TAZ signaling remains unclear.

Methods: Methods: Liver fibrosis was induced in male C57BL/6 mice by intraperitoneal injection of CCl_4 (0.5–0.7 mL/kg in olive oil) for 5 weeks. Animals were divided into control, CCl_4, CCl_4 + dapagliflozin (25 mg/kg/day), and dapagliflozin-only groups. Hepatic fibrosis was evaluated using histological staining (H&E, Sirius Red, and Masson's Trichrome). Collagen deposition was quantified by hydroxyproline content, and hepatic stellate cell activation was assessed by α-smooth muscle actin (α-SMA) expression using qRT-PCR. YAP/TAZ signaling was evaluated by measuring YAP, TAZ, and downstream targets CTGF and CYR61.

Results: Results: CCl_4 administration induced severe hepatic injury and fibrosis, as evidenced by histopathological alterations, increased collagen deposition, elevated hydroxyproline content, and upregulation of α-SMA expression. These changes were accompanied by activation of YAP/TAZ signaling and increased expression of CTGF and CYR61. Dapagliflozin treatment significantly attenuated histological liver damage, reduced collagen accumulation, decreased hydroxyproline levels, and suppressed hepatic stellate cell activation. Furthermore, dapagliflozin inhibited YAP/TAZ signaling and downregulated profibrotic gene expression.

Conclusion: Conclusion: Dapagliflozin ameliorates CCl_4-induced liver fibrosis by reducing collagen deposition, inhibiting hepatic stellate cell activation, and suppressing YAP/TAZ signaling. These findings suggest a novel mechanistic role of SGLT2 inhibition in hepatic fibrogenesis and support its therapeutic potential in liver fibrosis.

keywords: Dapagliflozin, Liver fibrosis, Carbon tetrachloride (CCl_4), YAP/TAZ signaling pathway, Hepatic

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-149

Needs Assessment and Evaluation of the Establishment of a Master's Program in Medical Laboratory Quality Management

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Background and aim: Given the vital role of clinical laboratories in clinical decision-making, the quality of laboratory results is of particular importance. The rapid advancement of laboratory technologies, the increasing volume of diagnostic requests, and the necessity of complying with international quality standards have made the need for training specialized personnel in the field of laboratory quality management more evident than ever. This study was conducted to assess the necessity of and need for establishing a Master's degree program in Quality Management in Medical Laboratories.

Methods: This study was designed as a descriptive-analytical needs assessment. Data were collected using a 28-item questionnaire organized into four domains, including demographic information, needs assessment, the content of educational syllabi, and the required skills. The face and content validity of the questionnaire were confirmed by experts, and its reliability was also established. The questionnaire was distributed to and completed by students, graduates, specialists, and faculty members in the field of laboratory sciences. The data were analyzed using descriptive and inferential statistical methods.

Results: The findings revealed that the vast majority of respondents considered the establishment of a Master's degree program in Medical Laboratory Quality Management both necessary and beneficial. Furthermore, participants emphasized the importance of specialized training in quality management, quality control, quality assurance, accreditation standards, and practical skills aimed at enhancing laboratory performance. Regarding the curriculum and core competencies, there was a strong consensus on the need to design a practical, needs-based program tailored to the real-world demands of clinical diagnostic laboratories.

Conclusion: The findings of this study indicate a clear need for the establishment of a specialized educational program in the field of medical laboratory quality management. Given the central role of quality in ensuring the validity of laboratory results and patient safety, the introduction of this program could contribute to the training of competent professionals, the improvement of laboratory services, and alignment with national and international standards. Therefore, it is recommended that educational policymakers and authorities in the field of laboratory sciences take the necessary steps to plan for the establishment.

keywords: Needs assessment, Quality management, Medical laboratory, Master's degree, Laboratory sciences,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-150

The Dual Metabolic Effects of Hydroxychloroquine: Glycemic Benefits and Hypoglycemic Risk in Autoimmune and Insulin-Resistant Populations

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Background and aim: Hydroxychloroquine (HCQ), which has been used as an immunomodulatory medication, is increasingly recognized for its capacity to increase insulin sensitivity and lower blood glucose. Research indicates that HCQ may improve glycemic control in a number of clinical populations; however, these advantages may come with a higher risk of hypoglycemia, which could have complicated metabolic effects. To understand its metabolic impact and clinical implications, a thorough synthesis of the evidence is required.In this review, the effects of HCQ on insulin sensitivity and glycemic outcomes were summarized, and the trade-off between glycemic benefits and hypoglycemic risk during long-term HCQ use was examined.

Methods: PubMed, Scopus, Web of Science, and Google Scholar were used to perform a narrative literature review. Combinations of the terms "hydroxychloroquine," "insulin sensitivity," "glycemic control," "HbA1c," "fasting plasma glucose," "type 2 diabetes," "metabolic syndrome," and "autoimmune diseases" were used to find studies published between 2015 and 2026. Included were cross-sectional studies, case-control studies, cohort studies, randomized controlled trials, mechanistic investigations, meta-analyses, and review articles. Research on infectious diseases, such as malaria and COVID-19, was not included. With a focus on insulin sensitivity, HbA1c, fasting plasma glucose, dose-response relationships, metabolic safety, and hepatic outcomes, the evidence was critically synthesized.

Results: HCQ's beneficial metabolic effects were consistently shown in the reviewed literature. Significant drops in HbA1c and fasting plasma glucose were found in several clinical trials, especially with long-term treatment and doses of about 400 mg/day. Additionally, data showed that certain patient populations had lower insulin requirements and better insulin sensitivity. The results, however, highlighted the dual metabolic effects of HCQ: although HCQ improves insulin responsiveness and glycemic control, its glucose-lowering effects may raise the risk of hypoglycemic episodes, particularly in vulnerable people and those on concurrent antidiabetic medication. Furthermore, a number of reports emphasized the necessity of keeping an eye out for any potential hepatic complications while undergoing long-term treatment. Overall, treatment duration, dosage, and underlying patient characteristics seemed to have an impact on the amount of metabolic benefit.

Conclusion: Based on available data, HCQ may be a useful adjunctive treatment for enhancing insulin sensitivity and glycemic control in autoimmune and insulin-resistant individuals. However, the coexistence of hypoglycemic risk and metabolic benefits highlights the significance of careful dose consideration and customized monitoring. To better define the balance between safety and efficacy and to elucidate its role in managing metabolic comorbidities, more long-term studies are necessary.

keywords: Hydroxychloroquine; Insulin Sensitivity; Glycemic Control; Hypoglycemia; Autoimmune Diseases; Metabolic Syndrome.

PBi-151

Combination of Curcumin Supplementation and Aerobic Exercise Improves Lipid Profile and Antioxidant Enzyme Activity in Type 2 Diabetic Wistar Rats: A Synergistic Effect

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Background and aim: Type 2 diabetes mellitus (T2DM) affects 11.4% of Iran's adult population and is associated with dyslipidemia and oxidative stress, which account for 65-80% of diabetes-related deaths. Curcumin has potent antioxidant and lipid-lowering properties, while aerobic exercise improves insulin sensitivity. However, the combined effects of these two interventions in T2DM remain underexplored. This study aimed to evaluate the combined effects of curcumin supplementation and aerobic exercise on lipid profiles and oxidative stress in T2DM Wistar rats.

Methods: Thirty-five male Wistar rats (180-220 g) were divided into seven groups (n=5 each): healthy control (Control), healthy+curcumin (Control+Cur), healthy+curcumin+exercise (Control+Cur+Ex), untreated T2DM (T2DM), T2DM+curcumin (T2DM+Cur), T2DM+aerobic exercise (T2DM+Ex), and T2DM+curcumin+aerobic exercise (T2DM+Cur+Ex). T2DM was induced by intraperitoneal injection of nicotinamide (110 mg/kg) followed by streptozotocin (50 mg/kg). Curcumin (30 mg/kg) was administered via gavage three times weekly for 4 weeks. The aerobic exercise protocol consisted of a 4-week treadmill program (10-22 m/min, 15-30 min, 5° incline). Serum lipid profile (triglycerides, total cholesterol, LDL, HDL) and antioxidant enzyme activities (catalase, superoxide dismutase, glutathione peroxidase) were measured using enzymatic kits. Data were analyzed by one-way ANOVA with Tukey's post-hoc test (p0.05). The experimental protocol was approved by the Animal Ethical Committee of Islamic Azad University, in accordance with the NIH Guide for the Care and Use of Laboratory Animals (Publication No. 85-23, 1985).

Results: The T2DM+Cur+Ex group showed the most significant improvements across all parameters. Compared to T2DM group, the combination treatment significantly reduced triglycerides (p0.0001 vs. curcumin alone and exercise alone), total cholesterol (p0.01 vs. curcumin, p0.05 vs. exercise), and LDL cholesterol (p0.0001 vs. both monotherapies). HDL cholesterol increased significantly only in the combination group compared to T2DM and T2DM+Ex groups (p0.05). Regarding antioxidant enzymes, only the combination group achieved significant restoration of superoxide dismutase activity (p0.001 vs. T2DM). Glutathione peroxidase activity was highest in the combination group (p0.01 vs. curcumin, p0.001 vs. exercise). No significant differences were observed among healthy control groups.

Conclusion: The combination of curcumin supplementation and aerobic exercise produced significantly greater improvements in lipid profile and antioxidant enzyme activities than either intervention alone in T2DM rats, demonstrating a synergistic effect. Curcumin likely acts through Nrf2 activation and NF-κB inhibition, while exercise enhances insulin sensitivity via AMPK and PGC-1α pathways. These findings suggest that combining curcumin with aerobic exercise represents a promising adjunctive therapeutic strategy for managing dyslipidemia and oxidative stress in T2DM. Further clinical studies are warranted to translate these findings to human populations.

keywords: Diabetes, Curcumin, Aerobic Exercise, Dyslipidemia, Oxidative Stress

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-152

Synthesis of magnesium oxide–doped hydroxyapatite for enhancing anticancer drug release

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Background and aim: Cancer treatment is often limited by the non-specific distribution and systemic toxicity of conventional chemotherapeutic agents. Therefore, the development of biocompatible and controlled drug delivery systems has gained considerable attention in recent years. Hydroxyapatite (HA), due to its excellent biocompatibility and similarity to the mineral phase of bone, has emerged as a promising carrier for drug delivery applications. However, pure HA exhibits limited drug loading and release properties. This study aims to synthesize magnesium oxide-doped hydroxyapatite (HA-MgO) nanoparticles and investigate their potential as a pH-responsive carrier for improving the controlled release behavior of the anticancer drug doxorubicin.

Methods: Magnesium oxide-doped hydroxyapatite nanoparticles were synthesized using a precipitation method under controlled conditions. Different concentrations of MgO were incorporated into the HA structure to evaluate their influence on physicochemical properties. The synthesized nanocomposites were characterized using X-ray diffraction (XRD) for phase identification, Fourier-transform infrared spectroscopy (FTIR) for functional group analysis, scanning or transmission electron microscopy (SEM/TEM) for morphology evaluation, and Brunauer–Emmett–Teller (BET) analysis for surface area determination. Doxorubicin was loaded onto the synthesized nanoparticles through an adsorption process, and drug loading efficiency was determined spectrophotometrically. In vitro drug release studies were carried out in phosphate buffer solutions at pH 7.4 and pH 5.5 to simulate physiological and tumor microenvironments, respectively. Release kinetics were further analyzed using common mathematical models, including Higuchi and Korsmeyer–Peppas equations.

Results: The synthesized HA-MgO nanocomposites exhibited successful incorporation of magnesium oxide into the hydroxyapatite structure without the formation of undesirable secondary phases. Morphological analyses suggested nanoscale particles with enhanced surface characteristics suitable for drug adsorption. MgO incorporation was associated with increased surface area and improved porosity, which are expected to facilitate higher drug loading efficiency compared with pure HA. Drug release experiments demonstrated a pH-dependent behavior, with faster release observed under acidic conditions resembling the tumor microenvironment. Such selective release may reduce systemic toxicity while improving therapeutic efficiency. Kinetic analysis indicated that the release profile followed diffusion-controlled mechanisms, consistent with Higuchi and Korsmeyer–Peppas models. Overall, the findings suggest that HA-MgO nanocomposites have considerable potential as smart carriers for controlled anticancer drug delivery applications.

Conclusion: The present study highlights the potential of magnesium oxide-doped hydroxyapatite nanoparticles as a promising platform for targeted anticancer drug delivery. Incorporation of MgO may improve structural characteristics, drug loading capacity, and pH-responsive release behavior of hydroxyapatite-based carriers. The observed controlled release under acidic conditions suggests enhanced suitability for tumor-targeted therapy while minimizing adverse systemic effects. Further biological investigations, including cytotoxicity and cellular uptake studies, are required to validate the clinical applicability of these nanocomposites and their potential role in future cancer treatment strategies.

keywords: Hydroxyapatite nanoparticles Magnesium oxide doping Anticancer drug delivery Doxorubicin pH-responsive

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-153

Evaluating the Role of Novel Inflammatory Markers in the Early Detection of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) in Diabetic Patients

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Background and aim: Background: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is a prevalent comorbidity in patients with Type 2 Diabetes Mellitus (T2DM), often progressing silently toward steatohepatitis and fibrosis. While traditional liver enzymes (ALT/AST) are widely used, they frequently lack the sensitivity required for the early detection of metabolic liver injury, necessitating the search for more precise biochemical indicators. Objective: This systematic review aims to evaluate the diagnostic efficacy and clinical utility of novel inflammatory biomarkers in the early identification of MASLD within the diabetic population.

Methods: Methods: Following PRISMA guidelines, a comprehensive search was conducted across PubMed, Scopus, and the Cochrane Library. Studies focusing on emerging markers, including high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and various adipokines, were analyzed. The quality of the included studies was assessed using the Newcastle-Ottawa Scale and the Cochrane Risk of Bias tool.

Results: Results: The synthesized evidence indicates that novel inflammatory markers, particularly those associated with the adiponectin-leptin axis and pro-inflammatory cytokines, demonstrate superior sensitivity and specificity compared to conventional liver function tests. A strong positive correlation was observed between systemic inflammatory loads and the severity of hepatic steatosis. Furthermore, the integration of these biomarkers with clinical indices significantly enhances the predictive value for early-stage MASLD, allowing for the differentiation between simple steatosis and steatohepatitis.

Conclusion: Conclusion: Novel inflammatory markers serve as potent tools for the early detection of MASLD in diabetic patients. Integrating these biomarkers into routine clinical screening may facilitate timely therapeutic interventions, potentially halting the progression to advanced fibrosis and cirrhosis.

keywords: MASLD, Type 2 Diabetes, Inflammatory Markers,

PBi-154

A Descriptive Study of Brain Tumor Patterns in a Medical Center in Zahedan

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Background and aim: We wanted to see what the brain tumor cases looked like at Khatam Al-Anbia Hospital in Zahedan—specifically, how many were benign versus malignant, which types showed up the most, and whether age or gender played a role. The hope is that this sort of local data can help spot high-risk groups and maybe improve how we diagnose and treat these tumors.

Methods: This was a simple descriptive cross-sectional study. We looked at brain tumor samples from our hospital over 40 weeks and analyzed the data using SPSS version 16.

Results: In that period, we had 25 cases. Most of them—64%—were benign. The most common benign type was Pilar cysts (16%), followed by Epidermoid cysts (9%). We also saw a handful of others: Dermoid cysts (4%), Colloid cysts (4%), Glial tumors (4%), Granuloma (4%), and one case of Lipomyelomeningocele (4%). On the malignant side, they made up 36% of the total. Carcinoma and Oligodendroglioma were tied at 12% each. Then there was Astrocytoma (4%), Medulloblastoma (4%), and Meningioglioma (4%). The average age of patients was 33 years. What really stood out was the gender split: only 24% were male, while 76% were female.

Conclusion: So in our study, benign tumors were definitely more common than malignant ones, with Pilar cysts leading the pack. Among the malignant ones, Carcinoma and Oligodendroglioma were equally frequent. The female predominance was pretty striking. And with a mean age of 33, it's a reminder not to rule out brain tumors just because the patient is young. Overall, this gives us a decent snapshot of what brain tumors look like in this particular population.

keywords: Brain Tumor, Benign, Malignant

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-155

Protective Role of Salix alba Extract Against Endothelial Injury and Early Atherogenic Changes in Experimental Hypercholesterolemia

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Background and aim: Atherosclerosis is a progressive inflammatory disease of the arterial wall characterized by lipid accumulation and endothelial impairment. Reduced endothelial nitric oxide synthase (eNOS) activity, diminished nitric oxide (NO) availability, and increased expression of adhesion molecules including vascular cell adhesion molecule-1 (VCAM-1) contribute to vascular inflammation and atherogenesis. Salix alba (white willow), a medicinal plant containing salicin and abundant phenolic constituents, possesses antioxidant and anti-inflammatory activities and may exert favorable effects on lipid metabolism. The present study investigated the influence of S. alba extract on endothelial function and molecular mediators involved in atherosclerotic development in rabbits with diet-induced hypercholesterolemia.

Methods: Twenty-five male New Zealand rabbits were randomly divided into five groups (n = 5): a control group receiving standard chow, a high-cholesterol diet (HCD) group (0.5% cholesterol), two HCD groups treated with S. alba extract at doses of 60 and 120 mg/kg/day, and an HCD group receiving aspirin (120 mg/kg/day). Oral treatments continued for eight weeks. Serum lipid profile and atherogenic index of plasma (AIP) were measured. In addition, aortic tissue samples were assessed for nitrite concentration as an indicator of NO bioavailability, and the mRNA expression levels of eNOS, VCAM-1, AMP-activated protein kinase-α1 (AMPK-α1), sterol regulatory element-binding protein-1c (SREBP-1c), and lectin-like oxidized LDL receptor-1 (LOX-1) were quantified using real-time PCR.

Results: Feeding rabbits with an HCD resulted in marked dyslipidemia, elevation of AIP, suppression of aortic nitrite content and eNOS expression, and increased VCAM-1 expression. These alterations were associated with reduced AMPK-α1 expression and enhanced expression of SREBP-1c and LOX-1. Administration of S. alba extract significantly improved serum lipid abnormalities, enhanced NO bioavailability and eNOS expression, and attenuated VCAM-1 expression compared with untreated HCD animals. The higher dose (120 mg/kg/day) produced more pronounced protective effects, showing efficacy comparable to that observed with aspirin treatment.

Conclusion: The findings indicate that Salix alba extract mitigates endothelial dysfunction induced by hypercholesterolemia through modulation of lipid metabolism, suppression of vascular inflammatory responses, and restoration of the eNOS/NO pathway. These results suggest that S. alba may serve as a promising adjunctive strategy for preventing or slowing atherosclerotic progression.

keywords: Salix alba L., Atherosclerosis, Endothelial dysfunction, Lipid metabolism

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-156

Cell-Free Therapeutic Potential of Whartons Jelly MSC-Derived Secretome for Mitigating Oxidative Stress-Induced Damage in Bovine Sperm

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Background and aim: Oxidative stress (OS) is a major cause of sperm damage during cryopreservation, impairing sperm function and reducing fertility potential. The secretome derived from Wharton's jelly mesenchymal stem cells (WJ-MSCs) contain a diverse repertoire of bioactive molecules with antioxidants and cytoprotective properties. This study investigated the potential of WJ-MSC-derived secretome to protect bovine sperm against oxidative stress-induced damage.

Methods: Bovine semen samples were randomly assigned to three experimental groups: control, DMEM-treated, and WJ-MSC-secretome-treated. Oxidative stress was induced using hydrogen peroxide (H_2O_2). Human WJ-MSCs were isolated from umbilical cord Wharton's jelly, and the secretome was harvested from the conditioned medium of passage-3 cultures. Following treatment, sperm samples were incubated at 38.5°C for 10 h. Total motility, progressive motility, viability, plasma membrane integrity, and acrosome integrity were evaluated.

Results: Under oxidative stress conditions, treatment with WJ-MSC-derived secretome significantly improved total motility (P 0.0001 vs. control and DMEM), progressive motility (P = 0.0027 vs. control; P = 0.0213 vs. DMEM), viability (P 0.0001 vs. control and DMEM), plasma membrane integrity (P 0.0001 vs. control and DMEM), and acrosome integrity (P = 0.0002 vs. control; P 0.0001 vs. DMEM) compared with the control and DMEM-treated groups.

Conclusion: WJ-MSC-derived secretome effectively attenuated oxidative stress-induced damage and preserved key functional parameters of bovine sperm. These findings demonstrate the promising potential of WJ-MSC-derived secretome as a novel cell-free therapeutic approach for sperm preservation and future applications in reproductive biotechnology and male infertility management.

keywords: Bovine sperm; Wharton's jelly mesenchymal stem cells; Secretome; Oxidative stress;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-157

Advances in Molecular Diagnostics for Early Cancer Detection: A Systematic Review of Clinical Biochemistry Markers

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Background and aim: Early detection of malignancy is critical for improving patient survival rates. Recent advancements in clinical biochemistry and molecular biology have facilitated the identification of novel biomarkers with high sensitivity and specificity. This systematic review evaluates the current clinical utility of circulating molecular markers for the early diagnosis of high-prevalence carcinomas.

Methods: A comprehensive search was conducted across PubMed, Scopus, and Embase databases for studies published between 2018 and 2026. Systematic reviews and clinical validation studies focusing on non-invasive molecular markers—including circulating tumor DNA (ctDNA), microRNAs, and exosomal proteins—were selected based on PRISMA guidelines. Inclusion criteria required studies to report diagnostic accuracy metrics, specifically sensitivity, specificity, and Area Under the Receiver Operating Characteristic (AUROC) curves. Data synthesis focused on comparing the diagnostic efficacy of these novel markers against traditional protein-based clinical biochemistry assays (e.g., PSA, CEA). Quality assessment was performed using the QUADAS-2 tool to evaluate risk of bias in the included trials.

Results: Out of 680 screened records, 22 studies met the criteria for inclusion. Analysis revealed that multi-marker panels combining ctDNA mutation analysis with protein biomarkers significantly outperformed single-marker assays, showing an average sensitivity of 88% compared to 65% for traditional markers. Exosomal microRNA profiling demonstrated high tissue-specificity, particularly in pancreatic and colorectal cancer detection, with AUROC values consistently exceeding 0.90. However, substantial heterogeneity was observed in standardized pre-analytical processing and assay cutoff values across clinical settings. Furthermore, the integration of liquid biopsy techniques into routine clinical biochemistry workflows was found to reduce diagnostic delay by an average of 4.2 weeks compared to conventional imaging and biopsy-based protocols.

Conclusion: Molecular diagnostics represent a robust evolution in clinical biochemistry. Integrating multi-omic liquid biopsy panels improves diagnostic precision over conventional markers. Future efforts must prioritize standardization of analytical protocols and large-scale validation to ensure clinical reproducibility.

keywords: Cancer, Circulating Tumor DNA (ctDNA), Liquid biopsy, Biomarkers

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-158

Molecular Mechanisms of Chemoresistance in Solid Tumors: A Systematic Review

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Background and aim: Cancer remains a leading cause of mortality worldwide, largely due to the development of resistance to therapeutic interventions. Understanding the biochemical and molecular alterations driving chemoresistance is essential for effective treatment strategies. This systematic review consolidates current knowledge on the key molecular mechanisms underlying resistance to common chemotherapeutic agents in solid tumors.

Methods: This systematic review was conducted following PRISMA guidelines. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, and Google Scholar using keywords including "cancer biochemistry," "chemoresistance mechanisms," "drug resistance," "solid tumors," "molecular targets," and "signaling pathways." Peer-reviewed original research articles and systematic reviews published in the last decade focusing on the molecular basis of chemoresistance in major solid tumors (e.g., breast, lung, colorectal cancer) were included. Studies investigating cellular, genetic, and epigenetic factors contributing to resistance were prioritized. Data extraction focused on identified resistance mechanisms, involved pathways, and potential therapeutic targets.

Results: The search yielded 520 articles, of which 25 were deemed eligible for inclusion based on predefined criteria. Key findings highlighted the critical role of altered cellular metabolism (e.g., enhanced glycolysis, altered nucleotide synthesis) in conferring resistance. Aberrant signaling pathways, including PI3K/Akt, Wnt/β-catenin, and NF-κB, were frequently implicated in promoting cell survival and inhibiting apoptosis upon drug exposure. Furthermore, the review identified the significance of drug efflux pumps (e.g., P-glycoprotein), DNA repair mechanisms, and the tumor microenvironment (e.g., hypoxia, stromal cells) in mediating resistance. Epigenetic modifications, such as DNA methylation and histone alterations, were also shown to play a crucial role in silencing drug-sensitive genes or activating resistance pathways.

Conclusion: Chemoresistance in solid tumors is a multifactorial process driven by complex biochemical and molecular alterations. Targeting these key mechanisms, including metabolic reprogramming, dysregulated signaling pathways, and epigenetic modifications, offers promising avenues for overcoming therapeutic resistance. Future research should focus on combination therapies and the development of novel agents that specifically target these resistance pathways to improve patient outcomes.

keywords: Cancer, Drug resistance, Chemoresistance, Solid tumors, Signaling pathway

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-159

Biomimetic Exosomal Drug Delivery Systems for Facilitating Blood-Brain Barrier Penetration in Glioblastoma Therapy: A Systematic Review (2016–2026)

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Background and aim: Glioblastoma (GBM) remains the most lethal central nervous system malignancy, characterized by a dismal prognosis due to the restrictive blood-brain barrier (BBB) and multidrug resistance (MDR) phenotypes. Classical synthetic nanocarriers often lack biological identity, leading to rapid clearance by the hepatic reticuloendothelial system (RES). Engineered exosomes, as endogenous biomimetic membrane vesicles, offer a novel targeted drug delivery paradigm due to their superior biocompatibility and active transcytosis potential. This systematic review comprehensively analyzes the structural efficacy of exosomal platforms in enhancing BBB permeability and suppressing human GBM models.

Methods: Following the PRISMA guidelines, a comprehensive search was conducted across PubMed, Scopus, and Web of Science using a combined MeSH/TiAb syntax for ("exosomes" OR "biomimetic vesicles") AND "blood-brain barrier" AND ("glioblastoma" OR "glioma") AND "drug delivery" conducted from January 2016 up to June 2026. Inclusion criteria targeted peer-reviewed, original experimental research evaluating human glioma cell lines (e.g., U87MG, U251) and human patient-derived xenograft (PDX) models. Studies solely utilizing non-human cell lines, review articles, and bibliometric analyses were excluded. Study selection and data extraction were performed independently by two investigators. Methodological quality and risk of bias were rigorously appraised using the Joanna Briggs Institute (JBI) tool. Ultimately, 17 high-quality experimental articles were selected from 69 retrieved studies for final qualitative synthesis.

Results: Systematic analysis of the 17 included studies demonstrated that membrane modification of human mesenchymal stem cell (hMSC) and NK cell-derived exosomes with peptide ligands (Angiopep-2, iRGD, folic acid, and RGE peptide) significantly enhanced active BBB transcytosis via LRP-1 and NRP-1 receptors. This biomimetic approach mediated a 65% evasion rate against hepatic RES macrophages, preserving enzymatic homeostasis (ALT/AST). Evidence validated three primary homing platforms: first, theranostic multi-functional systems encapsulating Superparamagnetic Iron Oxide Nanoparticles (SPIONs) and NIR-II optical agents for high-resolution photoacoustic imaging and synergistic photothermal therapy; second, co-delivery of apoptotic agents (Temozolomide (TMZ), doxorubicin) with VEGF-inhibiting anti-angiogenic factors; and third, siRNA delivery targeting collagen matrices to induce methuosis/ferroptosis in TMZ-resistant cells. Microfluidic formulation achieved a 32% drug-loading efficiency, yielding robust in vivo tumor suppression in humanized models without systemic toxicity.

Conclusion: Engineered biomimetic exosomes facilitate non-invasive drug transport across the BBB and enable multimodal combinatorial therapeutics against human glioblastoma models. This modified platform represents an efficient strategy to overcome chemoresistance and accelerate personalized medicine translation in glioblastoma management.

keywords: Exosomes, Blood-Brain Barrier, Glioblastoma, Biomimetic Drug Delivery, Targeted Therapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-160

Polarity-Guided Fabrication of Starch Nanoparticles for Biomedical Applications: Influence of Encapsulated Compound Hydrophilicity and Hydrophobicity on Encapsulation Performance

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Background and aim: Starch nanoparticles (SNPs) have emerged as promising biodegradable and biocompatible carriers for drug delivery and other biomedical applications. The physicochemical properties of encapsulated compounds, particularly their hydrophilicity and hydrophobicity, play a critical role in determining nanoparticle fabrication efficiency, stability, and release behavior. This review aimed to systematically evaluate major SNP fabrication strategies and examine how compound polarity influences method selection, particle characteristics, encapsulation efficiency, and biomedical performance. The study further sought to provide a practical framework for selecting appropriate fabrication approaches for diverse therapeutic agents.

Methods: A comprehensive literature review was conducted using PubMed, Scopus, and Web of Science databases to identify studies published between 2010 and 2025. Thirty-four relevant studies investigating starch nanoparticle fabrication and drug encapsulation were included. Fabrication techniques were classified into bottom-up approaches (nanoprecipitation, emulsion/microemulsion, emulsion cross-linking, dialysis, and sacrificial template methods) and top-down approaches (ball milling and ultrasonication). Data regarding particle size, morphology, encapsulation efficiency, loading characteristics, release profiles, starch modifications, and biomedical applications were extracted and comparatively analyzed. Particular attention was given to the relationship between fabrication strategy and the hydrophilic, hydrophobic, or amphipathic nature of the encapsulated compounds.

Results: The reviewed studies demonstrated that compound polarity strongly influences nanoparticle formation and encapsulation outcomes. Bottom-up methods produced particles ranging from approximately 30 to 870 nm with encapsulation efficiencies between 20.5% and 97.56%, offering precise control over morphology and drug loading. Hydrophilic compounds generally exhibited superior performance in aqueous-based systems, including emulsion cross-linking and sacrificial template approaches. Hydrophobic compounds achieved higher encapsulation efficiencies in nanoprecipitation, dialysis, and emulsion systems containing organic phases or chemically modified starches. Amphipathic compounds displayed variable encapsulation behavior and required optimization of solvent composition and processing parameters. Across biomedical applications, SNPs enhanced drug solubility, stability, controlled release, and therapeutic performance, particularly in cancer treatment and infectious disease management.

Conclusion: The hydrophilic or hydrophobic nature of encapsulated compounds is a key determinant in selecting suitable starch nanoparticle fabrication methods. Tailoring fabrication strategies to compound polarity can significantly improve nanoparticle characteristics, encapsulation efficiency, and drug release behavior. Chemical modification of starch further expands formulation versatility and enhances compatibility with diverse therapeutic agents. These findings provide a rational basis for designing SNP-based delivery systems and support their continued development for advanced biomedical and pharmaceutical applications.

keywords: Starch Nanoparticles, Drug Delivery, Encapsulation Efficiency, Hydrophilic Compounds, Hydrophobic Compounds

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-161

The Role of Lactate in Microenvironmental Remodeling in Breast Cancer: Biochemical Mechanisms and Clinical Implications

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Background and aim: Breast cancer (BC) is the most common cancer in women worldwide and has shown an increasing incidence rate in many countries. Breast cancer subtypes respond differently to conventional treatment. Hence, attention to epigenetic changes for novel therapeutic strategies and personalized therapy has increased. Lactate accumulation from aerobic metabolism (the Warburg effect) is important in cancer; therefore, research into lactate metabolism and lactylation has become a growing area of interest.

Methods: This review was conducted using available research articles from prior years (2020 – 2025), focusing on the keywords breast cancer, lactylation, and microenvironment remodeling. Also sourced from PubMed and other similar databases for compiled resources.

Results: Studies have shown that metabolic reprogramming in breast cancer produces large amounts of lactate. Lactate, the end product of glycolysis, is closely related to lactylation in the tumor microenvironment (TME). Lactate accumulation in the TME enhances tumor progression by activating oncogenic signaling pathways, such as HIF-1α, acidifying the TME, inhibiting immune cell activity, helping tumor cells escape immune recognition, and promoting invasion and metastasis. It also interacts with amino acid and fatty acid pathways, promotes angiogenesis, and modulates immune functions.

Conclusion: Previous studies have shown that lactate and lactylation are key mediators linking metabolic reprogramming with epigenetic regulation in breast cancer. Targeting lactate metabolism or lactylation pathways could represent new treatment opportunities and have the potential to optimize precision medicine strategies for improving outcomes for breast cancer patients' survival. For this reason, Future studies are essential to convert the results into specific and personalized therapeutic strategies for breast cancer management.

keywords: breast neoplasms; lactic acid; tumor microenvironment; biochemical phenomena

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-162

MicroRNAs as diagnostic biomarkers in diabetes male infertility

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Background and aim: This study conducts an in-depth review of the correlation between testis tissue changes and circulating microRNAs (miRNA) in diabetes-induced male reproductive complications, drawing upon both animal and clinical studies. The original articles published in English that specifically investigate miRNAs linked to male infertility in humans or animals with either type I or II diabetes mellitus were included.

Methods: The relevant articles were gathered from the PubMed, Google Scholar, Cochrane Library, and ScienceDirect databases. The quality of study was assessed utilizing the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Prevalence Studies. We collected an overall number of 1989 citations relating to our research subject. Following the elimination of articles based on the criteria, a total of 20 papers were included in the study.

Results: Aberrant expression profiles of 25 miRNAs were identified in diabetes associated with male reproductive issues, with 15 miRNAs exhibiting increased expression and 10 miRNAs showing decreased expression. Among the chosen publications, eighteen were identified as low-risk and two were classed as moderate quality. The dysregulated miRNAs were linked to testicular injury, disrupted steroid production, decreased sperm development and quality, and erectile dysfunction. The results demonstrate that the miRNA–mRNA network is linked to the pathological progression of diabetic testicular damage or erectile dysfunction. From a therapeutic perspective, the identification of circulating miRNAs could be beneficial in the timely identification and prevention of diabetes problems, such as diabetes-induced male infertility. Among all signaling pathways influenced by modified miRNAs, the Bax-caspase-3, MAPK, PI3K-Akt, and eNOS-cGMP-PKC were the main deregulated pathways.

Conclusion: This review highlights 25 dysregulated miRNAs in the tes tes or serum of individuals with diabetes who experience reproductive difficulties. This systematic study stands out for its exhaustive review of dysregulated miRNAs in the blood and testes of those with diabetes, encompassing both animal and clinical investigations. This is the first time such a comprehensive report has been compiled. The results demonstrate that the miRNA–mRNA network is linked to the pathological progression of diabetic testicular damage or erectile dysfunction. From a therapeutic perspective, the identification of circulating miRNAs could be

keywords: MicroRNAs · Diabetes · Erectile dysfunction · Spermatogenesis · Steroidogenesis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-163

Acute Cholestatic Jaundice with Fever in an 18-Year-Old Male: A Case Report

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Background and aim: Acute jaundice accompanied by fever and elevated liver enzymes in young adults requires prompt evaluation for infectious, obstructive, and drug-related causes. Differentiating between viral hepatitis, cholestatic disease, and medication-associated liver injury is essential for timely management and prevention of complications. Acyclovir is generally considered low-risk for clinically apparent liver injury, but liver test abnormalities may occur during herpesvirus infections or after treatment.

Methods: An 18-year-old male with no previous medical history presented to Shahid Beheshti Hospital, Hamadan, Iran, with a 1-week history of fever, weakness, lethargy, and jaundice. The patient had visited the hospital twice during this period, and intravenous acyclovir was administered during the second visit. His symptoms progressively worsened over the following week. Comprehensive laboratory evaluation included complete blood count, liver function tests (AST, ALT, ALP, bilirubin fractions), renal function tests, electrolytes, viral serology, and urinalysis. Physical examination assessed for jaundice, hepatomegaly, and signs of systemic infection.

Results: Laboratory findings on admission revealed: WBC 5400/mm³, RBC 5.43 million/mm³, Hb 17.1 g/dL, Hct 51.4%, platelets 131,000/mm³, ESR 12 mm/h, blood sugar 89 mg/dL, urea 17 mg/dL, creatinine 1 mg/dL, AST 208 U/L, ALT 155 U/L, ALP 448 U/L, total bilirubin 15.3 mg/dL, direct bilirubin 7.8 mg/dL, sodium 137 mEq/L, potassium 4.4 mEq/L, calcium 8.55 mg/dL, and amylase 50 U/L. Leukocyte differential showed polymorphonuclear cells 50%, lymphocytes 33%, monocytes 6%, eosinophils 2%. Urinalysis was positive for bilirubin and trace blood. Viral tests were negative. The patient also had constipation.

Conclusion: This case demonstrates acute jaundice with mixed hepatocellular-cholestatic laboratory abnormalities in a young patient. The marked hyperbilirubinemia with elevated ALP and transaminases supports a cholestatic hepatobiliary process. The differential diagnosis should include viral hepatitis, obstructive causes, and possible drug-related liver injury. Careful clinical correlation and further diagnostic workup, including imaging and serial liver function testing, are necessary before attributing the condition to medication-related injury.

keywords: Jaundice, Cholestasis, ALP, Hyperbilirubinemia, Case Report

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-164

Severe Hyperandrogenism with Markedly Elevated LH/FSH Ratio (24.5) in a 25-Year-Al Woman with PCOS: A Case Report Correlating Laboratory Findings with Clinical Presentation

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Background and aim: Polycystic ovarian syndrome (PCOS) is the most prevalent endocrine disorder in women of reproductive age (5–10%), characterized by hyperandrogenism, ovulatory dysfunction, and metabolic abnormalities. The pathophysiology involves excessive androgen production by ovaries and/or adrenal cortex, disrupting follicular maturation. In obese patients, adipose tissue Converts androgens to estrogen, leading to increased LH via positive estrogen feedback on the pituitary and decreased FSH via negative feedback. Low FSH prevents normal follicular maturation, resulting in amenorrhea. Hormonal profiling is critical for PCOS diagnosis and differentiation from other hyperandrogenic disorders (e.g., androgen-secreting tumors, congenital adrenal hyperplasia).

Methods: This is a single-case descriptive report of a 25-year-old woman who presented at the Endocrinology Clinic of Shahid Beheshti Hospital, Hamadan, Iran, with progressive facial hirsutism, acne, oily skin, and secondary amenorrhea. Clinical examination included physical assessment (hirsutism, acne, blood pressure, pulse). Laboratory evaluation measured serum hormone levels: FSH, LH, oestradiol, and testosterone using immunoassay techniques. Diagnosis was based on Rotterdam criteria: (1) ovulatory dysfunction, (2) clinical/biochemical hyperandrogenism, and (3) elevated LH/FSH ratio. Management plan included weight loss, metformin, and anti-androgen therapy.

Results: Clinical findings: Facial hirsutism (progressive over 1.5 years), acne, oily skin, secondary amenorrhea (last period 4 months ago), irregular cycles, overweight. Blood pressure: 13/8 mmHg, pulse: 76/min. No significant medical history. Laboratory findings: Parameter Patient Value Normal Range Interpretation FSH 1.1 U/L 2–8 U/L 0.5× (low) LH 27 U/L 6–13 U/L 2.1× (high) LH/FSH ratio 24.5 2–3 8× (markedly elevated) Oestradiol 194 nmol/24h 10–55 nmol/L 3.5× (high) Testosterone 8.1 nmol/L 1–2.1 nmol/L ~4× (severe hyperandrogenism) Diagnosis: PCOS confirmed by ovulatory dysfunction (amenorrhea), clinical hyperandrogenism (hirsutism, acne), biochemical hyperandrogenism (testosterone 4× normal), and elevated LH/FSH ratio (24.5).

Conclusion: This case demonstrates classic PCOS with severe biochemical hyperandrogenism. Laboratory findings (LH/FSH = 24.5, testosterone 4× normal) correlate perfectly with clinical symptoms (hirsutism, amenorrhea, acne). The markedly elevated LH/FSH ratio is diagnostic for PCOS and distinguishes it from other hyperandrogenic disorders. Management should include: (1) weight loss (5–10%) to improve ovulation and reduce androgens, (2) metfor min for insulin resistance and cycle regulation, (3) anti-androgen therapy (cyproterone acetate) for hirsutism and acne, and (4) long-term monitoring for diabetes, hypertension, and ovarian cancer risk. Early diagnosis through hormonal profiling is essential

keywords: PCOS, hyperandrogenism, hirsutism, secondary amenorrhea, LH/FSH ratio, testosterone, clinical biochemistry,

PBi-165

Circular RNAs as emerging biomarkers in rheumatoid arthritis: implications for diagnosis and and clinical management

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Background and aim: Noncoding RNAs (ncRNAs), including lncRNAs, miRNAs, and circRNAs, are key regulators of gene expression with growing clinical importance. CircRNAs are stable, covalently closed RNA molecules with tissue-specific expression that function in miRNA sponging and transcriptional regulation. Increasing evidence links circRNA dysregulation to various diseases, especially autoimmune disorders. In rheumatoid arthritis (RA), altered circRNA expression is associated with disease onset and progression. Due to their stability and detectability in biological fluids, circRNAs are emerging as promising biomarkers for early diagnosis, disease monitoring, and potential personalized therapeutic approaches in RA.

Methods: In this study, the MEDLINE®/PubMed and Scopus databases were searched for relevant publications. Keywords such as "rheumatoid arthritis", "circular RNAs", "biomarker", and "clinical application" were used, along with advanced Boolean search strategies to optimize sensitivity and specificity of the search. This work was conducted as a narrative review aimed at critically synthesizing and integrating current evidence regarding the role of circRNAs in RA pathophysiology and their emerging clinical applications.

Results: High-throughput profiling and qRT-PCR analyses in RA have consistently demonstrated a broad dysregulation of circRNAs across peripheral blood mononuclear cells, plasma, and fibroblast-like synoviocytes, highlighting their strong translational relevance. Several circRNAs, including circRNA_104871, circRNA_003524, and circRNA_103047, are significantly upregulated, while others such as circ_0005732 and circ_0072428 are downregulated, forming a distinct disease-associated expression signature. Clinically, plasma circRNAs such as circ_0005008 and circ_0005198 show high diagnostic performance and correlate with established disease activity indices (DAS28, ESR, CRP, RF), supporting their value as both diagnostic and severity-linked biomarkers. Functionally, circRNA-miRNA regulatory axes modulate key pathogenic processes in RA, including synovial inflammation, angiogenesis, and fibroblast-like synoviocyte proliferation, migration, invasion, and apoptosis

Conclusion: CircRNAs represent not only reproducible molecular biomarkers with high clinical diagnostic accuracy but also mechanistically active regulators of RA pathophysiology, underscoring their potential for future biomarker-guided stratification and targeted therapeutic development. However, considerable challenges persist in this field, which could hinder the translation of novel circRNA functions into clinical practice.

keywords: Rheumatoid arthritis, Circular RNAs, autoimmune disorders, biomarker

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PBi-166

Patient-Based Real-Time Quality Control (PBRTQC) in the Era of Artificial Intelligence: A Narrative Review

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Background and aim: Patient-Based Real-Time Quality Control (PBRTQC) is an emerging laboratory quality management approach designed to overcome limitations of conventional internal quality control (iQC). It uses real patient data to enable continuous monitoring of analytical performance and early detection of laboratory errors. Advances in statistical algorithms, artificial intelligence (AI), and machine learning (ML) have expanded its capabilities. This study aimed to review PBRTQC applications, benefits, challenges, and the role of AI and ML in its development.

Methods: This narrative review included studies published between 2019 and 2026. A PubMed search was performed using relevant keywords. A total of 71 articles were identified and managed in EndNote. After screening titles, abstracts, and full texts, 21 studies were selected based on relevance. Data were extracted and analyzed descriptively regarding PBRTQC concepts, algorithms, applications, and AI integration.

Results: The reviewed studies indicated that PBRTQC can detect analytical errors, particularly small and gradual systematic shifts, earlier than conventional quality control methods. Algorithms such as Moving Average (MA), Exponentially Weighted Moving Average (EWMA), and MovSum demonstrated effective performance in continuous quality monitoring. Findings showed a reduction in the number of patient results affected by analytical errors, faster detection of analytical instability, and decreased reliance on commercial control materials. Recent evidence suggested that artificial intelligence and machine learning–based models improve error detection sensitivity, reduce false-positive alerts, and enhance the management of complex and high-volume patient data. These findings highlight the potential of AI-supported PBRTQC systems for more efficient laboratory quality management. However, challenges remain, including the need for high-quality data, appropriate laboratory infrastructure, laboratory-specific validation, heterogeneity among studies, and limited evidence regarding AI-based applications.

Conclusion: PBRTQC is a novel and effective approach in laboratory quality management that enables real-time monitoring and earlier detection of analytical errors using patient data. Current evidence suggests that it can serve as a complementary tool to traditional internal quality control, improving analytical accuracy and patient safety. Moreover, integration of PBRTQC with artificial intelligence and machine learning offers promising potential for developing next-generation intelligent quality control systems in clinical laboratories. Further studies are required to support standardization and broader implementation.

keywords: Patient-based real-time quality control, Artificial intelligence, Quality management

PG-1

Efficacy and Safety of Personalized mRNA Neoantigen Vaccines in Glioblastoma Patients: A Systematic Review

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Background and aim: Glioblastoma (GBM) is the most aggressive primary brain tumor in adults, characterized by rapid progression, high intratumoral heterogeneity, and limited therapeutic response despite surgery, radiotherapy, and temozolomide. Personalized mRNA neoantigen vaccines have emerged as a novel precision-immunotherapy strategy designed to stimulate patient-specific T-cell responses against tumor-derived neoepitopes. Although early trials have reported promising immunogenicity, evidence regarding clinical benefit remains fragmented. This systematic review aimed to evaluate the efficacy, safety, and immune responses associated with personalized mRNA neoantigen vaccines in adult GBM patients.

Methods: A systematic search of PubMed, Embase, Scopus, Cochrane CENTRAL, ClinicalTrials.gov, and WHO ICTRP was conducted for studies published from 2022 onward. Two reviewers independently screened records, extracted data, and assessed methodological quality using RoB2 or ROBINS-I. Eligible studies included clinical trials and prospective interventional cohorts evaluating personalized mRNA neoantigen vaccines in histologically confirmed adult GBM. Outcomes included overall survival (OS), progression-free survival (PFS), treatment-related adverse events (TRAEs), and immunogenicity measures. Due to variation in study designs and outcome reporting, results were synthesized narratively.

Results: Five early-phase clinical studies met eligibility criteria, encompassing approximately 120 patients. Personalized mRNA neoantigen vaccines consistently induced robust CD4+ and CD8+ neoantigen-specific T-cell responses, with several studies reporting marked expansion of vaccine-responsive clonotypes. Median OS for newly diagnosed GBM ranged from 16 to 23 months, whereas recurrent cases showed OS between 9 and 13 months, suggesting a potential survival signal but limited by small sample sizes and lack of randomized controls. Safety profiles were favorable across all studies, with most adverse events mild to moderate and no treatment-related grade ≥3 toxicities consistently attributed to vaccination. Feasibility varied, with manufacturing turnaround influenced by sequencing depth, neoantigen selection pipelines, and clinical logistics.

Conclusion: Personalized mRNA neoantigen vaccines appear safe and strongly immunogenic in GBM patients, with early signals suggesting potential clinical benefit. However, current evidence remains insufficient to determine survival impact due to small, non-randomized studies. Larger, controlled trials integrating biomarker stratification and combination immunotherapies are needed to define the therapeutic value of this approach.

keywords: Glioblastoma, mRNA vaccine, neoantigen, personalized immunotherapy, immunogenicity

PG-2

A de novo ARID1B Variant Identified by Whole-Exome Sequencing in a girl with Neurodevelopmental Delay and Microcephaly

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Background and aim: ARID1B-related disorders are among the most common genetic causes of neurodevelopmental delay and intellectual disability. The ARID1B gene provides instructions for making a protein that forms a subunit of several different SWI/SNF protein complexes. SWI/SNF complexes regulate gene expression by a process known as chromatin remodelling. We present a case from a consanguineous family using whole-exome sequencing (WES) with enabled definitive diagnosis.

Methods: Due to the strong suspicion of a monogenic disorder and the background of consanguinity, whole-exome sequencing was conducted on the proband, followed by segregation analysis within the family.

Results: A 4-year-old girl, the second child of consanguineous parents, was referred suffered from global neurodevelopmental delay, microcephaly, and impaired speech. Family history revealed no relatives with intellectual disability. Physical and neurological examination confirmed significant developmental delay without dysmorphic features specific to a known syndrome. WES identified a heterozygote nonsense c.5653CT variant in the ARID1B gene, classified as pathogenic based on current ACMG criteria. This finding established the molecular diagnosis of ARID1B-related neurodevelopmental disorder. The result also suggested de novo occurrence or inherited heterozygous variant due to possible gonadal mosaicism in one parents.

Conclusion: This case emphasizes the diagnostic utility of WES in children with unexplained neurodevelopmental delay, particularly in consanguineous populations. Identification of a rare ARID1B mutation expands the known inheritance spectrum of ARID1B-associated disorders and provides essential information for genetic counselling and recurrence-risk assessment.

keywords: ARID1B, whole-exome sequencing, neurodevelopmental delay, microcephaly, consanguinity.

PG-3

Identification of a Novel ACADSB Variant for the Presymptomatic Diagnosis of 2-Methylbutyryl-CoA Dehydrogenase Deficiency through Newborn Screening in Iran

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Background and aim: 2-Methylbutyryl-CoA dehydrogenase deficiency (2-MBDD) is a rare autosomal recessive disorder of isoleucine catabolism. Early diagnosis via newborn screening is essential to prevent neurological sequelae. We report the first confirmed case of 2-MBDD in Iran.

Methods: A term male neonate born in 2022 was identified through the Iranian national newborn screening programme due to persistently elevated 2-methylbutyrylcarnitine (C5-carnitine) on dried blood spot tandem mass spectrometry. Confirmatory testing comprised plasma acylcarnitine profiling, urine organic acid analysis by gas chromatography-mass spectrometry, urine acylglycine analysis, and targeted Sanger sequencing of the ACADSB gene after informed consent. The variant was evaluated according to ACMG/AMP guidelines and in silico tools (PolyPhen-2, SIFT, MutationTaster, CADD). Management included carnitine supplementation (100 mg/kg/day) and regular clinical/biochemical monitoring.

Results: Diagnostic workup confirmed elevated C5-carnitine and 2-methylbutyrylglycine with a novel homozygous likely pathogenic ACADSB variant (c.907GC; p.Gly303Arg). The infant remained asymptomatic. After treatment initiation, C5-carnitine normalised to the intermediate range (0.4 µmol/L), with normal growth and neurodevelopment at follow-up.

Conclusion: This first Iranian case of 2-MBDD demonstrates the critical value of expanded newborn screening for presymptomatic diagnosis and effective management of rare metabolic disorders, preventing clinical manifestations and supporting the need for broader screening implementation and population-specific genetic research.

keywords: 2-Methylbutyryl-CoA dehydrogenase deficiency; ACADSB gene; Novel

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-4

Circulating microRNA-21 as an Early Diagnostic Biomarker in Colorectal Cancer

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Background and aim: Background: Colorectal cancer (CRC) is one of the leading causes of cancer-related mortality worldwide, and early detection significantly improves patient survival. Circulating microRNAs have emerged as promising non-invasive biomarkers for early cancer diagnosis. Among them, microRNA-21 (miR-21) is consistently overexpressed in various malignancies and detectable in serum and plasma, making it a strong candidate for early CRC screening. Aim: The aim of this study is to evaluate circulating microRNA-21 (miR-21) as a minimally invasive biomarker for the early detection of colorectal cancer.

Methods: Methods: This study is a narrative-based analytical investigation of published molecular studies evaluating serum and plasma levels of miR-21 in early-stage colorectal cancer. Data from peer-reviewed articles indexed in PubMed, Scopus and Web of Science were examined. Extracted variables included sample source, assay method, fold-change in miR-21 expression, and reported diagnostic sensitivity and specificity across studies.

Results: Result: Most reviewed studies reported a significant upregulation of circulating miR-21 in early-stage CRC patients compared with healthy individuals, with fold-change values typically ranging between 2- to 8-fold. The diagnostic sensitivity of miR-21 in early detection ranged between 70%–88%, and specificity ranged between 65%–82% depending on the assay type (qRT-PCR being the most commonly used). Studies utilizing combined biomarker panels (miR-21 + CEA or miR-21 + other miRNAs) demonstrated improved diagnostic performance.

Conclusion: Conclusion: Circulating miR-21 is a strong, minimally invasive, and reproducible biomarker for early CRC detection. Its elevated expression in early-stage patients and measurable stability in blood samples support its clinical utility. Further multi-center studies and standardized assay protocols are recommended to validate its integration into routine CRC screening programs.

keywords: Keywords(MeSH): microRNAs; Biomarkers; Colorectal Neoplasms; Early Detection of Cancer; Blood

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-5

Glycogen Storage Disease Type IXa in a 6-Year-Old Boy: A Case Report

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Background and aim: Background: Glycogen storage disease type IXa (GSD9A1) and type IXa2 (GSD9A2) are caused by a mutation in the PHKA2 gene on chromosome Xp22. This gene encodes the alpha-2 subunit of hepatic phosphorylase kinase.

Methods: Methods: Whole-exome sequencing was conducted to comprehensively analyze the protein-coding regions of the genome, allowing us to identify potential genetic variants associated with the condition in question. Following this, Sanger sequencing was performed to validate the findings and ensure accuracy in the detected variants, providing a robust confirmation of the results obtained from the initial whole-exome analysis. Whole-exome sequencing was conducted to comprehensively analyze the protein-coding regions of the genome, allowing us to identify potential genetic variants associated with the condition in question. Following this, Sanger sequencing was performed to validate the findings and ensure accuracy in the detected variants, providing a robust confirmation of the results obtained from the initial whole-exome analysis.

Results: Result: Upon conducting genetic testing, a rare missense variant in the PHKA2 gene was identified (p.Arg916Trp), which is believed to impair the normal function of the phosphorylase kinase enzyme. Further investigation through functional Sanger sequencing confirmed that both the mother and the child carry this pathogenic variant, indicating an inherited form of the disorder. The identified mutation was associated with a notable decrease in hepatic phosphorylase kinase activity, underscoring its pathogenic role. Following the initiation of treatment with raw cornstarch, an important source of glucose, the patient experienced a marked improvement in symptoms. Hypoglycemic episodes were significantly reduced, lactic acidosis was ameliorated, and liver function tests indicated a decrease in serum aminotransferases, reflecting improved liver function.

Conclusion: Conclusion: These findings not only expand the known spectrum of genetic mutations associated with glycogen storage disease type IX but also contribute valuable insights into the clinical presentations and underlying mechanisms of these two novel PHKA2 mutations. This case emphasizes the importance of genetic evaluation and early therapeutic intervention in managing glycogen storage diseases effectively.

keywords: Glycogen storage disease, PHKA2, Phosphorylase b kinase, Case report

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-6

Systematic Review and Synthesis: The Integrated WT1/MEG3/CA9 Signature as a Novel Framework in Colorectal Cancer Pathogenesis and Prognosis

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Background and aim: Current molecular classifications of colorectal cancer (CRC) often fail to fully capture disease heterogeneity and clinical outcome. Moving beyond the standard mutational axis, this systematic review investigates the collective role of three genes—WT1, MEG3, and CA9—which represent distinct but complementary oncogenic mechanisms.

Methods: A structured literature search was conducted in PubMed, Scopus, and Web of Science up to April 2025. Studies reporting on the expression, function, or clinical significance of WT1, MEG3, or CA9 in human CRC were included. Data were extracted and critically synthesized to evaluate their individual roles and collective potential.

Results: The synthesis confirms WT1's role as a context-dependent transcriptional regulator, MEG3's frequent epigenetic silencing via promoter hypermethylation with consequent loss of tumor-suppressive functions, and CA9's hypoxia-driven expression promoting invasion and chemoresistance. Critically, analysis of clinical data demonstrates that dysregulation of each marker is consistently associated with advanced tumor stage, metastasis, and inferior survival (e.g., hazard ratios 1.5 for poor outcomes). This review is the first to propose and systematically support the integrated WT1/MEG3/CA9 signature as a novel multi-dimensional biomarker panel.

Conclusion: The convergence of evidence from disparate biological domains (transcriptional, epigenetic, microenvironmental) suggests that the WT1/MEG3/CA9 signature offers a more holistic model for CRC subtyping and risk stratification than single-marker approaches. This systematic synthesis provides a foundational rationale for future translational studies. The immediate next step is the analytical validation of a unified assay and its testing in prospective cohorts to confirm clinical utility for personalized prognosis and therapy guidance in CRC.

keywords: Colorectal Cancer; Systematic Review; Biomarker Integration; WT1; MEG3; CA9

PG-7

Clinical and Neuroimaging Variability in Siblings With Succinic Semialdehyde Dehydrogenase Deficiency Due to a Homozygous ALDH5A1 Variant

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Background and aim: Succinic semialdehyde dehydrogenase deficiency (SSADHD) is a rare autosomal recessive neurometabolic disorder caused by pathogenic variants in the ALDH5A1 gene. The disease shows marked phenotypic heterogeneity, even among affected members of the same family. The study repports two sibs with different clinival features and same mutation.

Methods: Whole exome sequencing (WES) was performed for the proband, followed by Sanger sequencing for segregation analysis within the family.

Results: The proband is a 2-year-old girl presenting with global developmental delay. Brain magnetic resonance imaging (MRI) revealed abnormal distal signal intensity in the subcortical white matter of both frontal and parietal lobes. In addition, loss of signal void was observed in the left transverse sinus. Family history was significant for an affected sibling. Her 12-year-old brother had hypotonia at birth, neonatal jaundice, severe motor delay with sitting achieved at 1.5 years, absence of independent walking in early childhood, and eventual ability to walk later in life. He also exhibited dysmorphic features, including large ears. Brain MRI in the brother demonstrated cystic lesions and white matter volume loss. WES identified a pathogenic homozygous variant in the ALDH5A1 gene (NM_001080:c.637CT, p.Arg213Trp) in the proband. Sanger sequencing confirmed the same homozygous variant in the affected brother, while both parents were heterozygous carriers, consistent with autosomal recessive inheritance.

Conclusion: This report highlights intrafamilial phenotypic and neuroimaging variability associated with ALDH5A1-related SSADHD. Early application of WES enabled definitive diagnosis and genetic counseling. Recognition of variable clinical presentations is essential for timely diagnosis of SSADHD, particularly in families with affected siblings.

keywords: ALDH5A1, Succinic semialdehyde dehydrogenase deficiency, Developmental delay, White matter abnormalities,

PG-8

Identification of a Homozygous FBXL4 Missense Variant in Two Brothers With Severe Intellectual Disability by Whole Exome Sequencing

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Background and aim: Pathogenic variants in the FBXL4 gene are associated with mitochondrial DNA maintenance defects, typically presenting with early-onset neurodevelopmental impairment. Whole exome sequencing (WES) has become a key diagnostic tool in identifying the molecular basis of severe intellectual disability (ID), particularly in families with multiple affected children. The study revealed a pathogenic variant on FBXL4 gene using whole exome sequencing.

Methods: Whole exome sequencing was performed for the proband to investigate the underlying genetic etiology. Variant interpretation was conducted according to ACMG guidelines. Segregation analysis was subsequently performed.

Results: We report two affected brothers from the same family presenting with severe global developmental delay and intellectual disability. The proband is a 3-year-old boy, and his affected brother is 6 years old. Both children have never achieved independent walking or speech. No significant perinatal complications were reported. WES identified a homozygous missense variant in the FBXL4 gene, NM_012160.5:c.851CT, resulting in the amino acid substitution p.(Pro284Leu). The variant was classified as pathogenic/likely pathogenic. Segregation analysis confirmed the same homozygous variant in the affected brother, consistent with autosomal recessive inheritance.

Conclusion: This report expands the clinical spectrum associated with FBXL4-related neurodevelopmental disorders and underscores the utility of WES in diagnosing severe intellectual disability in families with multiple affected siblings. Early molecular diagnosis facilitates appropriate management and genetic counseling.

keywords: FBXL4, Intellectual disability, Mitochondrial disease, Whole exome sequencing, Autosomal recessive

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Tehran University of Medical Sciences (TUMS)
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PG-9

Integration of single-cell RNA sequencing with spatial transcriptomic analysis in high-grade serous ovarian cancer revealed new cross talk in tumor microenvironment

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Background and aim: High-Grade Serous Ovarian Carcinoma (HGSOC) is the fifth leading cause of gynecological cancer mortality, largely due to pervasive therapy resistance and aggressive metastasis. The tumor microenvironment (TME) plays a central role in this aggressive phenotype, yet the spatial orchestration of cellular crosstalk remains elusive. Emerging immunotherapies demand precise, druggable cell-surface targets. This bioinformatics-driven study sought to harness single-cell RNA sequencing (scRNA-seq) and spatial transcriptomics to meticulously map ligand-receptor (L-R) interactions in the HGSOC TME, with a focus on validating spatially conserved SPP1–CD44 and homophilic CD99–CD99 axes as potential immunotherapeutic targets to disrupt pro-tumorigenic crosstalk.

Methods: ScRNA-seq data from five treatment-naïve HGSOC tumors (GSE154600) were processed with Seurat v5.2.1 (R v4.4.2). Cluster-specific marker genes were identified and visualized with VlnPlot and FeaturePlot. Cell populations were annotated using integrated reference databases (CellMarker, Cell Taxonomy, and...). Intercellular communication was inferred using R package CellChat based on CellPhoneDB data base. Top-predicted L-R pairs underwent spatial validation by integrating independent Visium data (GSE211956; n=8 patients) from HGSOC tissue sections, employing deconvolution methods to assess co-expression, proximity, and niche-specific patterns.

Results: Unbiased clustering and marker-gene profiling resolved nine transcriptionally distinct cellular populations, dominated by malignant epithelial cells, cancer-associated fibroblasts (CAFs), tumor-associated macrophages (TAMs), T cells, and B/plasma cells. CellChat/CellPhoneDB analysis unveiled intricate communication networks across epithelial, immune, and stromal compartments, pinpointing SPP1-CD44 and the homophilic CD99-CD99 as dominant cell-markers and high-probability hubs. SPP1 (Osteopontin), as a protein secreted by malignant cells, engages CD44 on TAMs and CAFs to promote metastasis, stemness maintenance and therapy resistance. CD99-CD99 homodimers facilitate adhesion and migration in tumor-immune interfaces. Further analysis robustly confirmed these predictions, demonstrating significant co-localization of SPP1-expressing epithelial clusters with CD44+ myeloid/CAF cells in metastatic niches, alongside enriched CD99-CD99 interactions at invasive fronts, correlating with reduced $CD8^{+}$/NK-cell infiltration and increased CAF activation markers.

Conclusion: The spatial transcriptomic analysis confirmed of SPP1-CD44 paracrine signaling and CD99 homotypic adhesion and validated these pathways as fundamental components of HGSOC TME organization and aggressiveness. This integrated approach underscores the power of combining scRNA-seq with spatial technologies to pinpoint and verify high-priority therapeutic targets for precise oncology.

keywords: HGSOC, Single-cell Analysis, Cell-Cell Communication, Spatial Transcriptomics, SPP1-CD44, CD99

PG-10

Mapping the Spatial Architecture of Intercellular Communication in High-Grade Serous Ovarian Cancer Using Single-Cell and spatial Transcriptomics

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Background and aim: High-grade serous ovarian carcinoma (HGSOC), the deadliest gynecologic malignancy, harbors a heterogeneous and immunosuppressive tumor microenvironment (TME). Intercellular ligand–receptor(L–R) interactions drive tumor progression, immune suppression, and therapy resistance. Despite single-cell RNA sequencing (scRNA-seq) has advanced our understanding of cellular crosstalk, the spatial context of these signaling events remains underexplored. Herein, we integrated scRNA-seq alongside computational tools to delineate communication networks and infer statistically significant L-R pairs in HGSOC. Computationally prioritized interactions underwent spatial transcriptomics(ST) validation using high-resolution transcriptomics, revealing the MDK-NCL and APP-CD74 axes as key regulators of TME remodeling and pro-tumorigenic features, with implications for targeted interventions.

Methods: The scRNA-seq and visium spatial data from two cohorts of treatment-naïve HGSOC tumors (GSE211956: n = 8; GSE154600: n = 5) were processed using R package Seurat v5.2.1. Cell types were annotated using canonical markers, validated against CellMarker and the Human Cell Taxonomy databases. Intercellular signaling was inferred via CellPhoneDB, applying permutation-based statistics to identify significant L-R pairs, supplemented by R package CellChat for pathway enrichment and interaction scoring. High-priority axes (MDK-NCL and APP-CD74) were spatially mapped and validated through integration with GSE211956 dataset.

Results: Unbiased clustering identified nine transcriptionally distinct cell populations. The major compartments comprised malignant epithelial cells, cancer-associated fibroblasts (CAFs), tumor-associated macrophages (TAMs), T cells ($CD8^+$ and $CD4^+$) cells, and B/plasma cells. ScRNA-seq unveiled expansive L-R networks spanning malignant epithelial, myeloid, stromal, and... . MDK-NCL and APP-CD74 ranking among the highest-scoring interactions, exhibiting specificity in epithelial–myeloid and tumor–stroma dialogues. ST confirmed their enrichment in immunosuppressive niches, showing MDK-expressing cancer cells interacting with NCL+ macrophages to suppress CD8+ T-cell infiltration. Similarly, APP-CD74 predominated at invasive tumor-stromal interfaces and attenuated effector T-cell presence. ST confirmed the significant co-localization and co-expression of both MDK-NCL and APP-CD74 pairs within the HGSOC tissue architecture, supporting the in-silico predictions.

Conclusion: Integrated analysis identified MDK–NCL and APP–CD74 as pivotal, spatially restricted axes in HGSOC tumors. Both pathways emerge as promising targets for disrupting tumor–stroma and tumor–immune crosstalk. By leveraging computational strategies, our work advances precision oncology, offering new avenues for disrupting HGSOC progression and improving patient outcomes.

keywords: Single-cell RNA-seq, Spatial Transcriptomics, HGSOC, Tumor Microenvironment, Ligand-Receptor Interaction.

PG-11

Identification of a novel mutation in HEXA gene in a Tay-Sachs disease patient: A case report

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Background and aim: Background Tay-Sachs disease is an autosomal recessive disorder affecting the central nervous system caused by β-hexosaminidase. Tay-Sachs is a enzyme defect results from various mutations in α-subunit gene of this enzyme, resulting in GM2 ganglioside accumulation in lysosomes of nerve cells. This study aims to find Tay-Sachs pathogenic mutation in order to Whole Exome sequencing and Sanger confirmation.

Methods: The patient is a 2-year-old child who presented to a physician following muscle weakness, lack of attentiveness, lack of mobility, and mental retardation. DNA was extracted from the patient's blood, for molecular analysis and sequencing. In the present study, we report a novel pathogenic mutation, NM_001318825.2 c.1019+1GC in one affected child of a consanguineous family, causing Tay-Sachs disease. Sanger sequencing confirmed homozygosity of mutation in the proband and heterozygosity of this mutation in her parents, proposing it as the likely disease-causing mutation.

Results: Since date, NM_001318825.2 c.1019+1GC pathogenic variant has not been detected worldwide. This mutation locates on intron 8 donor splice site of the HEXA gene, and due to its improper operation, will cause Tay-Sachs disease.

Conclusion: Since date, NM_001318825.2 c.1019+1GC pathogenic variant has not been detected worldwide. This mutation locates on intron 8 donor splice site of the HEXA gene, and due to its improper operation, will cause Tay-Sachs disease.

keywords: Keywords: Central nervous system, Gene mutation, Lysosome, Hexosaminidase

PG-12

Epigenetic Alterations in Cancer: From Therapeutic Targeting to Multi Omics Driven Precision Oncology

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Background and aim: Epigenetic alterations critically influence cancer development, molecular heterogeneity, and response to therapy through reversible regulation of gene expression. Growing evidence highlights the clinical relevance of epigenetic biomarkers and targeted epigenetic therapies in cancer diagnosis, prognosis, and treatment stratification. The aim of this review is to summarize recent advances in cancer epigenetics, with an emphasis on translational applications, epigenetic based therapeutic strategies, and the integration of multi omics data to bridge laboratory findings with clinical decision making in precision oncology.

Methods: A comprehensive narrative review was performed to assess recent advances in cancer epigenetics with laboratory and clinical relevance. Peer reviewed articles published between 2022 and 2025 were retrieved from PubMed, Web of Science, and Scopus using keywords related to cancer epigenetics, DNA methylation, histone modifications, epigenetic therapies, multi omics, and precision oncology. Eligible studies included original research articles, systematic reviews, and clinical or translational studies published in English. Articles were screened based on relevance to epigenetic mechanisms, biomarker discovery, therapeutic applications, and laboratory to clinic integration. Selected studies were critically evaluated and qualitatively synthesized to highlight emerging epigenetic targets, therapeutic strategies, and translational implications in precision cancer medicine.

Results: Analysis of the selected studies demonstrated that epigenetic alterations, including aberrant DNA methylation patterns, histone modifications, and chromatin remodeling, are consistently associated with cancer initiation, progression, and therapeutic resistance. Recent clinical and translational studies highlighted the efficacy of epigenetic based therapies such as DNMT, HDAC, BET, and EZH2 inhibitors, particularly when used in combination with conventional chemotherapy or immunotherapy. Multi omics integration revealed improved identification of epigenetic biomarkers for diagnosis, prognosis, and therapy response prediction. Additionally, emerging approaches such as PROTAC based degraders and epigenetic editing showed promising preclinical outcomes, supporting their potential clinical translation. Overall, the findings underscore the growing role of epigenetics in bridging molecular discovery with precision cancer treatment.

Conclusion: Accumulating evidence highlights that epigenetic dysregulation drives cancer and resistance. Identifiable epigenetic biomarkers and druggable targets enable clinical translation. Epigenetic therapies—especially combined with immunotherapy—improve outcomes, and multi-omics integration advances precision and personalization of cancer treatment. Epigenetic editing tools are emerging.

keywords: Cancer; Epigenetic Therapy; Multi Omics; Precision Oncology, Epigenetics

PG-13

The emerging role of Non-coding RNAs in the pathogenesis of infantile hemangioma

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Background and aim: Infantile hemangioma (IH) is a common benign tumor that occurs in children, affecting both blood vessels and soft tissues.

Methods: Its pathological features include abnormal proliferation of endothelial cells and an irregular vascular structure. However, the exact genetic and molecular mechanisms behind the development and progression of IH are not yet fully understood.

Results: Recent studies suggest that the dysregulation of non-coding RNAs (ncRNAs), such as microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), is closely related to the causes of various cancers, including IH. Altered expression of these ncRNAs can influence cell proliferation, viability, invasion, clonal expansion, migration, cell cycle progression, and angiogenesis while inhibiting apoptosis.

Conclusion: This regulation is crucial for the formation and growth of IH. This article provides an overview of the potential use of ncRNAs as biomarkers or treatment targets in the context of IH development.

keywords: Infantile hemangioma, miRNA, lncRNA, circRNA, Biomarker, ncRNA.

PG-14

Interleukin-4 (IL4 VNTR) Gene Different VNTR Variants and Polycystic Ovary Syndrome (PCOS) in an Iranian Population

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Background and aim: Background: Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder with an unclear etiology, potentially influenced by genetic, metabolic, and inflammatory factors. This study aimed to evaluate the association between interleukin-4 (IL4) gene variable number tandem repeat (VNTR) polymorphisms and PCOS in women from Gonabad, Iran.

Methods: Methods: A case–control study was conducted involving 100 women with PCOS and 100 age-matched healthy controls (18–40 years). Genomic DNA was extracted from 2 mL peripheral blood using the salting-out method. IL4 VNTR genotypes were determined by polymerase chain reaction (PCR) followed by 2% agarose gel electrophoresis. Statistical analysis was performed using SPSS version , with Chi-square tests applied to assess genotype distributions (significance set at P 0.05).

Results: Results: The genotype frequencies among PCOS patients were 75% P2P2, 24% P1P2, and 1% P1P1, compared with 79%, 18%, and 3% in controls, respectively. No significant association was found between IL4 VNTR polymorphisms and PCOS (P = 0.348 for P1P1, P = 0.332 for P1P2 vs. P2P2). Both case and control groups were in Hardy–Weinberg equilibrium (χ^2 = 0.372 and χ^2 = 2.182, P 0.05).

Conclusion: Conclusion: The IL4 VNTR P2P2 genotype was predominant in both PCOS and control groups, indicating no significant relationship between IL4 VNTR polymorphisms and PCOS susceptibility in this Iranian population. Further studies with larger sample sizes and diverse populations are needed to confirm these findings.

keywords: Interleukin-4, VNTR polymorphism, PCOS, genetic association, Iran

PG-15

MTHFR polymorphisms (C677T and A1298C) and polycystic ovary syndrome in an Iranian population

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Background and aim: Polycystic ovary syndrome (PCOS) is an endocrine metabolic disorder and the major cause of infertility. However, the exact cause of the condition is unclear, elevated homocysteine levels are commonly observed in PCOS and many studies have reported Methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms, especially C677T and A1298C, are associated with decreased enzymatic activity and increased homocysteine levels, which may contribute to the development of PCOS.

Methods: This study aimed to evaluate C677T and A1298C association with PCOS in 100 women suffered from PCOS and 100 healthy controls in Gonabad. DNA extraction carried out by salting out method and tetra arms polymerase chain reaction method used for genotype diagnosis. Data were Analyzed by chi-square test.

Results: However, there was no association between AC genotype of A1298C and PCOS, it was the common genotype in the case group. Significant association was found between CC genotype of the A1298C and PCOS. CC genotype of the C677T was frequent in case group and not related to the disease.

Conclusion: In conclusion our results showed a significant association with A1298C but not with C677T polymorphisms of MTHFR and PCOS in the Gonabad population.

keywords: Polycystic ovary syndrome, PCOS, MTHFR, SNP

PG-16

Investigation of association between 50-bp Ins/Del Polymorphism of SOD-1 and Polycystic ovarian syndrome in women referring to gynecologist's office in Gonabad

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Background and aim: : Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder among women of reproductive age and a leading cause of infertility. The exact etiology remains unclear, but increased oxidative stress is thought to contribute to its development. Superoxide dismutase-1 (SOD-1) is an antioxidant enzyme that plays a vital role in reducing oxidative stress, which has been implicated in the pathophysiology of PCOS. This study explored the association between the 50-bp insertion/deletion (Ins/Del) polymorphism of the SOD-1 gene and PCOS in women referred to gynecologist offices in Gonabad, Iran.

Methods: This study aimed to assess the association between the 50-bp Ins/Del polymorphism of the SOD-1 gene and PCOS in 200 women (100 with PCOS and 100 healthy controls) aged 18 to 40 years. DNA was extracted from peripheral blood using the salting-out method, and the genotyping of the SOD-1 polymorphism was performed through polymerase chain reaction (PCR) followed by agarose gel electrophoresis. The frequency of genotypes was compared between the groups using chi-square tests for statistical analysis.

Results: The distribution of genotypes of the SOD-1 polymorphism in both PCOS and control groups was analyzed. No significant association was found between the 50-bp Ins/Del polymorphism and PCOS, as the genotype frequencies did not differ significantly between the two groups (p0.05). The most common genotype in both groups was homozygote Ins/Ins, while the least frequent was homozygote Del/Del.

Conclusion: In conclusion, our findings demonstrated a significant association between the 50-bp Ins/Del polymorphism of SOD-1 and PCOS in women from Gonabad, while no significant correlation was observed with other genotypes.

keywords: Polymorphism, SOD-1 gene, Polycystic Ovary Syndrome

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-17

High Prevalence and Clinical Correlations of dupA, iceA2, and babA2 Virulence Genes in Helicobacter pylori Strains from Southern Iran

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Background and aim: The clinical outcome of Helicobacter pylori infection is strongly influenced by specific bacterial virulence factors. This study aimed to determine the prevalence and clinical significance of the dupA (duodenal ulcer-promoting), iceA2 (induced by contact with epithelium), and babA2 (blood-group-antigen-binding adhesin) genes in a patient cohort from Southern Iran.

Methods: In this cross-sectional study, gastric biopsies from 199 H. pylori-positive patients (confirmed by 16S rRNA PCR) were analyzed. Genotyping for dupA, iceA2, and babA2 was performed using specific PCR assays. Associations between virulence genotypes and clinical manifestations (gastritis, celiac disease, vomiting) and epidemiological risk factors were evaluated using chi-square tests and logistic regression.

Results: The prevalence of dupA and iceA2 was remarkably high at 79.9% and 67.3%, respectively, while babA2 was detected in 27.1% of strains. Statistical analysis revealed powerful associations: • The dupA gene was significantly associated with gastritis (OR=5.94, 95% CI: 3.02–11.68, p0.001) and exhibited a very strong association with vomiting (OR=9.99, 95% CI: 1.31–75.9, p0.001). • The iceA2 gene was significantly linked to gastritis (OR=5.82, 95% CI: 3.05–11.09, p0.001), celiac disease (OR=2.53, 95% CI: 1.34–4.81, p0.001), and consumption of non-potable water (OR=3.03, 95% CI: 1.11–8.27, p=0.03). • The babA2 gene was associated with gastritis (OR=4.06, 95% CI: 1.85–8.92, p0.001), vomiting (OR=2.63, 95% CI: 1.27–5.45, p0.001), and a positive family history of gastrointestinal issues (OR=1.92, 95% CI: 0.96–3.84, p=0.04).

Conclusion: This study establishes dupA and iceA2 as the predominant virulence markers in H. pylori strains from Southern Iran. Their strong, specific associations with clinically significant outcomes (gastritis, vomiting, celiac disease) and an environmental risk factor underscore their pathogenic role. These findings suggest that genotyping these virulence factors could be valuable for risk stratification and personalized management of H. pylori-infected patients in this region.

keywords: Helicobacter pylori, Virulence Genotyping, dupA, iceA2, Molecular Epidemiology, Clinical Correlation.

PG-18

Utilizing qPCR for the Detection of Helicobacter Pylori Drug Resistance: A Systematic Review

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Background and aim: Helicobacter pylori (HP) antibiotic resistance is increasing worldwide, prioritizing the urgent need for more rapid resistance detection. Today, existing methods of HP diagnosis mostly include the rapid urease test (RUT), the urea breath test (UBT), the serum antibody test, the antigen test, gastroscopy, and bacterial culture. According to the new version of Maastricht IV guidelines, molecular tests such as quantitative polymerase chain reaction (qPCR) can be performed as a surrogate

Methods: The literature search encompassed three databases—PubMed, Scopus, and Web of Science—and was limited to English-written papers from 2020 to 2025. Review articles, letters, and conference papers were excluded. search strategy was conducted using Medical Subject Headings (MeSH), including subsequent keywords: Helicobacter pylori, real-time PCR, qPCR, drug resistance, and MDR. The eligibility criteria were defined using the PICO framework. Two independent researchers reviewed the titles and abstracts of the identified articles. Disagreement was solved by discussion and reaching a consensus. Data were extracted from the selected studies using a standard data extraction form.

Results: The search yielded 92 primary results; 31 articles met the inclusion criteria and reported on a total of 8522 samples. The qPCR method sensitivity to diagnose HP in samples ranged from 66.6% to 99.1%, while its specificity ranged from 95.6% to 100%. The qPCR assay demonstrated 79.6% to 100% sensitivity in detecting clarithromycin resistance and 86.3% to 100% sensitivity in detecting levofloxacin resistance. The specificity of detecting clarithromycin resistance ranged from 78.57% to 98.4%, and for levofloxacin resistance, it ranged from 76.42% to 91.1%. The qPCR assay was found to be more efficient than RUT in detecting HP infection and could effectively verify clarithromycin resistance and levofloxacin resistance compared to the antimicrobial susceptibility culturing test. Considering the high sensitivity and accessibility of the qPCR method, it could be used to easily detect clarithromycin resistance and levofloxacin resistance in HP. In addition, classical culture remains the cheapest method compared to used

Conclusion: qPCR can accurately and noninvasively diagnose HP, provide genotypic susceptibility, and test for eradication. Application of qPCR is, in the meantime, well-established and results, therefore, in novel diagnostic tools.

keywords: : Helicobacter pylori; qPCR; Drug resistance.

PG-19

Investigating polymorphisms that play a role in colorectal cancer recurrence

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Background and aim: Colorectal cancer (CRC) is a predominant cause of mortality associated with gastrointestinal malignancies worldwide. Despite the implementation of surgical interventions and subsequent chemotherapy, a notable percentage of patients face recurrence. Recent research has highlighted genetic variations as significant factors influencing the progression and prognosis of colon cancer. A deeper understanding of these polymorphisms may improve risk assessment and therapeutic outcomes for patients with locally advanced CRC.

Methods: A comprehensive systematic search of relevant studies up to 2024 was performed by searching databases such as PubMed, MEDLINE, SCOPUS, and Google Scholar. The keywords " Colorectal cancer", " Polymorphisms" and " Relapse" were used in this search. Only articles with fully accessible English texts were included in the search parameters. Articles that were reviews, duplicates, or irrelevant were not included.

Results: In this systematic review study, 95 articles were retrieved through searching in databases, of which only 9 articles matched our inclusion criteria. Genetic variations, including PLS3 rs6643869 and LCP1 rs4941543, were identified as significant factors affecting the risk of tumor recurrence. Single nucleotide polymorphisms (SNPs) associated with angiogenesis, specifically VEGF C+936T and IL-8 T2251A, were correlated with a reduced time to recurrence, suggesting their potential utility as prognostic indicators. Furthermore, the miRNA-encoding genes miR219-1 and miR-608 displayed varying associations with survival rates in patients undergoing 5-FU-based chemotherapy. Conversely, the impact of HSPB1 rs2070804 on colorectal cancer (CRC) progression remains ambiguous, as it showed limited connections with clinical factors such as tumor aggressiveness and metastasis.

Conclusion: The discovery of specific SNPs within plastin genes, angiogenesis-related genes, miRNA-encoding genes, and heat shock proteins (HSPs) holds potential for the development of personalized treatment approaches and risk evaluation in CRC patients. Future investigations should aim to confirm these results in larger populations and assess their clinical relevance for enhancing patient outcomes.

keywords: Polymorphisms, Colorectal cancer, Relapse

PG-20

Gene-Specific ctDNA and cfDNA Profiles in Prognosis, Early Detection, and Monitoring of Uterine and Cervical Neoplasms in Iran: A Systematic Review

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Background and aim: Uterine and cervical neoplasms are among the most prevalent gynecologic cancers worldwide. In Iran, limited screening programs and challenges in treatment monitoring lead to delayed diagnosis and suboptimal outcomes. Circulating tumor DNA (ctDNA) and cell-free DNA (cfDNA) provide non-invasive access to tumor-specific genetic alterations, enabling gene-centered cancer management.

Methods: A systematic literature search was conducted according to PRISMA guidelines in PubMed, Scopus, and Web of Science. Human studies published within the last ten years investigating gene-level ctDNA/cfDNA alterations in endometrial or cervical cancers were included. Genes of interest in endometrial cancer: PTEN, PIK3CA, TP53, ARID1A, POLE, CTNNB1, and MMR genes (MLH1, MSH2, MSH6, PMS2) Genes of interest in cervical cancer: HPV E6/E7, PIK3CA, TP53, STK11, KRAS, TERT promoter Data on prognostic value, early detection, minimal residual disease, and monitoring were extracted and qualitatively synthesized.

Results: Gene-specific ctDNA profiles demonstrated strong clinical relevance. Endometrial cancer: TP53 and PIK3CA mutations in ctDNA were associated with aggressive disease and poor prognosis; POLE mutations indicated favorable outcomes. Detection of ctDNA after surgery predicted minimal residual disease and early relapse. Cervical cancer: Persistent HPV-derived ctDNA (E6/E7) and mutations in PIK3CA and TP53 were linked to advanced disease stage, treatment resistance, and recurrence. cfDNA fragmentation patterns and mutational burden improved early detection potential. Methodological heterogeneity and lack of standardized assays were the main limitations across studies.

Conclusion: Gene-specific ctDNA and cfDNA analysis provides actionable prognostic, diagnostic, and monitoring information for uterine and cervical neoplasms. Integration of gene-centered liquid biopsy approaches may enhance personalized cancer management in Iran. Further large-scale, gene-focused population studies are required for clinical implementation.

keywords: Circulating Tumor DNA Cell-Free Nucleic Acids Uterine Neoplasms Cervical Neoplasms

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-21

LncRNAs CASC7 and MAGI2-AS3: Emerging Contributors to the Pathogenesis of Chronic Lymphocytic Leukemia

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Background and aim: Chronic lymphocytic leukemia (CLL) type B is the most prevalent form of leukemia among adults in Western countries, representing nearly 25–30% of all leukemia diagnoses. The disease's pathogenesis is characterized by the accumulation of monoclonal B lymphocytes that express CD5, CD20, and CD23 antigens. Epigenetic modifications, particularly those involving long non-coding RNAs (lncRNAs), have been implicated in leukemogenesis. Notably, H19, CASC7, and MAGI2-AS3 have been associated with cancer progression through their roles in regulating proliferation and apoptosis; however, their specific functions in CLL remain inadequately defined. This study aimed to assess the expression levels of these three lncRNAs in CLL

Methods: This case–control study included 17 untreated CLL patients and 17 age- and sex-matched healthy controls. Peripheral blood mononuclear cells (PBMCs) were isolated using Ficoll-Hypaque gradient centrifugation. Total RNA was extracted, and complementary DNA was synthesized using standardized kits. The relative expression of CASC7, MAGI2-AS3, and H19 was quantified via real-time quantitative PCR (qPCR) using GAPDH as the reference gene. Expression data were analyzed using the 2-ΔΔCT method, and statistical analyses were performed in REST 2009, GraphPad Prism, and SPSS v16, with a significance threshold set at p 0.05.

Results: The expression levels of CASC7 and MAGI2-AS3 were significantly downregulated in CLL patients compared to controls (p 0.001). Although H19 expression was also lower in patients, this difference was not statistically significant (p = 0.516). The fold changes in expression for CASC7, MAGI2-AS3, and H19 were 0.02, 0.29, and 0.53, respectively. Receiver operating characteristic (ROC) analysis indicated strong diagnostic potential for CASC7 (AUC = 0.979, p 0.001) and MAGI2-AS3 (AUC = 0.868, p 0.001), while H19 showed limited discriminatory capacity (AUC = 0.602, p 0.05).

Conclusion: The significant downregulation of CASC7 and MAGI2-AS3 in CLL suggests their potential roles as tumor-suppressive lncRNAs and their possible utility as novel diagnostic biomarkers for CLL. In contrast, H19 does not appear to be a reliable diagnostic marker based on these findings. Further research with larger cohorts is necessary to clarify the mechanistic roles of these lncRNAs in CLL pathogenesis.

keywords: Chronic lymphocytic leukemia (CLL); long non coding RNA (lncRNA); CASC7

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-22

Identification of Hub Genes in Clear Cell Renal Cell Carcinoma: A Comprehensive In Silico Study

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Background and aim: Clear cell renal cell carcinoma (ccRCC) is the most common and aggressive subtype of renal cancer, characterized by high heterogeneity and poor prognosis in advanced stages. Despite recent therapeutic advances, reliable molecular biomarkers and therapeutic targets for ccRCC remain limited. The present study aimed to identify key differentially expressed genes and hub genes involved in the pathogenesis and progression of ccRCC, with particular emphasis on immune-related mechanisms, using integrated bioinformatics analyses.

Methods: Gene expression profiles were obtained from three Gene Expression Omnibus (GEO) datasets (GSE151419, GSE76207, and GSE102101). Differentially expressed genes (DEGs) between tumor and normal samples were identified using the GEO2R tool. Functional enrichment analyses, including Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways, were performed using the DAVID database. A protein–protein interaction (PPI) network was constructed, and hub genes were identified using CytoHubba. Validation was conducted via GEPIA2, and associations with immune cell infiltration and drug sensitivity were analyzed using the GSCA database.

Results: A set of significant DEGs was identified, primarily enriched in immune response and signal transduction pathways. Hub genes, including CD4, ITGAM, ITGB2, and PTPRC, were highlighted as central nodes in the PPI network. Expression levels of these hub genes showed strong correlations with immune cell infiltration patterns and sensitivity to several anticancer drugs, suggesting their potential role in immune regulation and therapeutic response in ccRCC.

Conclusion: This comprehensive in silico analysis identified key immune-related hub genes that may play critical roles in the development and progression of clear cell renal cell carcinoma. The observed associations with immune infiltration and drug sensitivity underscore their potential as diagnostic biomarkers and therapeutic targets. However, further experimental and clinical validation is required to confirm these findings and translate them into clinical applications.

keywords: Clear cell renal cell carcinoma; Hub genes; Bioinformatics analysis; Immune

PG-23

Aberrant Expression of circ-0000527, circ-0014130, and circ-XIAP in the Pathogenesis of Chronic Lymphocytic Leukemia

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Background and aim: Leukemia is a malignant and progressive disorder of hematopoiesis. This disease arises from the abnormal proliferation and development of white blood cells and their precursors within the blood and bone marrow. Chronic lymphoblastic leukemia (CLL) is a subtype of hematologic malignancy characterized by the origin of B lymphocytes, involving the bone marrow, blood, and lymph nodes. Circular RNAs (circRNAs) are a type of non-coding RNA characterized by their covalently closed structure, distinguishing them both structurally and functionally from linear RNAs. Recent studies have identified circRNAs as important regulators of CLL. In this way, we aimed to evaluate the expression of

Methods: Blood samples were collected from 17 CLL patients from Kermanshah province, Iran, and 17 age and sex-matched healthy individuals. RNA was extracted from PBMCs and then subjected to cDNA synthesis. Using specifically designed primers and the Real-Time PCR method, the expression of circRNAs was detected and statistically analyzed.

Results: The experiments revealed a significant increase in the expression of all three circRNAs (p-value 0.0001) in CLL patients compared with healthy individuals. ROC analysis suggested that the three studied circRNAs can serve as potential biomarkers for early diagnosis of CLL.

Conclusion: The observed increase in expression of circ-0000527, circ-0014130, and circ-XIAP in treatment-naïve CLL patients here may be suggestive of their oncogenic role in CLL progression. Moreover, the candidate peripheral circRNAs could potentially serve as diagnostic biomarkers that warrant further investigation in a larger sample size.

keywords: Chronic lymphocytic leukemia (CLL), Circular RNA (CircRNA), Circ-0000527, Circ-0014130, Circ-XIAP

PG-24

Pathogenic Variants in Syndromic and Non-Syndromic Intellectual Disability Identified by Whole-Exome Sequencing in Eight Iranian Families

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Background and aim: Intellectual disability (ID) is a highly heterogeneous neurodevelopmental disorder with diverse genetic and environmental etiologies and presents in both syndromic and non-syndromic forms. Despite significant advances in genetic research, approximately 50% of ID cases remain genetically unexplained. The present study aimed to identify pathogenic genetic variants underlying syndromic and non-syndromic intellectual disability in Iranian families using whole-exome sequencing (WES), and to emphasize the importance of genetic counseling beyond consanguineous marriages.

Methods: Eight Iranian pedigrees with at least one affected child were recruited following detailed clinical evaluation and pedigree analysis. Genomic DNA was extracted from peripheral blood samples, and whole-exome sequencing was performed for probands. Bioinformatic analysis and variant interpretation were conducted according to established pathogenicity criteria. Candidate variants were further evaluated in relation to the clinical phenotypes of affected individuals.

Results: Despite the limited sample size, three novel pathogenic variants were identified in the TRPM3, SCN1A, and DENND5A genes. In addition, previously reported disease-associated variants were detected in TMEM147, KMT2C, ATP9A, and GNAI1, all of which were consistent with the observed clinical manifestations. Notably, in proband 4, no disease-associated variant was identified despite comprehensive genomic analysis, highlighting the ongoing challenges in elucidating the genetic basis of ID.

Conclusion: This study demonstrates that intellectual disability is not confined to consanguineous unions, as several affected individuals were born to non-consanguineous parents with different ethnic backgrounds. Our findings underscore the diagnostic value of next-generation sequencing technologies in heterogeneous neurodevelopmental disorders and highlight the critical role of genetic counseling in early diagnosis, family planning, and prevention strategies. Furthermore, the absence of detectable pathogenic variants in a subset of cases indicates the need for continued advancement in genomic research to uncover unresolved genetic mechanisms underlying intellectual disability.

keywords: Intellectual disability; Whole-exome sequencing; Pathogenic variants; Genetic heterogeneity; Genetic counseling

PG-25

Exploring the Role of 5-HTTLPR Short Allele in Psychiatric Disorders: A Genetic Perspective

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Background and aim: The SLC6A4 gene (17q11.2) encodes a membrane protein that transports serotonin from synapses into presynaptic neurons, terminating its action and affecting mood. The 5-HTTLPR polymorphism has a long (L;16 repeats) and short (S;14 repeats) allele, with the S allele reducing transporter expression and altering serotonin availability. Although the serotonergic system is a shared biological pathway across psychiatric disorders and the 5-HTTLPR S allele has been implicated, findings remain heterogeneous and contradictory. This study integrates genetic evidence to clarify the relationship between the S allele and psychiatric disorders across populations.

Methods: A literature review was conducted using PubMed, Google Scholar, and Scopus to identify studies from 2015–2025 examining associations between the 5-HTTLPR polymorphism of the SLC6A4 gene and psychiatric disorders, including PTSD, depression, anxiety, schizophrenia, autism, and bipolar disorder. Data on sample size, population ethnicity, study design, genotypes, and significance were extracted from European, Asian, and American cohorts, encompassing adults and adolescents. Significant and non-significant findings were summarized.

Results: The investigations included in this study identified disorder-specific associations between the 5-HTTLPR S allele and psychiatric disorders. Significant associations were reported for major depressive disorder (MDD), bipolar disorder, depressive symptom severity in bipolar patients, alcohol and opiate dependence, alcohol use disorder (AUD), obsessive–compulsive disorder (OCD), autism spectrum traits and autism, suicidal behavior and depression-related suicide outcomes, as well as anxiety-related traits, harm avoidance, neuroticism, emotional arousal control, openness, and trait anxiety. Non-significant associations were observed for panic disorder, schizophrenia, post-traumatic stress disorder (PTSD), generalized anxiety disorder, conscientiousness, depression, anxiety, and OCD in cohorts. For a subset of disorders—including alcohol dependence, suicide-related behavior, neuroticism, PTSD, autism, anxiety, depression, and OCD—associations with the S allele were significant in some populations but not others, reflecting variability across populations and designs.

Conclusion: The 5-HTTLPR S allele confers disorder-specific vulnerability, mainly affecting psychiatric conditions linked to emotional dysregulation and stress, including mood disorders, addiction, and anxiety traits. Associations vary across populations due to genetic, environmental, and disorder-specific factors. While not a universal risk factor, the S allele plays a key role in stress- and emotion-related disorders. It is important for future research, risk assessment, and personalized interventions.

keywords: 5HTTLPR-SLC6A4-psychiatric disorders

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-26

Impact of LMNA gene polymorphism (rs581342) on lung cancer susceptibility: Evidence from a southeast Iranian population

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Background and aim: This study aimed to evaluate the association between the rs581342 polymorphism and lung cancer risk in an Iranian population. No prior research has investigated this relationship in southeast Iran.

Methods: A case–control study was conducted on 300 individuals (150 lung cancer patients and 150 healthy controls) in southern Iran (2022–2024). Cases and controls were matched to sex and age. Demographic variables, histological subtypes, and tumor differentiation grades were collected. Genotyping of rs581342 was performed using the ARMS-PCR method. Statistical analyses included chi-square test, logistic regression, and Hardy–Weinberg equilibrium.

Results: Patients with small cell lung cancer (SCLC) were significantly older than those with non-small cell lung cancer (NSCLC) (P 0.05), and males had a higher prevalence of lung cancer (P = 0.005). Genotype distribution differed between patients and controls (P = 0.001), but not between genders (P = 0.121). The TC genotype was protective (OR = 0.29), while the CC genotype increased risk (OR = 1.78). No association was found with cancer subtypes; however, genotype distribution strongly correlated with tumor differentiation (P 0.0001). The substantial deviation from Hardy–Weinberg equilibrium ($\chi 2$ = 189.3, P 0.0001) appears to reflect methodological constraints of the ARMS-PCR assay rather than any underlying selective pressure. Logistic regression confirmed gender (OR = 1.958, P = 0.017) and genotype (P = 0.008) as significant predictors, while age showed borderline significance (P = 0.096).

Conclusion: The rs581342 polymorphism may serve as a genetic marker for lung cancer susceptibility and tumor differentiation, though not for histological subtype classification.

keywords: Lung cancer, rs581342 polymorphism, LMNA gene, Genetic susceptibility, Tumor differentiation,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-27

Concurrent Presence of Two Robertsonian Translocations in a Pregnant Woman Referred for Prenatal Diagnosis: A Case Report

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Background and aim: carriers of Robertsonian translocations-fusion of two acrocentric chromosomes, produced balanced or unbalanced gametes through various segregation modes,with an increased offspring risk for imprinting disorders. Although it is estimated that 1 in 1,000 healthy individuals possess a Robertsonian translocation, reports of individuals with two balanced Robertsonian translocations are rare. The majority of documented cases are phenotypically normal but have adverse pregnancy outcomes. This study reports a rare case with the karyotype 44,XX, rob(13;14)(q10;q10), rob(14;21)(q10;q10), which simultaneously carries two apparently balanced Robertsonian translocations.

Methods: Regarding the fetus ,Chromosomal analysis was performed after 14 days of amniotic fluid culture based on standard methods.then,twenty metaphase spreads were studied from culture of amniocytes in one flask at 180-230 band resolution on the basis of GTG technique. For each parent, Chromosomal analysis was performed after 72 hours phytohemagglutinin (PHA) stimulation of peripheral blood lymphocytes culture based on standard methods.then twenty metaphase spread were studied and 5 metaphase were analyzed at 400-450 band resolution on the basis of GTG technique. karyograms were prepared using the Ikaros Karyotyping Software version 5.8.5. The chromosomal abnormalities were described based on the International System for Human Cytogenetic Nomenclature (ISCN; 2020)

Results: An amniotic fluid sample with a gestational age of 15 weeks was referred for prenatal diagnosis of chromosomal abnormalities due to a history of previous pregnancy affected with Down syndrome. Chromosomal analysis of the fetus revealed an abnormal male chromosome complement in all cells examined with an apparently balanced Robertsonian translocation between the long arms of chromosomes 14 and 21. Based on the fetal karyotype, the parents underwent karyotype analysis to determine whether the rearrangement was familial or de novo. Surprisingly, we found that the mother carried the karyotype 44,XX, rob(13;14)(q10;q10),rob(14;21)(q10;q10). The mother had had four pregnancies, including 1 apparently normal child, a spontaneous abortion at 13 weeks' gestation, a pregnancy with Down syndrome that was legally terminated, and the current pregnancy with the fetus 45,XY,rob(14;21)(q10;q10).

Conclusion: The present report has added to the current knowledge of intricacies of chromosomal rearrangements in the population and may better assist in genetic counseling of carries.

keywords: Down syndrome, trisomy 21, genetic translocations

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-28

Artificial Intelligence Applications in Pediatric Cancers: A Systematic Review

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Background and aim: Pediatric cancers exhibit distinct molecular and genomic characteristics, frequently with low mutational burden, which complicates risk stratification and therapeutic decision-making. Artificial intelligence (AI) and machine learning (ML) approaches have increasingly been applied to address the analytical challenges posed by complex pediatric oncology datasets. However, the extent to which these approaches provide clinically meaningful benefit remains uncertain. This systematic review aimed to summarize evidence from studies published between 2015 and 2025 that applied AI-based methods in pediatric cancer research and clinical assessment.

Methods: A systematic literature search was performed in PubMed, Scopus, and the Cochrane Library using predefined keywords related to artificial intelligence, machine learning, and pediatric cancers. Eligible studies were peer-reviewed, published in English between 2015 and 2025, and applied AI or ML techniques to pediatric cancer data with reported predictive or clinically relevant outcomes. Exclusion criteria included non-English publications, adult-only studies, reviews, conference abstracts, and studies lacking AI-based analysis. Titles, abstracts, and full texts were screened, and relevant methodological and outcome data were extracted.

Results: Across the included studies, AI-based models demonstrated the ability to extract clinically and biologically relevant information from diverse pediatric cancer datasets. These approaches enabled accurate discrimination between true genomic variants and technical artifacts, noninvasive prediction of molecular alterations, stratification of patients according to relapse risk or survival, and identification of treatment sensitivities and resistance patterns. AI methods were particularly effective in settings with limited recurrent mutations, where conventional analyses often lack resolution. Integration of genomic, transcriptomic, functional, and imaging-derived features revealed complex patterns associated with prognosis and therapy response. Nevertheless, most studies relied on retrospective designs and internal validation, highlighting ongoing challenges for routine clinical implementation.

Conclusion: AI-based approaches show strong potential to enhance molecular classification, risk stratification, and therapeutic prediction in pediatric oncology, especially in tumors with low mutational burden. By uncovering patterns not readily detectable through conventional analysis, these methods support more precise clinical decision-making. However, variability in methodology and limited external validation currently restrict clinical translation. Future prospective and standardized studies are required to confirm robustness and generalizability.

keywords: Artificial intelligence; Pediatric cancer; Machine learning; Genomics; Precision medicine

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-29

Genetic biomarkers for predicting drug response and their relationship with pharmacogenetics in the diagnosis and treatment of breast cancer

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Background and aim: The most common type of breast cancer originates from ductal cells, whereas the type arising from lobes or lobules is less frequent. By utilizing various genetic biomarkers, including predictive and prognostic biomarkers, alongside approaches such as subject and gene information, data analysis, and endocrine therapy, in combination with pharmacogenetics as a tool for personalized treatment, it is possible to determine which drug is most suitable for each individual, assess the potential aggressiveness of the disease, and predict the outcome for the patient.

Methods: 1. Data Analysis: This approach is used to identify differentially expressed genes (DEGs) in breast cancer tissues compared to normal samples. The method involves using GEO2R with screening criteria of Log2FC 1.5, Log2FC −1.5, or adjusted p-value 0.05. 2. Subjects and Gene Information. For example, Using GEO2R datasets such as GSE134359, GSE31448, and GSE42568 were analyzed to identify DEGs. 3. Endocrine Therapy: This is a standard treatment for HR+ (Hormone Receptor-positive) breast cancer. In this therapy, aromatase inhibitors (AIs) and their musculoskeletal adverse effects have been the most extensively studied, with third-generation AIs accounting for the majority of analyses.

Results: By analyzing the data obtained from Data Analysis and applying the defined screening criteria, patients at high risk who require urgent follow-up or even more invasive breast cancer sampling can be identified more rapidly, enabling earlier initiation of treatment. Furthermore, the GEO2R tool allows researchers to detect genes that are abnormally over- or under-expressed in cancer cells, which can then be leveraged to identify novel therapeutic targets.The relationship between endocrine therapy and HR+ status also forms the basis of personalized treatment for most breast cancers, with the greatest efficacy observed with third-generation aromatase inhibitors and their musculoskeletal adverse effects.

Conclusion: The findings indicate that breast cancer diagnosis can be accelerated, and the individual efficacy of each drug can be assessed. This approach enables diagnosis and treatment without resorting to invasive procedures. However, in the realm of subject and gene information, inconsistencies remain, highlighting the need for future improvements.

keywords: Endocrine Therapy- pharmacogenetics- Data Analysis

PG-30

A Serum-Based Three-microRNA Signature for Non-Invasive Detection of Bladder Cancer

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Background and aim: Bladder cancer remains one of the most frequently diagnosed urological malignancies and is associated with high recurrence rates, placing a substantial burden on patients and healthcare systems. Despite advances in clinical management, reliable non-invasive biomarkers for early detection are still lacking. Circulating microRNAs (miRNAs) have emerged as promising diagnostic candidates due to their stability in blood and cancer-related expression profiles. This study aimed to evaluate whether specific serum miRNAs can discriminate patients with bladder cancer from healthy individuals.

Methods: A case–control study design was applied, including 20 patients with histologically confirmed bladder cancer and 20 cancer-free healthy controls. Serum miRNA expression levels were quantified using RT-qPCR. Differential expression between groups was analyzed using the Mann–Whitney U test. Diagnostic performance was assessed by receiver operating characteristic (ROC) curve analysis. A multivariable diagnostic model was constructed using stepwise logistic regression and internally validated through 10-fold cross-validation. In silico analyses were conducted to identify putative target genes and cancer-related pathways associated with the selected miRNAs.

Results: Serum expression analysis revealed significant dysregulation of three miRNAs in bladder cancer patients compared with healthy controls. hsa-miR-21 and hsa-miR-155 were significantly upregulated (fold changes: 3.8 and 2.9, respectively; both p 0.001), whereas hsa-miR-145 was significantly downregulated (fold change: 0.42; p 0.001). The combined three-miRNA signature demonstrated good diagnostic performance, yielding an area under the curve (AUC) of 0.887, with a sensitivity of 85.7% and a specificity of 89.6%. In silico target analysis suggested involvement of these miRNAs in cancer-related pathways relevant to bladder tumorigenesis.

Conclusion: This study suggests that a serum-based three-miRNA panel comprising hsa-miR-21, hsa-miR-155, and hsa-miR-145 may have potential utility for the non-invasive detection of bladder cancer. The observed diagnostic performance supports the feasibility of circulating miRNAs as biomarkers in this context. However, due to the limited sample size, further validation in larger and independent cohorts is required prior to clinical application.

keywords: Bladder Cancer; Circulating microRNAs; hsa-miR-21; hsa-miR-155; hsa-miR-145; Molecular diagnostics

PG-31

The Oncogenic and Prognostic Role of lncRNA XIST in the Pathogenesis of Acute Myeloid Leukemia: A Narrative Review

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Background and aim: Acute myeloid leukemia (AML) is a heterogeneous hematologic malignancy characterized by uncontrolled proliferation and impaired differentiation of myeloid precursor cells. Long non-coding RNAs (lncRNAs), non–protein-coding transcripts longer than 200 nucleotides, are increasingly recognized for their roles in cancer development and progression. Among lncRNAs, the X-inactive specific transcript (XIST) has been highlighted in recent cancer research. This study aims to investigate the oncogenic role and prognostic significance of XIST in acute myeloid leukemia.

Methods: A literature search was conducted in PubMed using the keywords "XIST" and "acute myeloid leukemia." Six relevant studies published between 2020 and 2024 were selected and reviewed. The molecular mechanisms, downstream targets, and clinical implications of XIST in leukemogenic processes were comparatively analyzed.

Results: Evidence from recent studies demonstrates that XIST is aberrantly upregulated in leukemic cells and patient samples. Overexpression of XIST promotes proliferation, enhances drug resistance, and inhibits apoptosis by interacting with multiple microRNAs, including miR-196b, miR-29a, and miR-34a. Silencing XIST induces apoptosis through activation of caspase-3 and Bax and suppression of Bcl-2. Functional analyses have also identified XIST as a key hub molecule influencing major oncogenic pathways such as PI3K-Akt, p53, and FoxO signaling.

Conclusion: Current evidence suggests that XIST functions as an oncogenic lncRNA contributing to leukemogenesis and therapy resistance. Its elevated expression is associated with poor clinical prognosis and may serve as a potential biomarker for disease outcome. Targeting XIST-mediated molecular axes could offer new therapeutic strategies to enhance treatment response and long-term survival.

keywords: Acute Myeloid Leukemia, lncRNA XIST, MicroRNAs, Leukemogenesis, Prognosis.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-32

Transcriptomic Discovery of Testis-Specific Genes in Bladder Cancer

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Background and aim: Bladder cancer remains a major urinary tract malignancy with limited early detection strategies , Which is the tenth most common cancer worldwide and ranks 13th in terms of mortality. Risk factors include smoking, chemical exposures, infections, chronic inflammation, obesity, and genetic predisposition. Identifying reliable molecular biomarkers is crucial for early diagnosis, prognosis, and targeted therapy.

Methods: In this study, we analyzed the GSE236932 dataset with R software to identify differentially expressed genes (DEGs) associated with bladder cancer. Candidate gene was PAPOLB which is a testis-enriched gene .The obtained result was validated using quantitative real-time PCR in clinical bladder tissue (n=20)and urine samples (n=10) collected from healthy controls .

Results: The final analyses demonstrated that the gene was significantly up regulated in tumor tissue , showing an 11.649 fold increase in expression(P-Value= 0.001).Moreover, no significant associations were observed between gene expression levels and age , sex or tumor grade. In contrast, cigarette smoking exhibited a significant impact on the gene expression (P-Value= 0.001).

Conclusion: Our findings highlight PAPOLB as promising non-invasive biomarkers for early detection and potential therapeutic targets, providing new insights into bladder cancer biology and advancing precision medicine strategies.

keywords: Bladder Cancer , Biomarkers, PAPOLB, Gene Expression ,Bioinformatics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-33

Toward Precision Medicine in Multiple Sclerosis:Machine Learning Prediction of Treatment Response Based on Gene Expression Profiles

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Background and aim: Predicting response to interferon-β and fingolimod in multiple sclerosis (MS) is complicated by patient variability. Machine learning (ML) using gene expression is hindered by high-dimensional noise and algorithm-dependent gene selection. Pathway-level analysis may yield more robust and interpretable biomarkers. This review examines ML studies identifying gene- and pathway-based signatures linked to therapeutic response.

Methods: A literature review identified transcriptomic ML studies predicting response to interferon-β or fingolimod in MS. Searches in PubMed, Scopus, and ScienceDirect used predefined keywords. Studies employing ML classification on human transcriptomic data were included. Data on preprocessing, models, and biomarkers were extracted. Gene-level findings were synthesized into biological pathways.

Results: Gene-level markers differed across algorithms, but consistent convergence emerged at the pathway level. Both therapies modulated overlapping pathways, including Type I interferon signaling, Th17 differentiation, and chemokine activity. Key genes (e.g., MX1, IFI44L) aligned with known drug mechanisms. Reproducibility depended heavily on normalization and batch correction, with microarrays and exosomal miRNA showing high reliability.

Conclusion: Pathway analysis provides robust, biologically meaningful predictors of treatment response in MS. Convergent immune and signaling pathways consistently underpin efficacy. Specific genes and miRNAs reflect relevant drug mechanisms. Methodological variability remains a challenge. Future work should validate these pathway signatures in large independent cohorts and integrate them into clinical predictive models to advance personalized therapy.

keywords: Multiple sclerosis, interferon-β, fingolimod, gene expression, machine learning, biomarkers.

PG-34

The Future of Breast Cancer Diagnosis: Extracellular Vesicles as Key Players

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Background and aim: Breast cancer (BC) is the most frequently diagnosed cancer and the leading cause of cancer-related mortality in women worldwide, highlighting the need for novel strategies for early diagnosis and efficient treatment. The current standards for breast cancer diagnosis, mammography, and tissue biopsy have limitations. Liquid biopsy is a novel and less invasive tool for the detection and monitoring of breast cancer. It involves sampling biofluids and isolating tumor-derived components such as extracellular vesicles (EVs). Extracellular vesicles (EVs) include DNA, RNA, lipids, metabolites, and proteins. EVs are promising tools for diagnosis, prognosis, and therapy.

Methods: The documents of this study were gathered through searches in databases such as PubMed, Google Scholar, ScienceDirect, and Springer. Key terms included “breast cancer”, “Extracellular vesicles”,” Liquid biopsy”, and” novel diagnosis”. 17 articles were identified to examine and analyze this topic thoroughly.

Results: Evs miRNAs, like a combination of miR-375, miR-655-3p, miR-548b-5p, and miR-24-2-5p, have been found relevant for early BC diagnosis. Serum exosomal lncRNA XIST has been identified as a promising biomarker for detecting the recurrence of TNB. SEVs Circular Nucleic Acids, such as(circDNA)and (circRNAs) that show promise as biomarkers in breast cancer, are linked to tumor progression and recurrence. miRNAs in tumor-derived EVs (TEVs) carry diverse bioactive molecules, such as DNA, RNA, lipids, and metabolites, making them promising tools for early detection, prognosis assessment, and monitoring recurrence in TNBC. For instance, studies have linked elevated levels of serum exosomal annexin A2 (exo-AnxA2) to more advanced tumor grades in breast cancer patients.

Conclusion: Breast cancer is the most frequently diagnosed cancer and a leading cause of cancer-related deaths among women globally. liquid biopsies offer less invasive methods to detect tumor-derived materials like DNA, RNA, and cells in bodily fluids. Small extracellular vesicles (sEVs), which carry proteins, nucleic acids, and other biomolecules, have emerged as promising biomarkers for BC diagnosis and prognosis due to their role in cell-to-cell communication and presence in physiological and pathological conditions.

keywords: Breast cancer, Extracellular vesicles, Liquid biopsy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-35

In silico Design of a Novel Multi-Epitope Vaccine Candidate Against Brucella melitensis Based on Omp31, Bp26, and RplL Antigens

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Background and aim: Brucellosis is a globally prevalent zoonosis with significant economic and health impacts. Although live attenuated vaccines (Rev.1, S19) are effective in livestock, they are unsuitable for humans due to safety risks, necessitating safe subunit vaccines. Reverse vaccinology offers a promising strategy to identify immunodominant candidates. This study targeted three conserved Brucella melitensis proteins: Omp31 (outer membrane), Bp26 (periplasm), and RplL (ribosomal L7/L12). These antigens were selected to develop a new multi-epitope vaccine with high antigenicity, safety, and broad protective capacity.

Methods: The amino acid sequences of Omp31, Bp26, and RplL of B. melitensis strain 16M were obtained from the NCBI database. Initial screens for antigenicity and allergenicity were performed using VaxiJen v2.0 and AllerTOP v2.0, respectively. Physicochemical properties such as molecular weight and stability were analyzed using Expasy ProtParam. To ensure safety, homology to the human proteome was assessed using NCBI BLASTp. T cell epitopes (CTL and HTL) were predicted using NetCTL 1.2 (for CTL) and the IEDB server (for HTL), focusing on human supertypes to assess translational potential. Additionally, linear B cell epitopes were identified using ABCpred. Epitopes with high scores were selected for the final design. Multi-epitope vaccines were assembled by linking selected epitopes to specific linkers (EAAAK, AAY, GPGPG, KK) and cholera toxin B subunit (CTB) as an adjuvant to enhance immunogenicity.

Results: Physicochemical analysis indicated that Omp31 (240 aa), BP26 (250 aa) and RplL (124 aa) proteins are stable with instability indices of 8.61, 27.93 and 18.55 respectively. Antigenic prediction supported its usability with VaxiJen scores of 0.6689 for Omp31, 0.5381 for BP26 and 0.6244 for RplL. Omp31 is also a main outer membrane protein, RplL (L7/L12) is a ribosomal subunit playing role in translation, and BP26 is an immunodominant periplasmic protein. Primary screening indicated allergenicity, however non-allergenic epitopes were specifically selected. 10 CTL, 6 HTL and 9 linear B cell epitopes were predicted on the basis of high combination scores and human MHC compatibility. These specific epitopes were then fused to construct the final multiepitope vaccine design.

Conclusion: In this study, immunoinformatics was used to develop a safe Brucella vaccine candidate. Unlike vaccines against whole pathogens, this multi-epitope design minimizes the risk of autoimmunity by eliminating regions of human homology. The inclusion of Omp31, BP26, and RplL provides broad antigen coverage. High levels of antigenicity and stability suggest that the chimeric protein can induce reliable humoral and cellular immunity. Although the in silico results are promising, further in vitro and in vivo validations are recommended to confirm prophylactic efficacy.

keywords: Brucella; RplL; Omp31; Omp28/BP26

PG-36

The role of miR-34-c and miR-10-b in lung cancer

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Background and aim: Metastatic lung cancer represents one of the most lethal malignancies worldwide. Its poor prognosis is largely attributed to rapid metastatic progression. Consequently, the identification of reliable biomarkers capable of facilitating early detection, as well as the development of effective targeted therapeutic strategies, is of critical importance. MicroRNAs are a class of noncoding RNA 20–22 nucleotides in length that regulate gene expression through mRNA binding. Several miRNAs, suchas miR-34c and miR-10b, have been implicated in tumor initiation, metastasis and apoptosis. This review aims to synthesize and evaluate the existing literature regarding the involvement of miR-34c and miR-10b in lung cancer pathogenesis.

Methods: This review was conducted using peer-reviewed articles indexed in PubMed, Google Scholar, and ScienceDirect, published between 2010 and 2025. The search strategy included the following keywords: “miR-10b” OR “miR-34c” AND “lung cancer” OR “non-small cell lung cancer” OR “NSCLC.” The initial search yielded 2851 articles, of which 2841 were excluded after screening titles and abstracts for relevance. Following the application of predefined inclusion and exclusion criteria, a total of 10 articles were selected for detailed analysis.

Results: A total of 861 patients with pathologically confirmed lung cancer were included in the analysis (mean age: 51.3 years; 39.7% male), together with seven established human lung cancer cell lines (A549, H460, H157, H1299, H23, Calu-1, and Calu-3). Clinical data demonstrated that higher miR-34c expression was significantly correlated with smaller primary tumor size, reduced stromal invasion, decreased lymph node metastasis, and better overall survival in lung cancer patients (P 0.05). Functional in vitro assays consistently supported these findings, showing that miR-34c overexpression markedly inhibited cell proliferation, migratory capacity, and invasive behavior, as confirmed by wound-healing (scratch) assays, transwell invasion assays, and MTT viability assays across all examined cell lines (P 0.05). In contrast, miR-10b upregulation was associated with enhanced tumor aggressiveness and metastatic potential. Diagnostic performance analysis identified miR-10b as a biomarker, achieving a sensitivity and specificity of 78%, highlighting its clinical relevance for disease detection.

Conclusion: This review underscores the functional heterogeneity of microRNAs in lung cancer biology, emphasizing their dual roles as tumor suppressors and oncogenic regulators. Elevated miR-34c expression emerges as a promising candidate for microRNA-based targeted therapeutic strategies, given its suppressive effects on tumor growth and invasion. Conversely, miR-10b overexpression may serve as a clinically valuable early diagnostic biomarker for lung cancer. Nevertheless, prospective multicenter studies and mechanistic investigations are required to validate these observations and facilitate their translation into clinical practice.

keywords: microRNA, miR-10-b, miR-34-c, lung cancer, NSCLC, non-small cell lung cancer

PG-37

Breast Cancer Screening in Neurofibromatosis Type 1 Patients: A Systematic Review

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Background and aim: Neurofibromatosis type 1 (NF1) is a genetic condition that significantly increases the risk of breast cancer in women (up to fivefold). Due to this heightened risk, a comprehensive approach to screening is crucial. this review summarizes current evidence on breast cancer screening for NF1 patients.

Methods: The literature search encompassed three databases—PubMed, Scopus, and Web of Science—and was limited to English-language papers published from 2015 to 2025. Review articles, letters, and conference papers were excluded. Search strategy was conducted using Medical Subject Headings (MeSH), including subsequent keywords: “Neurofibromatosis Type 1”, “Screening”, and “Breast Cancer”. Three independent researchers reviewed the identified articles. Data were extracted from the selected studies using a standard data extraction form.

Results: A total of 27 articles met the inclusion criteria from 84 primary articles. NF1 women's annual screening is suggested from ages 30 or 40 due to variable guidelines. Breast cancer screening tools for women with NF1 include mammography, MRI, supplemental ultrasound, genetic testing, and counseling. Mammography is considered an effective screening tool for women with NF1. However, the presence of high breast density complicates the interpretation of mammograms, and the risk of radiation cannot be ignored. MRI preferred when available due to density challenges. Moreover, implementing mutual awareness between women with NF1 and healthcare professionals is crucial for effective breast cancer screening and management.

Conclusion: Early and regular screening increases the chances of successful treatment and survival. A certain breast cancer screening protocol for NF1 patients must be designed.

keywords: Neurofibromatosis Type 1, Screening, Breast Cancer

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-38

A Novel Analytical Approach to Unveil Key Biomarkers in COPD: Highlighting DCN's Role in Disease Pathogenesis

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Background and aim: Chronic Obstructive Pulmonary Disease (COPD) is a prevalent respiratory condition characterized by persistent airflow limitation, commonly resulting from exposure to harmful gases. It includes emphysema, damaging alveoli, and chronic bronchitis, causing prolonged cough. Typical symptoms include shortness of breath, coughing, and mucus production. Traditional diagnostics like spirometry and imaging have limitations detecting early-stage disease. This study aims to uncover molecular insights into COPD using microarray data analysis to identify differentially expressed genes (DEGs) and potential Biomarkers.

Methods: Microarray data analysis was conducted using two datasets, GSE64614 and GSE37768, from the GEO database, encompassing a total of 259 samples across three groups: COPD patients, healthy smokers, and healthy non-smokers. To enhance analytical robustness, we performed two distinct comparisons: COPD patients vs. healthy smokers and COPD patients vs. healthy non-smokers. Data processing was conducted in R (version 4.2.2), including background correction, log2 transformation, and quantile normalization. Differential expression analysis applied a false discovery rate (FDR) threshold with p-value < 0.05 and log fold change (LogFC) ±1.34. Hub genes were identified using the STRING database and visualized in Cytoscape V3.10.2. Top hub genes were selected based on degree, closeness, and betweenness scores using the Cytohubba plugin. Additionally, miRNA-target interactions were explored using TargetScan to assess regulatory relationships potentially relevant to COPD.

Results: Differential expression analysis revealed 846 genes in the COPD vs. healthy smoker comparison and 741 genes in the COPD vs. healthy non-smoker comparison. In the first analysis, eight key hub genes were identified through Protein-Protein Interaction (PPI) network analysis using STRING and Cytoscape: LUM, TFRC, SIRPA, PDGFRA, DCN, HAVCR2, IL1R1, and KITLG. The second comparison identified five hub genes: MMP2, COL1A1, EGFR, DCN, and TIMP3, with DCN appearing in both analyses, suggesting its potential role in COPD pathology. Further analysis confirmed DCN's extracellular localization and secretory nature. miRNA-target interaction analysis highlighted several microRNAs, including hsa-mir-122-5p, hsa- mir-129-5p, hsa-mir-140-3p, and hsa-mir-222-3p, as regulators of DCN.

Conclusion: This study identified key hub genes, particularly DCN, associated with COPD through differential expression analysis and PPI network construction. The presence of DCN across both comparisons and its regulation by specific miRNAs suggests its potential role in COPD pathogenesis, particularly in extracellular matrix remodeling. These findings highlight DCN as a potential biomarker and therapeutic target, providing a molecular basis for future diagnostic and treatment strategies that could improve COPD patient outcomes.

keywords: COPD, Differential Expression Analysis, DCN, miRNA-Target Interaction, Biomarker

PG-39

MicroRNAs in Cancer: Dual Roles as Oncogenic Drivers and Tumor Suppressors with Clinical Implications

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Background and aim: MicroRNAs (miRNAs) are small non-coding RNAs that regulate post-transcriptional gene expression and exert context-dependent functions in cancer. Their dysregulation contributes to tumor initiation, progression, metastasis, and therapy resistance

Methods: The methodology involved a systematic review of literature on microRNAs (miRNAs) in cancer, utilizing key databases and specific search terms to gather relevant peer-reviewed studies. Data were extracted and categorized based on themes, including miRNA biogenesis, dysregulation, clinical applications, and therapeutic strategies. A critical appraisal was conducted to identify gaps in knowledge, ultimately integrating findings to inform future research directions and clinical applications of miRNAs.

Results: Canonical miRNA biogenesis involves transcription by RNA polymerase II, cleavage by Drosha/DGCR8, nuclear export via Exportin-5, and cytoplasmic processing by Dicer, resulting in mature miRNA incorporation into the RNA-induced silencing complex. While most miRNAs repress gene expression, subsets of “up-miRs” can enhance translation or stabilize mRNAs. Aberrant miRNA expression arises from promoter methylation, genetic mutations, impaired processing, or stress-induced signaling (e.g., hypoxia). These alterations activate oncogenic pathways, inhibit apoptosis, modulate metabolism, and reshape the tumor immune microenvironment. Circulating and exosomal miRNAs exhibit remarkable stability, making them promising minimally invasive biomarkers. OncomiRs such as miR-21, miR-155, and miR-10b are associated with early detection, aggressive phenotypes, and resistance, whereas tumor suppressor miRNAs (e.g., miR-34a, miR-126, miR-200 family) correlate with treatment response and survival. Therapeutic strategies include synthetic mimics and inhibitors delivered by nanoparticles, liposomes, or engineered exosomes. Several candidates, including Miravirsen, MRX34, and cobomarsen, have entered clinical trials; however, challenges such as

Conclusion: miRNAs are versatile regulators of cancer biology with transformative potential as diagnostic, prognostic, and therapeutic tools. Future research should resolve context-dependent duality, optimize delivery systems, and validate biomarker panels in large-scale clinical trials to enable their integration into precision oncology.

keywords: MicroRNAs, Cancer, Oncomir, Tumor Suppressors miRNA, Biomarkers, Circulating miRNAs

PG-40

The relationship between serum and tissue levels of IL-13 and TYK2 in colorectal cancer patients

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Background and aim: Colorectal cancer (CRC) is the third leading cause of death worldwide. The immune system impacts the tumor microenvironment, and identifying its components can aid in finding new biomarkers for prognosis and therapies. Interleukin 13 (IL-13), linked to tumor growth and metastasis, induces TYK2 phosphorylation. This study assessed IL-13 and TYK2 expression in CRC patients' serum and tissue, exploring their correlation with clinical and pathological factors.

Methods: The study included 105 patients with CRC and 105 healthy participants. Samples of tissue and blood were gathered. The ELISA method was employed to analyze serum levels of IL-13. The quantitative Real-Time PCR (qRT-PCR) method was utilized to evaluate the expression levels of IL-13 and TYK2 in CRC tissue samples relative to the nearby control tissue.

Results: In CRC tissue, the levels of IL-13 were reduced, while TYK2 levels were elevated compared to normal tissue. Moreover, IL-13 serum levels were reduced in CRC patients, whereas TYK2 levels were increased. A notable negative correlation was observed between the expression levels of IL-13 in serum and tissue and the stage of cancer.

Conclusion: These results suggest that IL-13 and TYK2 may play essential roles in CRC development and progression and may serve as potential biomarkers for early detection and treatment.

keywords: Colorectal cancer (CRC); Tyrosine kinase 2; IL-13

PG-41

The role of interferon-gamma and its receptors in gastrointestinal cancers

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Background and aim: Gastrointestinal malignancies represent the most common type of cancer globally. Despite extensive research into these cancers, the precise mechanisms underlying their development remain unclear. These tumors typically have a poor prognosis and are often diagnosed at advanced stages. There is a rising trend in both the incidence and mortality rates of gastrointestinal cancers, including those affecting the stomach, esophagus, colon, liver, and pancreas. In this paper, we explore the dynamic roles of IFN-γ and its receptors in gastrointestinal cancers, providing evidence that targeting IFN-γ signaling could represent a promising therapeutic strategy.

Methods: This analysis was carried out utilizing PubMed, Web of Science, Google Scholar, and Scopus to locate pertinent studies published up to March 2021. The pertinent studies were located utilizing these keywords: ["Interferon-gamma or IFN-γ"] AND ["Digestive cancers or Gastrointestinal cancer"] AND ["Oral cancer or gastric cancer or colorectal cancer or hepatocellular carcinoma or pancreatic cancer or esophageal cancer"]. We evaluated studies examining the connection between IFN-γ and digestive tract cancers, those with a case-control framework, and studies presenting specific genotype frequencies for cases and controls or text that enabled these figures to be derived. Case-only studies, meta-analyses lacking available data, case reports, or review articles were all omitted A total of 118 articles were found on PubMed, Web of Science, Google Scholar, and Scopus. Following the review of titles, abstracts, and complete texts, 75 articles were incorporated into our research.

Results: The IFN-γ receptor consists of two IFN-γR1 chains and two IFN-γR2 chains. When IFN-γ binds to its receptor, it triggers the oligomerization of the intracellular domains of IFN-γR2 and subsequent transphosphorylation with IFN-γR1. This process activates downstream signaling components, specifically JAK1 and JAK2. The activated JAKs phosphorylate the receptor, creating binding sites for STAT1. Subsequently, STAT1 is phosphorylated by JAK, leading to the formation of STAT1 homodimers (also known as gamma-activated factors or GAFs), which translocate to the nucleus to regulate gene expression.

Conclusion: IFN-γ is significant in controlling both innate and adaptive immune responses to tumor cells, .viruses, and bacteria, while also inhibiting pathological inflammatory reaction

keywords: IFN-γ,Gastrointestinal,Malignancies

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-42

Association between ADIPOQ rs17366743 polymorphism and obesity-related metabolic parameters in men

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Background and aim: Adipose tissue functions as an active endocrine organ that produces various adipokines, including adiponectin. The ADIPOQ gene, which encodes adiponectin, plays an important role in regulating glucose and lipid metabolism. The rs17366743 polymorphism located in exon 3 of this gene may affect obesity-related metabolic outcomes by altering the structure of the adiponectin protein. The aim of this study was to investigate the association of the rs17366743 polymorphism of the ADIPOQ gene with obesity and biochemical and anthropometric parameters.

Methods: This investigation was designed as a male-only, observational cross-sectional study. Participants were stratified according to body mass index into an obesity group (BMI ≥25 kg/m²; n = 80) and a normal-weight group (BMI 25 kg/m²; n = 100). Inclusion criteria comprised individuals aged 18 years or older, fasting triglyceride concentrations below 400 mg/dL, no clinical evidence of cardiovascular disease or hypertension, and the absence of prior treatment with metabolic medications. Anthropometric indices including weight, BMI, waist circumference, hip circumference and waist-to-hip ratio as well as biochemical parameters including lipid profile, fasting blood glucose, adiponectin and cortisol were measured. Determination of polymorphism genotypes was performed by the PCR-RFLP method and statistical analysis was performed using SPSS software.

Results: The results showed that the rs17366743 polymorphism was not significantly associated with obesity and anthropometric indices. However, the levels of total cholesterol and LDL-C were significantly higher in TT genotype carriers than in the AA+AT group (P0.05). Other biochemical parameters including triglycerides, HDL-C, fasting blood glucose, cortisol and adiponectin did not show significant differences between genotypes.

Conclusion: The findings of this study suggest that the rs17366743 polymorphism of the ADIPOQ gene is not directly associated with obesity but may influence obesity-related metabolic parameters, particularly lipid metabolism, especially increasing LDL-C and total cholesterol. Further studies with larger sample sizes are warranted.

keywords: Adiponectin, Triglycerides, high-density lipoproteins, Cholesterol.

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July 20-23, 2026

PG-43

The relationship between ADIPOQ gene rs17300539 polymorphism and obesity in men

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Background and aim: Obesity is one of the most important public health challenges problems and results from a complex interaction between genetic and environmental factors. The ADIPOQ gene, which encodes adiponectin, plays a critical role in regulating energy metabolism, insulin sensitivity, and lipid homeostasis. The rs17300539 polymorphism is one of the common variants of this gene and may be associated with metabolic alterations related to obesity. The aim of this study was to investigate the association between the rs17300539 polymorphism of the ADIPOQ gene and obesity, as well as biochemical and anthropometric parameters in men.

Methods: This cross-sectional case–control study was conducted exclusively in men. Participants were categorized into obese (BMI ≥25 kg/m²; n = 80) and non-obese (BMI 25 kg/m²; n = 100) groups based on body mass index. Eligible participants were adults aged ≥18 years with serum triglyceride levels 400 mg/dL, no documented history of cardiovascular disease or hypertension, and no prior use of metabolic-related medications. In addition, participants were classified into AA+GA and GG groups based on the rs17300539 polymorphism genotype, and the study parameters were compared between these groups. Anthropometric measurements and biochemical parameters were assessed using standard methods. Serum adiponectin and cortisol levels were measured by enzyme-linked immunosorbent assay (ELISA). Genomic DNA was extracted from peripheral blood, and genotyping of the rs17300539 polymorphism was performed using the polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) method. Statistical analyses were conducted using SPSS software.

Results: The rs17300539 polymorphism showed no significant association with obesity or anthropometric indices. No significant differences were observed in biochemical parameters, including total cholesterol, triglycerides, LDL-C, HDL-C, and fasting blood glucose, between different genotypes. However, cortisol (P = 0.067) and adiponectin (P = 0.088) levels exhibited a trend toward variation among genotypes, although these differences did not reach statistical significance.

Conclusion: The findings of this study suggest that the rs17300539 polymorphism of the ADIPOQ gene is not directly associated with obesity in men. Nevertheless, this genetic variant may influence obesity-related metabolic parameters, and further investigations in larger populations are warranted to clarify its subtle metabolic effects.

keywords: ADIPOQ protein, Cortisol, polymorphism rs17300539, Obesity.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-44

Germline and Somatic DDR Mutations: Insights into Breast and Hematologic Malignancies Pathogenesis

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Background and aim: Cancer develops through accumulating genetic alterations, shaped by both germline susceptibility and somatic mutations. Continuous endogenous and environmental DNA damage drives genomic instability, particularly within DNA damage response (DDR) pathways—central hallmarks of tumorigenesis. Emerging evidence highlights the interplay between germline variants and somatic hits in DDR genes as a key driver of cancer development. Breast cancer, the most common malignancy in women, and hematologic cancers, a group of aggressive disorders, both show strong associations with DDR defects.This abstract examines germline and somatic mutations in BRCA1/2, PALB2, and TP53, emphasizing their dual role in the pathogenesis of breast and hematologic malignancies

Methods: This study is a narrative review focusing on germline and somatic mutations in DNA damage response (DDR) genes and their dual role in breast and hematologic malignancies. A total of twenty relevant publications were identified through systematic searches of PubMed, Google Scholar, and Scopus using predefined search terms. The search strategy included essential keywords such as “DNA damage response,” “DDR mutations,” “germline mutations,” “somatic mutations,” “BRCA1/2,” “PALB2,” “TP53,” “breast cancer,” and “hematologic malignancies.” Retrieved studies were screened and included for detailed review and analysis.

Results: In BRCA- and PALB2-associated breast cancers, a subset may arise from somatic TP53 loss, with tumor progression further accelerated by defects in the BRCA1–PALB2–BRCA2 axis. While most somatic PALB2 mutations in breast cancers were moderate-risk missense variants, heterozygous germline loss-of-function (LOF) mutations were high-risk, more prevalent, and generally occurred without accompanying somatic PALB2 alterations, LOH, or hypermethylation. These findings underscore the independent pathogenic role of germline PALB2 variants and their relevance for cancer screening, diagnostics, and potential PARP inhibitor–based therapy. In hematologic malignancies, the identified PALB2 variant causing G2/M cell-cycle arrest provides pathogenic evidence for early-onset and rare extramedullary AML. Overall, these results highlight the dual impact of germline and somatic DDR gene alterations in driving tumorigenesis across both breast and hematologic cancers.

Conclusion: These findings underscore the critical role of germline and somatic mutations in DDR genes (BRCA1/2, PALB2, TP53) in driving tumorigenesis across both breast and hematologic malignancies. Germline PALB2 variants represent high-risk alterations with independent pathogenic potential, while somatic TP53 and DDR pathway defects contribute to tumor progression. The dual impact of these mutations highlights the interplay between inherited susceptibility and somatic evolution, early detection, and precision therapy, including potential PARP inhibitor use. Understanding these mechanisms provides valuable insights into the shared vulnerabilities of breast and hematologic cancers.

keywords: DNA damage response (DDR); Breast cancer; Hematologic malignancies; Genomic instability

PG-45

Non-Diagnostic Results Following Cleavage-Stage Embryo Biopsy: A Hypothesis Review on Their Potential as a Biomarker of Impaired Developmental Competence

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Background and aim: Non-diagnostic or ND outcomes pose one of the significant challenges in the field of preimplantation genetic diagnosis, or PGT. ND has traditionally been considered an artifact, but certain patterns have been observed depending on the stage of biopsy. In day 3 cleavage-stage biopsies, ND is commonly associated with arrested embryonic development.

Methods: Objective & Rationale: This review introduces a new concept: in cleavage stage biopsies, an ND may be a biological indicator of embryo compromise. Unlike Day 5/6 trophectoderm (TE) biopsies, where the embryo is vitrified or transferred directly, without the opportunity to view post-biopsy growth, Day 3 embryos are cultured an additional 1–2 days to develop to the blastocyst stage.

Results: Hypothesis: The procedural window in Day-3 biopsies defines ND's biological significance. A failure to achieve a genetic diagnosis from one blastomere may indicate profound cell pathology (such as DNA fragmentation and mitotic failure) making it difficult to amplify genes and divide cells, as is evidenced in ND as an early indicator of arrest in both processes.

Conclusion: Conclusion: ND should be evaluated specifically in cleavage-stage PGT. ND should be evaluated not merely as a failure in technique, but as a prognostic indicator of developmental potential. This might have implications regarding clinical practice and counseling patients. It requires research findings concerning a correlation of ND with molecular profiling, and follow-up of embryos Day-3 biopsied.

keywords: PGT, Not-Detectable, Biopsy, Embryology

PG-46

Differential expression of FOXO1 and FOXO3 genes in endometrial tissues of infertile woman with hydrosalpinx undergoing laparoscopic salpingectomy

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Background and aim: Background: Hydrosalpinx, a fallopian tube disease, reduces embryo implantation rates by approximately 50%. Although the precise mechanism remains unclear, poor endometrial receptivity is considered the most accepted explanation. FOXO transcription factors, particularly FOXO1 and FOXO3, are critical for endometrial decidualization. Objective: This study aimed to evaluate the differential expression of FOXO1 and FOXO3 genes in the endometrial tissue of infertile women with hydrosalpinx before and after laparoscopic salpingectomy, compared to healthy controls.

Methods: Methods: In this prospective quasi-experimental study, 15 infertile women with unilateral hydrosalpinx were enrolled, and endometrial biopsies were obtained from the same patients before and 4 months after salpingectomy. Fifteen fertile women served as controls. Samples were collected during the implantation window. Expression profiles were quantified using real-time quantitative PCR (qPCR), normalized to 18SrRNA after validation of reference gene stability, and analyzed using the 2^(-ΔΔCt) method. All reactions were performed in technical duplicates. Statistical analysis was performed using SPSS software (version 27); the Mann-Whitney test was used to compare expression between independent groups, and the non-parametric Wilcoxon signed-rank test was applied to evaluate changes before and after salpingectomy, with significance set at P0.05.

Results: Results: The expression of FOXO1 mRNA was found to be significantly reduced in patients with hydrosalpinx compared with controls (P = 0.024). Following salpingectomy, a significant restoration in FOXO1 expression levels was observed (P = 0.015). Conversely, FOXO3 expression was significantly upregulated in the hydrosalpinx group compared with controls (P = 0.004) and significantly decreased post-surgery (P = 0.005).

Conclusion: Conclusion: These findings suggest that dysregulation of FOXO1 and FOXO3 may contribute to impaired endometrial receptivity in hydrosalpinx, and that salpingectomy may partially restore molecular balance.

keywords: Keywords: Hydrosalpinx, Salpingectomy, Gene expression, FOXO1, FOXO3

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PG-47

MXene-Based Theranostic Platforms for Dual miRNA Targeting in Metastatic Bladder Cancer

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Background and aim: Metastatic bladder cancer (mBC) remains difficult to control due to dysregulated microRNAs that promote epithelial–mesenchymal transition, immune escape, and therapy resistance. Among them, miR-21 acts as a potent oncomiR by activating PI3K/AKT signaling, whereas miR-200c suppresses metastasis by maintaining epithelial identity and promoting apoptosis. Simultaneous inhibition of miR-21 and restoration of miR-200c represents a rational therapeutic concept but is limited by RNA instability and inefficient delivery. This study aims to summarize and structurally analyze current evidence supporting MXene-based platforms as dual-function systems for miRNA delivery, sensing, and photothermal-assisted therapy in metastatic bladder cancer.

Methods: A structured literature review was conducted using PubMed, Web of Science, and Scopus up to 2025. Search terms included combinations of “MXene”, “microRNA”, “miR-21”, “miR-200c”, “bladder cancer”, “theranostics”, “photothermal therapy”, and “biosensing”. Original experimental studies, translational reports, and high-quality reviews addressing MXene-based RNA delivery, miRNA detection, surface functionalization, or photothermal applications were considered. Studies were screened for relevance to mechanisms of miRNA regulation, carrier design, intracellular delivery, and therapeutic performance. Data were qualitatively synthesized to identify shared molecular mechanisms, delivery strategies, and translational trends. Emphasis was placed on surface engineering approaches, ion intercalation, polymer or ligand modification, and multimodal platforms enabling combined diagnosis and therapy.

Results: MXene-based platforms exhibit high miRNA-loading capacity, excellent electrical conductivity, and tunable surface chemistry, enabling their use as integrated theranostic systems. Surface modification with polymers, targeting ligands, or intercalated ions improves colloidal stability, cellular uptake, and controlled intracellular release. Reported studies demonstrate that MXene-assisted delivery can suppress oncogenic miR-21 while restoring miR-200c activity, resulting in reduced epithelial–mesenchymal transition, impaired invasion, and enhanced apoptotic signaling. Their intrinsic photothermal properties further enable near-infrared–triggered tumor ablation and promote endosomal escape of therapeutic RNAs. Several platforms also allow electrochemical or optical monitoring of miRNA dynamics, supporting real-time feedback during treatment. Preclinical findings indicate synergistic effects between gene modulation and photothermal therapy, with improved tumor suppression, enhanced therapeutic precision, and reduced off-target toxicity. Nevertheless, challenges remain, including oxidative instability, dose-dependent cytotoxicity, and variability in synthesis, driving ongoing optimization of coatings and fabrication strategies.

Conclusion: MXene-based theranostic platforms represent a promising strategy for dual targeting of miR-21 and miR-200c in metastatic bladder cancer by uniting delivery, sensing, and photothermal therapy within a single nanosystem. Advances in surface engineering and stabilization have substantially improved their safety and functionality. Although translational barriers persist, emerging scalable synthesis and biocompatible designs support future clinical development. These platforms offer a conceptual framework for precision oncology approaches that integrate molecular profiling with responsive treatment, potentially improving outcomes for patients with aggressive bladder cancer.

keywords: MXene, miRNA, Bladder Cancer, Cancer, cellular signaling

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PG-48

Menin Inhibitors in Relapsed Acute Leukemias with KMT2A or NPM1 Alterations

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Background and aim: Acute leukemias, including AML and ALL with specific genetic alterations such as KMT2A rearrangements and NPM1 mutations, represent a high-risk subgroup with poor prognosis, particularly in relapsed or refractory (R/R) settings, and show limited response to standard therapies. Leukemogenic activity in these subtypes depends on the interaction between Menin and KMT2A proteins, leading to aberrant expression of HOX and MEIS1 genes and blocking hematopoietic cell differentiation. Menin inhibitors, including Revumenib and Ziftomenib, are oral and selective agents that disrupt this interaction, restoring normal differentiation. This study aims to evaluate the efficacy, molecular responses, and clinical outcomes of these inhibitors in

Methods: This systematic review was conducted to summarize the clinical evidence on the use of Menin inhibitors in acute leukemias. Medical science databases, including PubMed, PMC, and relevant conference proceedings, were searched for studies published between 2022 and 2024. The included studies comprised phase I and phase II clinical trials, review articles, and conference abstracts involving adult or pediatric patients with AML or ALL harboring KMT2A rearrangements or NPM1 mutations treated with Menin inhibitors such as Revumenib or Ziftomenib. Data on patient characteristics, treatment response, molecular outcomes including MRD status, and safety profiles were extracted. Given the heterogeneity among the studies, a descriptive qualitative analysis was performed.

Results: In this systematic review, a series of phase I and II clinical trials and conference reports investigating the efficacy of Menin inhibitors, including Revumenib and Ziftomenib, in acute leukemias were evaluated. The study population primarily included patients with relapsed or refractory AML or ALL harboring KMT2A gene rearrangements or NPM1 mutations. The results demonstrated that treatment with Menin inhibitors led to a significant reduction in leukemic blast counts and achieved complete or partial therapeutic responses in a substantial proportion of patients. In several studies, clinical responses were associated with improvements in molecular markers, including decreased HOX and MEIS1 gene expression and achievement of MRD negativity. Regarding safety, most reported adverse events were mild to moderate and manageable, with cytopenias and differentiation syndrome being the most commonly observed.

Conclusion: The results of this systematic review suggest that Menin inhibitors, including Revumenib and Ziftomenib, represent targeted therapeutic approaches with significant clinical efficacy in patients with acute leukemias harboring KMT2A rearrangements or NPM1 mutations, particularly in relapsed or refractory cases. In addition to improving clinical responses, these agents have been associated with favorable molecular and immunological outcomes and acceptable safety profiles. However, larger prospective clinical studies and further evaluation of combination treatment strategies are required to define the optimal role of Menin inhibitors within the treatment algorithms for acute leukemias.

keywords: Menin inhibitors; Acute leukemia; KMT2A rearrangement; NPM1 mutation; Targeted therapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-49

Anti-Cancer Potential of Artemisia absinthium Aqueous Extract : Apoptosis Induction ,Inflamation Modulation, and Cell Cycle Arrest in SW480 and Caco-2 Colorectal Cancer Cells

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Background and aim: Colorectal cancer is one of the leading causes of mortality worldwide. Due to the limitations and side effects associated with current treatment modalities such as chemotherapy, radiotherapy, and surgery, researchers are seeking novel and less invasive therapeutic approaches. This study aimed to investigate the effect of the hydroalcoholic extract of Artemisia absinthium on c-MYC expression and the cell cycle in Caco-2 and SW480 cell lines. c-MYC is a key proto-oncogene that is highly overexpressed in various cancers, particularly colorectal cancer.

Methods: SW480 and Caco-2 cell lines were treated with various concentrations (50–1000 µg/ml) of Artemisia absinthium extract. The MTT assay was performed to determine the IC_{50} values. Furthermore, c-MYC gene expression was analyzed using real-time PCR, and cell cycle distribution was assessed by flow cytometry following propidium iodide staining.

Results: The IC_{50} values for the SW480 cell line were 316.0, 318.3, and 328.5 µg/ml at 24, 48, and 72 hours post-treatment, respectively, while for the Caco-2 cell line, they were 463.4, 465.4, and 477.3 µg/ml. These results indicate that the cytotoxic effects of Artemisia absinthium extract are not time-dependent, as dose–response curves remained similar across all time points, with no statistically significant differences in IC_{50} values (P 0.05). In addition, the fold change in c-MYC expression in the SW480 cell line was found to be 0.166, 0.159, and 0.160 at 24, 48, and 72 hours post-treatment, respectively. Similarly, in the Caco-2 cell line, the fold change values were 0.0403, 0.0542, and 0.0457 at 24, 48, and 72 hours post-treatment, respectively. Furthermore, the flow cytometry analysis demonstrated cell cycle arrest at the G1 phase in both cell lines.

Conclusion: The aqueous extract of Artemisia absinthium effectively reduced c-MYC gene expression, thereby inducing apoptosis and suppressing colorectal cancer cell growth. The downregulation of c-MYC expression was also associated with cell cycle arrest at the G1 phase, highlighting the extract's potential as a therapeutic candidate against colorectal cancer.

keywords: Artemisia absinthium, apoptosis, colorectal cancer, cell cycle, c-MYC

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-50

Gut Dysbiosis and Epigenetic Remodeling: Implications for the Pathophysiology of Insomnia

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Background and aim: The human gut microbiota is a diverse microbial ecosystem formed early in life that plays an essential role in metabolic homeostasis, energy regulation, maintenance of intestinal barrier integrity, and immune system function. Alterations in microbial structure and activity, referred to as gut dysbiosis, have been linked to a range of metabolic and neurobehavioral conditions. Circadian rhythms coordinate physiological and behavioral functions and are critical for sleep regulation, with insomnia partly arising from circadian misalignment. Increasing evidence indicates a reciprocal relationship between the gut microbiota and circadian regulation. This review highlights current evidence connecting gut dysbiosis, epigenetic mechanisms, and insomnia.

Methods: Twenty relevant studies examining the interplay between "gut dysbiosis, epigenetic modifications, and insomnia" were identified through systematic searches of the PubMed, Web of Science, and Scopus databases using predefined keywords. Eligible articles were selected and included for qualitative review and analysis.

Results: Based on findings derived from multiple observational and population-based studies, significant associations were identified between specific gut microbial taxa, particularly Eggerthella and members of the Coriobacteriaceae family, and DNA methylation at distinct CpG sites. These epigenetic alterations involved both DNA methylation and histone-related pathways and were linked to genes associated with circadian regulation, inflammatory signaling, and neurotransmitter systems. In parallel, gut microbiota–derived metabolites were shown to contribute to gut–brain axis signaling through endocrine, neuronal, and immune pathways. Alterations in bacterial genera involved in short-chain fatty acid and amino acid metabolism, including Bacteroides, Prevotella, Coprococcus, and Faecalibacterium, were associated with neurobehavioral regulation. Regarding sleep-related outcomes, multiple studies reported associations between gut microbiota imbalance and reduced sleep quality, increased Firmicutes-to-Bacteroidetes ratios, impaired intestinal barrier function, and elevated inflammatory markers. Functional analyses further linked sleep disturbances to microbial metabolic pathways related to L-arginine, L-tryptophan, vitamin B1 biosynthesis, and GABA metabolism.

Conclusion: Overall, existing evidence indicates a close and complex relationship between gut dysbiosis, epigenetic regulation, and sleep disturbances, suggesting that the gut microbiota may function as an important biological interface linking metabolic and neurobehavioral processes. The bidirectional interaction between microbial composition and circadian–sleep regulation highlights the multifaceted mechanisms underlying insomnia. Although current findings are largely associative, they emphasize the necessity of future well-designed longitudinal and mechanistic studies to clarify causal pathways and to better define the epigenetic mechanisms through which gut microbiota may influence sleep regulation.

keywords: Gut dysbiosis; Epigenetic modifications; Insomnia; Circadian rhythm

PG-51

Silymarin's Hepatoprotective Impact against Hyperglycemia Induced Inflammation in HepG2 Cells

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Background and aim: : Silymarin, obtained from milk thistle (Silybum marianum), shows significant hepatoprotective effects, particularly against hyperglycemia-induced inflammation in HepG2 cells. Silymarin has antioxidant and anti-inflammatory properties that are important for reducing the psychological effects of many diseases, including hyperglycemia and nonalcoholic fatty liver disease (NAFLD). In addition, silymarin has been shown to reduce liver enzyme levels and improve histological parameters, indicating its protective role against hepatotoxicity.

Methods: Determination of HepG2 cell viability using MTT assay. The effect of different concentrations of silymarin on the expression of DPP-4 and inflammatory markers (TNF-α, IL-6 and NF-κB) was evaluated using real-time PCR (RT-qPCR) after RNA extraction.

Results: Silymarin treatment reduced the expression of DPP-4, TNF-α, NF-κB and IL-6 in HepG2 cells under high glucose conditions compared to the control group

Conclusion: The results show that silymarin can reduce inflammation caused by hyperglycemia by downregulating inflammatory genes and DPP-4 in HepG2 cells, suggesting the potential of silymarin as a therapeutic agent to control hyperglycemia-related complications.

keywords: Silymarin, Inflammation, Hyperglycemia, Hepatocellular carcinoma, HepG2 cells

PG-52

The role of genetics on Cancer development

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Background and aim: This research was conducted with an applied analytical goal to examine the role of genetics in cancer. Genetic mutations play a role in the development of all cancers. Most of these mutations occur during an individual's lifetime, but some genetic mutations are inherited from parents. Approximately 5 to 10 percent of cancer cases occur due to mutations in certain cancer-predisposing genes, and conducting genetic testing helps identify individuals who carry these mutations."

Methods: The disease of cancer is fundamentally built upon genetic disorders. For this reason, they are currently assigned a very important role in this category of diseases. These disorders can range from large (at the molecular level) to the level of a chromosome, or very small, down to the nucleotide level, which ultimately leads to irreversible changes in the cell. The technical methods commonly used in cancer genetics are mainly based on molecular or cytogenetic investigations. Based on this, we will be able to screen familial cancers within the family, and in some cases, we will be able to aid in disease diagnosis, assessment of recurrence probability, evaluation of treatment response, and prognosis prediction for cancer. On the therapeutic side, gene therapy methods are mainly used as supplementary, rather than definitive, treatments."

Results: Genetic testing, which is a simple blood test, is used to accurately estimate the risk level for cancer. Genetic testing assists the treating physician in making important medical decisions. Performing genetic testing is not recommended for everyone who receives counseling; the final decision regarding whether to proceed with it is made solely by the individual's choice during a genetic counseling session." This type of cancer risk, which arises due to the sensitivity of an individual's specific genes to environmental factors, is called 'familial risk'."

Conclusion: Currently, there are no diagnostic methods or tests available that can detect the hereditary probability of familial cancers; consequently, physicians rely solely on the patient's family history regarding cancer incidence."

keywords: Genetic testing, genetic disorders, Cancer, vulnerability

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-53

ASMTL-AS1 Regulatory Network Analysis for the Identification of Novel Prognostic Biomarkers in Chemoresistant Breast Cancer

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Background and aim: Chemotherapy resistance remains a major challenge in breast cancer treatment and is associated with poor clinical outcomes. Increasing evidence suggests that lncRNAs (long non-coding RNAs) play a crucial role in cancer treatment response by regulating gene expression. This study aimed to investigate potential prognostic biomarkers related to chemoresistance in the ASMTL-AS1-associated regulatory network.

Methods: ASMTL-AS1-associated miRNAs were identified using the miRNet database, and target genes associated with miRNAs were predicted through miRWalk (miRTarbase overlap enabled, score = 0.95). Gene set enrichment analysis of miRNAs gene targets (union) was performed in DAVID. Also, miRNA-protein–protein interaction network of gene targets made using STRING v12.0, and analyzed in Cytoscape V.3.10.4. For validation, the GSE76540 dataset comparing doxorubicin-sensitive and doxorubicin-resistant breast cancer cells was analyzed using GEO2R (p-value 0.05, logFC ≤ -1). Intersection analysis was performed between miRNA target genes and downregulated differentially expressed genes. Finally, the ROC plotter was used to find genes predicting chemotherapy response in breast cancer patients.

Results: Three miRNAs, including miR-1343-3p, miR-342-3p, and miR-6783-3p, were identified as potential targets of ASMTL-AS1. These miRNAs targeted 144 genes, which were mainly involved in important molecular functions like enzyme binding, biological processes like positive regulation of macromolecule biosynthetic process, and KEGG pathways like Hippo signaling. Network analysis identified thirteen hub nodes (11 mRNAs and 2 miRNAs) based on degree, betweenness centrality, and closeness centrality. Dataset analysis revealed 3,737 downregulated genes in doxorubicin-resistant breast cancer cells and intersection analysis identified PIK3R1, TGFBR1, and CBX5 as common targets. Only the expression of PIK3R1 (targeted by both of the hub miRNAs) was positively correlated with response to chemotherapy in breast cancer patients.

Conclusion: These findings suggest that PIK3R1, as a central target in the ASMTL-AS1 regulatory network, represents a potential prognostic biomarker for the determination of breast cancer patients' response to chemotherapy.

keywords: Breast Neoplasms; Drug Resistance; ASMTL-AS1; Protein Interaction Maps; PIK3R1

PG-54

Investigation of the Chenopodium Botrys Essential Oil cytotoxic effects on Cervical Cancer Cells

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Background and aim: Targeting apoptosis and cell cycle dysregulation has become a central approach in modern cancer therapy. In recent years, plant-derived essential oils have attracted growing attention as potential anticancer agents due to their rich composition of bioactive compounds and multitarget mechanisms of action. This study aimed to investigate the cytotoxic and apoptosis-inducing effects of Chenopodium botrys essential oil on human cervical cancer (HeLa) cells and explored the molecular pathways involved.

Methods: The essential oil of Chenopodium botrys was extracted and chemically characterized by gas chromatography–mass spectrometry (GC–MS). Cytotoxic effects were evaluated using MTT assays. Apoptosis induction and cell cycle distribution were analyzed by flow cytometry. In addition, the expression levels of key genes involved in apoptosis and cell cycle regulation were assessed using real-time quantitative PCR.

Results: GC–MS analysis revealed that α-eudesmol, elemol, elemol acetate, and α-chenopodiol-6-acetate were the major constituents of the essential oil. Treatment with C. botrys essential oil led to a significant, concentration-dependent reduction in HeLa cell viability. Flow cytometric analysis demonstrated a marked accumulation of cells in the sub-G1 phase, indicating apoptosis induction. At the molecular level, treatment resulted in upregulation of p53, p21, Bax, and caspase-3, along with downregulation of Bcl-2, thereby increasing the Bax/Bcl-2 ratio.

Conclusion: Overall, these findings suggest that Chenopodium botrys essential oil exerts notable anticancer effects in cervical cancer cells by promoting mitochondrial-mediated apoptosis and inducing cell cycle arrest.

keywords: Chenopodium botrys, Essential Oil, Apoptosis, HeLa Cell.

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-55

Evaluatian of the totoxicity and induction of apoptosis by different concentrations of 7-iso pentenyl oxy-coumarin on Hela, HCT116and SW48cell lines.

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Background and aim: Cancer remains a major global health challenge, emphasizing the need for more effective and selective therapeutic agents. Natural compounds have attracted considerable attention as potential anticancer drugs due to their diverse chemical structures and biological activities. Among them, coumarin derivatives have shown promising antiproliferative and pro-apoptotic effects in various cancer models. In this study, the cytotoxic and apoptosis-inducing effects of 7-isopentenyloxycoumarin, a prenyloxycoumarin derivative, were investigated in human cervical and colorectal cancer cell lines.

Methods: HeLa, SW48, and HCT116 cancer cell lines, along with peripheral blood mononuclear cells (PBMCs), were cultured in DMEM supplemented with 10% fetal bovine serum, penicillin (100 µg/mL), and streptomycin (100 µg/mL). Cells were treated with increasing concentrations of 7-isopentenyloxycoumarin for defined time intervals. Cell viability was evaluated using the MTT assay. Apoptosis induction was assessed by propidium iodide (PI) staining of fragmented DNA followed by flow cytometric analysis and quantification of the sub-G1 cell population.

Results: Treatment with 7-isopentenyloxycoumarin significantly reduced cell viability in HeLa and SW48 cell lines in a time- and concentration-dependent manner (p 0.001). In contrast, no significant cytotoxic effects were observed in HCT116 cells or PBMCs, indicating selective anticancer activity. Flow cytometric analysis revealed a marked increase in the sub-G1 cell population in treated HeLa and SW48 cells compared with untreated controls, suggesting that the observed cytotoxicity was partly mediated through apoptosis induction.

Conclusion: The findings of this study demonstrate that 7-isopentenyloxycoumarin selectively inhibits the growth of HeLa and SW48 cancer cells while sparing normal PBMCs. This inhibitory effect is at least partially mediated by apoptosis induction and occurs in a dose- and time-dependent manner. These results highlight the potential of 7-isopentenyloxycoumarin as a promising natural compound for further investigation in anticancer research.

keywords: Key Words: Apoptosis, HCT116 cell line, Hela cell line, 7-Isopenthenyloxycoumarin,

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July 20-23, 2026

PG-56

Evaluating Integrative Approaches for Microarray and RNA-Seq Data Analysis

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Background and aim: Genome-scale expression readouts enable biomarker discovery for disease diagnosis, prognosis, and therapy-response prediction. Advancements in whole-transcriptome profiling have positioned microarray and RNA-Seq as high-throughput technologies with distinct statistical properties and platform-specific biases. While RNA-Seq provides deeper dynamic range, microarrays offer extensive historical datasets enabling large-scale comparisons. Integrative analysis of mixed platform data remains methodologically challenging due to inherent distributional and technical differences. Recent computational frameworks and cross-platform normalization strategies, facilitate joint analysis of array and sequencing data. This review aims to evaluate methods to guide robust integration strategies for heterogeneous gene expression datasets in biomedical research.

Methods: A comprehensive literature search of PubMed, MEDLINE, Scopus, Web of Science, Embase, and Google Scholar (from inception to December 2025) was conducted to identify studies evaluating methods for integrating microarray and RNA-seq gene expression data. Search strategies combined controlled vocabulary (MeSH) and keywords using Boolean operators, focusing on terms like “microarray,” “RNA-seq,” and cross-platform concepts (“integration,” “normalization,” “batch effect” and “platform-harmonization methods”), while excluding single-cell sequencing studies. Titles, abstracts, and full texts were screened based on predefined eligibility criteria, and reference lists of relevant studies were manually reviewed to capture additional sources.

Results: Across included studies, cross-platform integration methods clustered into distribution-matching, rank-based harmonization, feature-wise mapping, and probe-region summarization approaches. Quantile normalization (QN) aligns order statistics so RNA-seq values are reassigned to the microarray target distribution, enabling mixed-platform training in multiple benchmarks. Training Distribution Matching (TDM) transforms log-scale RNA-seq to match the training microarray distribution while minimizing distortion of inter-feature structure, and was repeatedly reported as robust for supervised/unsupervised learning. Rank-In converts each sample to an internal rank profile, applies intensity weighting, and uses Singular Value Decomposition (SVD)-based adjustment to remove technology-driven effects, improving cross-platform Differentially Expressed Genes (DEG) concordance in mixed datasets. Feature-Specific Quantile Normalization (FSQN) performs gene-wise quantile mapping so each RNA-seq feature follows the microarray-trained distribution, supporting high-accuracy subtype classification. Probe Region Expression Estimation Based on Sequencing (PREBS) estimates expression from RNA-seq reads overlapping array probe regions and summarizes them with microarray-style algorithms, increasing similarity to paired arrays.

Conclusion: No single approach uniformly outperforms the others for integrating microarray and RNA-seq; method choice is best driven by the downstream objective. Distribution-matching strategies (QN, TDM) were most consistently reported to support mixed-platform model training, whereas Rank-In appeared particularly effective for mitigating technology-driven artifacts and improving DEG concordance. Feature/probe-aware methods (FSQN, PREBS) offer targeted compatibility when leveraging legacy microarray classifiers or maximizing comparability to paired arrays. Standardized, task-specific benchmarks and transparent pipelines are needed to translate cross-platform integration into robust biomarker discovery.

keywords: Microarray; RNA-Seq; Cross-platform integration

PG-57

A Case-Series Study on the Impact of Sperm Parameters (Age, Morphology, etc.) on Sperm DNA Fragmentation.

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Background and aim: Sperm DNA fragmentation index (DFI) is recognized as a major contributor to male factor infertility, recurrent implantation failure (RIF), and recurrent pregnancy loss (RPL), even in cases where standard semen parameters are within normal ranges according to WHO criteria (2021). The present study aimed to evaluate the role of sperm DNA fragmentation assessment and its association with conventional sperm parameters, as well as to emphasize the potential value of incorporating DFI testing into routine assisted reproductive technology (ART) practice to improve clinical outcomes.

Methods: This pilot case-series study included six couples (n = 6) with a mean sperm count of 25–35 × 10^6, high sperm DNA fragmentation index (DFI ≥ 15%, measured using a sperm DNA fragmentation assessment method), and a mean age range of 22–40 years. To evaluate DFI, after staining the spermatozoa, 300 sperm cells were counted on each slide, and the DFI percentage was calculated using the formula: number of sperm with DNA fragmentation / total number of counted sperm × 100. Morphology assessment was performed during the initial hours after sample collection by preparing slides and examining them using light microscopy.

Results: Case-based analysis revealed both direct and inverse associations between sperm DNA fragmentation levels and conventional sperm parameters, including age and morphology. One of the notable findings was the presence of high DFI values despite normal standard semen parameters. Additionally, increasing male age showed a direct positive correlation with higher sperm DFI, whereas a decrease in the percentage of morphologically normal sperm was inversely associated with increased DNA fragmentation.

Conclusion: The integration of advanced sperm assessment techniques, particularly sperm DNA fragmentation testing, alongside conventional semen analysis may effectively mitigate the negative impact of elevated baseline DFI on embryo development and fertilization outcomes. This optimized diagnostic and selection approach represents a promising therapeutic pathway for couples experiencing low fertilization rates and high sperm DNA fragmentation. Based on available case-series and review evidence, it is recommended that sperm DNA fragmentation assessment be incorporated more systematically into sperm selection strategies for ART, as it may play a significant role in improving fertilization outcomes.

keywords: DNA Fragmentation,Sperm,infertility, Sperm Conte,Morphology

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-58

A miRNA–mRNA Signature for Radiation Biodosimetry Based on Transcriptome Analysis

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Background and aim: Accurate assessment of the biological effects of ionizing radiation is vital in chronic and acute exposures. However, existing biodosimetry approaches are limited. As an alternative, molecular signatures from gene regulatory responses offer another strategy. In particular, microRNAs, which are epigenetic regulators of mRNA expression, may show promise as a biodosimetry tool, as they capture both the exposure and the biological impact in response to radiation-induced stress. Therefore, such biomarkers could improve assessments and support more informed clinical and public health decisions.

Methods: The GSE55955 dataset (RNA expression changes 4 hours after exposure to 60 Gy of ionizing gamma radiation) was obtained from the GEO database and analyzed using GEO2R. Genes with p-value 0.05 and $|LogFC| \geq 1$, along with the top 10 upregulated and top 10 downregulated microRNAs (p-value 0.05), were considered differentially expressed genes and microRNAs (DEGs, DEMs). miRNA targets were predicted using miRWalk (score = 0.8, miRDB) and miRNet. Genes overlapping between DEGs and predicted targets were identified. Gene enrichment analysis was performed using DAVID on common genes. A miRNA-protein-protein interaction (PPI) network of the common genes was constructed and analyzed using the CytoHubba plugin of Cytoscape v3.10.3 to identify hub miRNAs/genes based on topological parameters (Degree, Closeness, Betweenness, Stress, MCC, and EPC), and key hub genes were defined as those common across all parameters.

Results: Analyzing GSE55955 identified 701 DEGs and 20 DEMs. For DEMs, miRWalk and miRNet predicted 4,376 and 13,969 targets, respectively. When predicted targets and DEGs overlapped, 156 common genes were found. Functional enrichment analysis identified intracellular signaling, cell communication, and regulation of cellular component biogenesis as the top biological process terms. In terms of cellular components, enriched terms included nucleoplasm, cytosol, and cell junction. Regarding molecular functions, the top terms were protein binding and activity, as well as phosphotransferase and protein kinase binding and activity. Finally, KEGG pathway analysis highlighted the Axon guidance, Cellular senescence, and p53 signaling pathways. A merged network, comprising 126 nodes and 204 edges, was constructed. Key hub miRNAs/genes identified included hsa-miR-574-5p, hsa-miR-30a-3p, hsa-miR-30a-5p, hsa-miR-423-5p, MDM2, CCND1, and CDKN1A. MDM2 is the target of hsa-miR-30a-3p, and the target of hsa-miR-423-5p is CDKN1A.Other key hub genes did not match based on the microRNA-target interaction network.

Conclusion: In this study, hsa-miR-30a-3p and hsa-miR-423-5p, together with their targets MDM2 and CDKN1A, were identified as miRNA–mRNA regulatory signatures associated with cellular responses to ionizing radiation.

keywords: Biodosimetry; Biomarkers; Gene Expression; MicroRNAs; Protein Interaction Maps

PG-59

Comparison of Molecular and Bioinformatics Technologies with Traditional Methods in Diagnosing Gastrointestinal

ALI RAVA [1] © ℗

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Background and aim: This study aims to evaluate novel laboratory methods for diagnosing gastrointestinal diseases and compare them with traditional approaches.

Methods: This systematic review was conducted by searching articles in Google Scholar and Scopus databases from 2020 to 2025. Inclusion criteria comprised studies that examined novel laboratory methods, while exclusion criteria included studies lacking sufficient data or clinical reviews without laboratory emphasis. From 2,500 initial articles, 12 studies were selected after screening

Results: Multiplex PCR, metagenomic sequencing, and machine learning in endoscopic image analysis have enhanced diagnostic accuracy and speed compared to traditional methods. Additionally, the use of metallic nanoparticles in molecular imaging and targeted drug delivery for gastrointestinal cancer treatment represents a novel approach. Furthermore, studies demonstrated that biological compounds such as plant extracts can be effective in inhibiting certain gastrointestinal pathogens. Clinical examinations of COVID-19 patients also revealed that certain laboratory markers, including elevated liver enzymes and decreased immune cells, can serve as biomarkers for predicting disease severity

Conclusion: The findings indicated that molecular methods and bioinformatics-based approaches have successfully overcome the limitations of traditional methods and have become the gold standard in diagnosing gastrointestinal diseases. However, challenges such as high costs and the need for advanced equipment remain, necessitating future research to focus on optimizing these methods

keywords: Laboratory methods, PCR, Gastrointestinal diseases, Molecular diagnostics, Medical imaging, Genetic

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PG-60

The role of the phosphodiesterase gene in subclinical hypothyroidism and its association with miscarriage in pregnant women

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Background and aim: Background Thyroid hormones play a vital role in metabolism and fetal growth, and any disruption in their levels can have serious consequences, including miscarriage. Recently, evidence has emerged regarding the genetic role in the onset of subclinical hypothyroidism (SCH) and miscarriage.

Methods: In this review study, various articles were collected by searching different scientific databases using the keywords phosphodiesterase, hypothyroidism, and miscarriage.

Results: The results of studies indicate that the PDE8B gene is responsible for encoding an enzyme that degrades cyclic adenosine monophosphate (cAMP), a key signaling molecule in thyroid hormone signaling. Variations in this gene may affect the efficacy of cAMP and consequently influence thyroid hormone levels. Investigations show that several polymorphisms, such as rs4704397, rs2046045, and rs6885099, in the PDE8B gene may be associated with changes in thyroid hormone levels and the risk of subclinical hypothyroidism (SCH). These changes might directly impact the phenotypic activities of this gene in pregnant women. Studies such as the research by Yang et al. (2019) reported that PDE8B may be significantly associated with SCH in pregnant women. Gruneford et al. (2019) also examined the relationship between the rs4704397 polymorphism in PDE8B and miscarriage, finding that this polymorphism has a significant association with thyroid hormone levels.

Conclusion: Conclusion The PDE8B gene has been identified as a key factor in the occurrence of subclinical hypothyroidism and its association with miscarriage. A better understanding of genetic variability and its role in these disorders could enhance diagnostic and therapeutic approaches during pregnancy.

keywords: Miscarriage, Hypothyroidism, Genetic polymorphism, PDE8B

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-61

Decreased expression of hsa-miR-142-3p and hsa-miR-155-5p in common variable immunodeficiency and involvement of their target genes and biological pathways

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Background and aim: Common variable immunodeficiency (CVID) is characterized by immune dysregulation and recurrent infections. MicroRNAs, particularly hsa-miR-142-3p and hsa-miR-155-5p, play critical roles in immune regulation. In knockout mouse models, the loss of these miRNAs resulted in immune defects with a CVID-like phenotype, including impaired T cell activation and cytokine production. These models highlighted their involvement in immune signaling pathways like NF-kB and JAK-STAT. This study investigates the expression of hsa-miR-142-3p and hsa-miR-155-5p in CVID patients, exploring their target genes and the biological pathways involved in the disease's pathogenesis.

Methods: hsa-miR-142-3p and hsa-miR-155-5p expression were assessed in a cohort of unresolved CVID cases and compared to healthy controls. Experimentally validated targets of these miRNAs were identified. A protein–protein interaction (PPI) network was constructed using the common target genes of both miRNAs, and hub genes were determined based on centrality metrics. The expression of these hub genes was investigated in GEO datasets and compared to control datasets. Gene ontology (GO) and pathway enrichment analyses were performed for the target genes, and the results were visualized in Cytoscape using the ClueGO and EnrichmentMap plugins.

Results: Hsa-miR-142-3p and hsa-miR-155-5p expression were significantly reduced in CVID patients. Evaluation of the PPI network demonstrated some hub genes in which pathogenic mutations have been reported in inborn errors of immunity (IEI), and other hub genes directly contribute to immune responses and the pathophysiology of IEI. Expression analysis of hub genes showed that they were significantly dysregulated in validating the CVID cohort. The pathway enrichment analysis indicated the involvement of the FOXO-mediated signaling pathway, TGFβ receptor complex, and VEGFR2-mediated vascular permeability.

Conclusion: Considering the dysregulation of hsa-miR-142-3p and hsa-miR-155-5p in CVID and the known role of their target genes in the immune system, their involvement in the pathogenesis of CVID can be suggested.

keywords: common variable immunodeficiency; epigenetic; microRNA; systems biology

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-62

Enhanced CAR-T Anti-Tumor Activity via CRISPR PD-1 Disruption in Relapsed B-Cell Malignancies

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Background and aim: Chimeric antigen receptor(CAR)T-cell therapy operates as an effective immunotherapy treatment which eliminates cancer cells through its precise targeting method.The treatment produced excellent clinical results for patients who had B-cell malignancies that failed to respond to treatment.However,the clinical achievements of CAR-Tcell treatment face obstacles which involve relapse cases and resistance development.Tumor antigen loss which includes CD19mutation and alternative splicing together with CAR-Tcell exhaustion throughPD-1/PD-L1signaling pathways lead to these treatment failures.CRISPR/Cas9technology functions as a genome-editing tool.This technology uses guideRNA to direct the Cas9enzyme toward DNA.allowing scientists to achieve precise gene disruption.This review aims to discuss how CRISPR/Cas9technology improvesCAR-Tcell anti-tumor effectiveness throughPD-1gene deletion.

Methods: This review article was conducted using articles published in PubMed, Google Scholar, and ScienceDirect between 2022 and 2026. The keywords were "CRISPR-Cas9 , CAR-T cell , PD-1 , B-cell Malignancies." A search of these databases resulted in 67 articles being found, 43 of which were excluded based on titles and abstracts. A total of 24 articles were selected according to the inclusion criteria.

Results: Finally,24 articles were included in the study.The PD-1/PD-L1 interaction in refractory B-cell malignancies which includes relapsed/refractory non-Hodgkin lymphoma restricted CAR-Tcell functions because it blocked intracellular signaling pathways and caused T cell exhaustion.The researchers used CRISPR/Cas9technology during CAR-Tcell production to create a PDCD1gene knockout by directing Cas9 to exon2 of the gene with a guide RNA.Cas9 create a double-strand break which the cell repaired through non-homologous end joining(NHEJ),resulting in frameshift insertions or deletions that caused the complete loss of PD-1 surface expression.Following the infusion of edited CAR-Tcells, the PD-L1 on lymphoma cells did not activate inhibitory pathways in the infused cells after the patient received the edited CAR-Tcell.The PD-1-disrupted CAR-Tcells maintained continuous CAR activation while their effector functions improved through increased cytokine secretion and cytotoxicity and their ability to survive in the body improved.The results showed better tumor control in living organisms while decreasing the need for systemic PD-1 inhibition.

Conclusion: CRISPR/Cas9 technology disruption of PD-1 led to enhanced CAR-T cell activity against B-cell tumors because it enabled the cells to resist PD-L1 immune suppression and it extended their lifespan while decreasing their rate of CAR T-cell exhaustion. However, further research needs to be done in this field.

keywords: CRISPR-Cas9 - CAR-T cell - PD-1 - B-cell Malignancies

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-63

Accuracy of Personalized ctDNA Assays for Minimal Residual Disease (MRD) Detection After Curative Resection of Colorectal Cancer: A Systematic Review

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Background and aim: Colorectal cancer (CRC) is a serious health concern worldwide, with a high rate of recurrence among treated patients. The current methods of surveillance in patients after surgery are also less efficient at detecting minimal residual disease (MRD) in the early stages. "Liquid biopsies" or circulating tumor DNA testing is a sensitive technique in which changes in a tumor's genomic pattern can be traced in plasma. This review will attempt to assess the sensitivity of such methods in tracing minimal residual disease in CRC.

Methods: This review article was conducted using articles published in PubMed, ScienceDirect, Google Scholar, and Web of Science until January 2026. The keywords were Circulating Tumor DNA, Colorectal Cancer, Minimal Residual Disease, and Molecular Diagnostic Techniques. By searching these databases, 68 articles were found. After reading titles and abstracts, 38 of them were removed, and 30 articles were selected under the inclusion criteria. All articles were chosen from English-language sources.

Results: In prospectively observed studies, tumor-informed personalized ctDNA assays were highly accurate in assessing Multi-Omics for Health and Disease (MOHD) following curative resection in colorectal cancer. Large series studies, including GALAXY and BESPOKE CRC, found that “a small proportion of patients were ctDNA-positive in the postoperative period, but it was strongly predictive of recurrence and poor disease-free survival (DFS) and overall survival (OS). Sensitivities were 72% in the early postoperative period, rising above 90% with repeat analysis, with specificities generally 90%, yielding high positive predictive values. ctDNA was more informative than conventional clinicopathologic risk factors and helped divide patients eligible for Adjuvant therapy. There were, however, some limitations, including true negatives with low tumor shedding, true positives with Clonal Hematopoiesis–Derived DNA (CLHD), among others: the current lack of standardization of assays, study timing of sampling, practicalities, and psychological effects.

Conclusion: Based on clinical studies, the use of personalized, tumor-informed ctDNA is rational and useful in detecting MRD after curative colorectal resection. Although these methods are highly accurate in terms of prognosis of recurrence and survival, further standardization, studies on timings, and interventional studies are needed to incorporate these methods into practice.

keywords: Circulating Tumor DNA; Colorectal Cancer; Minimal Residual Disease; Molecular Diagnostic

PG-64

Dysregulated microRNAs as Diagnostic Biomarkers for Cervical Cancer: Discovery and Validation

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Background and aim: Cervical cancer remains a significant global health concern, impacting over half a million women annually. The primary cause is a persistent infection with hr-HPV, which disrupts various cellular processes crucial for normal function. This disruption leads to genetic instability, including changes in the expression of miRNAs and their corresponding host genes, which far-reaching consequences for cellular regulation. To investigate novel biomarker for diagnosis of cervical cancer, we analyzed the datasets in Gene Expression Omnibus (GEO). The aim of this study is to investigate selected GSEs, identification of differentially expressed miRNAs and their target genes along with studying the enriched pathways.

Methods: We collected major datasets of cervical cancer in GEO, and analyzed the deafferented expression of normal and cancer samples online with GEO2R. Then, 38 GSEs including tissues and human cell lines were evaluated and analyzed. In the following, dysregulated miRNAs were identified and the common target genes of miRNAswere selected by targetscan and miRDB databases. Finally, enriched molecular pathways from EnrichR database were investigated.

Results: We identified 9 miRNAs and 85 target genes with significantly altered expression levels in cervical cancer that were consistent with the predicted results. Moreover, deregulation of these genes will change 45 biological pathways. These miRNAs are miR-218-5p, miR-92a-5p, miR-155-5p, miR-20a-5p, miR-34a-5p, miR-375-3p, miR-29a-3p, miR-let-7b-5p, and miR-27a-3p that molecular pathways such as PI3K-Akt, NF-κB, MAPK, P53, Hippo, PTEN, TGFB, and cell cycle checkpoints are involved in their expression.

Conclusion: Alterations in miRNA expression play an important role in pathogenesis of cervical cancer, affecting several biological pathways and hallmarks of cancer, such as immune system regulation, cellular cycle regulation and energy metabolism. Therefore, their study can help to develop diagnostic and prognostic biological markers and effective treatment for cervical cancer. Identifying this molecular genomic signature could open new avenues for developing therapeutic strategies for cervical cancer, particularly in the realm of precision medicine.

keywords: microRNAs (miRNAs), Cervical cancer, GEO, Bioinformatics, Diagnosis

PG-65

Intelligent Medicine: Genetic Data Analysis with the Help of Artificial Intelligence for Cancer Treatment

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Background and aim: Recent advancements in Next-Generation Sequencing (NGS) and Artificial Intelligence (AI) have enabled the analysis of genomic data for personalized cancer diagnosis and treatment.

Methods: This study, a systematic review based on PRISMA guidelines, investigates the applications of AI in cancer genomics, focusing on NGS technologies (such as WGS, WES, RNA-seq), machine learning algorithms (SVM, RF) and deep learning (CNN, Transformers), and clinical tools (such as Watson for Genomics, Tempus).

Results: The results indicate that AI identifies genetic variants (SNPs, CNVs, somatic mutations) with 85-97% accuracy and has improved treatment response rates by up to 60% in cancers like breast, lung, and melanoma. However, challenges such as the scarcity of diverse genomic data (less than 5% of TCGA data from the Middle East), data heterogeneity, high computational demands, and ethical considerations have limited the widespread adoption of these technologies. In Iran, the lack of indigenous data banks and computational infrastructure, particularly for breast cancer, has hindered the development of precision medicine. Recommendations include establishing local data banks, developing bias-resistant algorithms, standardizing data, and formulating ethical frameworks.

Conclusion: It is expected that by 2030, the integration of AI with genomics and technologies such as CRISPR will transform cancer treatment into a fully personalized process. This study emphasizes the necessity of investment in infrastructure and international collaborations, especially in developing countries like Iran, to bridge existing gaps in precision medicine.

keywords: Artificial Intelligence, Cancer Genomics, Precision Medicine, Next-Generation Sequencing

PG-66

Homeobox B4 gene expression is upregulated by ghrelin through PI3-kinase signaling pathway in rats bone marrow stromal cells

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Background and aim: Ghrelin, a 28 amino acid peptide, has diverse physiological roles. Phosphatidylino-sitol-bisphosphate 3-kinase (PI3K) and mitogen-activated protein kinase (MAPK) are involved in some of the recognized actions of ghrelin. It has been shown that ghrelin upregulates HOXB4 gene expression but the real mechanism of this effect is not clear.

Methods: Rat bone marrow stromal cells (BMSCs) were cultured in DMEM. BMSCs were treated with ghrelin (100 µM) for 48 h. Real-time PCR for HOXB4 was performed from Control (untreated BMSCs), BG (BMSCs treated with 100 µM ghrelin), PD (BMSCs treated with 10 µM PD98059, a potent inhibitor of mitogen-activated protein kinase, and 100 µM ghrelin), LY (BM-SCs treated with 10 µM LY294002, a strong inhibitor of phosphoinositide 3-kinase, and 100 µM ghrelin) and SY (BMSCs treated with 10 µM LY294002 plus 10 µM PD98059, and 100 µM ghrelin) groups. Relative gene expression changes were determined using Relative expression software tool 9 (REST 9).

Results: HOXB4 gene has been overexpressed in ghrelin-treated BMSCs (p0.05). PI3K inhibition by LY294002 significantly downregulated the ghrelin-induced overexpression of HOXB4 (p0.05).

Conclusion: We can conclude that ghrelin, through PI3K/Akt pathway, may improve BMSC transplantation potency by reducing its apoptosis. Moreover, upregulating HOXB4 in BMSC and its possible differentiation to HSCs might in the future open the doors to new treatment for hematologic disorders. Therefore, activating the PI3K/Akt pathway, instead of using a non-specific inducer, could be the principal point to increase the efficiency of BMSC-based cell therapies in the future

keywords: BMSCs; HOXB4; MAPK; PI3K; ghrelin; rat

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-67

Modulation of IL1B, TNF, CXCL10, and CCL2 Gene Expression in Human Microglial Cells by Resveratrol Treatment: Dose-Response and Time-Course Study in an LPS-Induced Neuroinflammation Model

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Background and aim: Redox adaptation is a hallmark of tumor progression, enabling cancer cells to survive elevated oxidative stress. The KEAP1–Nrf2 signaling axis functions as a master regulator of antioxidant and cytoprotective gene networks. Although sulforaphane (SFN) is a potent Nrf2 activator, the transcriptional dynamics of KEAP1 and downstream antioxidant genes in breast cancer remain insufficiently characterized.To define the dose-dependent and temporal transcriptional regulation of the KEAP1–Nrf2 axis in response to SFN in MCF-7 breast cancer cells.

Methods: MCF-7 cells were treated with escalating concentrations of SFN (2.5–10 μM) for 24 hours or with 5 μM SFN for 8–48 hours. The relative mRNA expression of KEAP1, HMOX1, GCLC, and NQO1 was measured using qRT-PCR and calculated using the $2^{-}\Delta\Delta Ct$ method.

Results: SFN caused strong transcriptional activation of Nrf2 target genes in a dose- and time-dependent manner. The highest transcriptional activation was achieved at 5 μM, with HMOX1 showing the highest induction level, which was 5.80 ± 0.65-fold change, p 0.001, followed by NQO1 and GCLC. Meanwhile, the transcriptional levels of the inhibitory component of the antioxidant pathway, namely KEAP1, were significantly down-regulated, with a 0.62 ± 0.08-fold change, p = 0.002. The transcriptional activation of antioxidant genes reached its maximum at 24 hours, with the transcriptional levels of the inhibitory antioxidant component of the antioxidant response, i.e., KEAP1, still down-regulated at 48 hours

Conclusion: These studies show that SFN stimulates the sustained activation of the KEAP1/Nrf2 pathway through coordinated activation of cytoprotective genes and suppression of KEAP1 transcriptional activation. These studies provide insights into transcriptional regulation of KEAP1 as a mechanism of prolonged redox signaling in breast cancer cells and provide a mechanistic rationale to target redox adaptive pathways using dietary isothiocyanates. The data show that SFN activates KEAP1/Nrf2 signaling by maintaining its activation, and this is mediated by the induction of cytoprotective genes that, at the same time, suppress KEAP1 gene expression. This

keywords: Sulforaphane, KEAP1–Nrf2 Signaling, Breast Cancer, Oxidative Stress, Redox Adaptation

PG-68

New Biomarker Panels for Pancreatic Cancer Detection

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Background and aim: Pancreatic ductal adenocarcinoma (PDAC) remains one of the deadliest malignancies, largely due to late diagnosis. CA19-9, the current biomarker, lacks sensitivity and specificity for detection of early-stage disease. New techniques of molecular testing and liquid biopsy look promising. We aim to evaluate the diagnostic performance of novel biomarkers, including circulating tumor DNA (ctDNA), exosomal microRNAs, methylated DNA panels, and protein signatures, for the early detection of PDAC.

Methods: We conducted a systematic review of studies published between 2020-2026 using 5 keywords in PubMed, Scopus, Web of Science, and Google Scholar that assessed the sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) of candidate biomarkers in PDAC versus healthy controls and benign pancreatic diseases.

Results: A multi-analyte panel combining ctDNA mutations (KRAS, TP53) with methylated markers (e.g. ADAMTS1, BNC1) achieved an AUC of 0.92 for stage I-II PDAC. Exosomal miR-10b, miR-21 and miR-155 had a pooled sensitivity of 84% and specificity of 90%. A plasma protein signature (CA19-9, TSP-1, LRG1, TIMP1) improved early detection AUC to 0.90 compared with CA19-9 alone (AUC 0.75). Moreover, detection of KRAS G12D in pancreatic cyst fluid had 98% specificity for high-grade dysplasia.

Conclusion: Novel biomarkers, especially in combination with multi-marker panels or liquid biopsy, are valuable tools to improve the detection of early-stage PDAC. Further prospective validation in high-risk cohorts is needed prior to clinical implementation.

keywords: Pancreatic Cancer Biomarker Detection Sensitivity Specificity

PG-69

From genome to extracellular vesicles: diagnostic and prognostic approach

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Background and aim: Genomic analysis in combination with extracellular vesicle (EV) profiling provides a novel paradigm for non-invasive disease characterization. This abstract summarizes recent advances of the association of genetic alterations with EV cargo, which together hold great potential for diagnosis and prognosis in cancers and other pathologies.

Methods: A systematic literature review was performed using PubMed, Scopus, and Web of Science (2018–2026). Keywords included “extracellular vesicles,” “genome,” “diagnostic biomarkers,” and “prognosis.” Studies correlating genomic mutations (e.g., EGFR, KRAS, TP53) with EV-associated nucleic acids, proteins, and lipids were analyzed. Emphasis was placed on liquid biopsy applications.

Results: EVs derived from tumours carry DNA fragments that reflect the mutational landscape of the parental cells and enable the detection of driver mutations and clonal evolution. Correlation of EV mRNA and microRNA profiles with genomic signatures improves diagnostic sensitivity (AUC 0.85 in several cohorts). EV load and cargo (e.g., miR-21, PD-L1 mRNA) predict therapy response and survival in lung, pancreatic and breast cancers, prognostically. Combining multi-omics (genome + EV proteome/transcriptome) improves risk stratification over single-modality approaches.

Conclusion: The genome-to-EV axis is a platform that combines molecular genetics with real-time systemic monitoring. For clinical translation, standardization of EV isolation and sequencing protocols is needed. Composite genomic-EV biomarkers require prospective validation in further studies.

keywords: Extracellular vesicles Genome Diagnostic biomarkers Prognosis

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-70

Post-Ovulatory Epigenetic Alterations in Murine Oocytes: Assessing the Role of DNMT3A and DNMT3L in Laboratory-Based Aging Models

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Background and aim: Epigenetics studies heritable changes in gene expression without alterations in DNA sequence. In mammalian oocytes, epigenetic mechanisms are essential for genomic stability, embryonic development, and establishment of maternal imprints. DNMT3A is the primary enzyme responsible for de novo DNA methylation, whereas DNMT3L acts as a key cofactor enhancing its activity. Both are crucial for proper oocyte development and epigenetic programming. This study investigated the expression of DNMT3A and DNMT3L in oocytes exposed to in vivo and in vitro aging and evaluated their potential relevance to assisted reproductive technologies.

Methods: Forty-five female Balb/c mice were superovulated using a regimen of HMG and HCG injections. Oocytes were collected and categorized into three experimental groups: control (freshly isolated oocytes), in vivo aging (oocytes aged within the oviduct), and in vitro aging (oocytes aged in laboratory culture medium). Total RNA was extracted from pooled oocytes, and cDNA was synthesized using reverse transcription. Quantitative real-time PCR (qRT-PCR) was employed to assess the relative mRNA expression levels of DNMT3A and DNMT3L. All reactions were performed in triplicate to ensure technical reproducibility. Statistical analysis was conducted using one-way ANOVA with GraphPad Prism software, and a p-value of less than 0.05 was considered statistically significant.

Results: qRT-PCR revealed significant upregulation of DNMT3A (2.8-fold, p 0.01) and DNMT3L (3.2-fold, p 0.001) in the in vitro aging group compared to control and in vivo groups. This coordinated overexpression suggests maladaptive activation of de novo methylation pathways under laboratory conditions, potentially disrupting epigenetic programming.

Conclusion: The upregulation of DNMT3A and DNMT3L under in vitro conditions indicates an epigenetic stress response in aged oocytes. This increase may represent a compensatory mechanism for genomic stability or lead to aberrant hypermethylation. These findings provide insights into oocyte quality decline in ART and emphasize the need for optimized culture conditions. The coordinated overexpression suggests these enzymes as potential biomarkers for oocyte quality assessment. Future research should explore functional consequences and strategies to mitigate these epigenetic alterations.

keywords: Oocyte aging, DNA methylation, DNMT3A, DNMT3L,POV.

PG-71

Oxidative Stress and Protective Interventions in Male Reproductive Dysfunction: A Systematic Review

معصومه شمایل راد [1] © Ⓟ

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Background and aim: اختلالات تولیدمثلی مردان یکی از مشکلات مهم سلامت باروری است که می‌تواند تحت تأثیر عوامل محیطی، متابولیک و فیزیولوژیک قرار گیرد. استرس اکسیداتیو یکی از سازوکارهای اصلی آسیب به سیستم تولیدمثل نر محسوب می‌شود و می‌تواند بر کیفیت اسپرم، ساختار بافت بیضه، متابولیسم انرژی و تنظیم مولکولی مؤثر باشد. با توجه به اهمیت شناسایی عوامل آسیب‌رسان و نیز مداخلات محافظتی، این مطالعه با هدف مرور سیستماتیک شواهد موجود درباره نقش استرس اکسیداتیو و راهکارهای کاهنده آن در اختلالات تولیدمثلی نر انجام شد.

Methods: در این مرور سیستماتیک، سه مطالعه تجربی مرتبط با اختلالات تولیدمثلی نر بررسی شدند. این مطالعات شامل آسیب تولیدمثلی ناشی از کادمیوم، اختلال تولیدمثلی مرتبط با دیابت، و تغییرات فصلی مؤثر بر کیفیت اسپرم در گاومیش نر بودند. داده‌های مربوط به پارامترهای اسپرم، وضعیت آنتی‌اکسیدانی، شاخص‌های استرس اکسیداتیو، تغییرات بافتی، بیان ژن‌های مرتبط با آپوپتوز، آنتی‌اکسیدان و متابولیسم انرژی استخراج و به صورت توصیفی تحلیل شدند.

Results: یافته‌ها نشان دادند که در هر سه مطالعه، استرس اکسیداتیو با کاهش کیفیت اسپرم، اختلال در اسپرماتوژنز و تغییر در نشانگرهای مولکولی همراه بود. مواجهه با کادمیوم موجب تخریب بافت بیضه، کاهش زنده‌مانی، تحرک و تعداد اسپرم، افزایش گونه‌های فعال اکسیژن و تغییر در بیان ژن‌های مرتبط با آپوپتوز و استروئیدوژنز شد. در مدل اسپرم مشاهده شد، در حالی که درمان با عصاره Zataria multiflora موجب بهبود پارامترهای اسپرم، افزایش فعالیت آنزیم‌های آنتی‌اکسیدانی و افزایش بیان ژن‌های PK و IRS گردید. همچنین در مطالعه مربوط به گاومیش‌های نر، تنش گرمایی فصلی با افزایش استرس اکسیداتیو و افت کیفیت اسپرم همراه بود، در حالی که در نمونه‌های با کیفیت بالاتر، فعالیت بیشتر سیستم آنتی‌اکسیدانی، کاهش DNA دیابت، افزایش آسیب اکسیداتیو، التهاب و قطعه‌قطعه شدن نشانگرهای آپوپتوزی و تغییرات مطلوب در وزیکول‌های خارج‌سلولی مشاهده شد.

Conclusion: شواهد موجود نشان می‌دهد که استرس اکسیداتیو نقش محوری در بروز اختلالات تولیدمثلی نر ناشی از عوامل محیطی، متابولیک و فصلی دارد. همچنین مداخلات آنتی‌اکسیدانی و ترکیبات محافظتی می‌توانند از طریق بهبود وضعیت اکسیداتیو، تنظیم بیان ژن‌های مرتبط و حفظ ساختار بافتی و عملکرد اسپرم، اثرات آسیب‌رسان را کاهش دهند. با این حال، برای تعمیم این یافته‌ها به سطح بالینی، انجام مطالعات بیشتر ضروری است.

keywords: استرس اکسیداتیو، ناباروری مردان، کیفیت اسپرم، آنتی‌اکسیدان، تولیدمثل نر

PG-72

The Impact of Estradiol, Estrogen Receptor-Alpha, and rs2234693 Polymorphism on Sperm Quality in Infertile Men

معصومه شمایل راد [1] © Ⓟ

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Background and aim: اسپرماتوژنز، فرآیند تولید اسپرم، تا حدی توسط استرادیول از طریق تعامل آن با گیرنده و تغییرات ژنتیکی در ژن ESRα تنظیم می‌شود. درک ارتباط بین سطوح استرادیول، بیان (ESRα) استروژن آلفا برای روشن شدن ناباروری مردان ضروری است. هدف این مطالعه، تجزیه و تحلیل ارتباط بین سطوح سرمی ESRα با کیفیت اسپرم در مردان نابارور بود ESRα و پلی‌مورفیسم‌های ژن ESRα استرادیول، سطوح سرمی.

Methods: این مطالعه گذشته‌نگر شامل مردان نابارور مراجعه‌کننده به مرکز باروری، بیمارستان وابسته دانشگاه علوم پزشکی ملیوجیانگ برای ملیت‌ها، و گروه کنترل از مردان سالم بدون سابقه باروری، بین اکتبر ۲۰۱۶ تا مارس ۲۰۱۷ بود. داده‌های مربوط به کیفیت اسپرم (شامل غلظت اسپرم، درصد اسپرم‌های با تحرک پیشرونده و درصد اسپرم با مورفولوژی طبیعی)، سطوح سرمی استرادیول و پزشکی استخراج شد. تحلیل‌های همبستگی پیرسون و اسپیرمن برای ارزیابی ارتباط بین سطوح استرادیول، سطوح و پارامترهای کیفیت اسپرم انجام شد. مقایسه‌ها بین گروه‌های نابارور و کنترل، و در گروه نابارور بر اساس ESRα طبقه‌بندی‌های مختلف کیفیت اسپرم و ژنوتیپ‌ها صورت گرفت.

Results: تحلیل داده‌های این مطالعه نشان می‌دهد که سطوح سرمی استرادیول و گیرنده استروژن آلفا (ESRα) به طور قابل توجهی در مردان نابارور افزایش یافته و با پارامترهای کلیدی کیفیت اسپرم، شامل غلظت، درصد تحرک پیشرونده و مورفولوژی طبیعی، همبستگی منفی معنادار دارند. این یافته‌ها مکانیسم‌های بالقوه اختلال در اسپرماتوژنز ناشی از دیس‌تنسیون هورمونی را برجسته می‌سازند، جایی که افزایش استروژن ممکن است به طور مستقیم یا غیرمستقیم ESRα در ژن rs2234693 بر سلامت و عملکرد اسپرم تأثیر منفی بگذارد. از سوی دیگر، پلی‌مورفیسم ESRα ، علیرغم ارتباط تئوریک با عملکرد گیرنده، در این جمعیت مورد مطالعه فاقد قدرت پیش‌بینی‌کنندگی قابل توجهی برای کیفیت اسپرم یا سطوح هورمونی بود. بنابراین، تمرکز بر ارزیابی و مدیریت پروفایل‌های هورمونی، به ویژه استرادیول و ESRα ، به عنوان عوامل مهم در پاتوفیزیولوژی ناباروری مردان، و در نظر گرفتن محدودیت پلی‌مورفیسم‌های خاص در پیش‌بینی نتایج بالینی، رویکردی مؤثرتر در تحقیقات و درمان‌های آینده خواهد بود.

Conclusion: ممکن است تأثیر منفی ESRα یافته‌ها حاکی از آن است که سطوح بالای سرمی استرادیول و احتمالاً ژن rs2234693 بر کیفیت اسپرم و باروری مردان داشته باشد. در مقابل، پلی‌مورفیسم‌های تک‌نوکلئوتیدی در جایگاه ESRα به نظر می‌رسد تأثیر کم یا هیچ اثری بر این پارامترها دارند. این نتایج نقش بالقوه اختلالات هورمونی را در خاص، احتمالاً سهم قابل توجهی ندارند SNP ناباروری مردان برجسته می‌کند و نشان می‌دهد که تغییرات ژنتیکی در این.

keywords: ESRαناباروری مردان، استرادیول، کیفیت اسپرم،

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-73

Evaluating the Role of Novel Biomarkers in Early Cancer Diagnosis Using Molecular Techniques in Peripheral Blood Samples

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Background and aim: Cancer detection at an early stage plays a vital role in enhancing patient survival rates; unfortunately, traditional diagnostic methods, such as tissue biopsy and serological markers, suffer from low sensitivity and cannot detect tumor heterogeneity or are not suitable for screening purposes. The application of peripheral blood liquid biopsy as a potential non-invasive approach for cancer detection and monitoring has gained considerable attention in recent years. This review highlights the application of molecular biomarkers such as ctDNA, EVs, and miRNAs in cancer detection using advanced molecular methods.

Methods: The aim of the present review is to outline recent advances (2025–2026) in peripheral blood biomarker research in the areas of genomics, epigenomics, proteomics, and transcriptomics. Special emphasis will be given to highly sensitive technologies, including next-generation sequencing, digital PCR, mass spectrometry, and machine learning based integration. Performance characteristics of biomarkers in terms of sensitivity, specificity and area under the curve will be discussed based on meta-analyses, systematic reviews, and large-cohort studies.

Results: The ctDNA methylation-based approaches provided high levels of precision, which reached 0.972 for breast cancer and 0.952 for early HCC. The multi-omic contents of exosomes helped identify patients with early-stage breast cancer from healthy people. The machine-learning approach based on cfDNA fragmentation and methylation provided the sensitivity of 86% and 81% correspondingly with 94–99% specificity for various types of cancer. With regard to the AI-powered tests to find 14 types of cancer, their sensitivity was 58.4% at 92% specificity. Compared to real-time PCR, NGS-based liquid biopsy was better to detect mutations in EGFR in NSCLC.

Conclusion: The use of liquid biopsy based on the analysis of peripheral blood represents an innovative tool for cancer diagnosis at an early stage. The application of molecular-based methodologies for the analysis of ctDNA, exosomes, miRNAs and multi-omic patterns, along with artificial intelligence technologies, represents an innovative approach.

keywords: liquid biopsy; circulating tumor DNA; early cancer detection; methylation; multi-omics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-74

A Homozygous FGF3 Candidate Variant in Three Affected Siblings with Congenital Hearing Loss in a Consanguineous Family

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Background and aim: Hereditary hearing loss (HL) is a highly heterogeneous condition. While 70–80% of cases are classified as non-syndromic hearing loss (NSHL), many "non-syndromic mimics" exist in which HL may be the first or only presenting symptom of an underlying syndromic condition. The FGF3 gene is typically associated with LAMM syndrome, characterized by labyrinthine aplasia, microtia, and microdontia; however, rare variants may present with incomplete phenotypes, challenging clinical diagnosis. This study aimed to identify the genetic basis of congenital HL in this family and potential pathogenic relevance of the identified FGF3 variant.

Methods: We investigated a consanguineous Turkish-ethnic Iranian family with three siblings affected by congenital sensorineural HL. Whole-exome sequencing (WES) was performed on the proband, followed by variant prioritization based on inheritance pattern, allele frequency, predicted pathogenicity, and clinical relevance. Candidate variants were validated and tested for familial segregation using Sanger sequencing. Initial genetic analysis for SLC26A4 variants, including c.1061TC and c.164+1del, revealed that they were in cis configuration in the proband's Father, thus ruling them out as the primary cause of the proband's phenotype. Subsequent WES analysis identified a rare homozygous missense variant in the FGF3 gene, NM_005247.4:c.463GA; p.Val155Met, in the proband and affected siblings.

Results: The p.Val155Met variant, located in the beta-sheet structure of the fibroblast growth factor 3 protein, is extremely rare in public databases. In silico prediction tools, including CADD: 29, MetaRNN: 0.79, and DEOGEN2: 0.88, predicted the variant to be deleterious. Although the variant is currently classified as a Variant of Uncertain Significance (VUS) according to ACMG criteria, segregation analysis confirmed that all three affected siblings were homozygous, while the parents and unaffected siblings were heterozygous or wild-type. Protein stability prediction using mCSM, SDM, and DUET suggested increased stability of the mutant protein, as indicated by negative ΔΔG values. Molecular docking analyses further indicated a potential effect on interactions with FGFR1 and FGFR2 receptors. Notably, the p.Val155Met residue is adjacent to p.Ser156Pro, which has previously been linked to syndromic HL.

Conclusion: Our findings suggest that the homozygous FGF3 p.Val155Met variant is a strong candidate for the HL phenotype in this family. This case highlights the importance of considering FGF3 in patients with apparently non-syndromic HL and underscores the role of "non-syndromic mimics" in the diagnostic odyssey of hereditary deafness. Further functional studies are warranted to clarify the pathogenicity of this variant.

keywords: Non-syndromic hearing loss, FGF3, variant of uncertain significance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-75

Reclassification of a Homozygous LHFPL5 Variant from VUS to Pathogenic in Two Unrelated Iranian Families with Congenital Hearing Loss

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Background and aim: LHFPL5 encodes an auxiliary component of the mechanotransduction (MET) complex in cochlear hair cells and is essential for normal auditory function. Pathogenic variants in this gene are a known cause of autosomal recessive non-syndromic hearing loss (NSHL). However, interpretation of rare missense variants may remain uncertain without sufficient clinical and segregation evidence. This study aimed to evaluate the pathogenicity of a rare homozygous LHFPL5 variant and to support its reclassification through segregation analysis and ACMG criteria.

Methods: A consanguineous Iranian family with congenital sensorineural HL was investigated. Whole-exome sequencing (WES) was performed in the proband to identify the underlying genetic cause. Candidate variants were prioritized based on inheritance pattern, population frequency, predicted functional impact, and known association with hearing loss. The selected variant was validated by Sanger sequencing, and segregation analysis was performed in available family members. During routine laboratory analysis of another affected, unrelated individual with congenital HL, the same LHFPL5 variant was incidentally identified. This additional observation, together with segregation data and in silico evidence, was incorporated into ACMG-based variant reinterpretation.

Results: A homozygous missense variant in LHFPL5 (NM_182548.4:c.410CT; p.A137V) was identified in the affected proband. The variant is located in exon 1, affects a highly conserved amino acid residue, and is rare in population databases. In silico analyses supported a deleterious effect. Segregation analysis showed that the affected individuals were homozygous for the variant, whereas the healthy parents were heterozygous carriers, consistent with autosomal recessive inheritance. Notably, the same variant was also observed in a second unrelated family from the same population. Based on the accumulated evidence, the variant was upgraded from Variant of Uncertain Significance (VUS) to Pathogenic according to ACMG criteria, including PP1, PS4, PM1, PM2, PP2, and PP3.

Conclusion: This study supports the pathogenic role of the LHFPL5 c.410CT (p.A137V) variant in congenital HL and highlights the importance of segregation analysis in resolving VUS.

keywords: Non-syndromic hearing loss, LHFPL5, and variant of uncertain significance.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-76

Host Genetics and Environmental Determinants of the Human Microbiome in Health and Disease (Narrative Review)

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Background and aim: The human microbiome is a complex, dynamic ecosystem shaped by the interplay of host genetic, hormonal and environmental factors. Recent investigations have shown that both community composition and functional traits vary at multiple body sites as the urinary microbiome and fecal microbiome relate to age, sex, diet, immunity and genetic background. However, their relative contribution is not yet fully understood, partly due to a lack of sequencing resolution and population specificity in prior studies .This narrative review summarizes evidence on environmental determinants, sex-related differences, microbiome function, and host genetics in human microbiome development

Methods: This narrative review aims to provide a synthesis of literature on human microbiome determinants, including host genetics, environmental factors, sex differences and immune status influencing gut (GI), urinary microbiomes and virome. An unsystematic PubMed search was carried out. Recent relevant articles were qualitatively appraised and thematically organized, without formal inclusion criteria or meta-analytic methods.

Results: Multiple interacting factors contribute to shaping the human microbiome, including host genetics, sex hormones, immune status and environmental exposures within the context of diet, age and early life conditions. Coupled with gene environment interactions, these determinants affect microbial diversity and composition across body sites and further result in inter individual variability.

Conclusion: At present, evidence supports a complex multi-factorial network of host genetic, hormonal and environmental determinants that structure the human microbiome. Environmental factors (diet, age, and interpersonal contact) are significant contributors to short-term variation in the microbiome; yet host genetics and sex hormones contribute to more consistent and individual-specific microbial signatures. Gaining deeper insights into these interactions will be crucial for formulating individualized microbiome-based diagnosis and treatment strategies.

keywords: Human microbiome , Urinary microbiome , host genetics , environmental

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-77

MicroRNA Biomarkers in Apoptosis-Mediated Cancer Diagnosis, Prognosis, and Therapy

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Background and aim: MicroRNAs identified as post-transcriptional regulators of gene expression, having significant involvement in regulation of complex functionally PCD networks. In human cancers, the dysregulation and aberrant expression of these RNAs leads to evasion of apoptosis, a fundamental hallmark of tumour survival, uncontrolled progression and aggressive chemoresistance. The purpose of this review is to provide a comprehensive assessment of the clinical exploitable specific tissue-dependent and circulating miRNAs as a non-invasive tool for early-stage cancer diagnosis and accurate prognostic prediction, together with the analysis of their druggability as novel genetic therapeutics to reactivate intrinsic and extrinsic apoptotic routes in cancer cells.

Methods: A full systematic review, metadata extraction, and bioinformatic analysis were performed within the PubMed, Scopus, and Web of Science databases to obtain validated miRNA expression profiles significantly associated with suppression of apoptosis in cancer. Clinical samples from tumor tissue and liquid biopsies (serum and plasma) of patients were analyzed. Quantitative real-time PCR-based datasets of expression levels of downstream target genes, such as Bcl-2, Bax, Mcl-1, and different Caspases, were directly associated with particular miRNA levels. Sophisticated computational target prediction (TargetScan, miRDB) were employed to identify binding sites of specific miRNAs at the 3'-UTR of the target genes. Survival Kaplan-Meier curves and multivariate Cox regression analyses were used to investigate prognostic association between unique miRNA signatures and overall survival of patients.

Results: The compiled data showed that up-regulated oncomiRs potently silenced important pro-apoptotic molecules such as Bax and Apaf-1, and down-regulated tumor-suppressor miRNAs cause the pathogenic over-expression of anti-apoptotic proteins like Bcl-2 or Mcl-1. Notably, the dysregulated circulating miRNAs had an excellent diagnostic accuracy (AUC 0.85) for early-stage tumors versus healthy controls. Aberrant expression of miRNAs has been reported to be significantly associated with high histological tumor grade, enhanced metastatic ability and poor overall patient survival. Therapeutically, delivery of synthetic miRNA mimics or antisense antagomirs by targeted formulation restored caspase-dependent apoptotic signaling and markedly sensitized refractory tumor cells to standard chemo- as well as emerging nanomedicine-based drug delivery systems.

Conclusion: Deregulated miRNA-apoptosis pathways represent powerful biomolecular signatures detectable in bodily fluids for early cancer detection and accurate prognostic prediction. Targeted manipulation of these miRNAs by next generation oligonucleotides represents a very promising therapeutic approach to circumvent chemoresistance through selective induction of tumor cell suicide. In the end, taking these miRNA-apoptosis axes to the clinical will be the anticipated impact to bring benchside molecular oncology and personalized medicine together nutritional for monitoring therapeutic responses in real-time and providing powerful, multi-target gene therapies that have potential to transform current standards in oncology.

keywords: MicroRNA, Apoptosis, Cancer Biomarkers, Chemoresistance, Targeted Therapy.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-78

Activation of NF-κB Pathway in Solid Tumors and its Role in the Regulation of Apoptosis in Tumor Cells

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Background and aim: It is essential to find new and more effective treatments to cancers. One of the key properties associated with cancer cells is their ability to resist apoptosis. Nuclear factor-κB (NF-κB) transcription factor plays a key role in many physiological processes such as immune responses, cell proliferation, inflammation, and cell death by regulating the transcription of over 400 genes. The aim of this study was to investigate the activation of NF-κB pathway in various solid tumors and its role in the regulation of apoptosis in tumor cells.

Methods: Activation of NF-κB and its associated mechanisms, the role of this pathway in tumor cell apoptosis, the effects of NF-κB activation on gene expression levels of various apoptosis-related genes, and therapeutic approaches targeting components of the NF-κB-related apoptosis pathway were investigated in different types of solid tumors in vitro and in vivo.

Results: Continuous activation of NF-κB factors was found in various types of solid tumors such as breast, ovarian, colon, pancreatic, thyroid, bladder and prostate carcinomas, and melanomas. In most tumor cells, activated NF-κB protected the cell from apoptosis, through induction of several survival genes such as TRAF1, TRAF2, IAPs (c-IAP1, c-IAP2, XIAP), FLIP, IEX-IL, Bcl-2, Bcl-xL and BfI-1. In addition, the signaling mechanisms that control NF-κB activity were involved in resistance to chemo- and radio- therapies. NF-κB inhibition restored TNF-α-induced apoptosis in ovarian cancer and hepatocellular carcinoma, sensitized lung cancer cells to apoptosis, and reversed Bcl-2-driven chemoresistance in breast cancer. Inhibition of NF-κB in Hodgkin/Reed–Sternberg cells led to the loss of expression of anti-apoptotic effectors and JNK activation. Inhibition of NF-kB survival pathway in pancreatic ductal adenocarcinoma cells induced apoptosis after autophagy inhibition. Likewise, downregulation of NF-kB pathway was followed by apoptosis induction in colorectal cancer cell lines.

Conclusion: The findings of this study showed that activation of NF-κB occurs in several solid tumors and inhibits apoptosis through regulation of expression of more than 30 survival-related genes. This pathway was involved in cancer development and progression, as well as in resistance to chemo- and radio- therapies. Hence, anti-NF-κB therapy may rescue many cases of cancers and may be considered as a therapeutic target. However, targeting the NF-κB pathway alone was not sufficient to induce apoptosis in cancer cells and combination of various inhibitors are required to achieve therapeutic potential.

keywords: NF-κB, Tumor Cell Apoptosis, Solid Tumors

PG-79

CRISPR Base Editing: A Precision Therapeutic Strategy for β-Thalassemia: A Systematic Review

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Background and aim: β-Thalassemia is a pretty common inherited blood condition worldwide,which comes from mutations within the HBBgene leading to reduced or even absent β-globin synthesis.This then drives ineffective erythropoiesis and microcytic-hypochromic anemia, many of the patients may need long term transfusions.The advances in gene editing methods, like CRISPR-base editing can improve the treatment options for this disorder.Base Editing, allows a precise DNA base change into another base,without generating double-stranded DNA breaks,thereby reducing the chance of unwanted mutations that are often linked with the usual CRISPR/Cas9approach.The aim is to review the potential of CRISPR-base editing as a therapeutic approach for β-thalassemia

Methods: This review article was conducted using articles published in PubMed, Google Scholar, and ScienceDirect between 2023 and 2026. The keywords were CRISPR Base Editing, β-Thalassemia, Precision Therapy, Base Editors. A search of these databases resulted in 47 articles being found, 28 of which were excluded based on titles and abstracts. A total of 19 articles were selected according to the inclusion criteria.

Results: . Finally,19 articles were included in the study.The therapeutic goal for β-thalassemia was either the direct correction of HBBmutations or the reactivation of fetal hemoglobin(HbF)expression.the first strategy involved the direct correction of HBBmutations that caused reduced(β+)or absent(β0)β-globin production.For common β-thalassemia mutations,such as CD39 and IVS2-1,Adenine-base editors(ABEs)were used to restore the normal nucleotide sequence through targeted A-to-G conversion,thereby correcting the pathogenic variant.The second approach was aimed at imitating hereditary persistence of fetal hemoglobin(HPFH)to reactivate HbF.The focus was on the regulatory areas within HBG1and HBG2promoters which are normally silenced postnatally.Cytosine-base editors(CBEs)were used to introduce HPFH related mutations by disrupting the LRF binding site within the HBG promoters and ABEs were used to create mutations that provided new KLF1 activator binding sites.The result of both base-editors modification was greater levels of γ-globin expression and HbF production and consequently an improvement in hemoglobin functionality and a decrease in the ineffective erythropoiesis observed in models.

Conclusion: CRISPR-based base editing has shown great promise as a potential therapy for β-thalassemia by correcting mutant genes that are responsible for β-thalassemia and increasing the level of fetal hemoglobin. However, further research needs to be done in this field.

keywords: CRISPR Base Editing- β-Thalassemia- Precision Therapy-Base Editors

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-80

A Novel Homozygous GAD1 Nonsense Mutation in a Patient with Spastic Quadriplegic Cerebral Palsy

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Background and aim: Cerebral palsy (CP) is traditionally viewed as the consequence of environmental insults during central nervous system development. However, recent evidence suggests a significant genetic component, particularly in cases of spastic quadriplegic CP. While CP is characterized by permanent motor impairment, its clinical heterogeneity often masks underlying monogenic etiologies. Among the implicated genes, GAD1—which encodes the essential GABA-synthesizing enzyme, GAD67—has emerged as a key candidate in early-onset spastic quadriplegia, highlighting the critical role of the GABAergic inhibitory system in maintaining neural circuit homeostasis. This study investigates the mutation causing spastic quadriplegic CP in a boy from an Iranian consanguineous family.

Methods: Whole-exome sequencing (WES) was utilized to identify disease-causing variants. Sanger sequencing was employed to confirm that this variant was inherited in a homozygous state within the family.

Results: Analysis identified a novel homozygous nonsense variant in GAD1 (c.87CA; p.Y29X; NM_000817.3). This mutation introduces a premature stop codon at position 29, leading to the truncation of the GAD67 protein. According to the ACMG guidelines, this variant is classified as “pathogenic.” In the co-segregation analysis, Sanger sequencing confirmed that both parents were heterozygous carriers of the GAD1 c.87CA variant, while the patient was homozygous, demonstrating an autosomal recessive inheritance pattern consistent with the family pedigree. These molecular findings strongly implicate the loss-of-function GAD1 mutation as the underlying cause of the patient’s severe neurodevelopmental phenotype and spastic quadriplegic cerebral palsy.

Conclusion: The identification of a novel GAD1 mutation underscores the critical role of comprehensive genetic testing in diagnosing spastic quadriplegic cerebral palsy. Given the phenotypic overlap with other neurodevelopmental disorders, such genomic insights are essential for accurate diagnosis and clinical management. This finding expands the mutational spectrum of GAD1-related disorders and reinforces the diagnostic value of family screening, especially in populations with high rates of consanguinity. Ultimately, this study provides deeper insights into the genetic architecture of early-onset spastic quadriplegia and supports precision medicine approaches for affected families.

keywords: GAD1/ Genetic testing /Spastic quadriplegic cerebral palsy/ Whole-exome sequencing /neurodevelopmental

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-81

A Novel Homozygous PIGC Variant Identified in a Patient with Glycosylphosphatidylinositol Deficiency: A Case Report

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Background and aim: Glycosylphosphatidylinositol (GPI) anchor deficiencies are a group of rare inherited disorders caused by mutations in genes involved in GPI-anchor biosynthesis. Variants in the PIGC gene have been associated with developmental delay, epilepsy, and intellectual disability. This study aimed to identify and characterize a novel PIGC variant in a patient with clinical features suggestive of GPI deficiency.

Methods: This study investigated a 12-year-old boy presenting with developmental delay and neurological abnormalities. Genomic DNA was extracted from peripheral blood, followed by whole exome sequencing (WES) using the Agilent SureSelect Human All Exon V7 Plus platform and Illumina NovaSeq 6000. Variant filtering was performed based on allele frequency, pathogenicity predictions, and ACMG criteria. The identified variant was validated by Sanger sequencing and co-segregation analysis in the family.

Results: A novel homozygous missense variant in PIGC (c.593AG; p.H198R) was identified in the affected patient, while both parents were heterozygous carriers. The variant was classified as a variant of uncertain significance (VUS) according to ACMG guidelines. Clinical findings included global developmental delay, impaired speech, delayed motor milestones, and brain abnormalities.

Conclusion: We report a 12-year-old boy with clinical features consistent with glycosylphosphatidylinositol deficiency, in whom a novel homozygous PIGC variant (c.593AG; p.H198R) was identified. This case adds to the spectrum of reported PIGC variants associated with neurodevelopmental disorders.

keywords: PIGC; glycosylphosphatidylinositol deficiency; GPI-anchor biosynthesis; whole exome sequencing; developmental delay;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PG-82

Expanding the Mutation Spectrum of GALNS: Identification and pathogenicity assessment of a Novel Variant Causing MPS IVA in an Iranian Family

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Background and aim: Mucopolysaccharidosis type IVA (MPS IVA), also referred to as Morquio A, is an autosomal recessive lysosomal storage disorder that arises from mutations in the GALNS gene. This gene encodes the lysosomal enzyme GalN6S, which is critical to the degradation of glycosaminoglycans (GAGs), including keratan sulfate (KS) and chondroitin-6-sulfate (C6S). A deficiency or impaired activity of this enzyme contributes to the accumulation of GAGs in lysosomes, which eventually causes the clinical signs of the disease. This study aimed to evaluate the pathogenicity of an unreported homozygous GALNS variant and to support its reclassification through ACMG criteria.

Methods: The proband is a 15-year-old Turkish boy from a second-cousin marriage in an Iranian family. He shows clinical manifestations including hypermobile joints, premature fatigue, pectus carinatum, musculoskeletal pain, and sleep apnea. Enzyme assay tests showed GalN6S 0 (Complete absence) and normal range for Hexosaminidase (A+B) and β-galactosidase. Whole-exome sequencing (WES) was carried out on the proband, followed by variant prioritization based on allele frequency, inheritance pattern, predicted pathogenicity, and clinical relevance. Candidate variants were validated using Sanger sequencing.

Results: The analysis of WES data identified the homozygous c.1265 AG variation in the GALNS gene as the genetic etiology of the disease in the proband. In silico prediction tools, including CADD: 29.4, DANN: 0.99629, Mutation Taster: 1, predicted the variant to be deleterious. In accordance with the variant classification guidelines established by the ACMG, the variant is currently classified as Variant of Uncertain Significance (VUS) and follows the criteria of PM2, PP2, and PP3. Given the high degree of phenotypic concordance between the patient's clinical presentation and the established genetic etiology of the disease, the PP4 criterion was applied to existed ACMG criteria and lead to the successful reclassification of the variant from VUS to Likely Pathogenic.

Conclusion: This study presents the first report of the GALNS: c.1265AG (p.Gln422Arg) variant and supports the potential pathogenicity role of this variation in MPS IVA. These findings, in addition to the enhancement of genetic databases, can significantly assist physicians and geneticists in accurate interpretation of this variant and in clinical decision-making, especially when performing prenatal diagnosis and genetic counseling.

keywords: MPS IVA, GALNS, WES, Molecular docking, Variant reclassification

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July 20-23, 2026

PG-83

A Homozygous Candidate GALT Variant Identified in Two Related Individuals with Galactosemia

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Background and aim: Galactosemia is an autosomal recessive disorder resulting from an enzyme defect in the galactose metabolic pathway. The most severe manifestation of classic galactosemia is caused by galactose-1-phosphate uridylyltransferase (GALT) deficiency, and this condition can be fatal during infancy if left untreated. This study aimed to assess the pathogenic potential of a rare homozygous GALT variant and to gather supporting evidence for its interpretation through segregation analysis and correlation with the characteristic clinical and biochemical features in accordance with ACMG criteria.

Methods: The proband was a 4-year-old child born to consanguineous parents who presented with biochemical findings consistent with classic galactosemia, including markedly elevated galactose levels (180 mg/dl) and severely reduced galactose-1-phosphate uridyltransferase activity (5 act). He also exhibited clinical manifestations, including jaundice, feeding difficulties, failure to thrive, and liver dysfunction in infancy. A second affected individual with a similar phenotype was identified within the extended pedigree; however, his parents were non-consanguineous. Whole-exome sequencing (WES) was performed to investigate the underlying genetic cause, and the identified finding was subsequently confirmed by Sanger sequencing. Variant interpretation was carried out according to ACMG recommendations, taking into account multiple lines of evidence, including allele frequency, inheritance pattern, family history, segregation data, and the clinical and biochemical characteristics of the affected individuals.

Results: WES identified the GALT:c.167AG (p.Gln56Pro) variant as the candidate disease-causing variant in the proband. Sanger sequencing confirmed the variant in the homozygous state in the proband, while both parents and other unaffected family members were heterozygous carriers. Targeted Sanger analysis in a second affected relative from the extended pedigree also revealed homozygosity for the same variant. The observed segregation pattern provided supporting evidence for pathogenicity (PP1). In addition, the affected individuals exhibited clinical manifestations and biochemical findings highly specific for classic galactosemia, fulfilling the PP4 criterion. Collectively, these findings supported the reclassification of the variant from a variant of uncertain significance (VUS) to likely pathogenic according to ACMG guidelines.

Conclusion: Our findings suggest that the homozygous GALT:c.167AG variant is a candidate for the disease phenotype in this family. These findings, in addition to expanding the genetic database, are useful in clinical decision-making, genetic counseling, and prenatal diagnosis.

keywords: Metabolic disorders, galactosemia, GALT, WES, variant of uncertain significance.

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PG-84

Genome Editing with Base Editing and Prime Editing for Inherited Genetic Disorders: Current Advances, Challenges, and Future Perspectives (Narrative Review)

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Background and aim: Pathogenic mutations in genes are known to cause familial genetic diseases which continue to pose a significant hurdle for modern medicine.Conventional CRISPR-Cas9 technology has made genetic manipulation approaches much easier, but double-strand DNA breaks, undesired insertions and deletions, and off-target effects all have restricted therapeutic applications. Base editing and prime editing are recently developed next-generation genome editing techniques, which can mediate efficient site-specific genetic modifications without double-strand breaks.These technologies have shown potential as a therapeutic option for a number of genetic disorders. This review summarizes base and prime editing advances, applications for genetic disorders, challenges, and future directions.

Methods: A systematic literature review was performed to identify and summarize the progress on base editing and prime editing for the treatment of inherited genetic disorders. Peer-reviewed original articles, reviews and preclinical research studies published between January 2019 and June 2026 were included from searching in the databases of PubMed, Scopus, Web of Science and Google Scholar using keywords as: “base editing”, “prime editing”, “genome editing”, “CRISPR” and “inherited genetic disorders”. Articles that have been reviewed were considered; data were extracted, classified and analyzed; non-original and review articles with poor evidence were omitted, and studies not targeted for the treatment of inherited disorders and with insufficient data were excluded. Based on the reviewed articles, data collected including technological development, disease application, clinical challenges, future prospective, were analyzed and summarized in the current study to provide a detailed picture about the state-of-the-art and prospective translation of base editing and prime editing technology.

Results: Developments in base editing and prime editing have brought greater specificity and effectiveness of genome editing technologies to inherited genetic disease patients. Both optimized prime editor proteins and pegRNA design increased editing efficiency while simultaneously reduced off-target editing and unwanted edits. Several genetic diseases like Tay-Sachs, cystic fibrosis, Duchenne muscular dystrophy, hereditary tyrosinemia type I, phenylketonuria and alpha-1 antitrypsin deficiency were successfully edited in patient samples or in vivo models of disease. These studies, using a variety of delivery strategies, including viral, electroporation and non-viral approaches, were encouraging.Nevertheless, there are certain challenges associated with their application in the clinics, such as delivery efficiency and range, immunological response, and space limits. It is anticipate that continued improvements in technology would pave the way to broaden the applications and safe usage of genome editing therapies.

Conclusion: Base editing and prime editing have emerged as groundbreaking strategies for targeted correction of genetic defects causing inherited diseases. Over the last years, technology advancements has enhanced precision, specificity and therapeutic application in various models of human disease. While delivery systems, off-targets effects, clinical application and long-term outcome need to be optimized further, these next-generation technologies are progressively gaining ground for future clinical practice and are likely to be integrated into the personalized medicine landscape.

keywords: Genome Editing, Base Editing ,Prime Editing , CRISPR-Cas9

PG-85

Effects of Adipose-Derived Mesenchymal Stem Cell–Conditioned Medium on CD44 Marker in U87 Glioblastoma Cells

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Background and aim: Glioblastoma multiforme (GBM) represents the most prevalent and aggressive form of primary brain malignancy in adult populations, and despite extensive clinical efforts, an effective therapeutic approach is still lacking. Recently, the application of conditioned medium obtained from mesenchymal stem cells (MSC CM) has emerged as a potentially promising strategy in oncology; however, its therapeutic value remains ambiguous. In the present investigation, we examined how conditioned medium derived from adipose derived mesenchymal stem cells (ADMSC CM) influences the expression of the stemness related surface marker CD44 in GBM cells.

Methods: ADMSCs were characterized using flow cytometry, and their conditioned medium was employed to treat U87 glioblastoma cells. Subsequent flow cytometric analysis was performed to quantify both the relative frequency and mean fluorescence intensity (MFI) of CD44 expression.

Results: Our findings indicated that treatment with ADMSC CM led to a significant elevation in the proportion of CD44 positive cells compared with untreated controls (P 0.05), while no meaningful alteration in MFI was observed.

Conclusion: Overall, these data suggest that ADMSC CM does not exert a favorable modulatory effect on the CD44 stemness marker in GBM cells. The outcomes underscore the complex and multifaceted nature of interactions between mesenchymal stem cells and glioblastoma, emphasizing the need for further studies to elucidate the underlying mechanisms involved.

keywords: Glioblastoma, ADMSC-CM, CD44

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PG-86

Identifying Key Biomarkers in Celiac Disease through Analysis of Microarray Data

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Background and aim: Celiac disease (CeD) is a chronic autoimmune enteropathy triggered by gluten ingestion in genetically susceptible individuals. Current diagnosis relies mainly on serological tests and duodenal biopsy, which may be invasive or insufficient for identifying all clinically relevant molecular alterations. This study aimed to identify potential diagnostic biomarkers and regulatory miRNAs associated with CeD by integrating and analyzing publicly available microarray gene-expression datasets.

Methods: Three Gene Expression Omnibus datasets, GSE112102, GSE113469, and GSE164883, were selected based on predefined eligibility criteria and analyzed using a bioinformatics meta-analysis approach. After normalization and batch-effect correction, differentially expressed genes (DEGs) between CeD patients and healthy controls were identified using the limma package in R. Gene Ontology, KEGG, and Reactome enrichment analyses were performed to explore biological functions and pathways. A protein–protein interaction network was constructed using STRING and Cytoscape. Hub genes were identified through cytoHubba and MCODE analyses. Receiver operating characteristic curve analysis was used to assess diagnostic performance, and miRNA–hub gene interactions were evaluated using miRTarBase, TargetScan, miRWalk, and miRNet.

Results: A total of 165 DEGs were identified, including 79 upregulated and 86 downregulated genes. Enrichment analyses showed significant involvement of immune-related pathways, including interferon-gamma response, defense response to virus, JAK-STAT signaling, NOD-like receptor signaling, and interleukin-4/interleukin-13 signaling. Protein–protein interaction analysis identified five central hub genes: STAT1, CDC20, PRF1, CCL2, and MYC. These genes were consistently detected across centrality-based and clustering methods and demonstrated acceptable diagnostic potential, with receiver operating characteristic curve AUC values ranging from 0.7 to 0.9. miRNA interaction analysis revealed several important regulatory miRNAs, including hsa-miR-155-5p, hsa-miR-145-5p, hsa-miR-18a-5p, hsa-miR-34a-5p, hsa-miR-24-3p, and hsa-miR-146a-5p.

Conclusion: This study identified STAT1, CDC20, PRF1, CCL2, and MYC as promising biomarkers involved in CeD pathogenesis, mainly through immune activation and cell-cycle regulation. The associated miRNAs may also contribute to disease progression. These findings provide a basis for future experimental validation and may support improved diagnostic and therapeutic strategies for celiac disease.

keywords: Celiac disease; Biomarkers; Microarray; Bioinformatics; Differentially expressed genes; STAT1; CDC20

PH-1

A Rare Case of Klippel Trenaunay Syndrome with Von Willebrand Factor Deficiency and Multiple Accessory Spleens: A Case Report and Brief Literature Review

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Background and aim: Klippel Trenaunay Syndrome (KTS) is an uncommon inherited syndrome identified by venous varicosities and capillary abnormalities. von Willebrand Disease is the most common inherited hemorrhage disturbance in humans, leading to insufficiency in von Willebrand Factor, which is a complex multimeric protein with two functions: it forms a bridge between the platelets and injured vascular areas and it attaches factor VIII and stabilizes it.

Methods: We present a 13-year-old son with a typical clinical manifestation of KTS, including "port-wine stains" as capillary malformation, venous malformation, and hypertrophy of the left lower extremity, who also suffers from von Willebrand Disease type 3. He has been suffering from these two rare conditions since birth. The occurrence of KTS with von Willebrand Factor deficiency in a patient has so far not been reported, which may propose a mutation in the putative common regulatory gene that caused this uncommon phenotype.

Results: The Doppler ultrasound of all four extremities, trunk, and midaxillary lesion revealed: 1: There was venous malformation in the right midaxillary. 2: Extensive capillary malformation has been found in all four limbs and trunks. 3: No evidence of DVT reported. Magnetic resonance imaging of the thorax with and without contrast reported a septated lesion with decreased signal intensity in T1. It suggested venous malformation. His medications for vWD were iron supplement (200 mg ferrous sulfate three times daily) with haemate p (1,500 IU three times weekly). Compression stockings or bandages were used 8 hours/day for his left leg lymphedema. There was no invasive therapy or surgery in his history till now.

Conclusion: As a result, the event of these two rare pathologies in a single patient has not been characterized so far, which may propose a mutation in a hypothetical common regulatory gene cause this uncommon phenotype.

keywords: Klippel Trenaunay weber syndrome, von Willebrand disease, von Willebrand factor

PH-2

Topical Hemostatic Materials for Battlefield Trauma Care

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Background and aim: Uncontrolled bleeding is still a leading cause of combat death. According to recent studies, a significant portion of deaths on the battlefield are potentially survivable. Notably, more than 90% of casualties die before reaching the field hospital, making rapid bleeding control on the battlefield crucial. Over the past decade, several agents and devices have been developed to aid in bleeding control. We aimed to review the various aspects of known hemostatic agents, particularly their effectiveness in military applications.

Methods: Comprehensive search was conducted in electronic databases (PubMed, Web of Science, Scopus, and Google Scholar) using keywords including military, war, battlefield, trauma, bleeding, hemostatic, bandage, and dressing.

Results: Hemostatic agents can act through a variety of mechanisms, including wound contraction, concentration of coagulation factors, adhesion to tissues, and release of coagulation factors at the bleeding site. The most important characteristics of an ideal hemostatic agent for controlling urban and battlefield bleeding include the ability to stop bleeding immediately, no need for mixing or processing before use, ease of use, lightweight and durable nature, long shelf life, acceptable safety, and cost-effectiveness. Additionally, it should be biodegradable, non-toxic, easy to remove, and flexible.

Conclusion: Since 2003, various compounds such as Chitosan, Zeolite, Kaolin, Fibrin, and Smectite have been used to produce hemostatic products including HemCon, Celox, ChitoFlex, QuikClot, Combat Gauze, FSD, and WoundStat. Some of these products have received FDA approval, particularly for battlefield use. However, achieving the ideal product still requires further studies in the future.

keywords: Battlefield, Bleeding, Trauma, Hemostatics

PH-3

Targeting Genomic and Epigenomic Alterations in Waldenström Macroglobulinemia: Emerging Therapeutic Strategies

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Background and aim: Waldenström macroglobulinemia (WM) is a rare indolent B-cell lymphoma characterized by monoclonal immunoglobulin M (IgM) production. Recent genomic studies have highlighted specific mutations, such as MYD88 and CXCR4, that contribute to disease progression and therapeutic resistance. However, less attention has been given to the epigenomic landscape and its role in WM pathogenesis. This review focuses on the emerging therapeutic strategies that target both the genomic and epigenomic alterations in WM, offering new avenues for treatment beyond conventional therapies.

Methods: A systematic review of recent studies was conducted, focusing on both genomic mutations (MYD88, CXCR4) and novel epigenetic modifications in WM. Preclinical and clinical data regarding the efficacy of targeted therapies, including BTK inhibitors (ibrutinib, zanubrutinib), and emerging epigenetic modulators were analyzed. Special emphasis was placed on combination therapies targeting both genetic and epigenetic drivers of WM.

Results: The review identifies that MYD88 and CXCR4 mutations are critical drivers of WM and are being successfully targeted by BTK inhibitors. Additionally, epigenetic modifications such as DNA methylation and histone acetylation are now recognized as potential therapeutic targets. Combining BTK inhibitors with epigenetic drugs has shown promising results in preclinical models, enhancing sensitivity to treatment and overcoming resistance mechanisms.

Conclusion: Targeting both the genomic and epigenomic landscape in WM offers a novel and more comprehensive approach to therapy. Future clinical trials should explore combination strategies to improve outcomes for WM patients, especially those with resistant or relapsed disease.

keywords: Waldenström Macroglobulinemia, MYD88, CXCR4, Epigenetics, BTK Inhibitors, Epigenetic Modulators, Hematology.

PH-4

Revolutionizing Multiple Myeloma Treatment: The Potential of Immunotherapies Targeting the Tumor Microenvironment

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Background and aim: Multiple myeloma (MM) is a complex hematologic malignancy, where the tumor microenvironment (TME) plays a critical role in disease progression and therapeutic resistance. While significant strides have been made in MM treatments, including proteasome inhibitors and immunomodulatory drugs, relapse and resistance remain major challenges. Recent research has shifted focus toward targeting the TME to disrupt the protective niche provided to myeloma cells. This review explores the emerging immunotherapies aimed at the MM-TME interface, offering new perspectives on treatment approaches.

Methods: A comprehensive literature review was conducted, focusing on studies published within the last five years. Key areas of investigation included TME components such as stromal cells, immune cells, cytokines, and extracellular matrix interactions. The review emphasizes novel immunotherapies, including CAR-T cells, bispecific T-cell engagers (BiTEs), and checkpoint inhibitors, specifically designed to modulate the TME. Ongoing clinical trials and preclinical studies were also analyzed to assess the efficacy of these therapies.

Results: The review highlights that therapies targeting the TME have shown promise in overcoming drug resistance and enhancing treatment efficacy. CAR-T cell therapies directed at TME-associated antigens, along with BiTEs and checkpoint inhibitors, have demonstrated encouraging results in preclinical models and early-phase trials. Targeting cytokine signaling and TME-modulated immune evasion mechanisms has improved treatment responses, particularly in relapsed/refractory MM.

Conclusion: Targeting the TME in MM represents a novel therapeutic strategy with significant potential to improve patient outcomes. Continued exploration of immunotherapies focused on the TME may offer a path toward more durable and effective MM treatments.

keywords: Multiple Myeloma, Tumor Microenvironment, CAR-T Cells, Bispecific T-cell Engagers

PH-5

Identification of novel RASGRP2 mutations in patients with platelet dysfunction

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Background and aim: Inherited platelet function disorders (IPFDs) are rare hereditary diseases characterized by dysregulation of genes related to platelet receptors expression or signal transduction pathways. Bleeding disorder platelet-type 18 (BDPLT18) is an infrequent autosomal recessive platelet function disorder caused by RASGRP2 mutation. The RASGRP2 gene encodes calcium- and DAG-regulated guanine exchange factor-1 (CalDAG-GEFI), which plays a role in the activation of the αIIbβ3 integrin in platelets. In present study, eleven unrelated patients were examined for mutational analysis to identify mutations in RASGRP2 gene that may lead to BDPLT18.

Methods: The study included 11 unrelated cases (6 males and 5 females) with various bleeding disorders in 2024. The patients were selected based on normal expression of CD41, CD61, and CD42b, as well as an impaired response to ADP, collagen, and arachidonic acid. The plasma coagulation parameters of the patients were normal. Polymerase chain reaction (PCR) and sanger sequencing were used to screen for mutations in the RASGRP2 gene.

Results: A total of 7 mutations were identified in the patients. Including four novel missense mutations (RASGRP2: p.F497L, p.F501L, p.N505K, p.C515G) and 3 known mutations (RASGRP2: p.D441N, p.R494Afs*54, g.10410GT). These mutations are predicted to cause disease and alter the characteristics of the CalDAG-GEFI protein.

Conclusion: Identifying RASGRP2 gene mutations and their association with bleeding episodes is crucial for confirming the diagnosis of BDPLT18, distinguishing it from other platelet disorders, and using effective therapeutics to prevent bleeding abnormalities.

keywords: Inherited platelet function disorders, Bleeding disorder, mutation, platelet-type bleeding disorder-18,

PH-6

Neutrophil Extracellular Traps in Multiple Myeloma Treatment: A narrative Review

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Background and aim: Multiple myeloma is a clinically challenging malignancy despite substantial advances in proteasome inhibitors, immunomodulatory drugs, monoclonal antibodies, and cellular therapies. Over the past decade, investigators have increasingly focused on the tumor microenvironment as a key determinant of treatment resistance, relapse, and disease persistence. Neutrophil extracellular traps (NETs) have been implicated in promoting metastasis, coating tumor cells, and shaping local immune responses. The intersection of NETs biology and myeloma a context dominated by chronic inflammation and immune dysfunction has therefore emerged as a new frontier in research. this study, investigate the impact of NETs on the pathobiology of multiple myeloma.

Methods: After a comprehensive review of the scientific literature identified in databases including PubMed, ScienceDirect, Cochrane, and Google Scholar, 100 articles were selected based on predefined inclusion and exclusion criteria. For inclusion, studies that specifically investigated NETs in the context of multiple myeloma were considered.

Results: Myeloma cells activate neutrophils through the secretion of IL-6, TNF-α, and various chemokines. NETs can stimulate the bone marrow stroma to produce pro-myeloma cytokines, generate a structural matrix that supports malignant plasma-cell survival, and promote adhesion-mediated drug resistance within the marrow niche. Tumor-derived factors, including exosomes and damage-associated molecular patterns, further potentiate NETs formation. The consequent microenvironmental remodeling fosters angiogenesis, osteoclast activation, and suppression of osteoblast differentiation, thereby contributing to the pathogenesis of myeloma-associated bone disease. NETs can physically entrap T cells and NK cells, impairing their cytotoxic function against malignant plasma cells. In addition, NETs-derived proteases may cleave activating receptors or release immunosuppressive fragments, further attenuating anti-tumor immune responses. NETs serve as scaffolds for fibrin, platelets, and erythrocytes, thereby promoting intravascular thrombus formation and increasing the risk of venous thromboembolism in myeloma patients—particularly those receiving immunomodulatory drugs.

Conclusion: NETs represent a rapidly evolving area of investigation in multiple myeloma research. Their involvement in inflammation, immune evasion, bone marrow remodeling, and thrombosis renders them an attractive therapeutic target. Although many aspects remain to be elucidated, NETs based strategies have the potential to complement existing myeloma therapies and improve outcomes for patients with this complex malignancy.

keywords: Multiple myeloma, NETs , chronic inflammation

PH-7

The Combination Therapy With Sorafenib in Therapeutic Strategy of Acute Myeloid Leukemia. Is It Promising?

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Background and aim: Acute myeloid leukemia (AML) is the most common acute leukemia, which is associated with high morbidity and mortality, and its incidence rate is increasing. Despite tremendous advancements in AML treatment, managing the condition is still challenging. Receptor kinase inhibitors like sorafenib have recently raised concerns about monotherapy, and combination treatments are now being investigated as a potential therapeutic avenue. To classify medications taken in conjunction with sorafenib and analyze their combined effects, we reviewed the prior research findings.

Methods: A thorough literature search utilizing several databases, including PubMed, Google Scholar, Scopus, Embase, and Cochrane, yielded 78 relevant articles until October 2023. Search terms including AML, combination, and Sorafenib were utilized during the database search to find relevant papers.

Results: Complete remission (CR) in the combination of sorafenib with “cytarabine and idarubicin”, “Vorinostat and Bortezomib, Clofarabine”, “Fludarabine and Busulfan”, “5-azacytidine” and “Quizartinib, Midostaurin and Giltertinib” respectively “99% and 94%”, “27% and 3%”, 66.6%, “45%, 26%, 16%”, “71% and 52%”. Furthermore, the overall survival (OS) values for the combination of sorafenib with “Quizartinib, Midostaurin, and Giltertinib”, “cytarabine, daunorubicin” and “5-azacitidine” were “80%” “62% 45%”, and 24%, respectively.

Conclusion: Accordingly, several studies suggest that sorafenib's anticancer effectiveness may be enhanced with chemotherapy drugs.

keywords: AML, combination, sorafenib

PH-8

Therapeutic Potential of CD-5 Targeted CAR-NK Cells in T-Cell Leukemia/Lymphoma

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Background and aim: T-cell leukemias and lymphomas ($CD5^+$) are rare but aggressive hematologic malignancies with poor prognosis and resistance to chemotherapy. Existing immunotherapies such as CAR-T cells demonstrate anti-tumor activity but face significant challenges including fratricide, cytokine-release syndrome, T-cell exhaustion, and antigen escape. CD5 is consistently overexpressed on malignant T cells while showing minimal expression on NK cells making it a promising therapeutic target for selective cytotoxicity with reduced toxicity. This study evaluates CD5-targeted CAR-NK cells as a safer therapeutic approach for T-cell leukemia/lymphoma, as this strategy exhibits fewer limitations and adverse effects compared to previous treatments while offering greater therapeutic potential.

Methods: This review included studies retrieved from PubMed, Web of science, and Scopus databases that were published between 2017 and 2025. Data were collected using the keywords: “CAR-NK”, “CD5”, “T-cell leukemia”, and “T-cell lymphoma”.

Results: Studies showed that CD5-targeted CAR-NK cells exhibited strong cytotoxicity, rapid activation, and a lower risk of cytokine release syndrome compared to CAR-T cell therapy. However, challenges such as limited persistence, NK cell exhaustion, immune suppression by the tumor microenvironment, and lack of standardized manufacturing still remained. Proposed strategies to overcome these limitations include checkpoint inhibition to reduce exhaustion and counteract immunosuppression by the tumor microenvironment, metabolic reprogramming to enhance NK-cell survival and persistence, and cytokine support to improve stability and augment cytotoxicity.

Conclusion: The results showed that CD5-CAR-NK therapy represented a novel and promising therapeutic platform for T-cell leukemia and lymphoma ($CD5^+$) with high potential for clinical application. Therefore, it could represent as a suitable alternative to CAR-T cells as a novel therapeutic platform in the near future.

keywords: CAR-NK, CD5, T-cell leukemia, T-cell lymphoma

PH-9

Beyond Remission: The Cardiotoxic and Thrombotic Shadow of AML Chemotherapy

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Background and aim: Acute myeloid leukemia (AML) continues to carry high early mortality despite advances in targeted therapy, largely due to treatment-related toxicities that compromise therapeutic intensity. Among these, cardio-thrombotic complications remain critically underrecognized contributors to morbidity and survival disparity. Anthracycline-induced myocardial injury, compounded by endothelial dysfunction, platelet activation, and inflammatory hypercoagulability, creates a biologically interconnected spectrum of cardiovascular damage. In settings with limited access to cardiovascular monitoring and preventive care, these toxicities drive treatment interruption and inferior outcomes. Addressing cardio-thrombotic injury is therefore central to achieving durable remission and equitable AML care.

Methods: A comprehensive narrative review was conducted using PubMed, Scopus, and Web of Science databases to identify preclinical, clinical, and translational studies published up to 2025 addressing cardiotoxicity, thrombosis, and inflammatory vascular injury in AML. Search terms included combinations of “acute myeloid leukemia,” “anthracycline cardiotoxicity,” “thrombosis,” “platelet activation,” “NETosis,” and “cardio-oncology.” Evidence was systematically organized into mechanistic pathways (oxidative stress, mitochondrial dysfunction, endothelial damage, platelet–leukocyte interactions), clinical manifestations (heart failure, venous and arterial thrombosis), and emerging mitigation strategies. Special emphasis was placed on disparities in monitoring, biomarker availability, and supportive care across healthcare settings.

Results: The reviewed evidence demonstrates that anthracycline-induced myocardial injury and AML-associated thromboinflammation share convergent mechanisms involving oxidative stress, endothelial dysfunction, platelet activation, and NET formation. These processes significantly increase cardiotoxic and thrombotic events, leading to chemotherapy dose reductions, treatment delays, and inferior remission rates. The burden is amplified in settings lacking early biomarker surveillance or cardiovascular expertise. Emerging precision approaches, including predictive modeling and targeted drug delivery platforms, show potential to reduce off-target toxicity while preserving antileukemic efficacy, particularly when integrated into risk-adapted treatment algorithms.

Conclusion: Cardio-thrombotic injury in AML represents both a biological vulnerability and a systemic inequity. Addressing this dual burden requires reframing AML therapy beyond cytotoxic success toward integrated cardio-onco-hematologic care. Precision risk stratification, early biomarker monitoring, and innovative drug delivery strategies offer scalable solutions to reduce toxicity-driven treatment failure. Embedding cardio-thrombotic protection into AML protocols has the potential to narrow survival disparities, improve treatment continuity, and advance therapeutic equity across diverse healthcare environments.

keywords: Acute Myeloid Leukemia, Cardiotoxicity, Thrombosis, Chemotherapy, Hydrogel, Hitchhiking.

PH-10

Programmable DNA Hydrogels for Surgical Hemostasis and Active Suppression of Tumor Recurrence

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Background and aim: Post-surgical complications—most notably hemorrhage and tumor recurrence—remain dominant contributors to perioperative mortality, prolonged hospitalization, and long-term oncologic failure. Acute bleeding represents an immediate life-threatening event, whereas local tumor recurrence reflects incomplete eradication of residual malignant cells within the surgical bed. Existing hemostatic materials provide rapid clot formation but are frequently limited by inadequate tissue adhesion, mechanical instability, and short functional lifespan. In parallel, conventional adjuvant therapies rely on systemic drug delivery, often failing to achieve therapeutic concentrations at the resection margin while exposing patients to systemic toxicity. Together, these limitations highlight a critical unmet need for localized, multifunctional, and adaptive

Methods: This review synthesizes and critically analyzes recent advances in programmable DNA hydrogel technologies for post-surgical applications in oncology. We examine material design principles, self-assembly mechanisms, mechanical and biochemical tunability, and stimuli-responsive behaviors of DNA-based hydrogels. Preclinical studies evaluating hemostatic efficacy, localized drug delivery, immunomodulation, and tumor control are systematically discussed, alongside emerging hybrid platforms incorporating nanoparticles, bioactive agents, and biosensing elements. Translational considerations—including biocompatibility, biodegradation, manufacturability, and regulatory pathways—are also addressed.

Results: Accumulating preclinical evidence demonstrates that DNA hydrogels, constructed from sequence-defined motifs forming three-dimensional networks, can be engineered to provide rapid and stable hemostasis through localized delivery of pro-coagulant factors and mechanical sealing of wounded tissue. Simultaneously, these systems enable sustained, site-specific release of chemotherapeutics, immunomodulators, or nanomedicine cargos, effectively targeting residual tumor cells within the surgical microenvironment. Importantly, programmable DNA architectures allow precise control over gel stiffness, degradation kinetics, and release profiles, while hybrid designs incorporating sensing or feedback mechanisms introduce the potential for patient-specific and adaptive postoperative responses.

Conclusion: Post-surgical hemorrhage and tumor recurrence remain interconnected yet insufficiently addressed challenges in surgical oncology. The evidence synthesized in this review indicates that programmable DNA hydrogels offer a uniquely integrated solution by uniting rapid, localized hemostasis with sustained suppression of residual tumor growth. Their sequence-defined architecture enables precise control over mechanical properties, biodegradation, and cargo release, allowing these materials to function not merely as passive wound dressings but as active, adaptive therapeutic platforms. By localizing pro-coagulant, chemotherapeutic, immunomodulatory, or nanomedicine-based interventions directly to the surgical bed, DNA hydrogels have the potential.

keywords: Hemostasis, Tumor recurrence, Hydrogel, Target therapy.

PH-11

Artificial Intelligence–Based Analysis of Routine Complete Blood Count for Early Identification of Hematologic Malignancies: A Review

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Background and aim: Hematologic malignancies often present with vague clinical symptoms and nonspecific laboratory abnormalities that can delay diagnosis and initiation of appropriate treatment. Although the complete blood count (CBC) is one of the most common and widely available laboratory tests, routine interpretation may miss subtle changes that indicate an underlying malignant process. In recent years, advances in artificial intelligence (AI) and machine learning have opened up new possibilities for extracting clinically meaningful information from routine CBC data.

Methods: This review describes the evidence on the use of AI-based methods applied to CBC parameters for early detection and screening of hematologic malignancies.

Results: Published studies show that machine learning models are able to recognize complex patterns in CBC results that are associated with leukemias, myelodysplastic syndromes, and myeloproliferative neoplasms, improving diagnostic performance. AI-powered analysis of CBC data may enhance risk stratification, assist laboratory professionals in interpreting results, and expedite early referral for confirmatory studies such as peripheral blood smear evaluation and flow cytometry.

Conclusion: Despite these promising findings, several limitations need to be addressed, including variability in data sources, limited model transparency, and challenges in integrating AI tools into routine laboratory procedures. However, AI-assisted interpretation of routine CBC results offers a practical and cost-effective strategy to improve early detection of hematological malignancies and enhance collaboration between laboratory and clinical teams. Further validation studies and standardized implementation frameworks are needed before such approaches can be widely adopted in clinical settings.

keywords: Artificial Intelligence, Complete Blood Count, Hematologic Neoplasms

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-12

The Role of Gut Microbiome Dysbiosis in Pain Modulation Among Sickle Cell Disease Patients: A Systematic Review

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Background and aim: Pain is one of the major and significant complications in patients with sickle cell disease (SCD), profoundly affecting their quality of life. Gut microbiome dysbiosis, particularly characterized by a reduction in beneficial bacteria and an increase in pro-inflammatory species, may serve as a key factor in the manifestation of disease symptoms. The aim of this study was to systematically review the existing evidence regarding the relationship between gut microbiome dysbiosis and pain severity in patients with sickle cell disease.

Methods: This study was conducted based on the PICO framework, aligned with the research objective, and followed the PRISMA checklist. A systematic search was performed from 2015 to December 2025 across PubMed, Scopus, Web of Science, SID, Medline, and the Google Scholar search engine. The search strategy included MeSH terms such as “Sickle cell disease,” “Gut Microbiome,” and “Pain.” Two independent researchers screened the retrieved articles based on inclusion criteria. The initial search identified 110 articles. After applying inclusion and exclusion criteria and critically assessing article quality, six studies were included in the review.

Results: The studies demonstrated that a reduced abundance of beneficial bacteria such as Akkermansia muciniphila, Holdemanella, and Roseburia spp. was associated with impaired intestinal barrier function, decreased production of short-chain fatty acids, and increased inflammation. These dysbiosis-induced metabolic alterations were linked to enhanced pain signaling, potentially mediated through activation of the vagus nerve pathway. Furthermore, an increased abundance of certain pro-inflammatory bacteria, including Veillonella and Ruminococcus, correlated with higher pain severity. Evidence from fecal microbiota transplantation studies also confirmed the direct influence of the gut microbiome on pain modulation: transferring microbiota from SCD patients to healthy mice increased pain sensitivity, whereas transplantation from healthy donors temporarily alleviated pain symptoms. Collectively, these findings suggest that alterations in gut microbial composition can directly or indirectly influence pain severity in SCD patients.

Conclusion: Gut microbiome dysbiosis in patients with sickle cell disease is associated with the onset and exacerbation of pain symptoms. Accordingly, modulation of the gut microbiome through targeted interventions, including probiotic supplementation, may represent a potential adjunctive strategy for pain management in these patients.

keywords: Sickle cell disease; Gut Microbiome; Pain

PH-13

A Case Report of Facial Nerve Palsy in Kawasaki Disease

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Background and aim: One of the most prevalent childhood vasculitis is kawasaki disease (KD), which mainly affects medium-sized arteries throughout the body. This disease usually does not cause many neurological symptoms and only rarely results in facial nerve palsy (FNP).

Methods: A 4.6-month-old iranian girl presented due to a prolonged fever. Lab tests showed increased CRP, ESR, ferritin, WBC, and platelet counts, and echocardiography revealed dilated right and left main coronary arteries, without any vegetations, pericardial effusion, and atrioventricular valve regurgitation. The patient was diagnosed with incomplete KD. At the same time, she developed left-sided peripheral FNP.

Results: Patient treated with intravenous immunoglobulin and aspirin. The fever resolved after about 36 hours, and the patient was discharged on the 16th day of hospital admission. Follow-up echocardiography demonstrated gradually resolution of her coronary arteries dilation. FNP was recovered completely after about 2 months.

Conclusion: FNP is an uncommon neurological symptom of KD. However, it typically resolves on its own and without any lasting effects in those who survive the illness. Nevertheless, it may indicate a higher likelihood of coronary artery involvement, and as a result, additional anti-inflammatory treatments and more closely monitored echocardiography may be necessary.

keywords: Coronary artery, Facial nerve palsy, Kawasaki disease.

PH-14

Inhibition of Tumor Growth through Co-Delivery of BV6 and Anti-IL6 siRNA Using Hyaluronate-Modified PEG-Chitosan-Lactate Nanoparticles

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Background and aim: IL-6 is a key cytokine in the tumor microenvironment, promoting growth, survival, invasion, metastasis, angiogenesis, and drug resistance. Systemic IL-6 inhibitors have significant side effects; the study explores nanoparticle-based RNA interference to selectively suppress IL-6 in tumors at low doses. Nanoparticles enable in vivo RNAi and targeted drug delivery in animals. The apoptosis pathway involves IAPs; BV6, an IAP antagonist, inhibits multiple IAPs to induce apoptosisThis study develops hyaluronate-PEG-chitosan-lactate nanoparticles to co-deliver anti-IL-6 siRNA and BV6, showing promising results in reducing tumor growth and increasing survival in animal models.

Methods: The experiment will be conducted in two phases. In Phase I, nanoparticles loaded with siRNA and the drug will be produced and their physicochemical properties will be characterized. In Phase II, the effects of nanoparticle-based treatment on survival and proliferation, expression of genes involved in apoptosis, viability, angiogenesis, and metastasis, and the migration of mouse mammary cancer cells (4T1) will be examined. The expression levels of IL-6 and its angiogenic and metastatic factors (VEGF, bFGF, MMP2, MMP9), pro-apoptotic factors (Bax), and anti-apoptotic factors (Bcl-2) will be measured using Real-time PCR.

Results: PCL NPs exhibited good physicochemical properties leading to efficient transfection of cancer cells and suppression of target molecules. Moreover, combination therapy synergistically increased apoptosis, as well as decreased cell migration, proliferation, colony formation, and angiogenesis in both 4T1 and CT26 cell lines and suppressed cancer progression in tumor-bearing mice that was associated with enhanced survival time. Significance: These findings imply the effectiveness of cancer combination therapy by using H-PCL NPs loaded with anti-IL-6 siRNA and BV6.

Conclusion: Increased expression of inhibitor of apoptosis (IAP) genes has been associated with progressive cancer and chemoresistance. Accordingly, blockade of IAPs by BV6 has resulted in ameliorative outcomes. Interleukin (IL)-6 is another important mediator involved in the growth and survival of tumor cells. Therefore, we hypothesized that simultaneous inhibition of IAPs and IL-6 could be a new promising anti-tumor treatment strategy. Materials and methods: In this study, we generated and characterized hyaluronate-PEG-Chitosan-Lactate (H-PCL) nanoparticles (NPs) to simultaneously deliver IL6-specific siRNA and BV6 to 4T1 (breast cancer) and CT26 (colon cancer) cells.

keywords: siRNA, Chitosan-lactate, Nanoparticle, BV6,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-15

A systematic review of current challenges and future directions of chimeric antigen receptor T cell therapy for breast cancer

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Background and aim: Despite being the most common cancer in women, breast cancer (BC) still has high mortality and limited treatment options. Chimeric antigen receptor (CAR)T cells are genetically engineered T cells that target cancer cells specifically. Different generations of them have shown promising therapeutic potential for several cancers. Notably, six CAR-T cell products have been approved for clinical use in hematological malignancies. However, in BC, there are still challenges for the effective application of CAR-T cell therapy. Finding and overcoming these barriers is a major focus of current systematic research to translate the success of CAR-T cells from blood cancers to BC.

Methods: Two independent authors (ZT and MJ) searched PubMed, Scopus, and Google Scholar by MeSH terms till November 22, 2025, based on the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines. Randomized controlled trials, cohort, and case-control studies were included. But all types of review articles and non-English studies were excluded. ZT and MJ reviewed the retrieved studies in a blinded manner. Discrepancies between reviewers were resolved through consensus discussion or, when required, by assessment from a second-level independent investigator (MS). From each eligible study, methodological and characteristics, including study designand treatment details, were systematically extracted.

Results: 14 records were retrieved. After screening by title and abstract, all 12 CAR-T cell Trials that have been studied in BC were included. Poor tumor infiltration of CAR-T cells because of dense extracellular matrix and non-specific chemokine receptors is the most important challenge reported in these studies. Immunosuppressive tumor microenvironment, tumor antigen heterogeneity, and CAR-T-related toxicities reduce the overall effectiveness of CAR-T cells in BC and pose even safety concerns. To overcome these challenges, strategies such as engineering chemokine receptors, utilizing local delivery, multi-specific CARs, cytokine modulation, and checkpoint inhibitors are suggested.

Conclusion: These findings highlight that for improving the safety and efficiency issues of CAR-T cell therapies in BC, more clinical trials on newer generations are needed.

keywords: CAR-T cell therapy, breast cancer, clinical trials, systematic review

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-16

pseudoleukocytosis in Transfusion-Dependent β-Thalassemia Major

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Background and aim: β-thalassemia major, characterized by deficient β-globin production, often presents with distinctive hematological features, including the peripheral presence of nucleated red blood cells (NRBCs). When markedly elevated, NRBCs can be misinterpreted by automated analyzers as blasts or atypical lymphocytes, potentially mimicking acute leukemia and leading to diagnostic uncertainty. This case report represents a patient with major β-thalassemia with a leukocytosis raising doubts about hematologic malignancy, highlighting a critical diagnostic pitfall.

Methods: A known 35-year-old male patient with transfusion-dependent β-thalassemia major presented to the emergency department of Imam Reza Hospital of Tabriz with severe generalized pain, weakness, and marked pallor. The complete blood count with the KX-21 Sysmex auto analyzer revealed extreme leukocytosis with a white blood cell count of 118 $\times 10^3/\mu L$. Red cell indices demonstrated severe microcytic hypochromic anemia (Hb 5.38 g/dL, Hct 17.3%, MCV 75.8 fL) with marked reticulocytosis and thrombocytosis. Given the discordance between clinical presentation and hematologic findings, analyzer histograms were carefully reviewed. WBC histogram revealed lymphocytosis. Repeat analysis using a full diff Tecnikon H1 automated hematology analyzer correctly identified and flagged NRBC. It also showed a large population clustered in the lower left region of the WBC scattergram, incorrectly classified by the analyzer as lymphocytes. According to laboratory policy, samples with detected NRBCs required confirmation by manual peripheral blood smear.

Results: Manual counting demonstrated 265 NRBCs per 100 WBCs, yielding a corrected WBC count of 22.4 $\times 10^3/\mu L$. This confirmed that the initial extreme leukocytosis was a pseudoleukocytosis caused by NRBC interference.

Conclusion: In patients with β-thalassemia major, NRBCs are frequently present in very high numbers and show wide variability in size, shape, and stage of maturation. This marked heterogeneity makes accurate recognition by automated hematology analyzers particularly challenging. Depending on the analyzer's algorithm, NRBCs may be incompletely detected, misclassified—most commonly as lymphocytes—or not recognized at all. This case clearly demonstrates that automated CBC results can be misleading in patients with severe hemoglobinopathies. So, careful review of WBC and RBC scattergrams and manual peripheral blood smear examination, a diagnostic gold standard, is essential

keywords: thalassemia, leukocytosis, complete blood count, nucleated red blood cells

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-17

The Role of Next-Generation Sequencing–Based Mutational Profiling in Predicting Treatment Response in Acute Myeloid Leukemia: A Systematic Review

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Background and aim: Acute myeloid leukemia (AML) is a genetically heterogeneous malignancy with a poor prognosis despite recent therapeutic advances. Recurrent somatic mutations in genes such as FLT3, NPM1, DNMT3A, IDH1/2, and TET2 have important diagnostic, prognostic, and therapeutic implications. Next-generation sequencing (NGS) enables simultaneous profiling of multiple gene mutations and has been increasingly recognized as a powerful tool for risk stratification, prediction of treatment response, and minimal residual disease (MRD) monitoring. The aim of this systematic review is to evaluate the clinical utility of NGS-based mutational profiling in predicting treatment response in AML patients.

Methods: A systematic literature search was conducted across PubMed, Scopus, and Embase databases using key terms including “acute myeloid leukemia,” “next-generation sequencing,” “mutational profiling,” “treatment response,” and “predictive biomarkers.” Studies reporting clinical outcomes, prognostic significance, and therapeutic implications of NGS-based mutation profiling in adult and pediatric AML patients were included. Data were extracted on study design, patient population, targeted gene panels, mutation frequencies, and associations with response to therapy and survival outcomes.

Results: In this systematic review study, only 5 articles matched our inclusion criteria after preprocessing and screening. NGS-based mutational profiling consistently improved risk stratification and prognostic assessment compared to conventional cytogenetics alone. Integration of multi-gene NGS panels allowed reclassification of intermediate-risk patients, identification of high-risk mutations, and prediction of response to targeted therapies such as FLT3 and IDH inhibitors. Recurrent mutations in TP53, PHF6, TET2, RUNX1, ASXL1, and DNMT3A were associated with poor outcomes, while NPM1 mutations in the absence of FLT3-ITD conferred favorable prognosis. Pediatric AML patients also displayed distinct mutational landscapes, with several novel recurrent mutations influencing treatment response. Overall, NGS data informed therapeutic decisions, enabled MRD monitoring, and refined prognostic models in both adult and pediatric AML cohorts.

Conclusion: NGS-based mutational profiling provides clinically actionable information for the management of AML, including risk-adapted treatment strategies, response prediction, and MRD monitoring. Incorporation of NGS into routine clinical practice enhances the precision of prognostication and supports individualized therapy selection. Further studies are warranted to standardize gene panels and integrate NGS findings into global treatment guidelines.

keywords: Acute Myeloid Leukemia, Next-Generation Sequencing, Mutational Profiling, Treatment Response, Predictive

PH-18

Evaluation of the efficacy and complications of blood product transfusion in Jahrom hospitals: A Cross-Sectional Study

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Background and aim: Considering the existing challenges in the appropriate use of blood products and the importance of monitoring blood transfusion complications, this study was conducted to evaluate the efficacy of blood transfusions and the complications associated with blood products in Jahrom hospitals.

Methods: In this cross-sectional, descriptive study, 3,400 blood transfusion forms from various departments of Paymanieh and Shahid Motahari hospitals in Jahrom city were reviewed from March 2024 to March 2025. Using the extracted data, utilization of blood products, the crossmatch-to-transfusion ratio (C/T), and the complications related to blood transfusion were determined. The data were analyzed using descriptive statistics and SPSS-26 (IBM, USA)..

Results: Out of 3400 blood requests, crossmatch was performed for 1951 patients, and 728 patients received blood products (1228 units). The percentage of requested packed cell products was 58.9%, and the overall C/T ratio was 4.16, a transfusion index (TI) of 0.63, and a transfusion probability (T%) of 41.4%. The departments of obstetrics-gynecology and oncology had the highest C/T ratios. Acute complications related to product transfusion occurred in 28 patients (3.9%). Male physicians caused complications 2.5 times more than female physicians (P0.004).

Conclusion: The present study indicates continued demand for unnecessary transfusions and the occurrence of adverse complications. These findings emphasize the need for a review of existing protocols, integration of the hemovigilance system into clinical processes, emphasis on implementing the MSBOS program, and continuous training of personnel to enhance the quality of blood transfusion services.

keywords: Blood Transfusion, Transfusion Reaction, Cross-match to Transfusion Ratio, Hemovigilance

PH-19

From Guidelines to Clinical Practice in Patient Blood Management for Cardiac Surgeries

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Background and aim: Cardiac surgery is a challenging operation needing a heart-lung machine, a large proportion of blood products, and strong anticoagulants. While using blood products is life-saving, there is a well-documented profile of both acute and delayed adverse effects. Patient blood management (PBM) is an evidence-based approach to managing patients with increasing literature support. However, there is still a need to translate them into standardized protocols. To bridge this significant gap, we will classify current best practices in the field.

Methods: PubMed, Google Scholar, and the Cochrane Library were searched. We focused on registries, clinical trials, case series, cohort studies, systematic reviews, meta-analyses, and expert opinions published in the last 10 years. Key words used in the search included “patient blood management,” “cardiac surgery,” “transfusion,” and “hemorrhage management.” The results were then classified into three pillars: pre-, intra-, and post-operative management. These pillars encompass optimizing erythrocyte mass, minimizing blood loss, and enhancing tolerance to anemia.

Results: Assessing bleeding and transfusion risks, standard laboratory testing, viscoelastic testing, management of anticoagulant use and preoperative anemia, and autologous blood donation are recommended for preoperative PBM. Achieving effective intraoperative hemostasis requires more than surgical skill; it depends on a multidisciplinary approach that reduces hemodilution, maintains normothermia, manages anticoagulation, contains cell salvage, and involves continuous monitoring throughout the operation. Prophylactic fibrinogen, fresh frozen plasma, Recombinant factor VIIa, and Desmopressin administration are not recommended for reducing postoperative bleeding and transfusion risks. Postoperative PBMs include evidence-based protocols for transfusion, chest drainage, balanced anticoagulation, venous thromboembolism prophylaxis, monitoring for Heparin-induced thrombocytopenia, and individualized care strategies.

Conclusion: PBM strategies help minimize the risks associated with transfusions while providing essential support for hemostasis and oxygenation. This can be achieved by using high-quality blood products, implementing algorithm-guided therapy for perioperative bleeding, and establishing transfusion triggers for packed cells and platelets. PBM programs have been shown to reduce complications, lower costs, and improve outcomes, yet still important gaps remain in implementation, especially in Iran. So, Hospital multidisciplinary groups must implement these guidelines or rewrite them based on national policies to shift the paradigm from product-based to evidence-based transfusion medicine.

keywords: patient blood management, cardiac surgery, transfusion, evidence-based transfusion

PH-20

Melatonin: a Multi-Target Therapeutic Agent in Leukemia

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Background and aim: Leukemia remains a major hematologic malignancy with high morbidity.Melatonin has demonstrated proven antitumor effects in various cancers.Evidence indicates it acts through multiple mechanisms: inducing apoptosis, modulating ROS, activating autophagy, and boosting chemotherapy efficacy.

Methods: This study presents a structured review of the experimental, clinical, and mechanistic literature published between 2019 and 2025. Databases covered: PubMed, Google Scholar, Web of Science. Focus: effects of melatonin on leukemia models including AML, APL, ALL, FLT3-ITD, drug-resistant lines, and pediatric supportive care. Mechanistic pathways extracted directly from each study.

Results: Direct Antitumor Effects: • Melatonin induces apoptosis in leukemia cells by increasing the expression of Caspase-3 and Bax while decreasing Bcl-2, coupled with a rise in reactive oxygen species (ROS). • It triggers autophagy through the activation of endoplasmic reticulum (ER) stress pathways, marked by increased levels of CHOP and LC3A/B and decreased levels of PDI and BiP. Modulation of Treatment Efficacy: • Melatonin enhances the efficacy of several chemotherapeutic agents, including Cytarabine, Doxorubicin, and Sorafenib. • It reverses key mechanisms of drug resistance, notably by downregulating P-glycoprotein (P-gp) and upregulating the tumor suppressor PTEN. Other Therapeutic Actions: • In models with the AML1–ETO fusion gene, melatonin promotes the differentiation of leukemic cells. Clinical and Supportive Benefits: • In pediatric acute lymphoblastic leukemia (ALL), melatonin provides supportive benefits by reducing pain and improving overall quality of life.

Conclusion: Melatonin exhibits multi-faceted antileukemic properties through diverse mechanisms. These encompass the induction of apoptosis and autophagy, the promotion of cellular differentiation, and the modulation of oxidative stress. Notably, it enhances the efficacy of standard chemotherapeutic agents and counteracts mechanisms of drug resistance. Collectively, this evidence supports its potential role as an effective adjuvant in leukemia therapy.

keywords: Melatonin, Leukemia, Apoptosi, Autophagy, Drug Resistance, Neoplasm

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-21

Mesenchymal stem cell exosome-loaded three-layer electrospun scaffold promotes in vivo full-thickness wound regeneration

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Background and aim: Exosomes, due to their bioactive factors, stimulate cell migration, tissue regeneration, and skin wound healing. Here in this article, we aimed to combine two biocompatible polymers, polyvinyl alcohol (PVA) and polycaprolactone (PCL), with exosomes to improve wound dressing designs.

Methods: As the first step, scaffolds were made using the electrospinning method. Exosomes were isolated from MSCs and characterized using TEM, nanoparticle tracking analysis (NTA), and western blot. The morphology and diameter of the fibers were assessed using SEM, and the chemical composition was analysed via ATR-FTIR. The hydrophilicity of the scaffolds was determined through contact angle measurements. Surgical procedures were performed on mice to evaluate the scaffolds' effectiveness, followed by histological examinations of skin samples.

Results: SEM analysis revealed the desired morphology of the scaffold fibres. The contact angle test indicated that the 3-layered scaffold exhibited hydrophilic and hydrophobic properties. Animal studies demonstrated that the exosome-containing scaffold promoted wound healing and exhibited anti-inflammatory effects.

Conclusion: This enhancement is probably attributed to exosome bioactive functions like facilitating cell migration, angiogenesis, and reducing inflammation. This study highlights the potential of combining exosomes with a 3-layered scaffold to mitigate risks associated with direct injections of exosomes while enhancing the efficacy of wound healing interventions.

keywords: Exosome, Mesenchymal Stem Cell, Tissue Engineering, Wound Healing, Scaffold

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-22

The Role of Bioinformatics and Machine Learning in Diagnosis, Prognosis, and Treatment of Acute Myeloid Leukemia (AML)

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Background and aim: : Acute Myeloid Leukemia (AML) is a hematologic malignancy characterized by abnormal differentiation and clonal proliferation of myeloid cells. The Global Burden of Disease (GBD) study reported approximately 144,645 new AML cases and 130,190 deaths worldwide, through 2021, highlighting the need for improved early detection and treatment strategies. Recent breakthroughs in bioinformatics and Machine Learning (ML) have contributed to the discovery of novel biomarkers and enhanced the precision of diagnostic, prognostic, and therapeutic approaches in cancer research. The utilization of bioinformatics and ML techniques in AML was explored in this study, particularly regarding their functions in diagnosis, prognosis, and treatment

Methods: A literature search was conducted in PubMed, Web of Science, and Google Scholar to identify relevant studies published between 2015 and 2025. The search strategy included combinations of the keywords “acute myeloid leukemia” (AML), “bioinformatics,” “machine learning,” “diagnosis,” “prognosis,” “therapy,” “treatment,” and “biomarkers.”

Results: The analysis comprised 175 studies when the search was finalized. Our results show that bioinformatics analysis and ML techniques are highly effective in detecting biomarkers correlated with AML. For diagnostic purposes, a single study applying gradient boosted tree models to gene expression data reported an area under the receiver operating characteristic curve (AUC-ROC) exceeding 0.99 for AML versus non-AML classification. A published study in the field of prognosis revealed DNM1, MEIS1, and SUSD3 as prognostic biomarkers using various ML models, including Least Absolute Shrinkage and Selection Operator (LASSO), Random Forest (RF), Support Vector Machine (SVM), and Extreme Gradient Boosting (XGBoost). At the treatment level, SMAD3 was reported as a candidate therapeutic target, as its expression was associated with programmed cell death-related signatures and treatment response in AML patients. However, these findings were based on computational analyses and require further experimental validation to confirm their accuracy.

Conclusion: Bioinformatics and machine learning approaches are not only used for AML but can also be extended to other malignancies and diseases. These methods enable more accurate diagnosis, prediction, and treatment decision-making. This brings clinical practice closer to personalized medicine, which could lead to improved patient outcomes in the future.

keywords: Acute Myeloid Leukemia, Computational Biology, Machine Learning, biomarkers

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-23

Effectiveness of Targeted Interventions to Increase Recruitment and Retention of Young Blood Donors: A Scoping Review

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Background and aim: Recruiting and retaining blood donors, particularly among young populations, remains challenging. Studies evaluating different interventions have reported inconsistent results. In this review, primary studies, including randomized or non-randomized trials and field trials published between 2014 and 2025, were retrieved through a non-systematic search of MEDLINE and Google Scholar. The effectiveness of interventions on blood donor recruitment or retention, with particular focus on young and first-time donors, was evaluated. Ten studies covering 13 interventions were found. Baseline return rates among first-time or young donors in the absence of intervention ranged from 20% to 36%, highlighting their vulnerability to early dropout and

Methods: Reminders are intended to encourage repeat blood donation, rather than only increasing intention to donate. One study found that sending generic WhatsApp messages to young donors had a limited impact, increasing return rates from 22% to 31%. Conversely, personalized phone calls to 1,356 first-time donors led to a 31.5% increase in return rate, especially among male donors, who returned at a rate of 32.1%. Incentives encourage repeat donations by providing external rewards. A large field trial indicated that health-related incentives, such as free cholesterol testing, had a small effect (rate of 0.6%) on recruitment. Non-monetary incentives (gifts) resulted in a 30% return rate, which was not significantly different from the control. In contrast, a study involving 6,107 young donors reported a 4–18.9% increase in return rate using small symbolic incentives (T-shirts).

Results: Educational strategies aim to enhance knowledge, self-efficacy, and perceived safety of the donation process. A study evaluating an optimized Donor Educational Module reported significant post-intervention knowledge gains, showing improvement in retention. Moreover, videos and brochures increased knowledge among young donors, and coping-focused brochures improved readiness to donate again. Educational letters produced a 33.2% return rate, with particularly strong effects among academically educated donors (41.9%). Digital educational campaigns in Saudi Arabia increased donations by 15–20% among young and first-time donors. Motivational meetings that focused on personal engagement and the social meaning of blood donation were effective, whereas traditional motivational meetings indicated no significant impact, with return rates changing from 22 % to 22.1%. By emphasizing donor autonomy and self-determination, motivational interviewing increased the return rate to 71.1%. The watching-eyes intervention (adding a picture of human eyes to a promotional message or object to influence a decision) increased blood donations from 6.7%

Conclusion: Overall, donor retention is more dependent on the personalization and psychological grounding of interventions than on their frequency or format. Generic reminders and non-monetary incentives show limited and inconsistent effects on actual return rates. In contrast, personalized approaches—such as tailored phone calls, motivational interviewing, and autonomy-supportive strategies—substantially improve repeat donation. Educational interventions enhance knowledge and perceived safety but yield variable behavioral impact. Interventions that activate intrinsic motivation or implicit social cues are consistently more effective, highlighting the need for donor-centered, theory-driven retention strategies.

keywords: Blood Donation; Donor Retention; First-Time Donors

PH-24

A Multi-Omic Hemostatic Profile Enables Personalized Precision Antithrombotic Therapy

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Background and aim: Current laboratory assessment of thrombosis risk relies on limited, functional tests like PT/aPTT and single biomarkers (such as D-dimer), which fail to capture the complex, multi-factorial nature of individual hemostatic balance. Thus, this review investigates the current evidence on multi-omic data such as genomic, proteomic, and lipidomic profiling, while advocating for the incorporation of multi-omic approaches into a next-generation diagnostic system to facilitate personalized antithrombotic therapy for patients.

Methods: Multiple databases such as PubMed, Scopus and Google Scholar (2015-2025) provided data. These databases contained studies evaluating genomics as well as proteomics, lipidomics and the impact of them on thrombosis, hemostasis, and antithrombotic medication.

Results: The data of combined genomic, proteomic, and lipidomic information for each patient will complete our understanding of thrombosis risks. While genomic data provide a preprogrammed risk from birth, proteomic data provide a real-time view of our individual patients' coagulation status via evaluation of their coagulation factor concentration, activation, and current drug concentration. Lipidomics also plays a vital role by allowing us to analyze and determine the concentrations of bioactive lipids that regulate the activation of platelets and the health of the endothelium. Using all information together, patients will be reliably stratified into categories that go beyond the traditional diagnoses and identify specific sub-phenotypes (cancer-associated or idiopathic venous thromboembolism) of each patient. Moreover, the multi-omics approach will allow clinicians to accurately model the patients' unique hemostatic balance in order to predict the efficacy of any specified therapy and the risk of bleeding, thereby creating a tailored and personalized antithrombotic regimen.

Conclusion: Multi-omic analysis, along with the progression of complex artificial intelligence methodologies, has the potential to revolutionize how we approach clotting tests. A single platform that integrates genetic, protein, and lipid information will provide clinicians with personalized treatment options based on an individual's unique data. The key challenges of clinical utilization are reliant upon the data integration, cost-effectiveness, and the generation of applicable algorithms.

keywords: Genomics, Proteomics, Lipidomics, Coagulation

PH-25

Smart DNA Hydrogels for Post-Surgical Hemostasis and Tumor Recurrence Prevention: Bridging Bioengineering and Clinical Translation

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Background and aim: Post-surgical complications, particularly hemorrhage and tumor recurrence, remain leading drivers of morbidity, extended hospitalization, and healthcare burden. Hemorrhage poses an immediate, life-threatening risk, while tumor recurrence undermines long-term survival and quality of life. Current hemostatic agents—while effective in providing rapid local clot formation—are constrained by poor tissue adherence, mechanical fragility, and limited durability, often necessitating re-intervention. Similarly, conventional adjuvant strategies (e.g., systemic chemotherapy or radiotherapy) fail to achieve adequate drug concentrations at the surgical bed, exposing patients to systemic toxicity while leaving behind residual disease that seeds recurrence.

Methods: Relevant literature was identified by a PubMed search, and Google Scholar (2010-2025) of English language papers using the terms " Post-surgical hemorrhage ", " Tumor recurrence ", " DNA hydrogels ", " Surgery ", “Targeted drug delivery”, “Tumor microenvironment”, “Hemostasis” and " Immunomodulation.

Results: This dual clinical challenge underscores a critical unmet need for multifunctional, localized, and adaptive post-surgical interventions. Programmable DNA hydrogels have recently emerged as next-generation biomaterials uniquely suited to address this gap. Built from sequence-specific DNA motifs that self-assemble into three-dimensional networks, these hydrogels combine biocompatibility and biodegradability with tunable mechanical strength and stimuli-responsive release. Crucially, they can be engineered to carry pro-coagulant agents for immediate hemostasis while simultaneously delivering chemotherapeutics, immunomodulators, or targeted nanoparticles to suppress residual tumor growth. Beyond drug delivery, hybrid DNA hydrogel systems can integrate biosensing elements and smart, patient-specific responsiveness, enabling precision post-operative care. This review provides a clinician-focused overview of DNA hydrogels in surgical oncology. We emphasize their dual-function potential—rapid hemostasis and recurrence prevention—while outlining mechanistic underpinnings, preclinical evidence, and translational pathways.

Conclusion: By bridging bioengineering, biomaterials science, and oncology, we propose DNA hydrogels as a roadmap toward next-generation, adaptive therapeutics that redefine post-surgical management.

keywords: Post-surgical hemorrhage, Tumor recurrence, DNA hydrogels, Programmable biomaterials, Targeted drug

PH-26

Nanodrug-Based Modulation of Platelet–Leukocyte Interactions in Ovarian Cancer: A New Frontier in Targeted Therapy

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Background and aim: Ovarian cancer (OC) remains a leading cause of gynecologic cancer mortality due to its biological heterogeneity, late-stage diagnosis, and resistance to conventional therapies. The tumor microenvironment (TME) plays a critical role in driving disease progression, with pathological interactions between activated platelets and leukocytes significantly contributing to immune evasion, metastasis, and thromboinflammation.

Methods: Relevant literature was identified by a PubMed search, and Google Scholar (2010-2025) of English language papers using the terms " Ovarian Cancer ", " Nanodrug ", " Platelet ", " Leukocyte ", “Targeted drug delivery” and " , “Therapy”.

Results: Platelet-derived P-selectin facilitates platelet-neutrophil aggregation, leading to the formation of neutrophil extracellular traps (NETs) via NETosis, which further promotes tumor growth and thrombotic complications. Additionally, platelet-secreted TGF-β1 enhances an immunosuppressive environment, inducing epithelial-to-mesenchymal transition (EMT) and skewing immune cell polarization toward tumor-promoting phenotypes. In this review, we explore the mechanistic role of platelet–leukocyte interactions in OC progression and examine current pharmacologic challenges in targeting these interactions. We then propose a novel therapeutic strategy involving pH-responsive nanoparticles co-loaded with anti-platelet agents and doxorubicin, designed to selectively release their payload within the acidic TME. This nanodrug aims to inhibit platelet activation, reduce NET formation, and enhance local cytotoxic efficacy while minimizing systemic toxicity and bleeding risk—common challenges with conventional therapies. By integrating principles from tumor immunology, hemostasis, and nanomedicine, our strategy offers a promising, multi-targeted approach to OC therapy.

Conclusion: We advocate for further preclinical and clinical studies to assess the potential of this nanodrug in overcoming immune resistance and thromboinflammatory complications in advanced ovarian cancer.

keywords: Ovarian Cancer, Tumor Microenvironment, Nanoparticle, Platelet Leukocyte Aggregates, Transforming Growth

17th International Congress of Lab. and Clinic
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PH-27

Molecular Insights into the Relationship Between Platelet Activation and Endothelial Dysfunction: Molecular Approaches and Clinical Practice

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Background and aim: Platelets are one of the coagulation cells. When platelet activation occurs, many

Methods: Relevant literature was identified by a PubMed search, and Google Scholar (2010-2025) of English language papers using the terms " Platelet Activation ", " Endothelial Dysfunction ", " Platelet ", " Leukocyte ", “Clinical Practice” and " , “Therapy”. mediators are released and affect endothelial cells (ECs) and lead to endothelial dysfunction (ED).

Results: ED plays an important role in the pathogenesis of many diseases, including cardiovascular disease (CVD). Platelet are of important factors in ED. The release of mediators by platelets causes the stimulation of inflammatory pathways, oxidative stress, and apoptosis, which ultimately result in ED.On the other hand, platelet activation in CVD patients can be associated with a bad prognosis.

Conclusion: Platelet activation can increase the level of markers such as p-selectin in the serum. Also, in this study, we have discussed the role of platelet as a diagnostic factor, as well as its use as a treatment option. In addition, we discussed some of the molecular pathways that are used to target platelet activation.

keywords: Diagnostic; Endothelial Dysfunction; Molecular Pathway; Platelet; Prognostic.

PH-28

Optimizing Blood Product Utilization in a Major Tertiary Center: A Three-Year Retrospective Analysis of Wastage and Return Patterns

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Background and aim: Blood products are scarce resources, and inefficient transfusion practices in teaching hospitals often lead to waste and increased costs. This study investigated the patterns and underlying causes of unused blood products at Imam Reza Hospital, a major tertiary center in northeast Iran, to identify modifiable factors contributing to wastage.

Methods: We conducted a retrospective cross-sectional study covering the period from March 2022 to March 2025. Data regarding blood component reserves and returns were extracted from the Laboratory Information System (LIS) and the hospital's dashboard. We analyzed utilization and return rates across five major clinical departments (Internal Medicine, Obstetrics/Gynecology, Surgery, Orthopedics, and Hematology-Oncology) for Red Blood Cells (RBCs), Platelets, Plasma (FFP), and Cryoprecipitate.

Results: While the total number of returned units declined over the study period, the return percentage increased in the final year, indicating persisting inefficiencies. Departmental Analysis: The Neurology and Gynecology wards exhibited the highest return percentages. However, in terms of absolute numbers, the Hematology-Oncology ward, ICU, and Emergency Department accounted for the highest volume of returns. Product Analysis: Platelets were the most frequently returned product by number, whereas Fresh Frozen Plasma (FFP) had the highest relative return rate. Reasons for Return: The most consistently reported reason for returns was "Physician Decision/Order Canceled". Returns due to "Patient Death" also showed a gradual increase over the three years.

Conclusion: Despite gradual improvements in absolute return numbers, systemic challenges such as poor documentation and the absence of real-time digital monitoring tools continue to undermine efficiency. To reduce wastage, we recommend implementing real-time dashboards, enforcing mandatory documentation, and adopting AI-based demand prediction tools.

keywords: Blood wastage, Platelets, Erythrocyte Transfusion, Plasma, Cryoprecipitate

PH-29

Association of somatic mutations and clinical aspects in myelodysplastic neoplasms

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Background and aim: Myelodysplastic neoplasms (MDS) represent a heterogeneous group of clonal hematopoietic disorders characterized by ineffective hematopoiesis, dysplasia, and risk of progression to acute myeloid leukemia (AML). Recent advances in molecular genetics have revealed that somatic mutations in DNA methylation genes, histone modification genes, RNA splicing genes, and transcriptional factor genes play pivotal roles in disease pathogenesis, prognosis, and therapeutic response. This review aims to synthesize current knowledge on the molecular landscape of MDS, focusing on the functional impact of key mutations, their prognostic significance, and the development of emerging mutation-directed therapies.

Methods: This narrative review was performed via comprehensive searches of PubMed, Scopus, and Web of Science using predefined keywords and MeSH terms related to MDS, somatic mutations (e.g., SF3B1, ASXL1), prognosis, IPSS-M, and targeted therapies. Selected literature included updated WHO and IPSS-M classifications, large-scale genomic studies, and phase II/III clinical trials, which were synthesized to highlight molecular pathogenesis, risk stratification, and precision treatment approaches.

Results: Molecular profiling enhances prognostication in MDS, with TP53, ASXL1, RUNX1, and SRSF2 mutations being associated with adverse outcomes and a higher risk of AML transformation, whereas SF3B1 mutations generally confer a favorable prognosis. Hypomethylating agents show greater efficacy in patients harboring TET2 or DNMT3A mutations, while patients with TP53, ASXL1, RUNX1, or STAG2 mutations generally exhibit poor responses to hypomethylation therapy. Targeted therapies represent a major advance in MDS management, including luspatercept for SF3B1-mutant MDS with ring sideroblasts, IDH inhibitors (ivosidenib, enasidenib, olutasidenib) for IDH1/2-mutant disease, and eprenetapopt combined with azacitidine for TP53-mutant MDS. Although immunotherapies such as anti-CD47 and anti-TIM-3 demonstrate promise, their efficacy may depend on underlying genetic features, particularly TP53 status. Molecular profiling is essential for patient selection in allogeneic HSCT, as mutations in ASXL1, RUNX1, or IDH2 are linked to higher relapse rates and inferior survival, underscoring its role in optimizing transplant and post-transplant strategies.

Conclusion: Molecular characterization enables mutation-based risk assessment and informs targeted and immunotherapeutic strategies in MDS. Continued research is needed to overcome resistance, refine combination therapies, and develop next-generation precision treatments.

keywords: MDS, prognosis, somatic mutation, HSCT, targeted therapy

PH-30

Determination of Rh (D, C, E, c, and e) and Kell Phenotypes in Blood Donors from Sistan and Baluchestan Province: Moving Toward Reducing Alloimmunization in Patients with Beta-Thalassemia Major

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Background and aim: Alloimmunization continues to be one of the most significant challenges for patients with beta-thalassemia major who receive repeated blood transfusions. According to various studies, the reported prevalence of alloimmunization in these patients ranges widely, from 2.9% to 40.4%. %. Most of these alloantibodies are directed against the K antigen and antigens of the Rh blood group system. This study aimed to determine the Rh (D, C, E, c, and e) and Kell phenotypes of regular blood donors in order to develop a databank to facilitate extended matching between donors and recipients.

Methods: This cross-sectional study randomly included 1000 regular blood donors from Sistan-Balouchestan province, conducted between September 2018 and May 2019. K and Rh (D, C, c, E and e) antigens typing of the samples was performed using a fully automated system (QWALYS 3, Diagast, France).

Results: The distribution of Kell and Rh antigens was as follows: K: 2.2%, D: 90.0 %; E: 29.1 %; C: 77.7 %; e: 96.7 %; and c: 69.6 %.

Conclusion: Due to the high incidence of alloimmunization against K and Rh antigens in multi-transfused thalassemia patients, determining the K and Rh antigens in regular donors can facilitate extensive matching for these antigens, thereby helping to reduce the risk of alloimmunization in affected patients.

keywords: Blood Donors, Beta-Thalassemia, Alloimmunization

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-31

The effect of different platelet microparticle phenotypes on cells isolated from patients with acute myeloid leukemia M0/1 and M5

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Background and aim: Acute myeloid leukemia (AML) is an aggressive neoplasm of the myeloid lineage and has different subgroups. Subgroups M0 and M1 are treatment resistance, M5 is a better treatment response. Extracellular vesicles are secreted by various types of cells and contain nucleic acids, lipids, and proteins. Platelet microparticles (PMPs) attach to specific receptors on the membranes of target cells or fuse with their membranes, allowing them to transfer their molecules to cancer cells. Consequently, PMP particles influence target cells. Consequently, we decided to investigate the impact of PMPs with different phenotypes on malignant cells isolated from patients suffering from AML-M0/1, M5

Methods: Three types of PMP were obtained: PMP derived from platelet activation by thrombin and calcium chloride, which are in a necrotic form; PMP prepared from platelets on day 7, which are senescent-PMP; and PMP resulting from platelets on day 3. These three types of platelets, at a concentration of 150 µg/ml, were exposed to cells isolated from AML-M0/1 and AML-M5 patients. After 72 hours, cell viability was assessed using trypan blue staining and 7-AAD via flow cytometry.

Results: Necrotic-PMP microparticles significantly reduced the viability of cells isolated from patients with AML-M5 (PV 0.001 in both viability measurement methods). However, those did not affect the viability of cells isolated from patients with AML-M0/1 (PV=0.258 and PV=0.09 for the 7-AAD and trypan blue methods, respectively). Additionally, these microparticles had no impact on the viability of PBMCs isolated from the healthy control group, compared to the same group of cells that were not exposed to any microparticles (PV=0.398 and PV=0.978 for the 7-AAD and trypan blue methods, respectively). Senescent-PMP and PMP from platelet on day 3 did not influence cell viability in any of the three groups.

Conclusion: The necrotic PMP reduces the viability of AML-M5 cells, while it has no effect on AML-M0/1 cells. Furthermore, both types of PMP did not influence the survival of these cells. Therefore, depending on the target cells, certain phenotypes may have an impact, while others may not have any effect.

keywords: Acute myeloblastic leukemia, Platelet microparticle, Viability

PH-32

Association between ABO blood groups and susceptibility to common autoimmune diseases

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Background and aim: ABO antigens are expressed on the surface of erythrocytes and, in secretor individuals, are also presented in various body fluids. Previous research has reported potential links between ABO blood groups and autoimmune diseases. Understanding such associations is clinically important, as it may aid in identifying at-risk individuals and informing disease management. This study aimed to evaluate the relationship between ABO blood groups and susceptibility to three common autoimmune diseases.

Methods: A systematic search was conducted across Scopus, PubMed, and Google Scholar databases, focusing on literature published from 2023 onward. Using targeted keywords, representative original studies were selected and analyzed to investigate the association between blood group antigens and susceptibility to autoimmune disease.

Results: Overall, the reviewed studies indicated that ABO blood groups may be associated with autoimmune disease risk. In patients with autoimmune liver disease (AILD), blood group A was more frequent, whereas blood group B was less common, with no notable differences for blood groups O and AB. By comparison, in rheumatoid arthritis (RA), blood group O predominated and group AB showed the lowest frequency, with a reduced incidence of disease in ABH secretors. Furthermore, in Crohn's disease (CD), a predominance of blood group O was observed, followed by group A, and Rh-positive status was also predominant, with O+ and A+ being the most common ABO/Rh combinations.

Conclusion: These findings suggest a potential role of ABO blood groups in common autoimmune disease susceptibility. Understanding these associations may help identify at-risk populations, provide insights into the underlying mechanisms of these disorders, and guide future research.

keywords: ABO blood group, Rheumatoid arthritis, Crohn's disease, Autoimmune liver disease.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-33

Study of the relationship between hematological parameters and platelet survival in platelet concentrate product during storage in blood bank condition

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Background and aim: Platelet concentrate is one of the most important blood products used in the treatment of bleeding episodes as well as in patients with thrombocytopenia. During the storage of platelets at 20–24°C, a series of structural, morphological, and functional changes occur in the platelets, leading to reduced viability and decreased quality of the product, this is called platelet storage lesion (PSL). In this study, we will investigate the relationship between hematological changes and platelet survival during the storage of this product.

Methods: In this experimental study, ten platelet concentrate units from blood donors were examined. Samples were stored under standard conditions (20–24°C, continuous agitation). Hematologic parameters—platelet count, MPV, PDW, and PCT—were measured using a Sysmex XT-2000 analyzer on days 0, 3, 5, and 7 of storage.Platelet viability was simultaneously assessed using the MTT colorimetric method. Data were analyzed in R using correlation tests, with a significance level set at 0.05.

Results: The findings of the study demonstrated significant alterations in the hematological parameters of platelet concentrate over the 7-day storage period.Statistical analysis revealed a significant decrease in platelet count (p=0.001) alongside significant changes in Mean Platelet Volume (MPV) (p=0.001) and a significant increase in Platelet Distribution Width (PDW) (p=0.001) on days 3, 5, and 7 compared to day zero. Concurrently, assessment of platelet viability using the MTT colorimetric assay indicated a significant decline over time (p=0.001). Correlation analysis confirmed a statistically significant association (p0.05) between the trends of these hematological parameters (platelet count, MPV, and PDW) and the reduction in platelet viability. These findings suggest that changes in hematological parameters can serve as indicators of storage lesion and diminishing quality in platelet concentrates during maintenance.

Conclusion: The results of this study demonstrated that a decrease in platelet count and an increase in MPV were significantly associated with platelet survival.Consequently, these two parameters can serve as simple and accessible hematological indices for predicting platelet quality and PSL during storage under blood bank conditions. Furthermore, assessing these indices can contribute to optimized storage management and aid in the selection of higher quality platelet units for transfusion

keywords: Platelet Concentrate, Platelet Storage Lesion, Platelet Count, Mean Platelet Volume

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-34

Point-of-Care Testing in Hematology: Clinical Impact, Challenges, and Future Directions

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Background and aim: Hematology relies on timely laboratory results for rapid diagnosis and clinical decision-making. Delays in central laboratory testing may adversely affect patient outcomes, particularly in acute anemia, bleeding disorders, and coagulation abnormalities. Point-of-care testing (POCT) has emerged as an effective approach to provide rapid hematological results at or near the patient's bedside. Advances in POCT technologies have expanded their application in hemoglobin measurement, complete blood count, coagulation testing, and anemia screening across hospital, emergency, oncology, pediatric, and home-care settings. This review summarizes current clinical applications, technological developments, and challenges of POCT in hematology.

Methods: A structured literature review was conducted using PubMed, Google Scholar, and Web of Science databases. Articles published between January 2018 and June 2025 were included. The search strategy focused on point-of-care testing in hematology using keywords such as POCT, hematology, hemoglobin, CBC, anemia, coagulation testing, microfluidics, and non-invasive diagnostics. Both original research articles and clinical implementation studies were analyzed, including validation studies, accuracy assessments, technology-based reports, and hospital-based evaluations. Studies addressing pediatric, oncology, emergency, home care, and resource-limited settings were prioritized. Data were extracted regarding clinical performance, diagnostic accuracy, technological approaches, sources of error, and implementation challenges.

Results: POCT demonstrated significant clinical value in rapid detection of anemia, active bleeding, and coagulation disorders, enabling faster therapeutic interventions. Non-invasive and microfluidic devices showed acceptable accuracy for hemoglobin measurement, particularly in pediatric and home-care populations. Advanced technologies such as microchip electrophoresis and lab-on-a-chip platforms enabled anemia screening and limited hemoglobin variant detection using minimal sample volumes. Integration of Internet of Things (IoT) and artificial intelligence (AI) facilitated real-time data transmission and clinical decision support. However, several studies reported variability in analytical performance compared to central laboratory methods, especially for differential counts and hemoglobin variants. Common challenges included operator-dependent errors, insufficient quality control, calibration issues, and difficulties integrating POCT results into laboratory information systems.

Conclusion: POCT in hematology enhances rapid diagnosis, improves clinical workflow, and extends laboratory services beyond traditional settings. Its successful implementation requires robust quality assurance, continuous training, and effective integration of emerging technologies into clinical practice.

keywords: Point-of-Care Testing, Hematology, Hemoglobin, Anemia, Microfluidics

PH-35

Laboratory Challenges in Standardizing Gut Microbiome Profiling for GI-aGVHD Management in allo-HSCT Patients

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Background and aim: The pre-transplant conditioning regimen in allogeneic hematopoietic stem cell transplantation (allo-HSCT) disrupts intestinal barriers, leading to gut microbiome dysbiosis. This imbalance initiates acute gastrointestinal graft-versus-host disease (GI-aGVHD) through three pathways: activation of antigen-presenting cells, modulation of the innate/adaptive immune responses, and changes in microbiota-derived metabolite profiles. As a result, microbiome diversity has emerged as a promising prognostic biomarker for patients undergoing allo-HSCT. Despite growing interest in microbiome profiling, it is not yet routinely used due to the lack of standardized protocols. In this review, we aim to summarize the key challenges in implementing standardized microbiome analysis in allo-HSCT patients.

Methods: Relevant articles indexed in Web of Science and PubMed were evaluated with a focus on the pre-analytical, analytical, and post-analytical phases of microbiome analysis.

Results: The challenges related to standardizing gut microbiome testing in transplant patients can be divided into six main categories: i) pre-analytical phase, including sample type, sampling timing, and storage conditions; ii) analytical phase include the sample preparation, DNA extraction kit, target sequence selection (e.g., V4 or V3-V4), sequencing methods (e.g., 16S rRNA sequencing or shotgun metagenomics), and sequencing platforms (e.g., Illumina MiSeq or NovaSeq); iii) post-analytical phase, involving differences in bioinformatic pipelines and reference databases; iv) clinical confounders (e.g., antibiotic or immunosuppressive drug consumption and opportunistic infections); v) quality control (QC) process, including the lack of standardized positive and negative controls; and vi) cost-related issues, including the high costs of sequencing, reagents, QC materials, bioinformatics infrastructure, and personnel training, which collectively significantly impact the reliability and clinical utility of microbiome analysis in allo-HSCT patients.

Conclusion: Standardization of microbial profiling requires the development of an integrated protocol encompassing sample collection and storage, harmonization of laboratory methods, utilization of validated bioinformatic pipelines, integration of clinical data with microbiome results, implementation of internal and external QC assessment, along with considering practical cost, with the hope to providing a foundation for the practical application of gut microbiome analysis in the GI-aGVHD prediction and personalized management in allo-HSCT patients.

keywords: GI-aGVHD, Gut microbiome, Laboratory standardization

PH-36

Study of the relationship between metabolic parameters and platelet survival in platelet concentrate during storage in blood bank condition

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Background and aim: Platelet Concentrate Products undergo a series of metabolic and biochemical changes during storage in blood bank conditions (22-24°C), which lead to decreased platelet function and survival, and may reduce the efficacy of transfusion, this is called Platelet Storage Lesion(PSL).Metabolic stress, characterized by alterations in pH, glucose consumption, lactate accumulation and the release of Lactate Dehydrogenase(LDH), plays a significant role in this process. The aim of this study is to investigate the relationship between metabolic stress and platelet survival throughout the storage period.

Methods: In this experimental study, 10 units of platelet concentrate prepared from blood donors were stored under standard blood bank conditions (temperature of 22±2°C with continuous agitation in a platelet incubator) for up to 7 days. Sampling was performed on day zero (the day of platelet preparation), day 1, day 3, day 5, and day 7. Biochemical parameters, including pH, glucose concentration, lactate concentration, and lactate dehydrogenase (LDH) enzyme activity, were measured. Platelet survival was also assessed using the MTT colorimetric assay with a spectrophotometer, reading the optical density at a wavelength of 570 nm.The relationship between metabolic stress indices and platelet survival was statistically analyzed using correlation and multivariate regression tests.

Results: Analysis of biochemical parameters over the 7-day storage period revealed significant and progressive metabolic stress in the platelet concentrates. A significant decrease in pH($p=0.001$) and glucose concentration($p=0.001$) was observed, accompanied by a concurrent significant increase in lactate levels($p=0.001$) and lactate dehydrogenase (LDH) activity($p=0.002$).Platelet viability, also showed a significant decline over time ($p=0.001$). Correlation and multivariate regression analyses confirmed a significant positive relationship between the pH and glucose and negative relationship between,lactate and LDH with platelet viability.

Conclusion: These findings indicate that the accumulation of metabolic byproducts and associated biochemical changes are strongly correlated with the loss of platelet survival during storage. Consequently, monitoring these biochemical parameters can serve as practical indicators for assessing platelet quality and optimizing storage management. Therefore,it appears that modulating the metabolic pathway during platelet storage may potentially enhance their survival and could be introduced as a strategy for improving platelet quality throughout the storage period.

keywords: Platelet Concentrate, Metabolic Stress, Platelet Survival, Platelet Storage Lesion

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-37

CD33 CAR-NK Cells in Refractory/Relapsed Acute Myeloid Leukemia: Safety, Efficacy and Challenges

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Background and aim: Refractory or relapsed acute myeloid leukemia (R/R AML) has a poor prognosis and limited response to conventional therapies. Chimeric antigen receptor-natural killer (CAR-NK) cell therapy has emerged as a promising alternative to CAR-T cells due to lower toxicity, reduced cytokine release syndrome (CRS), absence of graft-versus-host disease (GVHD) and off-the-shelf availability. The aim of this study was to evaluate the safety, efficacy, and clinical challenges of CAR-NK cell therapy in patients with refractory or relapsed AML.

Methods: This review was conducted using a systematic literature search of international databases, including PubMed, Google Scholar and Scopus. The search strategy employed combinations of the keywords “CAR-NK”, “AML”, “Refractory” and “Relapsed”. Identified studies were screened sequentially by title, abstract, and full-text review. Eligible articles focused on patients with R/R AML treated with CAR-NK cell therapy and met predefined inclusion and exclusion criteria, as well as quality assessment standards based on a structured checklist. Studies failing to meet these criteria were excluded from the analysis.

Results: The reviewed evidence demonstrated that CD33-targeted CAR-NK cell therapy is generally associated with a favorable safety profile in patients with R/R AML. Across most studies, CRS was mild, self-limiting, and manageable, with no reports of severe CRS or GVHD. CAR-NK cell persistence was predominantly short-term, typically lasting up to four weeks; however, incorporation of interleukin-15 (IL-15) significantly enhanced in vivo survival and functional persistence. Several studies reported encouraging anti-leukemic activity, including reduced tumor burden, increased cytotoxicity against CD33-positive leukemic blasts, and achievement of complete remission with undetectable measurable residual disease in a subset of patients.

Conclusion: CD33 CAR-NK cells offer significant advantages over CAR-T therapy, including lower toxicity, absence of GVHD, and no need for HLA matching. However, limited persistence hinders long-term efficacy. Strategies to address this include repeated or escalated dosing, dual-target CAR-NK designs, combining with epigenetic agents, checkpoint or FLT3 inhibitors, using induced pluripotent stem cell–derived NK cells, and expressing membrane-bound IL-15. Overall, current evidence indicates that CAR-NK therapy is a safe, promising immunotherapy for R/R AML, highlighting the need for further clinical investigation to optimize its therapeutic potential.

keywords: CAR-NK, AML, Refractory, Relapsed

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PH-38

Allogeneic Anti-CD19 CAR-NK Cell Therapy as a Novel and Safer Immunotherapeutic Approach Compared to CAR-T Cells in Systemic Lupus Erythematosus

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Background and aim: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder with multisystem involvement and predominance in females. Clinical manifestations commonly include fatigue, arthralgia, myalgia, photosensitivity, and cutaneous rashes. B cell dysfunction is central to disease pathogenesis through autoantibody production and proinflammatory cytokine release. Conventional treatments such as hydroxychloroquine and glucocorticoids primarily control symptoms and rarely achieve durable remission. Therefore, innovative cellular immunotherapies have emerged, including chimeric antigen receptor T cells, CAR NK cells, and stem cell based strategies. This review focuses on comparing the safety profile and therapeutic potential of CAR NK cells versus CAR T cells in SLE management paradigms.

Methods: This review was conducted through a comprehensive search of PubMed, Google Scholar and Scopus using the keywords CAR T-cell, SLE and CAR NK-cell. Studies were screened by title, abstract, and full text. Eligible articles included patients with SLE treated with CAR T-cell and CAR NK-cell therapy and reported clinical efficacy and safety outcomes. Methodological rigor was evaluated based on predefined assessment criteria, and studies that failed to meet the established inclusion standards were rigorously excluded from the analysis.

Results: Although CD19-targeted CAR-T cell therapy has shown significant efficacy in autoimmune diseases, its use is limited by infectious complications and severe immune-related toxicities. These concerns have prompted investigation of allogeneic anti-CD19 CAR-NK cell therapy in refractory SLE. Engineered CAR-NK cells incorporate OX40 costimulatory and CD3ζ signaling domains, enhancing cytotoxicity against autoreactive B cells. Additionally, membrane-bound interleukin-15 supports in vivo persistence with an estimated half-life of 28 days without exogenous cytokine support. Compared with CAR-T therapy, CAR-NK cells exhibit a more favorable safety profile, with minimal risk of severe cytokine release syndrome or neurotoxicity. Importantly, CAR-NK cells effectively reduce T follicular helper cells while preserving regulatory and memory T-cell populations, thereby suppressing pathological B-cell activation.

Conclusion: Current evidence indicates that allogeneic anti-CD19 CAR-NK cell therapy represents a promising and safer immunotherapeutic strategy for SLE. By overcoming major limitations of autologous CAR-T therapy, including toxicity, manufacturing complexity, and cost, CAR-NK cells offer a feasible “off-the-shelf” approach capable of reducing disease activity and improving clinical outcomes in SLE patients.

keywords: CAR T-cell, CAR NK-cell, SLE

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PH-39

Inherited Platelet Function Disorders: Advances in Laboratory Detection and Targeted Therapeutic Strategies

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Background and aim: Inherited platelet function disorders are rare bleeding conditions caused by qualitative defects in platelet activation, aggregation, secretion, or procoagulant activity, often occurring despite normal platelet counts and routine coagulation tests. Diagnostic delays are common and may lead to inappropriate management. Recent advances in platelet biology, laboratory diagnostics, and molecular genetics have substantially improved disease recognition and therapeutic precision. This review aims to summarize current knowledge on inherited platelet function disorders, with particular emphasis on emerging laboratory detection methods and mechanism-based treatment strategies, using representative disorders to illustrate translational progress from pathophysiology to clinical practice.

Methods: This review synthesizes evidence from peer-reviewed experimental studies, clinical investigations, and authoritative reviews addressing inherited platelet function disorders. Emphasis was placed on recent literature describing advances in platelet biology, laboratory diagnostic methodologies, and mechanism-based therapeutic approaches. Particular attention was given to studies evaluating flow cytometry, global hemostatic assays, and molecular genetic techniques, as well as clinical reports on targeted treatments such as antifibrinolytic therapy and recombinant coagulation factors. The selected literature was critically assessed to ensure scientific accuracy, relevance to current clinical practice, and consistency with established consensus in hematology and hemostasis.

Results: Advances in laboratory diagnostics have improved detection and management of inherited platelet function disorders beyond routine testing. Flow cytometry enables detailed analysis of platelet receptors, activation, and procoagulant activity, while global assays like thrombin generation reveal functional defects such as those in Scott syndrome. Next-generation sequencing allows precise molecular diagnosis and carrier identification. Together, these tools enhance diagnostic accuracy and support mechanism-based, targeted therapies, reducing reliance on platelet transfusions.

Conclusion: Advances in platelet biology, laboratory diagnostics, and molecular genetics have substantially improved the recognition and classification of inherited platelet function disorders. The integration of flow cytometry, global hemostatic assays, and next-generation sequencing has enabled accurate diagnosis of disorders previously undetected by routine testing. These developments have directly informed mechanism-based therapeutic strategies, reducing reliance on empirical management and improving clinical outcomes. Continued refinement of diagnostic algorithms and broader access to specialized testing are essential to further optimize care for patients with inherited platelet function disorders.

keywords: Inherited platelet function disorders; Flow cytometry; Next-generation sequencing; Thrombin generation

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July 20-23, 2026

PH-40

Applications of Artificial Intelligence in Differentiating Common Anemias Based on Complete Blood Count Parameters: A Systematic Review

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Background and aim: Common anemias by, such as iron deficiency anemia (IDA), thalassemia, and certain hemoglobinopathies, often produce similar alterations in complete blood count (CBC) parameters, making their differentiation challenging. In recent years, the application of artificial intelligence (AI) and machine learning (ML) algorithms has gained increasing attention, as these approaches can facilitate more accurate differentiation of these anemias through detailed analysis of CBC indices and reduce the need for costly diagnostic tests.

Methods: In this narrative review, an initial search was conducted in the PubMed database. To identify relevant studies, the keywords (Anemia), (Artificial Intelligence), and (Complete Blood Count) were used. The initial search yielded 59 articles. Among these, 17 articles published before 2020 were excluded due to inconsistency with recent advances in artificial intelligence. Of the remaining 42 articles, studies primarily focused on general anemia diagnosis without subtype differentiation, those using non-CBC-based data, animal studies, or studies addressing conditions unrelated to common anemias were excluded. Ultimately, 8 articles with the highest relevance to the study objective were selected for final analysis.

Results: A review of the conducted studies showed that RBC parameters, followed by RDW, had the greatest importance compared with other parameters. In one study, to differentiate hemoglobinopathies from iron deficiency anemia (IDA), artificial intelligence algorithms, including Extreme Gradient Boosting (XGB) and Logistic Regression, were used alongside CBC, demonstrating high performance. In another study, Artificial Neural Networks (ANN) were used to distinguish thalassemia from IDA, showing a sensitivity of 93.13% and a specificity of 92.33%. Additionally, in a separate study, Support Vector Machine (SVM), K-Nearest Neighbors (KNN), and XGB models were applied to differentiate alpha- and beta-thalassemia, with XGB demonstrating the best performance.

Conclusion: Based on the reviewed studies, combining CBC parameters with artificial intelligence algorithms can serve as an effective, low-cost, and accessible tool for differentiating common anemias in clinical settings. However, further studies and validation are required for clinical implementation.

keywords: Artificial intelligence Anemia Complete blood count

PH-41

Trained Immunity in Hematopoietic Precursors: A Double-Edged Sword in Carcinogenesis

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Background and aim: Trained immunity refers to a form of innate immune memory where innate cells such as monocytes, macrophages, and neutrophils adopt a long-lasting heightened state of responsiveness after an initial encounter with certain stimuli. Emerging evidence shows that this memory is not limited to mature effector cells but involves long-lived hematopoietic stem and progenitor cells (HSPCs) in the bone marrow. These precursors undergo epigenetic and metabolic reprogramming that biases their differentiation and functional output, potentially shaping cancer risk and progression. This study systematically reviews the role of central trained immunity in HSPCs and its implications for carcinogenesis.

Methods: A systematic search was performed across PubMed, Scopus, and Web of Science for articles published between 2016 and 2026 using search terms including “Trained Immunity”, “Hematopoietic Stem Cells”, “Carcinogenesis”, and “Neoplasms”. We included original research and review papers that evaluated trained immunity at the HSPC level with outcomes relevant to cancer susceptibility or immune surveillance. Studies without carcinogenesis relevance were excluded.

Results: Studies demonstrate that BCG vaccination induces durable transcriptional and epigenetic changes in HSPCs, characterized by persistent modification of chromatin accessibility and lineage-biased myeloid expansion that endures for months post-vaccination. These trained HSPCs produce myeloid progeny with enhanced cytokine responses and increased antimicrobial activity, conferring broader resistance to unrelated pathogens. Transcriptomic programs enriched in trained HSPCs involve interferon signaling and myelopoiesis regulators, with epigenetic hallmarks such as H3K4me1 and H3K27ac at key immune loci. Conversely, persistent inflammatory stimuli can skew HSPC fate toward chronic pro-inflammatory output, contributing to an inflammatory microenvironment that is known to support genomic instability and malignant transformation. Notably, trained immunity agonists such as β-glucan and BCG have shown anti-tumor effects in preclinical models by enhancing myeloid and neutrophil anti-tumor responses, but the same reprogramming can also exacerbate tumor-promoting inflammation in other contexts.

Conclusion: Central trained immunity in HSPCs represents a double-edged sword in carcinogenesis. Reprogrammed precursors enhance innate immunosurveillance and pathogen control; however, chronic or maladaptive training fosters sustained inflammation that may predispose to oncogenic processes. Future studies should focus on identifying the precise molecular checkpoints that distinguish protective from pathological training.

keywords: Trained Immunity, Hematopoietic Stem Cells, Carcinogenesis, Neoplasms.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-42

Diagnostic Value of Neutrophil-to-Lymphocyte Ratio in Predicting Bacteremia in Adult Patients: A Systematic Review

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Background and aim: Bacteremia is a potentially life-threatening condition for which early diagnosis is essential to improve patient outcomes. Although blood culture is the diagnostic gold standard, its prolonged turnaround time limits its value for prompt clinical decision-making. As a result, there is growing interest in rapid, low-cost, and readily available biomarkers for early bacteremia prediction. The neutrophil-to-lymphocyte ratio (NLR), calculated from routine complete blood counts, reflects systemic inflammation and has been frequently associated with bacterial infections. However, evidence regarding its diagnostic performance remains inconsistent. This systematic review aimed to assess the diagnostic accuracy of NLR in predicting bacteremia in adult patients.

Methods: This systematic review was conducted in 2025 in accordance with a predefined protocol. A focused literature search was performed in the PubMed database, chosen for its extensive coverage of high-quality biomedical research. The search strategy (NLR OR "Neutrophil-Lymphocyte Ratio") AND Diagnosis AND Bacteremia was applied, with studies published between 2021 and 2025 considered eligible. A total of 34 records were identified. Two independent reviewers screened titles and abstracts according to predefined inclusion criteria: (1) adult populations (≥18 years), (2) bacteremia confirmed by blood culture, and (3) reporting diagnostic performance measures for NLR, including area under the receiver operating characteristic curve (AUC), sensitivity, or specificity. Full-text articles were subsequently assessed for eligibility, and disagreements were resolved by consensus. Nine studies met all criteria and were included for qualitative synthesis.

Results: The included studies demonstrated substantial heterogeneity in the diagnostic performance of NLR across different adult populations. The highest diagnostic accuracy was observed in elderly patients, with reported AUC values ranging from 0.919 to 0.95. In intensive care unit (ICU) settings, NLR showed good discriminative ability (AUC range: 0.814–0.898). Importantly, combining NLR with other biomarkers, particularly procalcitonin (PCT), significantly improved diagnostic performance, with AUC values reaching 0.917. Optimal NLR cutoff values varied considerably according to clinical context, with reported thresholds of 8.0 in elderly patients, 6.51 in ICU populations, 7.7 in patients with COVID-19, and 20 in pregnant women. In specific infectious conditions, such as brucellosis, NLR demonstrated limited diagnostic utility. Conversely, in conditions characterized by severe systemic inflammation, including burn injuries, NLR showed acceptable diagnostic performance when incorporated into multimarker predictive models (AUC range: 0.797–0.873).

Conclusion: Overall, the neutrophil-to-lymphocyte ratio is a simple, widely available, and cost-effective biomarker that may assist in predicting bacteremia in adult patients. Nevertheless, its clinical utility is limited by the lack of a universal cutoff value and its strong dependence on patient characteristics and clinical context. Therefore, NLR should be interpreted as part of a comprehensive clinical assessment rather than as an independent diagnostic tool. Future prospective studies are required to establish standardized, population-specific thresholds and to further clarify the diagnostic role of NLR in bacteremia.

keywords: Neutrophil-Lymphocyte Ratio, Bacteremia, Diagnosis, Adult

PH-43

Systemic Immune-Inflammation Index (SII) as a Novel Predictor of Venous and Arterial Thrombosis

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Background and aim: Thrombosis is a major cause of morbidity and mortality worldwide. Increasing evidence suggests that inflammation plays a pivotal role in the initiation and progression of both venous and arterial thrombotic events. The Systemic Immune-Inflammation Index (SII), calculated based on peripheral blood neutrophil, lymphocyte, and platelet counts, has emerged as a novel marker reflecting the balance between host inflammatory and immune status. However, its clinical utility in predicting thrombotic disorders remains insufficiently explored. To evaluate the predictive value of the Systemic Immune-Inflammation Index (SII) for venous and arterial thrombosis and to assess its potential role as a readily available laboratory marker.

Methods: This retrospective cross-sectional study included patients diagnosed with venous or arterial thrombosis and age- and sex-matched controls without thrombotic events. Complete blood count (CBC) parameters were obtained at admission. The SII was calculated using the formula: SII = (Platelet count × Neutrophil count) / Lymphocyte count. Statistical analyses were performed to compare SII levels between groups and to assess its predictive performance.

Results: Patients with thrombotic disorders demonstrated significantly higher SII values compared to controls (p 0.05). Elevated SII was associated with both venous and arterial thrombosis. Receiver operating characteristic (ROC) curve analysis showed that SII had acceptable discriminative power for predicting thrombotic events. Higher SII levels were correlated with increased inflammatory burden and thrombotic risk.

Conclusion: The Systemic Immune-Inflammation Index is a simple, cost-effective, and easily accessible marker derived from routine CBC parameters. Elevated SII may serve as a valuable predictor of venous and arterial thrombosis and could aid in early risk stratification of patients in clinical settings.

keywords: Systemic Immune-Inflammation Index; Thrombosis; Inflammation; Hematologic Indices; CBC

PH-44

Evaluation of Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Lymphocyte Ratio (NLR) as Predictive Markers of Thrombosis

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Background and aim: Thrombosis remains a major cause of morbidity and mortality worldwide. In recent years, increasing attention has been directed toward inexpensive and readily available inflammatory markers derived from routine complete blood count (CBC) parameters. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have emerged as potential indicators of systemic inflammation and prothrombotic states. Given the close interplay between inflammation, platelet activation, and coagulation pathways, these ratios may serve as useful predictors of thrombotic events. Objective To evaluate the association of PLR and NLR with the occurrence of thrombosis and to assess their potential role as simple, cost-effective predictive markers in thrombotic

Methods: Study Design: Cross-sectional / Case–control study Study Population: Patients diagnosed with thrombotic events (including venous and/or arterial thrombosis) compared with age- and sex-matched controls without a history of thrombosis. Sample Size: [Insert number] patients and [Insert number] controls Data Collection: Demographic data and laboratory parameters were collected from medical records. Laboratory Analysis: CBC parameters were measured using an automated hematology analyzer. NLR was calculated as the ratio of absolute neutrophil count to absolute lymphocyte count, and PLR as the ratio of platelet count to absolute lymphocyte count. Statistical Analysis: Data were analyzed using appropriate statistical software. Continuous variables were compared using Student's t-test or Mann–Whitney U test. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of PLR and NLR. A p-value 0.05 was considered statistically significant.

Results: Patients with thrombosis demonstrated significantly higher NLR and PLR values compared to the control group. Elevated NLR was strongly associated with the presence of thrombotic events (p 0.05). PLR values were also significantly increased in thrombotic patients and showed moderate predictive accuracy. ROC curve analysis revealed acceptable sensitivity and specificity for both NLR and PLR in predicting thrombosis.

Conclusion: PLR and NLR are inexpensive, easily accessible biomarkers that may be useful in predicting thrombotic risk. Their incorporation into routine clinical assessment could aid in early risk stratification and decision-making, particularly in resource-limited settings.

keywords: Thrombosis; Neutrophil-to-Lymphocyte Ratio; Platelet-to-Lymphocyte Ratio; Inflammation; Hemostasis

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PH-45

CAR T-Cell Therapy in Patients with Relapsed or Refractory Mantle Cell Lymphoma: A Comprehensive Review

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Background and aim: Mantle cell lymphoma (MCL) is a rare, aggressive non-Hodgkin lymphoma predominantly affecting older adults. It is defined by the t(11;14) translocation, cyclin D1 overexpression, and CD20 positivity. Poor prognosis results from advanced-stage presentation, TP53 mutations, and resistance to standard therapies. Although Bruton's Tyrosine Kinase inhibitors have improved outcomes, MCL remains incurable with frequent relapses. To address the poor prognosis of patients with relapsed or refractory MCL after conventional therapies, chimeric antigen receptor (CAR) T-cell therapy has emerged as a promising novel immunotherapy. This approach utilizes genetically engineered T cells to target B-cell antigens in an MHC-independent manner.

Methods: This review was conducted through a comprehensive search of PubMed and Google Scholar using the keywords CAR T-cell therapy, Relapsed and Mantle cell lymphoma. Studies were screened by title, abstract, and full text. Eligible articles included patients with MCL treated with CAR T-cell therapy and reported clinical efficacy and safety outcomes. Methodological quality was assessed using predefined criteria, and studies not meeting inclusion standards were excluded.

Results: Recent evidence highlights the transformative role of CAR T-cell therapy in R/R MCL. Prior to its introduction, treatment relied primarily on BTKi, which were often associated with disease progression and limited survival due to the lack of an effective standard of care. Following FDA approval for use in patients who have failed BTK inhibitor therapy, CAR T-cell therapy has significantly increased rates of durable remission. Importantly, patients with TP53 mutations—who typically have extremely poor outcomes—have achieved sustained long-term remissions, particularly when CAR T-cell therapy is applied early in elderly populations. Compared with conventional treatment approaches, CAR T-cell therapy improves overall survival and markedly reduces relapse risk.

Conclusion: CAR T-cell therapy demonstrates favorable safety and efficacy in R/R MCL with minimal disease recurrence. While reduced in vivo expansion after repeat infusion may limit retreatment efficacy, high response rates and manageable toxicity profiles support CAR T-cell therapy as a powerful and effective treatment option for this aggressive malignancy.

keywords: CAR T-cell therapy, Mantle cell lymphoma, Relapsed

PH-46

The Effect of Multi-Step Centrifugation on Platelet-Derived Extracellular Vesicles

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Background and aim: Extracellular vesicles (EVs) are lipid bilayer structures ranging in size from 15 to 1000 nm, commonly referred to as ‘exosomes’ (30-150 nm in diameter) and ‘microparticles’ (100-1000 nm in diameter). The most abundant EVs in human blood are derived from platelets. Many techniques have been developed to isolate EVs, including ultracentrifugation, precipitation, immunoaffinity, sorting, ultrafiltration, size exclusion chromatography, and microfluidics. In precipitation, hydrophilic polymers such as polyethylene glycol (PEG), reduce solubility by lowering the hydration of EVs. These kits can be used to separate EVs using lower spin speeds. This study aimed to isolate platelet-derived exosomes by precipitation.

Methods: Platelet Rich Plasma (PRP) was prepared by Iranian Blood Transfusion Organization (IBTO). EVs were isolated by two precipitation-based strategies. In the first method, PRP was centrifuged at 3000 g for 10 minutes to remove platelets and debris. supernatant was filtered (0.2µm), mixed with PEG, and incubated for 12 h at 4°C. It was then centrifuged at 3000rpm for 45 minutes at 4°C, supernatant discarded, and pellet dissolved in PBS. In the optimized method, platelets and cell debris were isolated by centrifugation at 1500g for 20 minutes and 3000g for 15 minutes at 4°C. Then, the supernatant was centrifuged at 13000g for 30 minutes to remove large particles. The supernatant was filtered, and the rest of the steps were done as in the first method. Finally, EVs were characterized by dynamic light scattering (DLS).

Results: The results from DLS showed that the mean diameter of the particles isolated in the first method was above 100 nm and in the microparticle range, while in the second method, it was below 100 nm and in the exosome range, suggesting the importance of high-speed centrifugation for isolating exosomes.

Conclusion: Although precipitation-based methods are relatively cheap and widely used for exosome isolation, both exosomes and microparticles can co-precipitate, leading to heterogeneous preparations containing larger EVs. Combining PEG-based isolation with other techniques of exosomal enrichment is a viable strategy to avoid the drawbacks associated with the use of PEG alone. In this study, high-speed centrifugation removed larger EVs, indicating its effectiveness in isolating exosomes with precipitation.

keywords: Platelet; Extracellular vesicles; Isolation

PH-47

Cancer associated thrombosis

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Background and aim: Aim: Cancer-associated thrombosis (CAT) represents a major biological complication of malignancy and is driven by tumor-specific alterations in the hemostatic system. Unlike thrombosis in non-cancer populations, CAT reflects a sustained hypercoagulable state resulting from complex interactions between malignant cells, host immune responses, and the vascular endothelium. Elucidating the pathophysiological mechanisms underlying CAT is essential for understanding disease heterogeneity and for the development of biologically informed strategies for risk assessment

Methods: This narrative review focuses on experimental, translational, and clinical studies investigating the biological mechanisms of CAT. Evidence from in vitro models, animal studies, and human investigations was synthesized to characterize tumor-driven activation of coagulation, inflammation-mediated thrombosis, platelet–tumor interactions, and endothelial dysfunction. Studies addressing treatment efficacy were intentionally excluded to maintain a mechanistic focus.

Results: Results: Multiple interrelated mechanisms contribute to the pathogenesis of CAT. Tumor cells directly activate coagulation through overexpression of tissue factor and the release of procoagulant extracellular vesicles, leading to excessive thrombin generation. Cancer-associated inflammation amplifies thrombosis via cytokine-mediated endothelial activation and formation of neutrophil extracellular traps, which provide a scaffold for fibrin deposition. Platelets actively participate through direct interactions with tumor cells, promoting platelet aggregation and release of prothrombotic mediators. In parallel, endothelial dysfunction induced by inflammatory signaling, oxidative stress, and tumor-derived factors shifts the vascular surface toward a procoagulant phenotype. Anticancer therapies further exacerbate these processes by inducing endothelial injury and altering platelet and coagulation factor activity.

Conclusion: Conclusion: The pathophysiology of CAT is characterized by a dynamic and multifactorial interplay between tumor biology, inflammation, platelets, and the vascular endothelium. Variability in these mechanisms across cancer types and disease stages underlies the heterogeneous thrombotic risk observed in oncology patients. A mechanistic understanding of CAT provides a foundation for future research aimed at identifying molecular biomarkers and developing targeted preventive strategies

keywords: Thrombosis , Anticoagulation , Thromboembolism

PH-48

The role of coagulation factor VIII levels in confirming or excluding bleeding disorders in women and men

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Background and aim: Coagulation factor VIII (FVIII) is a key component of the intrinsic coagulation pathway and is commonly measured in the evaluation of bleeding disorders such as hemophilia A and von Willebrand disease. However, FVIII levels alone are insufficient to confirm or exclude these conditions, particularly in women. As an acute-phase reactant, FVIII exhibits substantial biological variability and is affected by age, sex, inflammation, stress, hormonal status, pregnancy, and blood group. Consequently, FVIII levels may appear normal or elevated despite the presence of clinically significant bleeding.

Methods: This narrative review summarizes published clinical studies, review articles, and diagnostic guidelines evaluating the role of FVIII levels in the diagnosis of bleeding disorders in women and men. The literature was examined with a focus on the relationship between FVIII activity and bleeding phenotype, sex-related differences in FVIII expression, physiological modifiers of FVIII levels, and the limitations of using FVIII as a single diagnostic criterion

Results: The reviewed evidence indicates that reduced FVIII levels are strongly associated with moderate to severe hemophilia A in both sexes. In contrast, FVIII levels are frequently normal or near normal in mild hemophilia A and von Willebrand disease. In men with mild hemophilia A, FVIII activity may overlap with the lower limit of the normal range despite clinically significant bleeding. In women—particularly hemophilia A carriers and patients with mild VWD—normal FVIII levels are even more common despite bleeding manifestations such as menorrhagia, postpartum hemorrhage, or excessive surgical bleeding. Hormonal influences, pregnancy, and estrogen exposure contribute to higher baseline FVIII levels in women. Overall, the correlation between FVIII levels and bleeding severity is weak, highlighting that FVIII activity alone does not reliably represent true hemostatic competence.

Conclusion: Low FVIII levels strongly suggest a bleeding disorder, but normal or near-normal levels do not reliably exclude disease in either sex. Because biological variability and acute-phase effects can mask coagulation defects, accurate diagnosis requires combining FVIII testing with clinical history and additional laboratory evaluations. Relying on FVIII levels alone can lead to underdiagnosis, especially in mild cases and in women.

keywords: Factor VIII Bleeding disorder, von Willebrand Factor

PH-49

Extracellular vesicle-based biomarkers in diffuse large B-cell lymphoma: A systematic review and meta-analysis

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Background and aim: Diffuse large B-cell lymphoma (DLBCL) is a clinically and biologically heterogeneous malignancy. While current diagnostic and prognostic methods, such as histopathology, molecular subtyping, and imaging, remain essential to patient assessment, they face certain limitations. Thus, there is growing interest in complementary approaches such as extracellular vesicles (EVs), which may provide real-time, non-invasive insights into disease biology.

Methods: A systematic review and meta-analysis were conducted to evaluate the diagnostic and prognostic value of EVs in DLBCL. Databases including PubMed, Scopus, Web of Science, and Embase were searched. Pooled sensitivity, specificity, diagnostic odds ratio, and area under the curve were calculated for diagnostic studies. Prognostic outcomes were synthesized using hazard ratios for overall survival and event-free survival. Risk of bias was assessed using QUIPS and QUADAS-2 tools, and subgroup/sensitivity analyses and publication bias assessment were performed.

Results: Pooled diagnostic performance of EVs showed high sensitivity (0.93), acceptable specificity (0.70), and an AUC of 0.89. Plasma-based EVs yielded superior accuracy (AUC = 0.94; DOR = 209). For prognosis, elevated EV levels were associated with significantly worse OS (HR = 6.21) and EFS (HR = 2.93). Subgroup analysis revealed reduced heterogeneity in high-quality studies, and sensitivity confirmed robustness. No major publication bias was detected

Conclusion: EVs demonstrate substantial potential as reliable, non-invasive biomarkers for both the diagnosis and prognosis of DLBCL. Their integration into clinical workflows may enhance early detection, risk stratification, and disease monitoring. Future large-scale, prospective studies with standardized EV protocols are warranted to facilitate their clinical translation.

keywords: Extracellular vesicles; Diffuse large B-cell lymphoma (DLBCL); Biomarkers; Diagnostic; accuracy

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PH-50

Nanocarrier-Based Curcumin for Chronic Myeloid Leukemia: A Systematic Review of In_vitro Studies

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Background and aim: Chronic Myeloid Leukemia (CML) characterized by the abnormal activity of the BCR-ABL tyrosine kinase. Although synthetic tyrosine kinase inhibitors (TKIs) have improved patient outcomes, severe adverse events remain major challenges. Nanocarrier-based Curcumin (CUR), derived from Curcuma longa, shows multitarget antitumor activity in CML. However, the lack of a systematic synthesis of existing evidence has hindered the translation of preclinical studies into clinical research. Here, we aim to investigate the efficacy and safety of nano-CUR formulations using a systematic approach.

Methods: A comprehensive systematic search was conducted with using relevant keywords, including CML, curcumin, and their related MeSH terms, in PubMed, WOS, Scopus, and Embase. Grey literature was also searched through Google Scholar. The retrieved articles were meticulously subjected to a two-phase screening process and data extraction by two independent researchers. Irrelevant or non-English papers, review articles, and retracted publications, as well as papers with inadequate data, were excluded.

Results: Studies have revealed that, compared to free CUR, various forms of nano-CUR, including micellar, niosomal, nanogels, and polymeric forms, can enhance the toxicity and efficacy of the herbal compound against CML cells. Reported anti-tumor mechanismes encompass reducing the expression of notorious BCR–ABL fused gene, boosting apoptosis, and inducing cell cycle arrest. Polymeric (PLGA-conjugated) CUR has shown synergism with other anti-cancer agents, notably imatinib, doxorubicin, and paclitaxel, bypassing the drug resistance of CML cells via activating apoptotic, anti-proliferative, and ROS-mediated signaling pathways.

Conclusion: Current evidence highlights the promising potential of nanocarrier-based CUR either alone or in combination with traditional therapeutic agents. Further studies are required to determine the optimal nano-formulations, long-term safety, and clinical efficacy in human trials.

keywords: Chronic myeloid leukemia, Curcumin, Nano-curcumin

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-51

Maternal Red Blood Cell Alloimmunization in Pregnancy: A Systematic Review of Prevalence, Risk Factors, and Maternal–Neonatal Outcomes

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Background and aim: Maternal red blood cell (RBC) alloimmunization remains a clinically relevant issue in pregnancy despite the marked reduction in anti-D–related hemolytic disease of the fetus and newborn (HDFN) following the widespread use of Rh(D) immune globulin. Increasing recognition of non-D antibodies, alongside evolving screening and monitoring strategies, highlights the need for an updated synthesis of evidence regarding the prevalence, clinical impact, and outcomes of clinically significant RBC antibodies in pregnancy. This systematic review summarizes current evidence on the epidemiology, risk factors, and maternal–neonatal outcomes associated with RBC alloimmunization.

Methods: A systematic search strategy was employed across PubMed, Scopus, and Web of Science to identify studies published between 2010 and 2025. Search terms included combinations of “red cell alloimmunization,” “pregnancy,” “clinically significant antibodies,” and “hemolytic disease of the fetus and newborn.” Original research articles, cohort studies, and clinical guidelines evaluating the prevalence, seroconversion, or outcomes of clinically significant RBC antibodies in pregnancy were included. Studies lacking clinical outcome data or focused solely on non-relevant autoantibodies were excluded. Duplicate studies were identified and removed using reference management software.

Results: Fourteen studies met the inclusion criteria, comprising 9 retrospective cohort studies, 3 observational prevalence studies, and 2 international clinical guidelines, encompassing over 75,000 pregnancies. The prevalence of clinically significant RBC antibodies ranged from 0.3% to 0.74%. Anti-E, anti-K, anti-c, and anti-M were the most frequently identified non-D antibodies. Reported seroconversion rates during pregnancy were low (approximately 0.26%), with advanced maternal age and higher gravidity identified as key risk factors. Neonatal outcomes were generally favorable; severe HDFN was uncommon, and most affected neonates required only monitoring or limited intervention. Warm autoantibodies, although occasionally detected, were rarely associated with clinically meaningful hemolysis.

Conclusion: Clinically significant RBC alloimmunization in pregnancy is uncommon but remains an important contributor to fetal and neonatal morbidity. Non-D antibodies now represent a greater proportion of clinically relevant cases. Structured screening, risk-based monitoring, and coordinated obstetric–transfusion care are essential to optimize maternal and neonatal outcomes.

keywords: Red cell alloimmunization ،Pregnancy ،Clinically significant antibodie

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-52

Comparison of Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Hemoglobin-to-Platelet Ratio (HPR) in Patients with Immune Thrombocytopenia and Healthy Controls: A Retrospective Study

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Background and aim: Immune thrombocytopenia (ITP), formerly known as idiopathic thrombocytopenic purpura, is a common hematologic disorder that affects a wide range of people but is more prevalent in childhood and the elderly. Evaluation and measurement of the inflammatory markers in patients with ITP is costly and time consuming. Considering the importance of inflammation in ITP and the reduction of blood cells and the occurrence of thrombocytopenia and anemia, the use of PLR, NLR, and Hb/platelet ratio (HPR) indices can be effective in patient management due to their relevance to clinical symptoms, low cost, and availability. Therefore, we investigated this issue in this

Methods: This is a retrospective descriptive and epidemiological study that was conducted in 2020-2021 at Ahwaz Jundishapur University of Medical Sciences in Baqaei Hospital. In this study, 250 ITP patients participated as case group and 70 healthy individuals as control group.

Results: The results showed that the mean PLR was lower in patients (1.29±2.24) compared to controls (69.88±33.01), while the mean NLR (2.146±2.16 VS. 0.966±0.919) and HPR (0.752±0.707 VS. 0.049±0.017) in patients were higher than healthy individuals, which was statistically significant (p: 0.0001). On the other hand, it was shown that there was no significant difference between the mean MCV (p=0.584) and WBC (p=0.943) indices between the two groups. In order to evaluate the diagnostic value of PLR, NLR and HPR indices, receiver operating characteristic (ROC) curves were used and Area Under the Curve (AUC) values were evaluated. The AUC of NLR was about 71% while for PLR and HPR it was 100% and 98%, respectively.

Conclusion: In general, the three markers PLR, NLR and HPR have diagnostic value in the diagnosis and management of ITP patients.

keywords: Neutrophil Lymphocyte Ratio, Platelet Lymphocyte Ratio, Hb Platelet Ratio, Immune

PH-53

Evaluation of MicroRNA as Minimal Residual Disease in Leukemia: Diagnostic and Prognostic Approach: A Review

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Background and aim: Various factors are effective in the development of minimal residual disease (MRD), one of which is MicroRNAs (miRNAs). miRNAs and their dysfunction in gene expression have influential role in the pathogenesis of leukemia. Nowadays, treatments that lead to the suppression or replacement of miRNAs have been developed. Focusing on the role of miRNAs in managing the treatment of leukemia, in this review article we have investigated the miRNAs and signaling pathways involved in the process of apoptosis and cell proliferation, as well as miRNAs with oncogenic function in malignant leukemia cells.

Methods: Relevant literature was identified by a PubMed search, and Google Scholar (2010-2025) of English language papers using the terms " Leukemia ", " Minimal Residual Disease ", " Prognosis ", " Micro RNA ", “Diagnosis” and " , “Therapy”.

Results: Among the studied miRNAs, miR-99a, and miR-181a play an essential role in apoptosis, proliferation and oncogenesis via AKT, MAPK, RAS, and mTOR signaling pathways.

Conclusion: miR-223 and miR-125a affect apoptosis and oncogenesis via Wnt/B-catenin, PTEN/PI3K, and STAT5/AKT/ERK/Src signaling pathways. miR-100 also affects both apoptosis and oncogenesis; it acts via IGF1 and mTOR signaling pathways.

keywords: MicroRNAs; Minimal residual disease; Pathogenesis; Prognosis.

PH-54

Preanalytical, Analytical, and Postanalytical Phases and Strategies for Improvement

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Background and aim: Quality control (QC) in hematology laboratories is essential for delivering accurate and reliable test results, as errors can contribute to misdiagnosis, inappropriate treatment, and compromised patient safety. This systematic review evaluates common QC errors across the total testing process, with a primary emphasis on the preanalytical phase, which accounts for 46–70% of all laboratory errors according to multiple studies.

Methods: A comprehensive literature search was performed for peer-reviewed articles, guidelines, and studies published between 2018 and 2024. Inclusion criteria focused on reports detailing QC protocols, error types, frequencies, and interventions in hematology settings. Data were extracted on error occurrences in preanalytical (e.g., sample collection and handling), analytical (e.g., instrument performance), and postanalytical phases (e.g., result reporting), along with the effectiveness of reduction strategies.

Results: Preanalytical errors were the most prevalent, including clotted samples, insufficient volume, labeling errors, hemolysis, and transportation issues. These often stem from improper collection techniques or inadequate mixing of anticoagulated tubes. Analytical errors primarily involved internal QC failures and instrument bias, while postanalytical errors included turnaround time delays and reporting inaccuracies. Strategies for mitigation showed promising results: regular staff training and education reduced human-related errors; standardization of procedures and automation minimized manual interventions; robust quality management systems with audits improved monitoring; and advanced tools, such as digital morphology analyzers and patient-based QC, enhanced error detection and overall reliability.

Conclusion: The findings confirm that preanalytical errors, particularly clotted samples and insufficient volume, dominate in hematology laboratories, aligning with global reports where rejection rates range from 0.3–9%. Analytical automation has reduced phase-specific errors, but ongoing calibration remains critical. Implementing comprehensive interventions—training programs, standardized workflows, automation, and advanced QC tools—can significantly lower error rates, improve diagnostic accuracy, and enhance patient outcomes. Future research should prioritize large-scale studies on innovative QC strategies in diverse settings to further minimize risks and support evidence-based laboratory improvements.

keywords: Preanalytical errors, Quality control, Hematology laboratory, Error reduction

PH-55

Ruxolitinib as a Novel Salvage Therapy for Secondary Hemophagocytic Lymphohistiocytosis

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Background and aim: Hemophagocytic lymphohistiocytosis (HLH) represents a disorder driven by immune overactivation, featuring excessive cytokine release and compromised function of natural killer and cytotoxic T-cells. It can manifest as primary or secondary (triggered by infections, malignancies, or autoimmune conditions). If it remains untreated, it may cause severe organ damage and death. Standard treatments, drawn from pediatric protocols like HLH-94 and HLH-2004, include agents such as dexamethasone, etoposide, cyclosporine, and intravenous immunoglobulin, but up to 30% of cases remain unresponsive, prompting exploration of novel options. Adult guidelines rely on extrapolated data, with limited prospective evidence.

Methods: This case involved a 38-year-old female initially presenting with fever, rash, pancytopenia, and Epstein-Barr virus (EBV) infection (14,900 copies/mL). After brief improvement and discharge, she was readmitted with worsening symptoms. Diagnosis confirmed secondary HLH based on seven criteria: fever, splenomegaly, pancytopenia, hypertriglyceridemia, hypofibrinogenemia, hyperferritinemia, elevated soluble IL-2 receptor, and bone marrow hemophagocytosis. Initial therapy included dexamethasone (up to 25 mg/m²/day), intravenous immunoglobulin (1 g/kg), etoposide (37.5-75 mg/m² twice-weekly), and rituximab (375 mg/m² for EBV). Due to persistent progression, ruxolitinib (Janus kinase 1/2 inhibitor) was started at 20 mg twice daily as salvage therapy, based on murine model data, and later reduced to 10 mg daily for renal issues.

Results: Pre-ruxolitinib, ferritin peaked at 155,726 mcg/L, lactate dehydrogenase at 13,456 units/L, with rising liver enzymes and EBV load (657,000 copies/mL). Complications included thrombocytopenia-linked subdural hematoma and neutropenia-associated candidemia. After seven days of ruxolitinib, ferritin dropped to 24,098 mcg/L, lactate dehydrogenase decreased, fibrinogen rose to 374 mg/dL without transfusions, and liver function improved. However, pancytopenia and hepatosplenomegaly did not resolve. The patient experienced hematoma expansion and intraparenchymal hemorrhage, leading to death. Genetic testing ruled out primary HLH mutations.

Conclusion: In this refractory secondary HLH case, ruxolitinib showed reductions in inflammatory markers, but it is unclear if solely attributable to it versus the delayed effects of prior therapies. Combined with positive animal data, it indicates potential as an off-label option, though pancytopenia persisted and the outcome was fatal. Further research is needed on dosing, duration, efficacy, and safety in humans, including ongoing trials.

keywords: Inflammatory mediators, EBV-related conditions, HLH syndrome, Ruxolitinib therapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-56

Prognostic Value of KM T 2A and Downstream Gene Expression in AML Patients Undergoing Allogeneic Hematopoietic Stem Cell T ransplantation

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Background and aim: Background: Relapse following allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a major cause of treatment failure in acute myeloid leukemia (AML). KMT2A, an epigenetic regulator, maintains hematopoietic homeostasis by modulating HOXA9, MEIS1, and PRDM16 — genes critical for leukemic stem cell (LSC) self-renewal. Objectives: The present study evaluated the expression of KMT2A and its downstream targets in AML patients post-allo-HSCT to assess their prognostic potential.

Methods: Methods: Bone marrow (BM) samples from 42 participants (15 controls, 12 newly diagnosed AML, 15 post-HSCT RNA extraction, complementary DNA (cDNA) synthesis, and quantitative real-time PCR (qRT-PCR).

Results: Results: Significantly elevated expression of KMT2A and HOXA9 was observed in AML and HSCT-AML groups compared to controls (P 0.0001). PRDM16 expression increased markedly only in de novo AML (P 0.0001 vs. controls/HSCT-AML). MEIS1 showed no statistically significant differences across the groups; however, a non-significant increasing trend was observed in the de novo AML cohort. PRDM16 demonstrated exceptional diagnostic accuracy for AML (AUC = 0.966; sensitivity = 100%; specificity = 93.3%). Strong positive correlations existed between: KMT2A-PRDM16 (r = 0.818, P 0.0001); KM T2A-HOXA9 (r = 0.680, P 0.0001); HOXA9-PRDM16 (r = 0.699, P 0.0001). Higher post-HSC T PRDM16 expression correlated with increased platelet counts (P = 0.019) and CD34+ cell doses (P = 0.032).

Conclusion: Conclusions: PRDM16 is a highly sensitive and specific diagnostic biomarker for de novo AML. While KMT2A, HOXA9, and PRDM16 exhibit dysregulation in AML pathogenesis and post-HSCT, assessment of their expression at day +30 post-transplant did not predict early relapse. Integrating these genes into multi-parameter models or serial monitoring strategies may enhance prognostic utility.

keywords: Acute Myeloid Leukemia,KMT2A,HOXA9,MEIS1,PRDM16,Prognosis,Relapse

PH-57

Association Between Maternal Anti–HPA-1a Antibody Concentration and Disease Severity in FNAIT

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Background and aim: Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is due to maternal alloantibodies targeting fetal platelet antigens, predominantly human platelet antigen-1a (HPA-1a) in Caucasian populations. Severe thrombocytopenia may cause bleeding, including intracranial hemorrhage. Most cases are detected postnatally, as no accepted non-invasive antenatal marker preidentified high-risk pregnancies. Maternal anti-HPA-1a antibody concentration has been proposed as a predictor of disease severity, but its clinical utility remains uncertain. This systematic review evaluated whether maternal anti-HPA-1a antibody levels correlate with fetal or neonatal platelet counts and whether they can identify pregnancies at risk of serious FNAIT complications.

Methods: A systematic search of MEDLINE, EMBASE, and the Cochrane Library was implemented from inception to January 2016. Eligible English-language studies included at least five pregnant women with measured maternal anti-HPA-1a antibodies and corresponding fetal or neonatal platelet numbers. Studies were categorized as prospective screening of unselected pregnancies or retrospective analysis of suspected or confirmed FNAIT cases. Methodological quality was assessed using established criteria. Owing to substantial heterogeneity in study design, antibody assays, timing of sampling, and outcome definitions, results were synthesized descriptively.

Results: Thirteen studies were included (three prospective and ten retrospective). Most used the monoclonal antibody immobilization of platelet antigen (MAIPA) assay, while others used ELISA or platelet immunofluorescence. In prospective studies, higher maternal antibody levels were linked to an elevated risk of severe neonatal thrombocytopenia (50×10^9/L). Negative predictive values ranged from 88% to 95%, whereas positive predictive values were variable, limiting use for definitive diagnosis. Retrospective studies demonstrated significant correlations, particularly with simultaneous sampling and MAIPA quantification, and differences in thresholds may reflect transplacental IgG transfer and variable assay standardization.

Conclusion: Maternal anti-HPA-1a antibody levels are associated with FNAIT severity, especially when measured using standardized quantitative MAIPA assays at appropriate gestational time points. These antibody levels appear most useful for risk stratification and exclusion of severe disease rather than confirming high-risk cases or guiding antenatal treatment. Variability in laboratory methods and sampling timing remains a limitation, underscoring the need for assay standardization and further prospective studies before wider integration into antenatal screening and management strategies and clinical practice.

keywords: FNAIT; HPA-1a antibody; MAIPA assay; risk stratification

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-58

Point-of-Care INR Testing in Clinical Practice: Opportunities and Challenges

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Background and aim: Point-of-care (POC) coagulometers provide a rapid and reliable alternative to conventional laboratory-based international normalized ratio (INR) testing, enabling immediate result availability in time-sensitive clinical settings. Despite these advantages, their clinical utility remains underrecognized in many healthcare systems. POC testing also supports the expanding role of telemedicine, particularly in hematology. This study aims to evaluate the opportunities and challenges associated with the implementation of point-of-care INR testing across diverse clinical applications.

Methods: We identified relevant literature through a systematic search of the PubMed database covering the period from 2020 to 2025. The search strategy included the terms “point-of-care testing,” “international normalized ratio,” and “applications of point-of-care testing for INR measurement.”

Results: Point-of-care (POC) INR testing is predominantly applied in the monitoring of vitamin K antagonist therapy, offering rapid INR assessment and improved access to care, particularly in geographically remote or resource-limited settings. The reduced turnaround time compared with laboratory-based testing enables earlier clinical decision-making. Nonetheless, performance limitations have been documented, including decreased reliability at supratherapeutic INR values (3.5) and susceptibility to interference from lupus anticoagulant, which may lead to overestimation of INR results. Prior studies suggest that patient-specific correction factors may enhance measurement accuracy in selected cases. Beyond routine anticoagulation monitoring, POC INR testing has been utilized for perioperative bleeding risk assessment in warfarin-treated dental patients, although procedural complexity appears to be a stronger determinant of bleeding risk than INR alone. Additional applications include emergency medical services and the evaluation of venom-induced consumption coagulopathy, where rapid, portable testing offers practical advantages despite technical constraints.

Conclusion: Point-of-care INR testing demonstrates substantial potential in the management of a wide range of clinical scenarios, particularly those requiring rapid clinical decision-making. Nevertheless, further research is required to better define its optimal clinical applications and to address existing limitations related to accuracy, standardization, and implementation.

keywords: international normalized ratio, Point-of-care testing, coagulation tests

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-59

The Comparison of Genes and Molecular Pathway between Newly Diagnosed and Relapsed Acute Lymphocytic Leukemia (ALL) Patients: A Bioinformatics Analysis

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Background and aim: Acute lymphoblastic leukemia (ALL) is among the most common cancers in children, which leads to the death of many patients. ALL patients include new cases and the relapsed ones. The common genes between these two conditions can largely help in managing patients and preventing future relapses. Therefore, this study investigated the genes and molecular pathways between the two conditions using bioinformatics.

Methods: In this bioinformatic study, GSE102301 database was used. After determining differentially expressed genes (DEGs), gene ontology (GO) and the related Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways were analyzed (using GeneCodis4 software). Interactions between proteins were evaluated using STRING database and hub genes were identified based on the highest score. Finally, ROC curve analysis was used to determine the diagnostic value of hub genes.

Results: Based on the interaction between DEGs, 10 genes were selected as hubs, which included WDR75, MYBBP1A, DDX10, URB1, HEATR1, NOP14, PUM3, VARS1, EARS2 and SYK |logFC| 1 and p 0.05. The results showed that all the hub genes had diagnostic value (AUC=1).

Conclusion: Hub genes identified through bioinformatics analyses may serve as potential biomarkers; however, future studies need to examine these genes in clinical settings among the patients.

keywords: Acute Lymphocytic Leukemia, Bioinformatics, Diagnosis, Relapse

PH-60

Evaluation of Genes and Molecular Pathways Involved in Pathogenesis of Sickle Cell Anemia: A Bioinformatics Analysis and Future Perspective

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Background and aim: Sickle cell disease (SCD) is one of the hematological disorders characterized by a defect in the structure and function of globin chains. Hereditary factors play an important role in the pathogenesis of SCD. We aimed to investigate the genes and pathways related to the pathogenesis of SCD.

Methods: Microarray dataset was downloaded from the Gene Expression Omnibus (GEO) database. LIMMA package of R-software was used to detect UP and Down regulations between SCD and control subjects. Enrichment analysis and Protein-protein interaction (PPI) networks were performed using GeneCodis4 software and GeneMANIA database, respectively. PrognoScan database was used to evaluate the relationship between the hub genes and patients' survival.

Results: Overall, 447 DEGs were identified in SCD patients compared to control subjects. Out of 447 DEGs, 345 genes were up-regulated and 102 genes were down-regulated. Effective hub genes in SCD pathogenesis include SLC4A1, DTL, EPB42, SNCA, and TOP2A. In addition, hub genes had a high diagnostic value.

Conclusion: Evaluation of hub genes in SCD can be used as a diagnostic panel to detect high-risk patients. In addition, by identifying the UP and Down stream pathways, treatment strategies in the monitoring and treatment of patients can be designed.

keywords: Sickle cell; Gene; Molecular pathway; Pathogenesis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-61

In silico analysis of genes and molecular pathways involved in the pathogenesis of follicular lymphoma

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Background and aim: Follicular lymphoma (FL) is a common form of non-Hodgkin lymphoma, characterized by abnormal B-cell growth within the germinal center. Research has shown the role of genes and molecular pathways in the pathogenesis of FL. However, the main factor of pathogenesis has not been determined. Therefore, in this study, the genes and molecular pathways related to the pathogenesis of FL were evaluated using a systems biology approach.

Methods: In this study (bioinformatics analysis), the GSE32018 database was used for data analysis. This database was extracted from Gene Expression Omnibus (GEO). The sample of this database was 36, which included normal and FL samples. For this purpose, 23 cases were FL and 13 were healthy samples. Protein-protein interaction (PPI) is performed to show the interaction between DEGs. STRING software is used for this purpose. Associations between the hub genes, transcription factors, and microRNAs were assessed using the miRTarBase and TRRUST databases. The criteria used for data analysis included log fold change greater than one and p 0.05.

Results: After evaluating and analyzing the data, the results showed that 866 DEGs were identified between the control and FL samples. Of this population, 231 cases of UP regulation and 635 cases of downregulation were in FL samples compared to control samples. PPI network and hub gene analyses identified 7 hub genes, including RPL37A, MRPS7, RPS14, RPS28, RPL34, RPS20, and RPS3. According to the results, hsa-miR-191-5p has the highest interactions with hub genes among miRNAs, and KDM5A has the most interactions among TFs.

Conclusion: Identifying genes and molecular pathways can be effective in designing therapeutic strategies and preventing the proliferation of FL cells, thereby increasing patients' survival.

keywords: Follicular Lymphoma, Molecular Genetics, Bioinformatics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-62

Identification of IVS II-I (HBB:C.315+1 G>A) Mutation in a Transfusion-Independent Thalassemia Patient: A Case Report

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Background and aim: Thalassemia is a genetic blood disorder marked by reduced hemoglobin synthesis, often requiring transfusions. Mutations in the HBB gene largely determine disease severity. We present a rare case of a patient homozygous for the IVS II-I (HBB:C.315+1 GA) mutation, which abolishes the canonical splice donor site of intron 2, producing aberrant transcripts and resulting in beta-0 thalassemia. Despite this pathogenic variant, the patient has managed to remain transfusion-independent, highlighting an unusual clinical course that challenges conventional expectations of disease progression.

Methods: A 34-year-old female presented for premarital screening. Clinical, hematological, and genetic information were collected at both admission and follow-up.

Results: Laboratory analysis revealed microcytic anemia, with parameters including an MCV of 76 fL and an MCH of 25 pg. Hemoglobin electrophoresis showed HBF at 97.7% and HB A2 at 2.3%. Sequencing confirmed the presence of the IVS II-I (HBB:C.315+1 GA) mutation, validated by ARMS PCR after two repetitions of the tests. Notably, the patient has remained stable without any history of transfusions or supplementary therapies such as hydroxyurea that could elevate fetal hemoglobin levels.

Conclusion: This case suggests the possibility of additional mutations that may provide compensatory mechanisms, enabling the patient to exhibit a genetically major but phenotypically intermediate phenotype. The findings underscore the complexities associated with thalassemia presentations and highlight the critical need for comprehensive genetic analysis to understand the variability in individual patient responses. Further research into the underlying genetic factors will be essential to elucidate how certain patients with known pathogenic mutations can maintain transfusion-independent status. Such insights could ultimately lead to more tailored and effective therapeutic strategies for managing thalassemia.

keywords: IVS II-I, HBB:C.315+1 GA, Thalassemia, Transfusions, Beta-0 thalassemia

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-63

Evaluation of Genes and Molecular Pathways Involved in the Progression of Monoclonal Gammopathy of Undetermined Significance (MGUS) to Multiple Myeloma: A Systems Biology Approach

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Background and aim: Today, Monoclonal Gammopathy of Undetermined Significance (MGUS) is known as a plasma cell malignancy susceptible to evolving into the life-threatening stage, multiple myeloma (MM), without prominent clinical manifestations. Despite the discovery of advanced therapies and multiple pathogenic markers, the complexity of MM development has made it an incurable malignancy.

Methods: In this study, the microarray dataset was downloaded from the Gene Expression Omnibus (GEO) database and analyzed using the LIMMA package of R-software to determine differentially expressed genes (DEGs) in MGUS and MM compared to the control samples. Enrichment analysis of DEGs was evaluated using the GeneCodis4 software. Protein-protein interaction (PPI) networks were constructed via the GeneMANIA database, and Cytoscape visualized them. The Molecular Complex Detection (MCODE) plugin from Cytoscape was used to identify the key modules from the PPI network. Afterward, the hub genes were recognized using the cytoHubba plug-in in Cytoscape. Eventually, the correlation between hub-DEGs and MM-specific survival was evaluated via the PrognoScan database.

Results: A total of 138 (MM-normal) and 136 (MGUS-normal) DEGs were obtained from the datasets, and 62 common DEGs between MGUS and MM diseases (26 up-regulated and 36 down-regulated genes) were screened out for subsequent analyses. Following enrichment analyses and the PPI network's evaluation, FOS, FOSB, JUN, MAFF, and PPP1R15A involved in the progression of MGUS to MM were detected as the hub genes. The survival analysis revealed that FOS, FOSB, and JUN among hub genes were significantly associated with disease-specific survival (DSS) in MM.

Conclusion: Identifying the genes involved in the progression of MGUS to MM can help in the design of preventive strategies as well as the treatment of patients. In addition, their evaluation can be effective in the survival of patients.

keywords: Genes molecular pathway; MGUS; Multiple myeloma; Systems biology.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-64

Hydrogel-Mediated Oxygenation to Prevent Post-Surgical Breast Cancer Recurrence: Mechanistic Insights and Translational Perspectives

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Background and aim: Surgical resection removes the bulk of localized breast tumors, yet the act of surgery paradoxically generates a profoundly hypoxic, inflamed, and immunosuppressed tumor bed that becomes the biological engine of recurrence. Residual malignant cells exploit this postoperative niche to stabilize HIF-1α, undergo EMT-driven plasticity, remodel metabolism, and suppress cytotoxic immunity, processes that render conventional adjuvant therapies markedly less effective. Increasing evidence now positions hypoxia itself as the primary, targetable determinant of postoperative relapse.

Methods: Relevant literature was identified by a PubMed search, and Google Scholar (2010-2025) of English language papers using the terms " Breast Cancer ", " Tumor Microenviroment ", " DNA hydrogels ", " Hypoxia ", “Targeted drug delivery”, “Tumor microenvironment”, and " Immunomodulation."

Results: Hydrogel-mediated oxygenation has emerged as a mechanistically aligned strategy to reprogram this vulnerable microenvironment. Advanced injectable and implantable hydrogels can operate as localized oxygen bioreactors, via perfluorocarbon reservoirs, catalytic CaO_2/catalase constructs, photosynthetic microbes, or hybrid chemical–biological platforms, while simultaneously delivering chemotherapeutics, immunomodulators, or radiosensitizers. Restoring oxygen tension disrupts the hypoxia–HIF–EMT axis, reawakens T-cell and macrophage function, resensitizes dormant cells to adjuvant therapy, and prevents the establishment of a metastatic progenitor niche. Integrating materials-science design principles with mechanistic tumor-bed biology, this review delineates how oxygenating hydrogels remodel epithelial plasticity, DNA-damage responses, stromal signaling, and immune effector dynamics. Preclinical evidence consistently demonstrates significant reductions in local recurrence when these platforms complement standard adjuvants. We further evaluate translational constraints, including the safety of oxygen-generating chemistries, manufacturing scalability, and surgical workflow compatibility, and propose a roadmap for clinical deployment.

Conclusion: Collectively, these insights position hydrogel-mediated oxygenation as a new conceptual pillar in postoperative oncology, transforming the resection cavity from a sanctuary for residual malignancy into a therapeutically reconditioned microenvironment that supports durable disease control.

keywords: Tumor Hypoxia; Breast Cancer Recurrence; Hydrogel Oxygenation; Tumor Microenvironment; Postoperative

PH-65

Managing Toxicities of Bispecific Antibody Therapy in Hematological Malignancies

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Background and aim: Bispecific antibodies (BsAbs) are an emerging class of targeted immunotherapies, significantly advancing the treatment of hematologic malignancies by offering effective options for relapsed or refractory cases, but are associated with significant toxicities. Early complications include cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS), while delayed effects can involve graft-versus-host disease (GVHD), infections, cytopenias, immunosuppression, and tumor lysis syndrome. Awareness of these key adverse events is essential for safe and effective treatment. In this review, we aim to highlight the adverse effects associated with BsAbs therapies in clinical practice and to discuss strategies for prevention and management.

Methods: This narrative review was performed through a comprehensive search of multiple databases, including Web of Science, PubMed, Scopus, and Google Scholar, with no restrictions on publication date. The search strategy incorporated the keywords “bispecific antibodies”, “hematologic malignancies”, “cytokine release syndrome”, “neurotoxicity”, and “hematotoxicity “. Only full-text articles published in English were considered, and studies were selected based on predefined inclusion and exclusion criteria.

Results: Effective management of BsAb therapies relies on early detection using biomarkers and imaging, combined with timely interventions such as immunosuppressants, corticosteroids, and cytokine inhibitors. CRS prevention involves premedication with acetaminophen, diphenhydramine, and dexamethasone. ICANS is mainly managed with corticosteroids, with dosing based on severity. Effective CRS control with IL-6 inhibitors can help prevent ICANS, while severe cases may need mechanical ventilation. Fungal prophylaxis is considered in high-risk patients, especially during neutropenia or immunosuppressive therapy. Bacterial prophylaxis is used selectively for prolonged neutropenia. Vaccinations for influenza, COVID-19, and pneumococcus are recommended for patients and close contacts, with live vaccines avoided during B-cell depletion. Prevention and management of hematologic involves baseline evaluation, monitoring, early supportive care, modification of lymphodepleting regimens, and control of CRS with corticosteroids/tocilizumab. Severe cytopenias are managed with transfusions, thrombopoietin (TPO) agonists, granulocyte colony-stimulating factor (G-CSF), stem cell boosts, and intravenous immunoglobulin (IVIG) for hypogammaglobulinemia or recurrent infection.

Conclusion: In summary, despite significant advances in the treatment of hematologic malignancies with novel bispecific antibody therapies, their distinct and sometimes severe toxicity profiles remain a major challenge, necessitating careful monitoring, early intervention, and a multidisciplinary approach. Although substantial progress has been made in managing early complications such as CRS, ICANS, infections, and hematologic toxicities, late-onset events, particularly neurotoxicity, remain poorly understood. Ongoing research and the development of standardized guidelines are therefore essential to optimize safety, expand patient access, and improve overall outcomes.

keywords: Bispecific Antibody, Hematologic malignancies, Cytokine release syndrome, neurotoxicity, hematotoxicity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-66

Targeting of CTLA-4/TGF-β in related with Helicobacter pylori in gastric mucosa-associated lymphoid tissue

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Background and aim: Helicobacter pylori–driven gastric mucosa-associated lymphoid tissue (MALT) lymphoma arises through a highly specialized immunobiological circuit in which chronic antigenic stimulation converges with a progressively tolerogenic microenvironment to sustain malignant B-cell survival. Central to this evolution is the coordinated activation of the CTLA-4 checkpoint axis and the TGF-β regulatory cytokine network, which together impose a multilayered suppression of anti-lymphoma immunity. CTLA-4 upregulation on neoplastic B cells, reinforced by TGF-β–producing macrophages and T-cell subsets, establishes a durable immune-privileged niche capable of maintaining lymphomagenesis even after H. pylori eradication. Yet no gene-silencing strategy has been developed to dismantle this cooperative tolerance architecture, nor

Methods: Here, for the first time, we construct a fully integrated in silico framework—encompassing multi-isolate sequence interrogation, conserved-region extraction, rational siRNA engineering, thermodynamic and off-target filtration, Ago2 interaction modeling, and 100-ns molecular-dynamics validation—to identify siRNAs capable of suppressing CTLA-4 and TGF-β transcripts implicated in MALT lymphomagenesis.

Results: Five siRNA duplexes met all criteria for functional asymmetry, GC optimization, folding stability, target affinity, and Ago2 compatibility, with MD simulations confirming robust guide-strand retention and structural stability within the Ago2 catalytic cleft. This study marks the first systematic attempt to simultaneously destabilize the two dominant molecular pillars of immune escape in H. pylori–associated MALT lymphoma.

Conclusion: The resulting siRNAs provide a computationally validated blueprint for experimental translation and position RNA interference as a mechanistically targeted therapeutic strategy for refractory disease.

keywords: Helicobacter pylori, Mucosa-Associated Lymphoid Tissue, CTLA-4, TGF-β, Small Interfering RNA,

PH-67

Blood-Based Biomarker Approaches for Acute Lymphoblastic Leukemia (ALL) Diagnosis: A Systematic Review

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Background and aim: Acute Lymphoblastic Leukemia (ALL) is an aggressive blood cancer that mainly affects children, though adults can develop it as well. Early detection and careful monitoring are crucial for improving survival and treatment outcomes. Traditional bone marrow biopsies are invasive and can be stressful, especially for young patients. Blood-based biomarkers offer a less invasive way to detect and track the disease, potentially making diagnosis and follow-up easier and more comfortable.

Methods: This review examines recent research on blood-based biomarkers for ALL, focusing on circulating tumor DNA (ctDNA) and circulating microRNAs (miRNAs). Key genetic changes, including IKZF1, TP53, and NOTCH1, as well as miRNAs like miR-155 and miR-181a, were evaluated for their ability to help diagnose the disease and predict outcomes in both children and adults.

Results: Studies show that ctDNA can detect genetic mutations associated with ALL and help track minimal residual disease (MRD) and treatment response in real time. Circulating miRNAs, especially miR-155 and miR-181a, have emerged as promising markers that reflect disease activity and progression. Using these blood-based tests can reduce the need for repeated bone marrow biopsies and improve patient comfort. Combining ctDNA and miRNAs increases the accuracy of diagnosis and helps predict relapse risk more reliably.

Conclusion: Blood-based biomarkers are emerging as a powerful, minimally invasive tool for diagnosing and monitoring ALL. They can make care less stressful for patients—especially children—while helping doctors personalize treatment and improve outcomes. Larger clinical studies are still needed to confirm these findings and integrate them into everyday practice.

keywords: ALL, ctDNA, microRNAs, blood biomarkers, MRD

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-68

Dendritic Cell Vaccines in Multiple Myeloma: A Systematic Review of Safety and Efficacy

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Background and aim: Multiple myeloma (MM) is a complex hematologic malignancy that poses substantial therapeutic challenges, necessitating the exploration of innovative treatment strategies. Conventional interventions, including chemotherapy and hematopoietic stem cell transplantation, are often limited by adverse effects and high relapse rates. This systematic review aims to evaluate the potential of dendritic cell (DC) vaccination as an emerging immunotherapeutic approach in MM management, with the goal of broadening current treatment options.

Methods: A comprehensive systematic search was conducted across PubMed, Scopus, ProQuest, and Web of Science to identify relevant studies. Rigorous inclusion criteria were applied, and study quality was assessed using Cochrane risk-of-bias tools. Key evaluation parameters included rates of disease remission, survival outcomes, and immunological effects.

Results: From an initial pool of 2,923 studies, 15 met the eligibility criteria for inclusion. Analysis indicated that DC vaccination was effective in inducing both complete and partial remissions and enhanced immune responses. Notable increases in various immune cell populations and cytokine levels were observed, suggesting a multifaceted therapeutic mechanism underlying this intervention

Conclusion: This review highlights the potential of dendritic cell (DC) vaccination as a promising therapeutic strategy for multiple myeloma (MM). Despite the encouraging findings, further research is required to optimize administration protocols, enhance treatment efficacy, and ensure long-term safety and stability. Advancing our understanding and clinical application of DC vaccination could improve MM management and provide patients with more effective, personalized, and sustainable therapeutic options.

keywords: Multiple Myeloma, Dendritic Cells, Immunotherapy, Vaccination, Neoplasm Vaccines

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-69

When the Victim Becomes the Villain: Platelets as Drivers of Immune Dysregulation in ITP

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Background and aim: Immune thrombocytopenia (ITP) is a heterogeneous autoimmune disorder characterized by immune-mediated destruction of platelets and impaired platelet production. Although autoantibodies have historically been central to the understanding of ITP, current evidence demonstrates that its pathogenesis extends well beyond humoral mechanisms to involve complex dysregulation of both innate and adaptive immune responses. Multiple immune pathways—including autoreactive B and T cells, dendritic cell activation, and regulatory T cell deficiency—contribute to disease onset, progression, and chronicity. Moreover, ITP encompasses a broad spectrum of clinical and immunological subtypes, including primary idiopathic forms and secondary ITP associated with autoimmune diseases, infections, and inborn errors of

Methods: Relevant literature was identified by a PubMed search, and Google Scholar (2010-2025) of English language papers using the terms " Immune Thrombocytopenia ", " Platelet Activation ", " P-selectin ", " -selectin glycoprotein ligand 1 ", and " Transforming growth factor β,."

Results: This review offers a novel perspective on ITP pathogenesis, emphasizing the active immunoregulatory role of platelets as contributors to immune dysregulation. Far from being passive targets, platelets in ITP actively shape immune responses through crosstalk with immune cells, particularly $CD4^+$ T helper (Th) and $CD8^+$ cytotoxic T cells. This interaction, primarily mediated via the P-selectin–PSGL-1 axis, promotes Th1/Th17 polarization, enhances autoantibody production, and accelerates platelet destruction. In parallel, platelet-derived microparticles (PMPs) act as potent immune effectors by delivering pro-inflammatory cytokines and autoantigens that sustain chronic immune activation. Prolonged platelet activation also gives rise to a distinct subpopulation known as “hairy platelets”—exhausted, granule-depleted cells with altered surface phenotypes and sustained pro-inflammatory potential. Although functionally exhausted in terms of coagulation, these platelets retain immunostimulatory capacity through persistent phosphatidylserine exposure and cytokine release. By reframing platelets as active participants in the pathogenesis of ITP, this review proposes that targeting platelet activation, platelet–T cell

Conclusion: Such approaches could offer more precise and personalized treatment options, particularly for patients with chronic or refractory disease, by restoring immune balance and improving long-term outcomes.

keywords: Immune Thrombocytopenia, Platelet Activation, P-selectin, P-selectin glycoprotein ligand 1, Transforming

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-70

Exosome-Derived Molecular Signatures for Differential Diagnosis of Myelodysplastic Syndromes and Non-clonal Pancytopenia

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Background and aim: Differentiating myelodysplastic syndromes (MDS) from non-clonal causes of pancytopenia remains a major diagnostic challenge due to overlapping clinical features and nonspecific laboratory findings. Diagnosis still relies largely on invasive bone marrow examination and cytogenetic analyses, which may be inconclusive, particularly in early or low-risk disease. Despite advances in molecular diagnostics, reliable non-invasive biomarkers reflecting clonal hematopoiesis are lacking. Emerging evidence indicates that extracellular vesicles, especially exosomes, carry disease-specific molecular cargo with potential diagnostic value. This review aims to evaluate the diagnostic utility of exosome-derived molecular signatures, including microRNAs, proteins, and surface markers, in distinguishing MDS from non-clonal pancytopenia.

Methods: A narrative review was conducted using PubMed and Scopus databases to identify studies published over the past decade that investigated exosomal molecular profiles in patients with MDS or non-clonal cytopenias. Studies were assessed with emphasis on molecular reproducibility, diagnostic relevance, and their ability to differentiate clonal from reactive hematopoietic disorders.

Results: Comparative analyses of exosomes isolated from peripheral blood or bone marrow plasma demonstrate that patients with MDS exhibit reproducible molecular signatures distinct from non-clonal pancytopenia. Exosomal microRNA profiling consistently identifies panels of approximately 10–30 deregulated microRNAs in MDS, most notably upregulation of miR-21 and miR-155, along with dysregulation of miR-10a, miR-486, miR-34a, and members of the miR-181 family, which are implicated in clonal expansion, myeloid differentiation, and genomic stability. These microRNA patterns show relative stability across cohorts and disease stages, supporting their association with clonal hematopoiesis. Proteomic analyses further reveal enrichment of proteins involved in ineffective hematopoiesis and immune dysregulation, including TGF-β1, TNF-α, IL-6, S100A8/S100A9, and HSP70. Additionally, exosomal surface marker profiling demonstrates increased expression of CD34, CD33, CD117, CD63, and CD81. In contrast, non-clonal pancytopenia displays heterogeneous, non-specific exosomal profiles reflecting polyclonal cellular origins.

Conclusion: Exosome-derived molecular signatures, particularly microRNA panels complemented by proteomic and surface marker analyses, represent promising non-invasive tools for differentiating myelodysplastic syndromes from non-clonal pancytopenia. These molecular profiles reflect intrinsic features of clonal hematopoiesis and demonstrate greater specificity than conventional laboratory parameters. Integration of exosome-based biomarkers into diagnostic algorithms may reduce reliance on invasive bone marrow procedures, improve early disease detection, and support more accurate risk stratification in hematologic practice.

keywords: Exosomes; MicroRNA; Myelodysplastic Syndromes; Pancytopenia; Hematologic Diagnostics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-71

Therapeutic potential of metformin-based combination therapy in acute myeloid leukemia

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Background and aim: Acute myeloid leukemia (AML) is the most prevalent form of acute leukemia. Despite great efforts, the overall prognosis for patients with AML remains poor, and the mortality rate due to relapse is also considerable. Consequently, the disease poses treatment challenges. Several studies have indicated that metformin may serve as a beneficial adjunct to traditional anti-leukemia medications, especially enhancing their effectiveness against drug resistance; however, it is not effective when used as a standalone treatment. In this context, combination therapies are currently being explored as a promising treatment option.

Methods: This study is a narrative review. A comprehensive literature search across multiple databases, including PubMed, Google Scholar, Scopus, Embase and Cochrane, yielded 103 relevant articles up to July 2024. From an initial total of 103 articles, we excluded unrelated and duplicate articles, as well as those for which the full text was unavailable and review articles. Ultimately, 32 articles were included in the study. During the database search, we employed search terms such as AML, combination, and metformin to find relevant articles.

Results: According to the results of the studies, the combination of metformin with gilteritinib, sorafenib, 6-benzylthionosine, venetoclax, diclofenac, diflunisal, and cytarabine reduces intracellular ATP levels, inhibits glycolysis, halts the cell cycle, diminishes oxidative phosphorylation, increases the expression of anti-apoptotic proteins and increases cytotoxicity. This combination also induces apoptosis, reduces cell growth, and ultimately leads to a significant decrease in the burden of AML and an increase in overall survival for these patients.

Conclusion: Therefore, combining these drugs with metformin may enhance the synergistic effect and improve the treatment of AML patients.

keywords: AML; Combination; Metformin

PH-72

Comparison of Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Hemoglobin-to-Platelet Ratio (HPR) in Patients with Immune Thrombocytopenia and Healthy Controls: A Retrospective Study

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Background and aim: Immune thrombocytopenia (ITP), formerly known as idiopathic thrombocytopenic purpura, is a common hematologic disorder that affects a wide range of people but is more prevalent in childhood and the elderly. Evaluation and measurement of the inflammatory markers in patients with ITP is costly and time consuming

Methods: This is a retrospective descriptive and epidemiological study that was conducted in 2020-2021 at Ahwaz Jundishapur University of Medical Sciences in Baqaei Hospital. In this study, 250 ITP patients participated as case group and 70 healthy individuals as control group.

Results: The results showed that the mean PLR was lower in patients (1.29±2.24) compared to controls (69.88±33.01), while the mean NLR (2.146±2.16 VS. 0.966±0.919) and HPR (0.752±0.707 VS. 0.049±0.017) in patients were higher than healthy individuals, which was statistically significant (p: 0.0001). On the other hand, it was shown that there was no significant difference between the mean MCV (p=0.584) and WBC (p=0.943) indices between the two groups. In order to evaluate the diagnostic value of PLR, NLR and HPR indices, receiver operating characteristic (ROC) curves were used and Area Under the Curve (AUC) values were evaluated. The AUC of NLR was about 71% while for PLR and HPR it was 100% and 98%, respectively.

Conclusion: In general, the three markers PLR, NLR and HPR have diagnostic value in the diagnosis and management of ITP patients.

keywords: Neutrophil Lymphocyte Ratio, Platelet Lymphocyte Ratio, Hb Platelet Ratio, Immune

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-73

Specific Leukocyte Recruitment Integrins: An Important and Impressive Factor in The Atherosclerosis Process

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Background and aim: Atherosclerosis is a major underlying cause of cardiovascular diseases, which remain the leading causes of mortality worldwide. Early stages of atherosclerosis are characterized by the recruitment of inflammatory cells from the circulation and their transmigration across the vascular endothelium. This process is primarily mediated by cellular adhesion molecules expressed on endothelial cells and leukocytes in response to inflammatory stimuli. The aim of this review is to evaluate and summarize current evidence regarding the role of integrins, particularly β2 integrins, in the development and progression of atherosclerosis.

Methods: This review analyzes and synthesizes findings from experimental and clinical studies investigating the involvement of integrins in leukocyte recruitment, adhesion, and migration during atherogenesis, with a specific focus on β2 integrin subtypes.

Results: Evidence indicates that interactions between integrins and their ligands are essential for leukocyte rolling, tethering, and firm adhesion to the vascular endothelium. Integrins such as Macrophage-1 Antigen (MAC-1) and Lymphocyte Function-Associated Antigen-1 (LFA-1), as well as other β2 integrins including CD11c/CD18 and CD11d/CD18, play significant roles in mediating inflammatory cell adhesion and accumulation within atherosclerotic lesions.

Conclusion: Integrins, particularly β2 integrins, are critical regulators of leukocyte-endothelial interactions and inflammatory cell recruitment in atherosclerosis. Targeting integrin-mediated pathways may represent a promising therapeutic strategy for the prevention and treatment of atherosclerotic cardiovascular diseases.

keywords: Atherosclerosis; Integrins; β2 Integrins; Leukocyte Adhesion; Inflammation;

PH-74

Platelet-Derived Extracellular Vesicle microRNA-223: A Novel Biomarker for Deep Vein Thrombosis Laboratory Diagnosis

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Background and aim: Deep vein thrombosis (DVT) is a prevalent vascular disease that can result in life-threatening complications such as bleeding and pulmonary embolism. Therefore, early diagnosis is critical for timely treatment, despite the fact that it faces many challenges due to the lack of appropriate laboratory techniques. Activated platelets release extracellular vesicles that carry various cargoes, comprising microRNA-223, which regulates inflammation and thrombosis. This study examines the utilization of platelet-derived extracellular vesicles (PDEVs) microRNA-223 as a novel biomarker for DVT diagnosis.

Methods: In this study, we conducted a comprehensive search of Scopus, PubMed, and Google Scholar databases using the keywords " Deep vein thrombosis," "Platelet-derived extracellular vesicle," and " microRNA-223." Articles published between 2016 and 2025 were reviewed.

Results: According to the studies, PDEVs increased in DVT patients, which elucidates the enhancement of platelet activation, a key factor in thrombosis. Although the number of PDEVs elevated, miR-223 downregulated due to its role in the suppression of procoagulant factors such as tissue factors. This alteration in DVT compared to a normal person may be a part of a pathological process. These results demonstrate that increased PDEV count with a reduced miR-223 level is a significant marker, and their combination can be a sensitive and non-invasive way for early diagnosis.

Conclusion: Ultimately, harnessing PDEVs-miR-223 as a non-invasive method can be a promising approach for early detection and timely intervention, thus better patient management and diminishing health complications.

keywords: Extracellular vesicles, Deep vein thrombosis, microRNA-223

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-75

Prognostic Value of NLR, SIRI, and SII in Cardiovascular Diseases: An Evidence-Based Review of Original Clinical Studies

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Background and aim: Systemic inflammation plays a key role in the initiation, progression, and destabilization of atherosclerotic plaques and contributes directly to adverse cardiovascular outcomes. Hematologic inflammatory indices derived from routine complete blood counts, including neutrophil-to-lymphocyte ratio (NLR), systemic inflammation response index (SIRI), and systemic immune-inflammation index (SII), have emerged as accessible tools reflecting immune activation and inflammatory burden. Numerous original studies have explored their prognostic significance in acute and chronic cardiovascular settings.

Methods: An evidence-based review was performed using original clinical studies evaluating NLR, SIRI, and SII in patients with acute coronary syndrome (ACS), ST-elevation myocardial infarction (STEMI), and high-risk cardiovascular populations. Extracted data included cutoff values, hazard ratios (HR), odds ratios (OR), area under the curve (AUC), and endpoints such as major adverse cardiovascular events (MACE), all-cause mortality, cardiovascular death, and heart failure.

Results: Across studies, elevated NLR was consistently associated with adverse cardiovascular outcomes. Reported cutoff values ranged from 2.5 to 3.5, with higher NLR linked to increased risk of MACE and mortality (HR 1.6–2.8) and moderate discriminative performance (AUC 0.65–0.75). SIRI showed strong prognostic relevance, particularly in acute settings. Values above 4.5–5.0 were independently associated with higher short- and long-term mortality, with reported HRs of 2.0–2.6 and acceptable discriminative ability (AUC 0.70–0.78). SII demonstrated the most robust predictive performance. In STEMI patients undergoing PCI, elevated SII values (1200–1300 $\times 10^9$/L) were associated with markedly increased MACE risk (HR up to 4.09). In ACS patients with chronic kidney disease, SII $\geq$ 1159.84 $\times 10^9$/L independently predicted MACE (HR $\approx$ 1.86) and cardiovascular mortality (HR up to 7.7). AUC values ranged from 0.75 to 0.85, and inclusion of SII improved risk discrimination and reclassification.

Conclusion: NLR, SIRI, and SII are reliable, low-cost biomarkers for cardiovascular risk stratification. Among them, SII shows the greatest prognostic strength and improves risk reclassification beyond traditional models, while NLR and SIRI provide complementary information on systemic inflammatory activity.

keywords: SII, NLR, SIRI, MACE, ACS

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-76

Evaluation of prevalence and trends of HIV, HBV and HCV in blood donors in south iran: A retrospectiove study (12 years) based machine learning

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Background and aim: Today, various studies have been conducted in connection with the prevalence of viral infections in blood donors, however, considering that the transmission of viruses has not been eliminated in general, it is necessary to evaluate the transmission process and trends in donors. This evaluation can be the basis for the use of preventive strategies to prevent the transmission of infections through blood. In this study, we investigated the prevalence and trend of HIV, HBV and HCV infections in blood donors in Khuzestan province in the last 12 years.

Methods: This study is a retrospective descriptive analysis conducted using data collected from blood donors at the Khuzestan Blood Transfusion Organization between 2011 and 2022. The study anonymously examined the stored screening results of blood donors at Khuzestan blood donation centers for HBV, HCV, and HIV infections. Eligible donors were between 18 to 65 years of age, weighed over 45 kg, had a hemoglobin level above 12.5 g/dL, and did not have a history of serious illness, high-risk behavior, blood transfusion, surgery, hepatitis, or jaundice. Their blood pressure and body temperature were also within normal ranges. Donors who did not meet these criteria were excluded from the study.

Results: In related HBS, There was no significant association between positive results and gender or marital status. However, there is a significant association between positive results and self-exclusion status (p-value 0.012) as well as donor occupation (p-value 0.018). Also, a significant association was found between positive HCV results and self-exclusion status (p-value 0.03). About HIV, no significant association between positive results and gender, marital status, or self-exclusion status of donors. However, a significant association was found between positive HIV results and donor occupation (p-value 0.01).

Conclusion: The results of the present study showed a reduction in HBV, HCV, and HIV among donors. This confirms the effectiveness of the policy used by IBTO in recent years. Routine blood donation screening in Iran is based on serological tests, which cannot identify cases in the window period.

keywords: Human Immunodeficiency, Hepattis B Virus, Hepatitis C Virus, Blood Donor.

PH-77

Laboratory Approaches to APS

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Background and aim: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by the presence of antiphospholipid antibodies (aPLs) such as lupus anticoagulant (LA), anticardiolipin antibodies, and anti-β2-glycoprotein I antibodies. APS is associated with thrombotic events, pregnancy-related morbidity, and a variety of other clinical manifestations including autoimmune disorders, immune thrombocytopenia, and catastrophic APS (CAPS). The diagnosis of APS relies on both clinical criteria (thrombosis and/or pregnancy morbidity) and laboratory evidence of persistent aPLs.

Methods: The diagnosis of APS involves various laboratory assays to detect aPLs. These include: Immunoassays: For detecting anticardiolipin antibodies and anti-β2-glycoprotein I antibodies. Coagulation assays: For detecting lupus anticoagulant, which involves functional tests like the Russell Viper Venom test and activated partial thromboplastin time assay. Advanced functional tests: Experimental methods such as thrombin generation assays, rotational thromboelastometry, flow cytometric platelet activation, and surface plasmon resonance. Genetic studies: Whole exome sequencing and genome-wide association studies to identify genetic susceptibility loci

Results: Diagnostic Challenges: The diagnosis of APS is complicated by the variability in clinical presentation and the limitations of current laboratory assays. Standardization issues and interference from anticoagulant therapy are significant challenges. Clinical Manifestations: APS patients may present with a wide range of symptoms including thrombosis, pregnancy complications, autoimmune disorders, and CAPS. Treatment: Long-term anticoagulation with vitamin K antagonists is the standard treatment for thrombotic APS. Direct oral anticoagulants are generally not recommended for secondary prevention, especially in high-risk patients. Genetic Insights: Genetic studies have identified several loci associated with APS, suggesting a complex interplay between genetic predisposition and environmental trigger

Conclusion: APS is a complex autoimmune disorder with significant diagnostic and therapeutic challenges. Advances in laboratory diagnostics, including the development of new assays and genetic studies, are crucial for improving the diagnosis and management of APS. Early diagnosis and a multidisciplinary approach are essential for reducing morbidity and improving patient outcomes.

keywords: APS, LA, Thrombosis

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-78

An investigation into alterations in calcium levels in patients with leukemia and their impact on prognosis

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Background and aim: Leukemia is one of the major types of hematologic malignancies with a considerable prevalence among patients. According to epidemiological patterns, acute myeloid leukemia (AML) is the most common type in adults, accounting for approximately one-third of cases. Chronic lymphocytic leukemia (CLL) comprises about one-quarter to one-third of cases, while acute lymphoblastic leukemia (ALL) accounts for nearly one-fifth, and chronic myeloid leukemia (CML) represents about one-tenth of leukemia cases. Hypercalcemia is defined as a condition in which serum calcium levels exceed the normal range (8.5–10.5 mg/dL) and are reported above 11.5 mg/dL. Given the occurrence of hypercalcemia and calcium alterations in

Methods: These studies were conducted based on the PICO criteria and in line with the goal of realization and following the PRISMA checklist. This systematic review includes a comprehensive search from 2015 to 2024 in Pubmed databases and Google scholar search engine. MESH keywords such as " Leukemia" Hypercalcaemia “ were used in the search. Next, two independent researchers screened the retrieved articles based on the inclusion criteria

Results: A total of 742 articles were identified through the initial search. After title and abstract screening, 36 articles underwent full-text assessment, and 10 studies were finally included according to predefined inclusion and exclusion criteria. The selected studies comprised clinical, paraneoplastic, and molecular-functional investigations. The findings indicated that calcium dysregulation in leukemias is a heterogeneous phenomenon evaluated at systemic or intracellular levels. Clinically, hypercalcemia was largely independent of parathyroid hormone and vitamin D and was mainly associated with bone involvement, abnormal osteoclast activation via the RANK/RANKL pathway, inflammatory cytokine release, and paraneoplastic mechanisms. In several reports, severe hypercalcemia represented an initial disease manifestation or a marker of high disease activity and treatment resistance, particularly in chronic myeloid leukemia. Molecular studies demonstrated that disruption of intracellular Ca2+ homeostasis, especially persistent store-operated calcium entry and abnormal endoplasmic reticulum calcium release, leads to chronic Ca2+ accumulation and enhanced leukemic cell survival and drug resistance

Conclusion: Based on available evidence, hypercalcemia in leukemias is a complex, multifactorial phenomenon that is primarily considered a paraneoplastic manifestation and a systemic consequence of malignancy. In most clinical studies, calcium reflects disease activity, bone involvement, malignancy-related calcium imbalance, or treatment toxicity rather than acting as a direct regulator of cell survival or apoptosis. However, limited mechanistic studies indicate that persistent dysregulation of intracellular Ca^{2+} signaling, particularly via SOCE and ER–mitochondrial interactions, may promote leukemic cell survival and drug resistance, suggesting a potential future therapeutic target.

keywords: Leukemia - prognosis- hypercalcemia

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-79

Immunomodulatory Contributions of Mesenchymal Stem Cells and Their Extracellular Vesicles to the Treatment of Immune Thrombocytopenia

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Background and aim: Immune thrombocytopenia (ITP) is an acquired immune disorder that is defined by a persistent reduction in platelet numbers. Mesenchymal stem cells (MSCs), as multipotent cells characterized by low immunogenicity, pluripotent differentiation, and immunomodulatory ability, can play a critical role in the ITP pathogenesis. In this comprehensive literature review, the recent findings of potential therapeutic effects of MSCs and MSC-derived extracellular vesicles (EVs) in ITP are discussed.

Methods: The present systematic review was conducted by searching the literature in PubMed, Embase, Scopus, and Web of Science using keywords including Mesenchymal stem cell, MSC, Extracellular vesicles, EVs, exosome, Immune thrombocytopenic purpura, ITP. All original studies that discussed the potential effects of MSCs and their EVs on ITP pathogenesis and therapeutic targets were included in the analysis, in accordance with the PRISMA checklist.

Results: Accumulating experimental and clinical data demonstrate that MSCs derived from ITP patients exhibit reduced proliferative capacity, increased apoptosis, and compromised immunomodulatory function, accompanied by dysregulated cytokine secretion, such as elevated IL-6. Pharmacologic interventions, including glucocorticoids and selective CB2 receptor agonists, partially restored MSC viability through Bcl-2 upregulation, normalized inflammatory cytokine profiles, and re-established suppression of T-cell activation and TNF-α release. Clinical observations further indicate that hUC-MSC infusion in refractory ITP can induce sustained, though incomplete, hematologic responses lasting up to 12–17 months. Emerging evidence also suggests that MSC-derived extracellular vehicles recapitulate key immunoregulatory properties of MSCs, supporting their potential as a cell-free therapeutic modality in ITP.

Conclusion: MSCs and MSC-derived EVs exhibit significant immunomodulatory and anti-inflammatory effects relevant to ITP pathogenesis and treatment. Their ability to restore immune balance and improve hematologic outcomes highlights their promise as adjunct or alternative therapeutic strategies. Further controlled studies are required to define their clinical utility and optimize their application.

keywords: Immune thrombocytopenia, ITP, Mesenchymal stem cells, MSCs, Extracellular Vesicles, EVs.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-80

Kell and E Alloantibodies as the Main Causes of Alloimmunization in Transfusion-Dependent Thalassemia Patients: A Cross-Sectional Study

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Background and aim: Patients with major thalassemia require regular blood transfusions, and one of the most important complications of repeated transfusions is the development of alloantibodies. This study aimed to assess the frequency and characterize common types of alloantibodies in patient population.

Methods: This descriptive cross-sectional study was conducted on 45 patients with transfusion-dependent major thalassemia in Birjand, Iran. Antibody screening and subsequent antibody identification tests were performed to detect alloantibodies. Demographic, clinical, and laboratory data including age, gender, and relevant clinical parameters were extracted from the patients' electronic medical records. Data were analyzed using SPSS version 26, and the chi-square and Fisher's exact tests were applied to evaluate associations between variables.

Results: A total of 45 patients, comprising 21 males (46.6%) and 24 females (53.3%), with and age ranged from 1 to 36 years, were included in the study. The overall prevalence of alloantibodies was 2.2%-18.1% (95% CI). Four alloantibodies were identified, with anti-K being the most frequent (3 patients, 100%) followed by anti-E (1 patient, 33%). The most common ABO phenotype was type O (42.2%), while Rh antigens c and e, were present in 100% and 93.3% of patients, respectively. Seven patients (15.5%) had undergone splenectomy. No significant association were observed between alloimmunization and age group, gender, blood group, number of transfused blood units, or splenectomy status.

Conclusion: Given the detection of alloantibodies targeting the Kell and Rh (E) blood group systems in the thalassemia population, it is recommended that transfused blood units be matched at a minimum for Kell and Rh antigens.

keywords: Thalassemia, Alloimmunization, Alloantibody, Blood transfusion

PH-81

The combination therapy with Venetoclax in therapeutic strategy of acute lymphoblastic leukemia

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Background and aim: Acute lymphoblastic leukemia (ALL) is characterized by the malignant transformation and proliferation of lymphoid progenitor cells in the bone marrow, blood, and extramedullary sites. Leukemic cells can develop drug resistance both before and after treatment, complicating disease management. Combination therapy with Venetoclax has been shown to enhance the efficacy of standard anti-leukemia drugs. Therefore, this study aims to review combination treatment strategies as potential therapeutic alternatives, drawing on evidence from previous published literature.

Methods: A comprehensive literature search was conducted across English-language databases and studies were selected for their relevance and conceptual importance.

Results: Combination therapy involving venetoclax- together with agents such as azacitidine, blinatumomab, bortezomib, decitabine, ibrutinib, dinaciclib, and inotuzumab ozogamicin, has been shown to supress DNA methyltransferases activity, reduce proteasome function, and enhance cytolytic protein production. These therapeutic combinations promote cell-cycle arrest, modulate the expression of anti-apoptotic proteins, and collectively contribute to improved antileukemic activity. Overall, these effects may translate into better therapeutic responses in patients with ALL.

Conclusion: Venetoclax-based combination regimens demonstrate synergistic antileukemic effects and may offer superior therapeutic benefits for patients with ALL compared to single agent therapy.

keywords: Venetoclax, Acute lymphoblastic leukemia, chemotherapy.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-82

Clinical and Translational Relevance of Human Endogenous Retroviruses in Leukemia: A Narrative Review

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Background and aim: Human endogenous retroviruses (HERVs) are remnants of ancient viral infections integrated into the human genome and increasingly recognized for their potential roles in oncogenesis, immune regulation, and therapeutic response in hematologic malignancies. Altered expression of specific HERV families has been reported in leukemia patients, suggesting possible clinical and translational relevance. This narrative review aims to summarize patient-derived evidence on HERV expression in leukemia and to evaluate reported associations with disease characteristics, prognosis, and immunologic mechanisms relevant to clinical practice.

Methods: A narrative literature review was conducted to identify and synthesize human studies investigating the expression and clinical relevance of human endogenous retroviruses (HERVs) in leukemia. Electronic searches were performed in PubMed, Web of Science, and Google Scholar to retrieve English-language articles published within the last ten years. Search terms included “human endogenous retrovirus” or “HERV” in combination with “leukemia,” “acute myeloid leukemia (AML),” “acute lymphoblastic leukemia (ALL),” “chronic lymphocytic leukemia (CLL),” and related keywords. Studies were screened based on title and abstract, followed by full-text evaluation when appropriate. Eligible studies included those analyzing patient-derived samples and reporting clinical, prognostic, immunologic, or translational findings related to HERV expression. Experimental studies without clinical relevance and non-human studies were excluded. The selected evidence was qualitatively synthesized and organized according to leukemia subtype and HERV family, with particular emphasis on findings with potential implications for clinical practice and translational research.

Results: Evidence derived from patient samples demonstrates differential and subtype-specific expression patterns of human endogenous retrovirus (HERV) families across various forms of leukemia. Increased expression of HERV-K has been reported in peripheral B lymphocytes of patients with leukemia and lymphoma, suggesting a potential role in disease-related immune dysregulation. In pediatric acute lymphoblastic leukemia (ALL), elevated expression of HERV-K–derived np9 transcripts and HERV-R env has been associated with leukemic cell biology and disease characteristics. In acute myeloid leukemia (AML), aberrant expression of HERV-K9–derived elements, as well as HERV-Suppressyn and Syncytin-2, has been correlated with clinical outcomes and prognostic parameters, supporting their potential utility as biomarkers. Additional studies indicate that leukemia stem cells express multiple HERV families, generating shared antigenic epitopes that may be relevant for immunotherapeutic targeting. Furthermore, immunologic evidence suggests that HERV activation may contribute to T-cell responses and graft-versus-leukemia effects, highlighting a functional link between HERV expression, immune modulation, and

Conclusion: This narrative review integrates clinical and laboratory evidence indicating that HERV expression in leukemia is subtype-specific and clinically relevant. Patient-derived data support associations between selected HERV families and disease characteristics, prognosis, and immune responses, underscoring their potential value as biomarkers and translational targets. While current findings are largely associative, they provide a framework for future studies to clarify the functional and clinical significance of HERVs in leukemia and to explore their relevance in biomarker development and immunotherapy.

keywords: Human endogenous retrovirus; leukemia; biomarker; clinical relevance; immune modulation

PH-83

Hemophilia A and Mim8 in Prophylactic Treatment

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Background and aim: Hemophilia A is a hereditary bleeding disorder caused by factor VIII deficiency, leading to spontaneous bleeding and progressive joint damage. Prophylactic treatment with recombinant factor VIII (rFVIII) remains the standard approach, but frequent infusions can reduce adherence and affect quality of life (Bennett et al., 2020). Mim8, a bispecific monoclonal antibody, is emerging as a promising alternative, mimicking factor VIII activity while potentially reducing injection frequency (White et al., 2023)

Methods: I conducted a systematic literature search in PubMed, Scopus, and the Cochrane Library from 2015 to 2025, using keywords such as "Hemophilia A," "Mim8," "prophylaxis," and "factor VIII." Clinical trials, meta-analyses, and systematic reviews assessing prophylactic therapies in Hemophilia A were included. Key outcomes extracted were annual bleeding rate (ABR), infusion frequency, and safety profiles.

Results: Nine studies met inclusion criteria. Clinical trials indicated that Mim8 effectively reduced ABR compared with conventional rFVIII therapy (median ABR: 1.5 vs 3.8 episodes/year) (Bennett et al., 2021; Peyvandi et al., 2023). Patients on Mim8 required fewer infusions per month (1–2 vs 2–3 with rFVIII), contributing to improved adherence and quality of life (Gonzalez et al., 2022). Safety analyses revealed a lower incidence of infusion-related reactions and inhibitor development in Mim8-treated patients. Meta-analyses support that Mim8 provides comparable or superior efficacy to standard prophylaxis while decreasing treatment burden (Zhang et al., 2024)

Conclusion: Mim8 shows significant potential as a prophylactic therapy in Hemophilia A, offering effective bleed prevention with reduced infusion frequency. These features may enhance adherence and patient quality of life. Long-term studies are warranted to confirm safety and solidify Mim8's role as a standard prophylactic option.

keywords: Hemophilia A, Factor VIII, Bleeding disorders.

PH-84

Cancer-Associated Thrombosis: Pathophysiology and Treatment

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Background and aim: The aim of this systematic review is to evaluate the most effective treatment strategies for Cancer-Associated Thrombosis (CAT), focusing on the comparison between low-molecular-weight heparin (LMWH) and direct oral anticoagulants (DOACs). This review also explores the role of risk assessment models and identifies gaps in the current treatment approaches.

Methods: A systematic search of the literature was conducted using the databases PubMed, Scopus, and Cochrane Library. Studies were included if they assessed the treatment of venous thromboembolism (VTE) in cancer patients and compared LMWH and DOACs. Studies were selected based on inclusion criteria such as randomized controlled trials (RCTs), cohort studies, and clinical trials. The Cochrane Risk of Bias tool was used to evaluate the quality of studies. Key outcomes, including VTE recurrence, major bleeding events, and mortality, were extracted for analysis

Results: A total of 15 studies were included in the review. The studies consistently demonstrated that LMWH was more effective than warfarin in preventing recurrent VTE in cancer patients. Notably, the Hokusai-VTE Cancer trial showed that edoxaban (DOAC) was non-inferior to LMWH for preventing recurrent VTE, with a comparable risk of major bleeding (Raskob et al., 2018). Similarly, the CASSINI trial found that apixaban effectively prevented VTE recurrence without significantly increasing bleeding risk, even in high-risk cancer populations. The review also found that Khorana score was effective in predicting VTE risk in cancer patients, helping to guide treatment decisions. Furthermore, gastrointestinal cancers were associated with a higher risk of bleeding , particularly when using oral anticoagulants like DOACs.

Conclusion: Cancer-associated thrombosis is a significant complication of malignancy, and anticoagulation therapy remains the cornerstone of treatment. LMWH is the standard treatment for CAT, but DOACs, particularly apixaban and edoxaban, offer a promising alternative, with comparable efficacy and ease of use. However, the risk of bleeding in cancer patients with gastrointestinal malignancies requires careful patient selection. The use of risk prediction models such as the Khorana score is essential for personalizing therapy. Further research is needed to explore new treatment strategies and refine the management of CAT

keywords: Venous thromboembolism, low-molecular-weight heparin, edoxaban, apixaban

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-85

Diagnostic Value of Normal or Near-NormalFactor VIII Levels in Excluding Bleeding Disorders

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Background and aim: Factor VIII (FVIII) is an essential coagulation protein used for diagnosing bleeding disorders, particularly hemophilia A and von Willebrand disease (VWD). FVIII levels are commonly used to evaluate bleeding risk, with normal or near-normal levels often being interpreted as evidence against significant bleeding disorders (Mannucci & Tuddenham, 2001). However, FVIII levels are subject to numerous biological and environmental influences, such as hormonal fluctuations, pregnancy, stress, and inflammation, which can alter FVIII activity without indicating a true underlying bleeding disorder (Goudemand & Manco-Johnson, 2013). This systematic review examines the diagnostic utility of normal or near-normal FVIII levels in both men and

Methods: A comprehensive search was conducted in PubMed, Scopus, and Web of Science databases through December 2025. The following terms were used: “factor VIII,” “bleeding disorders,” “hemophilia A,” “von Willebrand disease,” “normal factor VIII,” and “diagnosis.” Inclusion criteria were clinical studies, cohort studies, and observational studies involving FVIII activity measurement in patients with bleeding symptoms. Studies focusing on severe hemophilia A or animal models were excluded. Data were extracted by two independent reviewers on FVIII levels, bleeding phenotype, and final diagnosis, with disagreements resolved through consensus (Liberati et al., 2009)

Results: From the 37 eligible studies (covering over patients), normal or near-normal FVIII levels were found in approximately 60% of individuals with clinically significant bleeding symptoms. This was particularly common in women, as well as patients with mild hemophilia A and VWD. Despite FVIII levels being within normal reference ranges, a substantial proportion of these patients exhibited severe bleeding events (Goudemand & Manco-Johnson, 2013). FVIII activity was found to be influenced by pregnancy, estrogen therapy, and inflammatory conditions, often resulting in transiently elevated FVIII levels in otherwise healthy individuals (Peyvandi & Garagiola, 2016). Several studies showed a weak correlation between FVIII levels and bleeding severity, indicating that FVIII testing alone lacks diagnostic sensitivity. In particular, FVIII levels failed to distinguish between mild bleeding disorders and healthy individuals in many cases . (Goudemand & Manco-Johnson, 2013)

Conclusion: Normal or near-normal FVIII levels are not sufficient to exclude bleeding disorders, particularly in individuals with mild bleeding symptoms. FVIII activity is influenced by various physiological and environmental factors, which can result in misleadingly normal values. Relying solely on FVIII levels to rule out bleeding disorders may lead to diagnostic delay or misclassification. A comprehensive diagnostic approach, including detailed clinical history, repeat testing, and additional coagulation assays, is essential to accurately diagnose bleeding disorders in both women and men (Peyvandi & Garagiola, 2016).

keywords: Factor VIII; Bleeding disorders; Hemophilia A; von Willebrand disease

PH-86

Low levels of coagulation inhibitors: A high-risk thrombotic factor in thalassemic patients

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Background and aim: The 1-thalassemia major (1-TM) is defined as a hereditary red blood cellrelated disease. Thrombotic events are associated with thalassemia in adult patients. Thus, the present investigation was aimed to examine some hemostatic parameters, including anti thrombin-III (AT-III), protein-C (PRC) and protein-S (PRS) in 1-TM patients.

Methods: Thirty B-TM patients who referred for routine follow-up admission to the thalassemia clinic of Kerman Special Disease Center alongside with 30 healthy subjects were selected and enrolled in the present study. Further registration, the peripheral blood specimens were collected after 3 weeks of last transfusion and then the plasma concentrations of AT-III, PRC and PRS were measured in them.

Results: We have observed that the concentrations of natural coagulation inhibitors (PRC and PRS) were significantly attenuated in 1-TM patients (P0.05), while the plasma level of AT-III was not remarkably differed in 1-TM patients in compare to healthy subjects.

Conclusion: According to the findings of present work, significant changes in the PRC, PRS and AT-III which could be observed in multi transfused 1-TM patients may attribute as critical risk factors for the development of upcoming thromboembolic events in their future life.

keywords: Thalassemia major; Thrombosis; Protein C

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-87

Frequency of Transfusion-Related Complications Among Blood Product Recipients in Hospitals of Bushehr Province, 2022–2024

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Background and aim: Blood transfusion, as one of the most essential and life-saving therapeutic interventions in modern medicine, has long played a crucial role in saving lives and improving patients' quality of life. Adverse reactions associated with blood and blood product transfusions represent a significant challenge to healthcare systems. Access to safe and healthy blood for recipients is not only a medical necessity but also a key indicator for evaluating the efficiency of healthcare systems worldwide.

Methods: This cross-sectional study was conducted using hospital records and transfusion data from Bushehr Province. The study population included all hospitalized patients who received blood and blood products. Data were analyzed using the chi-square test with a significance level of less than 0.05. Statistical analyses were performed using SPSS version 25.0 and STATA version 17.0.

Results: A total of 212 patients experienced adverse reactions following blood or blood product transfusions. Among them, 71 patients (33.5%) were aged 20–45 years. Regarding the severity of reactions, 201 patients (94.8%) had mild reactions, 10 patients (4.7%) had severe reactions, and 1 patient (0.5%) experienced a life-threatening reaction. The most common type of reaction was non-hemolytic, observed in 90 patients (42.5%), and the blood product most frequently associated with reactions was RBCs, reported in 123 cases (58%).

Conclusion: The findings of this study indicate that non-hemolytic reactions were the most prevalent transfusion-related complication, and most reactions were mild. The incidence observed in this study was lower than global averages. The most frequent symptoms included fever, chills, and pruritus.

keywords: Blood, Adverse reaction, Allergic reaction, Blood Transfusion Bushehr

PH-88

The Prognostic Significance of D-Dimer Concentrations for Clinical Outcomes Following Trauma: A Systematic Review and Meta-Analysis

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Background and aim: This study systematically reviewed the literature and performed a meta-analysis to quantify the relationship between admission D-dimer concentrations and injury outcomes in trauma patients.

Methods: We searched PubMed, MEDLINE/PubMed, and Web of Science for studies published between 2011 and 2023, and screened reference lists for additional reports. Two reviewers independently evaluated study quality using the Newcastle-Ottawa Scale. Primary endpoints were mortality and deep vein thrombosis (DVT).

Results: Eighty-four records were identified, 17 underwent full-text review, and 12 studies met inclusion criteria. Using a random-effects model to synthesize results, mean D-dimer levels were significantly higher in patients who experienced adverse outcomes compared with those who did not ($p = 0.0003$; standardized mean difference [SMD] = 0.51, 95% CI: 0.24–0.79). Higher admission D-dimer was also associated with mortality ($p = 0.03$; SMD = 0.42, 95% CI: 0.04–0.79) and with DVT ($p = 0.0008$; SMD = 0.79, 95% CI: 0.32–1.25).

Conclusion: The pooled evidence suggests that elevated D-dimer measured at admission is a potentially useful prognostic indicator for poor outcomes in trauma patients, including increased risk of death and DVT.

keywords: D-dimer, Meta-analysis, Mortality, Trauma brain injury, Deep vein thrombosis

PH-89

Role of some members of chemokine/ cytokine network in the pathogenesis of thalassemia and sickle cell hemoglobinopathies: a mini review

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Background and aim: The word of hemoglobinopathy is described for an array of disorders that affecting hemoglobin (Hb) functions. Hb is a molecule with 68 kDa molecular weight, serving as oxygen carrying metalloprotein. Hemoglobinopathy includes a wide range of Hb structural deficits varying from thalassemia to sickle cell disease. Cyto-chemokine network members are pivotally involved in the pathogenesis of hemoglobinopathies, however, the exact role of these mediators in the development of these disorders yet to be well addressed. Cytokines and chemokines are generated by inflamed endothelial cells that promote the expression of their respected receptors and further activate NF-κβ, recruit red blood cells

Methods: Cytokines and chemokines are generated by inflamed endothelial cells that promote the expression of their respected receptors and further activate NF-κβ, recruit red blood cells

Results: Cytokines and chemokines are generated by inflamed endothelial cells that promote the expression of their respected receptors and further activate NF-κβ, recruit red blood cells

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keywords: Cytokines and chemokines are generated by inflamed endothelial cells that

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-90

Clinical relevance of body mass index in hematopoietic stem cell transplantation outcomes: a narrative perspective

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Background and aim: :: Hematopoietic stem cell transplantation (HSCT) is an established therapeutic approach for malignant and non-malignant hematologic disorders. Despite advances in transplantation strategies, post-transplant outcomes such as engraftment kinetics, graft-versus-host disease (GVHD), and disease relapse remain heterogeneous. Body mass index (BMI) is a readily available parameter reflecting baseline nutritional and metabolic status. However, its clinical relevance, particularly when considered alongside routinely assessed laboratory markers, remains incompletely defined in the transplantation setting. This narrative perspective aims to explore the potential role of baseline BMI together with selected routine clinical and laboratory markers in relation to HSCT outcomes

Methods: A narrative clinical review was conducted together with a descriptive evaluation of baseline clinical characteristics from approximately 100 adult patients (≥18 years) undergoing HSCT. Both allogeneic and autologous transplant recipients were included, encompassing patients with malignant and non-malignant hematologic conditions. Demographic and baseline variables, including age, sex, and BMI, were collected as part of routine pre-transplant assessment. In addition, routinely available laboratory markers commonly reported in transplantation studies, such as inflammatory and biochemical parameters, were considered to provide broader clinical context. Transplantation-related outcomes of interest included engraftment time, the occurrence of GVHD, and post-transplant disease relapse. The available clinical information was reviewed to assess feasibility and clinical relevance without performing formal statistical analyses.

Results: and post-transplant disease relapse. The available clinical information was reviewed to assess feasibility and clinical relevance without performing formal statistical analyses. Results : The study cohort demonstrated heterogeneity in baseline BMI, age, sex, and routinely assessed laboratory characteristics among patients undergoing HSCT. In transplantation literature, routinely available inflammatory markers such as C-reactive protein (CRP) and biochemical markers such as lactate dehydrogenase (LDH) have been commonly incorporated into outcome assessment to reflect systemic inflammation, disease burden, and transplant-related stress. Within this clinical framework, the availability of baseline BMI alongside routinely collected laboratory markers provides a relevant context for considering their combined role in post-transplant outcomes, including engraftment dynamics, GVHD, and disease relapse. This descriptive evaluation supports the feasibility of integrating anthropometric and routine laboratory parameters into broader clinical risk assessment in HSCT.

Conclusion: BMI represents a simple and accessible clinical parameter that may contribute to integrated risk assessment in HSCT. Consideration of BMI alongside routinely assessed laboratory markers supports further systematic investigation of their combined role in transplantation outcomes. From a practical clinical perspective, these readily available parameters may be incorporated into routine pre-transplant evaluation without increasing diagnostic complexity.

keywords: Body mass index; hematopoietic stem cell transplantation;inflammatory markers;clinical outcomes

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-91

Efficacy and Safety of Mesenchymal Stromal Cell Therapy in Pediatric Steroid Refractory Acute Graft versus Host Disease: A Systematic Review (2020–2025)

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Background and aim: Steroid-refractory acute graft-versus-host disease (SR-aGVHD) is a severe and life-threatening complication in children undergoing allogeneic hematopoietic stem cell transplantation. Despite the introduction of newer therapies such as ruxolitinib, long-term efficacy in pediatric patients remains limited. This has prompted investigation into mesenchymal stromal cells (MSCs), which possess regenerative and immunomodulatory properties.

Methods: A PubMed search conducted in August 2025 initially identified 257 records. Limiting the search to studies published between 2020 and 2025 yielded 94 articles. After excluding non-English (n=90) and non-human studies (n=66), and focusing on pediatric populations (18 years), 23 studies remained. Following full-text review and quality assessment, 17 studies were included in the synthesis.

Results: The selected studies indicate that MSC therapy is both safe and effective in children with SR-aGVHD, typically administered weekly or biweekly at 1–2×10^6 cells/kg. Complete response rates reached up to 53%, with one-year overall survival (OS) ranging from 50% to 74%, and day-28 overall response rates (ORR) between 60% and 76%. Survival was consistently higher among early responders. Commercial remestemcel-L trials, including phase 3 and expanded access studies, reported OS of 67–74% and ORR of 65–70%, significantly outperforming placebo or historical controls. These benefits were further confirmed in larger pediatric cohorts through real-world registry data. Smaller studies using bone marrow-, umbilical cord-, and decidua-derived MSCs reported ORRs of 60–100% and OS of 50–67%. Across all studies, MSC infusions were well tolerated, with minimal long-term toxicity or infusion-related adverse events.

Conclusion: Pediatric MSC therapy for SR-aGVHD demonstrates favorable safety, durable survival among responders, and robust early response rates. Future research should prioritize pediatric randomized controlled trials, comparisons between MSC sources, and extended follow-up to validate long-term safety and efficacy.

keywords: Pediatric SR-aGVHD; MSC therapy; Hematopoietic stem cell therapy

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PH-92

PRP, Improves in Vitro Fertilization Outcomes in Patients with Diminished Ovarian Reserve

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Background and aim: Background & Aims Diminished ovarian reserve (DOR) is a clinical syndrome with reproductive and endocrine disorders. This study aimed to examine the effect intra ovarian platelet-rich plasma (PRP) administration on oocyte maturation, and embryo quality in DOR patients who underwent a controlled ovarian hyperstimulation (COH) cycle.

Methods: Materials & Methods This retrospective cohort study, involved 25 DOR patients trying to conceive by ART. Pre and post-intervention, demographic information was gathered. In the subsequent controlled ovarian hyperstimulation (COH) cycle oocyte maturation, embryo quality were measured.

Results: Results Although PRP treatment increased the number of oocytes obtained, this rise was not statistically significant. While the number of embryos obtained post-intraovarian injection in patients with DOR increased, the improvement was not statistically significant; however, the quality of the embryos did improve.

Conclusion: Conclusion Our study discussed how the PRP administration intra ovarian, can slow down the progression of the disease by increasing the maturation rate of oocytes and increasing the quality of embryos in women with DOR. Further research is needed to investigate the effect of PRP administration intra ovarian improving fecundity for women with DOR.

keywords: Key Words: Platelet-Rich Plasma; Fertilization in Vitro; Ovarian Reserve

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PH-93

Investigating the therapeutic effects of chimeric antigen receptor T-cell therapy in Multiple Myeloma patients

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Background and aim: Multiple myeloma (MM) is a hematological malignancy defined by the uncontrolled proliferation of plasma cells within the bone marrow, representing the second most common leukemia. Standard treatments include chemotherapy, autologous hematopoietic stem cell transplantation, proteasome inhibitors, immunomodulatory drugs, and monoclonal antibodies. Despite initial success, MM inevitably relapses, underscoring the urgent need for novel therapeutic strategies to address relapsed and refractory (R/R) disease. Chimeric antigen receptor (CAR) T cell therapy has recently demonstrated remarkable efficacy in R/R MM clinical trials. Our aim is to evaluate the therapeutic potential of CAR-T cell therapy as a promising approach for patients with R/R MM.

Methods: In this systematic review, studies were retrieved from PubMed, Scopus, Web of Science, and Google Scholar without time restrictions. The search strategy employed keywords/MeSH terms ("CAR-T cell" OR "Chimeric Antigen Receptor T Cell") AND ("Multiple Myeloma"), supplemented with free-text variations to maximize coverage. Study selection applied inclusion criteria of English-language publications involving MM patients treated with CAR-T cells, alone or in combination with chemotherapy or other therapies. Exclusion criteria eliminated non-MM diseases, non-CAR-T interventions, non-English studies, case reports, expert opinions, letters, and reviews. Clinical trials were prioritized. Data extraction was independently performed by two researchers, recording reference details, trial phase, patient demographics, sample size, intervention methods, dosing/route, responses, and adverse effects; disagreements were resolved by a third reviewer. Study quality was assessed using the Cochrane risk of bias tool for randomized trials. Data analysis and synthesis were conducted with R software version 4.2, ensuring methodological rigor.

Results: A total of 973 studies were initially identified. After removing duplicates and unrelated articles, 302 studies underwent screening, of which 85 were selected for title/abstract eligibility assessment. Following full-text evaluation, 12 studies met the inclusion criteria for this systematic review. These studies investigated the therapeutic efficacy of anti-CD19/anti-BCMA CAR T cell (10), Anti-BCMA CAR-T xell (28), BCMA-CAR T cell (88), LCAR-B38M CAR-T cell (171), BCMA-BBZ-OX40 CAR-T cells (22), and anti-GPRC5D CAR-T cells (33) in 351 patients across Phase I and II trials. Treatment responses included 221 complete responses (CR), 107 partial responses (PR) and. Eight patients developed extramedullary disease, while 12 exhibited elevated AST levels. Hematologic toxicities were frequent: neutropenia (116 n), leukopenia (119 n), anemia (75 n), and thrombocytopenia (127 n). Cytokine release syndrome (CRS) occurred in 304 patients, and neurotoxicity was reported in 50 patients. Despite 73 patients experiencing progressive disease (PD), and 56 patients died.

Conclusion: Based on our finding, CAR-T cell therapy offers substantial therapeutic potential for R/R MM, achieving high response rates across Phase I and II trials. Among 351 patients, notable outcomes included 221 complete and 107 partial responses, underscoring its efficacy. However, frequent hematologic toxicities, cytokine release syndrome, and neurotoxicity highlight the need for optimized safety strategies. Despite disease progression and mortality in some cases, CAR-T therapy represents a transformative advance, reinforcing its significance as a promising modality for improving outcomes in R/R MM management.

keywords: Multiple Myeloma, Chimeric Antigen Receptor, CAR-T cell, Immunotherapy.

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PH-94

Dendritic Cell Immunotherapy for Lymphoid Malignancies: A Systematic Review of Clinical and Immunological Outcomes

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Background and aim: Lymphoid malignancies, including lymphomas and chronic lymphocytic leukemia, remain associated with frequent relapse and limited long-term disease control despite advances in conventional therapies. Dendritic cell (DC)-based immunotherapy has emerged as a promising strategy to induce tumor-specific immune responses with an acceptable safety profile. This systematic review aimed to evaluate the clinical outcomes, immunogenicity, and safety of DC-based vaccination approaches in patients with lymphoid malignancies.

Methods: This systematic review was conducted in accordance with PRISMA guidelines and registered in the PROSPERO database. A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science from the database inception through January 01, 2026. Interventional clinical trials of any phase investigating DC-based immunotherapy in patients with lymphoid malignancies were included. Data on study characteristics, DC preparation and antigen-loading strategies, clinical efficacy, immune responses, and treatment-related adverse events were extracted and synthesized using proportional meta-analytic methods.

Results: A total of sixteen clinical studies involving 215 patients were included. Vaccination strategies employed autologous or allogeneic DCs loaded with tumor lysates, apoptotic tumor material, or defined tumor-associated antigens. Several studies combined DC vaccination with immunomodulatory agents such as lenalidomide or low-dose cyclophosphamide. Disease stabilization was achieved in 38% of patients, while partial remission was observed in 18% and complete remission in 12%. Immunological assessments demonstrated enhanced antigen-specific T-cell proliferation, increased effector T-cell activation, reduced regulatory T-cell frequencies, and elevated secretion of antitumor cytokines, including interferon-γ and interleukin-2. Treatment-related adverse events were predominantly mild and transient, most commonly limited to local injection-site reactions.

Conclusion: DC-based vaccination strategies in lymphoid malignancies appear to be safe and immunogenic, with clinical benefit primarily reflected by disease stabilization rather than high objective response rates. These findings suggest that DC immunotherapy may represent a viable approach for long-term disease control, particularly in patients with indolent disease or low tumor burden. Future clinical trials incorporating standardized protocols, optimized DC maturation and activation strategies, and rational combination approaches with other immunotherapies are warranted to improve therapeutic efficacy.

keywords: Dendritic cell immunotherapy, Lymphoid malignancies, Cancer immunotherapy, Clinical outcomes

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PH-95

Investigating the therapeutic effects of chimeric antigen receptor NK-cell therapy in Acute myeloblastic leukemia patients

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Background and aim: Acute myeloblastic leukemia (AML) is an aggressive hematologic malignancy characterized by genetic alterations and uncontrolled proliferation of myeloid precursors, producing immature leukocytes that impair bone marrow function. Current therapies, including chemotherapy and allogeneic transplantation, are limited by relapse, incomplete eradication of leukemic cells, and risks such as graft-versus-host disease (GVHD), underscoring the urgent need for novel strategies. Natural killer (NK) cell therapy offers promise by targeting residual disease without inducing GVHD. Our aim in this study is to review the potential therapeutic effects of chimeric antigen receptor NK Cell (CAR-NK) Cell in patients with AML.

Methods: In this systematic review; studies were included from Scopus, PubMed, WOS, and Google Scholar databases (to 2025). Two researchers independently and systematically searched using keywords: ("CAR-NK Cell" OR "Chimeric Antigen Receptor NK-Cell") AND ("Therapeutics") AND ("Leukemia, Myeloblastic, Acute"). Combining keywords and free text was used to broaden the search results. Subsequently, inclusion criteria were (English language, AML disease, CAR-NK cell therapy) and exclusion criteria (non-English, other leukemias, other cell therapy, AML animal models/cell lines). Clinical Trial studies were included; Case reports, experts' opinions, letters to editors, and reviews were excluded. Two researchers have individually extracted data, which includes the collected primary author's name, publication year, Trial Phase, patient characteristics, sample size, age range, sex, intervention methods, Route/dose, response, and side-effects. In instances of disagreement, a third researcher was consulted for further evaluation. Quality was assessed with RoB 2.0/ROBINS-I, and data synthesized using R (v4.2).

Results: A total 1905 studies were identified. After excluding duplicate and unrelated articles, 204 articles were screened; out of which 57 articles were selected for the screening of titles and abstracts eligibility assessment. After the full-text assessment, only 15 studies were included in this systematic review. These studies investigated the therapeutic efficacy Anti-CD33/CLL1 CAR-NK Cells (18), CD123-CAR-NK cells (12), anti-CD33 CAR-NK cells (10+27), NKX101-CAR NK cell therapy (61), QN-023a-CAR NK cell therapy _allogeneic CAR-NK cells targeting CD33_ (19), CAR.70/IL15-transduced CB-NK cells (80), anti-CD7 CAR-pNK cells(10), Off-the-shelf CAR-NK cells targeted CD123 (12), CLL1 CAR-NK cell injection (24) in 273 patients across Phase I and I/II trials. All these CAR-NK cell studies in AML patients are currently recruiting, and no clinical outcomes or results have yet been published, with only planned enrollment and study status publicly available.

Conclusion: This systematic review highlights the urgent need for innovative therapies in AML, where current options remain limited by relapse and GVHD. Our analysis of 15 ongoing Phase I/I–II clinical trials involving 273 patients demonstrates active investigation of diverse CAR-NK constructs, including anti-CD33, CD123, CLL1, NKX101, and others. Although clinical outcomes are not yet available, these studies collectively underscore the growing momentum of CAR-NK cell therapy as a promising, potentially safer immunotherapeutic strategy to improve efficacy, reduce relapse, and advance AML treatment paradigms.

keywords: CAR-NK Cell, Natural killer cell, Immunotherapy, Acute Myeloblastic Leukemia

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
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PH-96

Chimeric Antigen Receptor Natural Killer Cells in Relapsed/Refractory Acute Myeloid Leukemia: A Systematic Review of Clinical Trials

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Background and aim: Background Chimeric antigen receptor natural killer (CAR NK) cell therapies are currently being advanced as innovative immunotherapeutic modalities for the treatment of relapsed or refractory acute myeloid leukemia (AML). In contrast to CAR T cells, CAR NK platforms may offer significant anti-leukemic efficacy while exhibiting diminished toxicity profiles. We conducted a systematic review of five studies published from 2018 to 2025 that explored CAR NK constructs targeting CD33, CD123, NKG2D ligands, and dual CD33/FLT3 antigens.

Methods: Five studies, including preclinical assessments and phase I clinical trials, were found, three of which were carried out in China and two in the US. Three to ten patients with relapsed or refractory AML made up the sample sizes. NK cells were derived either from the NK 92 cell line (Tang, 2018), peripheral blood mononuclear cells (PBMCs) obtained from healthy donors (Mu, 2025), or allogeneic sources that were expanded ex vivo (Huang, 2025; Sauter, 2023; Muftuoglu, 2025). The constructs utilized included CD33 chimeric antigen receptor (CAR)NK cells that were genetically modified via retroviral transduction with TCRζ, CD28, and 4-1BB signaling domains; a novel CD33 CAR specifically designed to mitigate hematopoietic stem cell toxicity; CD123 CAR NK cells produced through lentiviral transduction; NKX101, a CAR targeting NKG2D ligands that co-expresses membrane-bound interleukin-15 to enhance persistence; and SENTI 202, a logic-gated CAR targeting CD33 and/or FLT3 to preserve healthy hematopoietic stem cells.

Results: Clinical efficacy was variable yet encouraging. Across studies, complete remission (CR/CRi) rates ranged from 33% to 80%, with MRD negativity achieved in 50–67% of responders. Median progression-free survival in one trial was 71.5 days, with overall survival of 137 days among patients achieving remission. Safety profiles were good: CRS occurred in 20–40% of patients, predominantly grade 1–2, with isolated grade 3–4 events. No cases of ICANS or GVHD were reported, and hematologic toxicities were temporary. NKX101 was notable for the absence of CRS or ICANS, though one patient experienced unrelated fatal sepsis.

Conclusion: In conclusion, CAR NK therapies demonstrate promising efficacy and safety in relapsed/refractory AML. These early-phase studies support clinical research, with ongoing trials anticipated to improve construct design, dosing strategies, durability of response, and long-term safety.

keywords: CAR; CAR NK; Acute myeloid leukemia; Relapsed; Refractory

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-97

Natural killer cell–based immunotherapy for AML in transplant and non-transplant settings: a systematic review

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Background and aim: Acute myeloid leukemia (AML) continues to pose a significant challenge in the field of hematologic oncology, characterized by elevated incidence rates, poor long-term survival outcomes, and considerable mortality, despite advancements in therapeutic interventions. Consequently, cell-based immunotherapies have garnered heightened scholarly interest, with natural killer (NK) cells emerging as particularly advantageous candidates due to their intrinsic anti-leukemic cytotoxic properties and their capacity to recognize malignant cells in an antigen-independent manner. Notwithstanding the increasing clinical interest, a thorough and systematic assessment of NK cell–based therapeutic strategies in the context of AML remains essential.

Methods: To assess clinical studies on NK cell therapy in AML, whether as an independent treatment or alongside hematopoietic stem cell transplantation (HSCT), this systematic review adheres to PRISMA guidelines. Relevant articles were identified through a systematic literature search of five major databases: PubMed, Scopus, Web of Science, Embase, and the Cochrane Library, with data extraction focused on NK cell origins, methods of isolation and expansion, clinical effectiveness, and safety outcomes.

Results: Subsequent to the exclusion of articles deemed non-relevant, a total of 48 studies were ultimately incorporated into this systematic review, consisting of 21 trials that encompassed AML alongside other hematologic malignancies, and 27 trials that exclusively concentrated on AML. A substantial 82% of the NK cells were derived from peripheral blood (PB), with the predominant purification techniques involving CD3 depletion and CD56 selection utilizing CliniMACS technology. Thirty-six percent of the studies implemented either prolonged expansion exceeding seven days or brief activation not surpassing 24 hours. NK cell therapy resulted in a complete remission (CR) rate of 37.1% and an event-free survival (EFS) rate of 71.3% in scenarios devoid of hematopoietic stem cell transplantation (HSCT); the overall survival (OS) subsequent to HSCT was recorded at 39.5%. Notably, the incidence of graft-versus-host disease (GVHD) remained relatively low, highlighting the favorable safety profile of NK cell therapy.

Conclusion: NK cell-based therapy constitutes a promising and well-accepted immunotherapeutic strategy for AML. Nonetheless, the optimization of NK cell proliferation, longevity, and clinical implementations necessitates additional exploration via extensive, rigorously controlled trials.

keywords: Natural killer cell, Acute myeloid leukemia, Cell therapy, Expansion,Adaptive transfer

PH-98

Thrombophilic Gene Polymorphisms and Their Contribution to Coronary Artery Disease: From Hypercoagulability to Atherothrombosis: A Systematic Review

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Background and aim: Coronary artery disease (CAD) is primarily driven by atherosclerosis and thrombosis. Genetic polymorphisms affecting coagulation and fibrinolysis pathways play a crucial role in CAD susceptibility. Key thrombophilic variants include Factor V Leiden (G1691A) and Prothrombin (G20210A), which increase clot formation risk. Polymorphisms in fibrinolysis genes such as PAI-1 (4G/5G) and tPA influence clot breakdown. Variants in homocysteine metabolism genes, notably MTHFR C677T and A1298C, affect vascular health via hyperhomocysteinemia. Platelet function is modulated by polymorphisms like GP IIIa (PLA1/A2) and Factor XIII Val34Leu. This review systematically evaluates the impact of these genetic variations on CAD development and progression.

Methods: A systematic literature search was performed across PubMed, Scopus, Web of Science, and Embase databases, covering publications from January 2015 to December 2025. The search strategy combined keywords and MeSH terms including "coronary artery disease," "thrombophilia," "gene polymorphism," "Factor V Leiden," "Prothrombin G20210A," and "MTHFR." Inclusion criteria were original research articles investigating associations between thrombophilic gene polymorphisms and CAD risk, severity, or clinical outcomes in adult populations. Exclusion criteria included review articles, case reports, conference abstracts, and non-English studies. Two independent reviewers screened titles, abstracts, and full texts according to predefined criteria, resolving discrepancies by consensus. Data extraction focused on study design, sample size, genetic variants studied, and clinical endpoints. Risk of bias was assessed using standardized tools such as the Newcastle-Ottawa Scale. Due to heterogeneity in study designs and populations, results were synthesized narratively.

Results: Recent studies consistently demonstrate a significant association between thrombophilic gene polymorphisms and increased risk of coronary artery disease (CAD). The Factor V Leiden mutation (G1691A) was found to increase CAD risk by approximately 1.8 to 2.4 times across diverse populations. Similarly, carriers of the Prothrombin G20210A variant showed a 1.5 to 2-fold elevated risk of thrombotic events contributing to CAD progression. Polymorphisms in the MTHFR gene (C677T) were linked to elevated homocysteine levels, with a 10–15% higher risk of CAD, particularly in individuals with homozygous mutations. Variants affecting fibrinolytic balance, such as PAI-1 4G/5G, were associated with increased thrombotic tendencies in 20–25% of studied cases. Combinational presence of multiple polymorphisms further amplified CAD susceptibility by up to 30%. However, heterogeneity in ethnicities and sample sizes calls for caution, highlighting the need for larger multicenter studies to confirm these findings.

Conclusion: It seems that thrombophilic gene polymorphisms, including Factor V Leiden and Prothrombin G20210A, play a significant role in increasing the risk and progression of coronary artery disease by promoting hypercoagulability and thrombus formation. Although current evidence supports the importance of these genetic variants in CAD pathophysiology, variability in study populations and methodologies limits definitive conclusions. Therefore, further large-scale, multicenter research is essential to validate these associations and integrate genetic profiling into personalized risk assessment and management strategies for CAD patients.

keywords: Thrombophilic Gene Polymorphisms, Coronary Artery Disease, Hypercoagulability, Factor V Leiden

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PH-99

Novel Therapies for Thalassemia and Sickle Cell Disease: The Transition from Bone Marrow Transplant to Gene Therapy

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Background and aim: Therapies for Thalassemia and Sickle Cell Disease (SCD) are evolving significantly. While Bone Marrow Transplantation (BMT) offers a cure, its application is severely hampered by the scarcity of suitable donors and the risk of Graft-versus-Host Disease (GVHD). This has driven a major paradigm shift toward advanced gene therapies. Ex vivo approaches, particularly those leveraging CRISPR-Cas9 technology to reactivate protective Fetal Hemoglobin (HbF) production, are emerging as powerful, highly personalized, and potentially curative alternatives. These novel modalities promise to overcome major limitations of BMT, ushering in a new era of precision medicine for these inherited blood disorders.

Methods: This review article employs a comprehensive, systematic literature review approach to delineate the therapeutic transition for beta-Thalassemia and Sickle Cell Disease (SCD) from established treatments to cutting-edge gene therapies. The methodology involved searching major biomedical repositories, specifically PubMed, Scopus, and Web of Science, for preclinical and clinical studies published between 2010 and 2025. Search terms focused on "gene therapy," "CRISPR," "BMT limitations," "Thalassemia," and "Sickle Cell Disease." The analysis proceeds through three distinct phases. Initially, we critically assess the inherent challenges of current standards, focusing on the donor scarcity and Graft-versus-Host Disease (GVHD) risks associated with allogeneic Bone Marrow Transplantation (BMT). Subsequently, the core of the review dissects modern platforms, giving prominence to *ex vivo* strategies utilizing genome editing (CRISPR/Cas9) to reactivate Fetal Hemoglobin (HbF). Finally, efficacy and safety data are synthesized from ongoing clinical trials, comparing long-term outcomes such as transfusion independence and reduced Vaso-Occlusive Crises (VOCs) to establish

Results: The systematic review synthesized data from 45 core studies comparing gene therapy outcomes to historical Bone Marrow Transplant (BMT) benchmarks. For beta-Thalassemia major patients receiving ex vivo lentiviral vector therapy, 92% achieved transfusion independence (12 months), confirming stable, long-term beta globin production. In parallel, Sickle Cell Disease (SCD) cohorts treated with autologous stem cells edited via CRISPR to reactivate Fetal Hemoglobin (HbF) showed a 96% elimination of severe Vaso-Occlusive Crises (VOCs) during the first year post-treatment. Safety analysis revealed that adverse events were predominantly linked to the required myeloablative conditioning chemotherapy, typical for both BMT and stem cell gene therapy. Crucially, the gene therapy cohorts demonstrated zero incidence of de novo chronic Graft-versus-Host Disease (GVHD), sharply contrasting with the 15-30% rate observed in mismatched BMT recipients. These findings confirm that modern autologous gene therapies provide highly effective, curative alternatives with a significantly improved, non-allogeneic safety profile.

Conclusion: This review affirms that gene therapy platforms represent the vanguard in managing Thalassemia and SCD, offering curative potential far exceeding the limitations of allogeneic BMT, particularly regarding donor compatibility and chronic GVHD risk. Both ex vivo vector-based methods and emerging CRISPR/Cas9 editing demonstrate high efficacy in achieving transfusion independence and eliminating VOCs. While conditioning chemotherapy remains a transient risk, the long-term safety and durable efficacy profiles position autologous gene therapy as the new standard of care, fundamentally altering the prognosis for patients with these debilitating hemoglobinopathies.

keywords: Gene Therapy ،Thalassemia ،Sickle Cell Disease (SCD) ،Bone Marrow Transplant

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PH-100

Unveiling the Biomarker Potential of Long Non-Coding RNAs in Acute Lymphoblastic Leukemia: A Systematic Review

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Background and aim: Long non-coding RNAs (lncRNAs) are regulatory RNA transcripts longer than 200 nucleotides that play essential roles in chromatin remodeling, cell cycle, migration, and Apoptosis by regulating processes related to RNA transcription and protein translation. Acute lymphoblastic leukemia (ALL), the most common pediatric hematological malignancy, is a heterogeneous disease predominantly affecting B-cell precursors, with T-cell ALL associated with poorer outcomes. Given the risk of relapse and treatment resistance, accurate risk stratification is essential. Emerging evidence indicates that lncRNAs have significant diagnostic and prognostic potential in ALL. This systematic review summarizes lncRNAs identified in ALL and their expression alterations in affected patients.

Methods: This systematic review was conducted in the PubMed, Scopus databases,Web of Science, and Bentham Science using the keywords "acute leukemia OR Acute Lymphoid Leukemia OR acute lymphoblastic leukemia OR Precursor Cell Lymphoblastic Leukemia-Lymphoma OR ALL" AND "long Noncoding RNA OR lncRNA OR Long Non-Translated RNA OR Long non-protein-coding RNA" AND "prognosis OR prognostic OR diagnosis OR recurrence OR survival OR outcome OR clinicopathological". Human studies investigating the relationship between LncRNAs and prognosis in ALL patients were included. The animal studies, reviews, meta-analysis, clinical trials, case reports, and non-English articles were excluded.

Results: Out of 961 articles reviewed and after removing 64 duplicate articles, 62 articles were included. All eligible studies investigating lncRNAs in B-cell and T-cell ALL were included in this systematic review. Data analysis identified at least 209 lncRNAs involved in the pathogenesis of ALL. Several of these lncRNAs were experimentally validated in clinical samples or ALL cell lines using qRT-PCR. In this systematic review their expression patterns are summarized according to sample type, size, and study outcomes. The reviewed studies demonstrated that dysregulated lncRNAs influence key biological processes, including cell proliferation, apoptosis, viability, migration, and invasion in ALL models. In addition, multiple lncRNAs showed significant diagnostic and prognostic value, with reported associations to clinical outcomes such as overall survival and response to therapy.

Conclusion: The findings of this systematic review highlight the significant role of lncRNAs in the development and progression of ALL. The consistent dysregulation of lncRNAs across studies supports their potential as non-invasive diagnostic and prognostic biomarkers. Beyond their biomarker utility, functional evidence indicates that lncRNAs actively regulate leukemic cell behavior, suggesting their promise as therapeutic targets. Continued investigation into lncRNA biology may contribute to improved risk stratification and personalized management of patients with ALL.

keywords: Acute lymphoblastic leukemia; Long noncoding RNAs; Biomarker; Diagnosis, Prognosis.

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Tehran University of Medical Sciences (TUMS)
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PH-101

Comparative Meta-Analysis of Droplet Digital PCR (ddPCR) and Real-Time Quantitative PCR (RT-qPCR) for BCR::ABL1 Detection in Hematologic Malignancies

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Background and aim: Chronic myeloid leukemia (CML) and Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL) are marked by the BCR::ABL1 fusion gene, crucial for disease progression. Monitoring BCR::ABL1 transcript levels is vital for assessing minimal residual disease (MRD), predicting relapse, and guiding treatment decisions, particularly regarding tyrosine kinase inhibitor (TKI) discontinuation. While traditional RT-qPCR has been the gold standard, its limitations—such as susceptibility to inhibitors and restricted multiplexing—have spurred interest in Droplet Digital PCR (ddPCR). This meta-analysis highlights the methodological, clinical, and practical advantages of ddPCR, emphasizing its potential to improve precision in molecular monitoring.

Methods: This meta-analysis synthesizes findings from 37 peer-reviewed studies retrieved from the Scopus database, focusing on comparisons between ddPCR and RT-qPCR for the detection of BCR::ABL1. The selected studies were relevant to hematologic malignancies, particularly CML and Ph+ ALL, and included publications from 2015 to 2024. Inclusion criteria encompassed original research that examined sensitivity, specificity, clinical utility, MRD monitoring, and challenges related to standardization. Data extraction involved a qualitative assessment of methodological differences (e.g., amplification, multiplexing, tolerance to inhibitors), clinical outcomes (e.g., relapse prediction, TFR), and real-world implications (e.g., cost, standardization). Due to heterogeneity in study designs and protocols, no formal statistical meta-analysis was performed; instead, a narrative synthesis was conducted, drawing insights from critical analyses and syntheses of the source documents. References were cross-verified for concordance on the International Scale (IS), and any gaps in multicenter validation were noted.

Results: Droplet Digital PCR (ddPCR) exhibits superior sensitivity and precision compared to Real-Time Quantitative PCR (RT-qPCR) in detecting low-abundance BCR::ABL1 transcripts in chronic myeloid leukemia (CML) and Philadelphia-positive acute lymphoblastic leukemia (Ph+ ALL). ddPCR's droplet partitioning enables absolute quantification without standard curves and allows multiplexing for variants and resistance mutations, while showing greater resistance to PCR inhibitors like SDS, EDTA, and heparin. Clinically, ddPCR enhances minimal residual disease (MRD) monitoring by identifying relapse risks earlier and reducing misclassifications of samples that RT-qPCR fails to detect. Cases positive by ddPCR but undetectable by RT-qPCR correlate with higher relapse risks. However, some studies indicate no significant sensitivity differences when standardized to the International Scale (IS). Real-world challenges for ddPCR include higher costs, more complex workflows, and variable standardization across laboratories. Initiatives like the EuroMRD consortium aim to develop quality control systems, while multicenter validation is needed for effective clinical integration.

Conclusion: Droplet Digital PCR (ddPCR) shows significant advantages over Real-Time Quantitative PCR (RT-qPCR) in detecting BCR::ABL1 transcripts in hematologic malignancies, offering improved sensitivity, precision, and clinical utility. Enhanced methodological features suggest ddPCR's potential for better molecular monitoring, but real-world implementation challenges need to be addressed through standardization and multicenter validation.

keywords: Droplet Digital PCR (ddPCR), Real-Time Quantitative PCR (RT-qPCR) ,BCR::ABL1 detection

PH-102

Hematologic Inflammatory Biomarkers NLR, PLR, and LMR as Diagnostic, Prognostic, and Predictive Tools in Solid Tumors

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Background and aim: Cancer-related inflammation plays a pivotal role in tumor initiation, progression, and therapeutic resistance. Easily accessible hematologic inflammatory biomarkers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR), have gained increasing attention as potential tools for cancer diagnosis, prognosis, and treatment response prediction. This review aims to synthesize current evidence on the clinical relevance of NLR, PLR, and LMR across common solid tumors.

Methods: A comprehensive review of the literature was conducted using major biomedical databases, including PubMed/MEDLINE, Embase, and Scopus, covering studies published from January 2010 to December 2025. Eligible studies evaluated the association of baseline or dynamic changes in NLR, PLR, and/or LMR with diagnostic accuracy, survival outcomes, or treatment response in patients with solid malignancies. Data were qualitatively synthesized, focusing on study design, tumor type, biomarker cut-off values, and reported clinical endpoints.

Results: Across a wide range of solid tumors, including lung, breast, colorectal, gastric, hepatocellular, and gynecologic cancers, elevated NLR and PLR were consistently associated with advanced disease stage, aggressive tumor biology, and poorer survival outcomes. Conversely, higher LMR was generally correlated with favorable prognosis and improved treatment response. Several studies demonstrated the predictive value of these indices in assessing response to chemotherapy, targeted therapy, and immune checkpoint inhibitors. Although optimal cut-off values varied among tumor types and study populations, the overall trends remained consistent, supporting their potential clinical utility. Importantly, these biomarkers offered prognostic information independent of traditional clinicopathologic factors in many analyses.

Conclusion: NLR, PLR, and LMR represent cost-effective, reproducible, and readily available inflammatory biomarkers with significant diagnostic, prognostic, and predictive implications in solid tumors. Their integration into routine clinical practice may enhance risk stratification and individualized treatment planning. However, heterogeneity in study methodologies and lack of standardized cut-off thresholds limit their immediate implementation. Prospective studies and harmonized analytical approaches are needed to validate their clinical application.

keywords: Inflammatory biomarkers, solid tumors, prognosis.

PH-103

Artificial Intelligence in the Early Diagnosis and Prognosis of Hematological Malignancies

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Background and aim: Hematological malignancies represent a major global health burden, arising from complex interactions between genetic susceptibility and environmental factors. Early detection is critical, as delayed diagnosis is associated with poor clinical outcomes and increased mortality. Beyond early diagnosis, accurate identification of high-risk patients and prediction of disease progression are essential for optimizing clinical decision-making, resource allocation, and patient safety, with the potential to improve survival outcomes. Artificial intelligence–based approaches have increasingly enhanced diagnostic accuracy and risk stratification in these diseases. This study aims to summarize recent advances in the application of AI for early diagnosis and prognosis in hematological malignancies.

Methods: Relevant literature was identified through a comprehensive search of the PubMed database, covering publications from 2020 to 2025. Search terms included “artificial intelligence,” “machine learning,” “diagnosis of hematological malignancies,” and “prognosis of hematological malignancies.”

Results: Machine learning (ML) enables the analysis of large, complex medical datasets, supporting improved diagnosis, risk stratification, and prognostic prediction in hematological malignancies. In one study using polycythemia vera as a disease model, artificial intelligence was employed to demonstrate that leukemic stem cells (LSCs) exhibit distinct morphological characteristics compared with normal stem cell counterparts. A conventional neural network trained on single-cell images achieved approximately 92% classification accuracy in the identification and quantification of LSCs; a cell population closely associated with disease initiation, progression, relapse, and therapeutic resistance across multiple hematological malignancies. In another study, various deep learning architectures were evaluated for early detection and outcome prediction in blood cancers, with the ResNetRS50 model demonstrating the highest accuracy (97%), particularly in identifying malignancy at early stages. Despite these promising findings, challenges related to data heterogeneity, limited model scalability, and unequal access to AI technologies continue to hinder widespread clinical implementation.

Conclusion: Recent advances in artificial intelligence have significantly enhanced the detection and classification of hematological malignancies. The continued integration of AI-based diagnostic and prognostic approaches into clinical practice holds promise for earlier detection, personalized therapeutic strategies, and improved patient outcomes.

keywords: artificial intelligence, prognosis of Hematological Malignancies, detection of blood cancer

PH-104

The Interplay Between Autoimmune Disorders Affecting the Coagulation and Platelet Systems and Their Implications for Cardiovascular Diseases: A Systematic Review

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Background and aim: Autoimmune diseases (AIDs) are chronic and heterogeneous disorders caused by dysregulated immune responses that may affect specific organs or multiple systems. Increasing evidence suggests a link between AIDs and cardiovascular disease (CVD). This systematic review aimed to evaluate the association between autoimmune diseases and cardiovascular risk, with a focus on underlying immunological and pathophysiological mechanisms.

Methods: A comprehensive literature search was conducted in PubMed, SCOPUS, and ScienceDirect databases. Studies assessing the relationship between autoimmune diseases and cardiovascular disease were screened, and 28 studies met the inclusion criteria and were included in the final analysis.

Results: Among the included cohort studies, 26 studies (92.8%) demonstrated a significant association between autoimmune diseases and increased cardiovascular risk. Key mechanisms contributing to this association included chronic inflammation, endothelial dysfunction, oxidative stress, and immune cell dysregulation. Immune components such as T cells, B cells, and neutrophils were shown to promote atherosclerosis through cytokine secretion, adhesion molecule expression, and thrombogenic activity. Conversely, two studies (7.1%) reported no statistically significant association.

Conclusion: Autoimmune diseases are strongly associated with an increased risk of cardiovascular disease through complex immunological and inflammatory mechanisms. Improved understanding of these pathways may guide the development of targeted therapeutic strategies to reduce cardiovascular complications in patients with autoimmune disorders.

keywords: autoimmune diseases; coagulation disorders; platelet dysfunction; cardiovascular disease; thromboinflammation

PH-105

Utility of Irradiated Blood Components: A Review of Indications, Outcomes, and Safety

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Background and aim: Blood transfusion is a life-saving therapeutic intervention; however, it may lead to serious immunological complications. Transfusion-associated graft-versus-host disease (TA-GVHD) is a rare but almost universally fatal condition caused by the engraftment and proliferation of viable donor T lymphocytes in the recipient. Irradiation of blood components using gamma or X-ray radiation is the most effective method to inactivate donor lymphocytes and prevent TA-GVHD.This systematic review aimed to evaluate the clinical indications, effectiveness, outcomes, and safety of irradiated blood components in preventing transfusion-associated graft-versus-host disease.

Methods: This study was conducted as a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, and Google Scholar from January 2000 to March 2025. The search strategy was developed using Medical Subject Headings (MeSH) and free-text terms, including: Irradiated Blood Components, Blood Irradiation, Transfusion-Associated Graft-versus-Host Disease, Blood Transfusion, Immunocompromised Host, and Hematopoietic Stem Cell Transplantation. Boolean operators (AND/OR) were applied. Inclusion criteria consisted of English-language randomized controlled trials, observational studies, and review articles evaluating the clinical application, safety, and outcomes of irradiated blood products in human subjects. Case reports, animal studies, duplicate publications, and articles without relevant outcome data were excluded.

Results: A total of 214 articles were identified through database searching. After removal of duplicates and screening of titles and abstracts, 38 articles were selected for full-text evaluation. Finally, 12 studies met the inclusion criteria and were included in the systematic review. The results demonstrated that irradiation effectively prevented the proliferation of donor T lymphocytes by inducing irreversible DNA damage, leading to a marked reduction in the incidence of TA-GVHD, particularly in high-risk populations such as hematopoietic stem cell transplant recipients, patients with congenital or acquired immunodeficiency, intrauterine transfusion recipients, and patients receiving HLA-matched platelet transfusions. Although irradiation was associated with biochemical and storage-related changes in red blood cells, no clinically significant adverse outcomes were reported when standard irradiation doses were applied.

Conclusion: Irradiation of blood components is a safe and essential strategy for the prevention of transfusion-associated graft-versus-host disease in high-risk patient populations. Despite minor alterations in blood product quality, the benefits of irradiation in preventing a nearly fatal transfusion-related complication clearly outweigh its limitations. Establishing standardized irradiation protocols, optimizing radiation doses, and harmonizing institutional guidelines are crucial for improving transfusion safety. Further large-scale studies are recommended to refine current practices and enhance patient outcomes.

keywords: Irradiated Blood Components; Blood Irradiation; Transfusion-Associated Graft-versus-Host Disease; Blood Transfusion;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-106

Effectiveness of Leukoreduction in Preventing Transfusion-Related Complications

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Background and aim: Blood transfusion is an essential therapeutic modality in clinical practice; however, it is associated with adverse events such as febrile non-hemolytic transfusion reactions (FNHTRs), alloimmunization, transmission of leukocyte-associated viruses, and transfusion-related immunomodulation (TRIM). Leukoreduction, defined as the removal of white blood cells from blood components, has been introduced to reduce these complications and improve transfusion safety. The present study aimed to systematically evaluate the effectiveness of leukoreduction in preventing transfusion-related complications and to assess its clinical benefits in transfusion medicine.

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, and the Cochrane Library from inception to December 2024. The search strategy was designed using Medical Subject Headings (MeSH) and related keywords, including: Leukoreduction, Blood Transfusion, Febrile Non-Hemolytic Transfusion Reaction, Alloimmunization, Cytomegalovirus, and Transfusion-Related Immunomodulation. Eligible studies included randomized controlled trials, observational studies, and meta-analyses that compared leukoreduced versus non-leukoreduced blood components in human subjects. Animal studies, case reports, duplicate articles, and studies without relevant clinical outcomes were excluded.

Results: A total of 482 articles were identified through database searching. After removal of duplicates and screening of titles and abstracts, 96 studies were assessed for full-text eligibility. Finally, 34 studies met the inclusion criteria and were included in the systematic review. The results showed that leukoreduction significantly reduced the incidence of febrile non-hemolytic transfusion reactions, decreased the risk of cytomegalovirus (CMV) transmission, and lowered the rate of HLA alloimmunization, particularly in chronically transfused patients. Evidence regarding its effects on transfusion-related immunomodulation and overall mortality was inconsistent; however, most studies supported an overall improvement in transfusion safety.

Conclusion: Leukoreduction is an effective strategy for reducing several transfusion-related complications and enhancing patient safety. Routine implementation of leukoreduction, especially in high-risk patient populations, is strongly recommended. Further large-scale studies are required to clarify its broader immunological and clinical effects.

keywords: Leukoreduction; Blood Transfusion; Febrile Non-Hemolytic Transfusion Reaction; Alloimmunization; Cytomegalovirus; Transfusion-Related

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-107

The Role of ASXL1 Mutations in Myeloid Leukemias: A Systematic Review

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Background and aim: Myeloid leukemias encompass a variety of clonal blood disorders originating from hematopoietic stem/progenitor cells.This group of diseases consists of Myelodysplastic Syndromes(MDS),acute myeloid leukemia(AML),myeloproliferative neoplasms(MPN) and chronic myelomonocytic leukemia(CMML).Characterized by hyperplastic, self-renewal,and differentiation of myeloid cells.The development of these diseases is facilitated by persistent genetic/epigenetic lesions,which perturb normal blood homeostasis.Of the genes that contribute to epigenetic regulation, the gene Additional Sex Combs-Like1(ASXL1)has gained attention and is central in myeloid leukemias.This systematic review will provide an in-depth and critical assessment of molecular biology mechanisms,clinical relevance,and prognostic implications of ASXL1 mutations in myeloid leukemia,with a particular focus on disease progression and treatment response.

Methods: In this review, a comprehensive search was conducted using the keywords "ASXL1" "myeloid leukemias" and "hematopoiesis" and "epigenetics" and "Myelodysplastic Syndromes" in the PubMed, Google Scholar, and Web of Science databases.

Results: Mutations of ASXL1, most being frameshift and nonsense mutations located in the last exon of this gene, are detected in 20–40% patients with myeloid leukemia. On one hand, mutations in ASXL1 disrupt chromatin function through Polycomb Repressive Complex 2(PRC2)-inhibition, augmented BRCA1-Associated Protein 1(BAP1)-induced deubiquitination canonicity and starkly reduced levels of instruction library constituent marks such as H2AK119ub and H3K27me3. This leads to ectopic activation of the oncogenic expression programs including AKT/mTOR and Bromodomain-containing protein 4(BRD4) transcription. On the other hand, mouse model studies are also in favor of a role of ASXL1 mutations in clonal hematopoiesis and leukemogenesis. In the linear context ASXL1 mutations have also been repeatedly associated with poor overall survival, lack of response to standard therapies and transformation in acute leukemia.

Conclusion: Mutations in the ASXL1 gene are very important for the development and evolution of myeloid leukemias. They are also to predict poor outcomes on their own.The new drugs like hypomethylating agents work for none of these patients. The only hope for patients with such high risk is the new drugs like allogeneic hematopoietic stem cell transplant.New drugs using other epigenetic regulators such as BRD4, HDAC, and BAP1 are likely to work very well. ASXL1 status should also be added to risk scores for precise treatments for people with myeloid cancers.

keywords: Asxl1, Asxl1 mutations, myeloid leukemia, Myelodysplastic Syndromes

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-108

Immunohematology Challenges in Multi-Transfused Patients: A Systematic Review of RBC Alloantibody Identification

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Background and aim: Blood transfusion is a lifesaving therapy for anemia and hypoxia but may induce immune-mediated complications due to exposure to donor red blood cell (RBC) antigens. One of the most significant is RBC alloimmunization, caused by antibody formation against non-self antigens, which can lead to delayed hemolytic transfusion reactions, reduced RBC survival, crossmatching difficulties, and increased transfusion needs. Patients with hemoglobinopathies, malignancies, and chronic transfusion dependence are particularly at risk. This systematic review summarizes current evidence on the immunopathogenesis, risk factors, and clinical consequences of RBC alloimmunization to enhance transfusion safety and patient outcomes.

Methods: A systematic search strategy was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Electronic databases including PubMed, Scopus, and Web of Science were searched to identify studies published between 2015 and 2025. Search terms were applied using various combinations related to “red blood cell alloimmunization,” “blood transfusion,” “alloantibodies,” “immunological mechanisms,” and “transfusion reactions.” Original research articles and review studies addressing the mechanisms, prevalence, antibody specificity, risk factors, detection methods, and clinical outcomes of RBC alloimmunization were eligible for inclusion. Studies involving non-human subjects, case reports, conference abstracts, and articles lacking sufficient or relevant data were excluded. Duplicate records were identified and removed using reference management software. Data were synthesized narratively with emphasis on immunopathogenesis, prevalence patterns, and preventive transfusion strategies.

Results: A total of 43 studies met the inclusion criteria,with an overall sample size of 8,916 patients. The systematic reviewed literature demonstrated that approximately 2–5% of transfused individuals developed detectable RBC alloantibodies; however, considerably higher rates were reported among multitransfused patients. Alloimmunization was most commonly directed against antigens of the Rh and Kell blood group systems, with anti-K and anti-E identified as the most prevalent antibodies. Female sex, a history of pregnancy, inflammatory conditions at the time of transfusion, and receipt of more than three transfusions were consistently associated with increased alloimmunization risk. Patients with hemoglobinopathies, including thalassemia and sickle cell disease, exhibited the highest alloimmunization rates, whereas individuals with leukemia receiving immunosuppressive therapy showed comparatively lower rates. Retrospective analyses indicated that a substantial proportion of alloantibodies, particularly those targeting Kidd and Lutheran antigens, became undetectable over time, thereby increasing the risk of delayed hemolytic transfusion reactions upon subsequent antigen exposure.

Conclusion: RBC alloimmunization remains a clinically significant complication of blood transfusion, particularly among multitransfused and high-risk patient populations. Implementation of preventive strategies such as extended antigen matching, universal leukoreduction, routine antibody screening, and accurate documentation of transfusion history is crucial for minimizing alloimmunization risk. Enhanced understanding of both recipient- and donor-related factors may contribute to improved transfusion practices, reduced immunological complications, and optimized long-term patient management.

keywords: Blood transfusion, RBC alloimmunization, Alloantibodies, Multitransfused patients, Transfusion reactions

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-109

Systemic Immune-Inflammation Index and Neutrophil-to-Lymphocyte Ratio in Immune Thrombocytopenia: A Cross-Sectional Study

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Background and aim: Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by immune-mediated platelet destruction and impaired thrombopoiesis, leading to an increased risk of bleeding. In addition to its autoimmune nature, ITP exhibits inflammatory features; however, the utility of routinely available inflammatory indices in reflecting disease-related inflammation remains unclear. The Systemic Immune-Inflammation Index (SII) and neutrophil-to-lymphocyte ratio (NLR) have emerged as simple, non-invasive markers of systemic inflammation. This study aimed to evaluate the association of SII and NLR with ITP and disease stage.

Methods: In this cross-sectional study, 69 blood samples from patients with ITP and healthy controls were collected at Baghaei Hospital, Ahvaz, between 2023 and 2024. Patients were classified as newly diagnosed or chronic. SII and NLR were calculated from complete blood count parameters. Group comparison, correlation analysis, and multiple linear regression were performed to assess the associations of these indices with disease status, age, sex, and disease stage.

Results: SII values were significantly lower in patients with ITP compared with healthy controls ($p = 0.01$), whereas NLR did not differ significantly between groups. Age demonstrated an independent positive association with SII ($p = 0.007$), while sex showed no significant association. In contrast, NLR was not significantly associated with either age or sex, although a borderline positive association with age was observed ($p = 0.069$). Neither SII nor NLR differed significantly between newly diagnosed and chronic ITP patients ($p = 0.24$ and $p = 0.34$, respectively). Correlation analysis demonstrated a stronger association between SII and platelet count (Spearman $r = 0.74$, p 0.0001) than between SII and NLR (Spearman $r = 0.48$, $p = 0.0005$).

Conclusion: Although SII significantly distinguished patients with ITP from healthy controls, NLR did not show a similar discriminatory ability. The stronger correlation of SII with platelet count than with NLR suggests that SII may be influenced substantially by thrombocytopenia, a defining feature of ITP. Therefore, caution is warranted when interpreting SII as an independent inflammatory marker in this disease. The lack of significant findings for NLR further suggests that these commonly used inflammatory indices may have limited utility in reflecting inflammatory activity in ITP.

keywords: Immune Thrombocytopenia; Systemic Immune-Inflammation Index; Neutrophil-to-Lymphocyte Ratio; Inflammation; Platelets

PH-110

The next-generation tools for non-invasive precision cancer diagnosis: CRISPR-based diagnostics for detection of ctDNAs.

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Background and aim: With the rapid advancement of liquid biopsy technologies, non-invasive approaches for precision cancer diagnostics have gained considerable attention. Cell-free DNA (cfDNA) circulating in the bloodstream and particularly its tumor-derived fractions, known as circulating tumor DNA (ctDNA) has emerged as a valuable biomarker for cancer detection, disease prognosis, assessment of response to treatment and even chemotherapies resistance (1). Nevertheless, the clinical implementation of ctDNA-based assays remains challenging, primarily due to the low abundance of mutant alleles and the resulting poor signal-to-noise ratio when detecting rare oncogenic mutations (2). To overcome these limitations, CRISPR-based technologies have been increasingly explored owing to their

Methods: CRISPR-CPPC technique is one of the CRISPR-Cas9 based strategy which, introduced for detecting the EGFR T790M mutation in patients with non-small cell lung carcinoma (NSCLC). In this workflow, ctDNA is first amplified by PCR, followed by incubation with the CRISPR/Cas9 complex for selective recognition and enrichment of the target sequence. The enriched DNA is subsequently quantified using droplet digital PCR (ddPCR), resulting in a highly sensitive assay with a reported sensitivity of 93.9% and a specificity of 100% (3). Building on similar enrichment principles, PASEA assay developed to KRAS mutation detection in plasma-derived ctDNA from patients with pancreatic cancer. In this approach, CRISPR-Cas9 selectively and continuously cleave wild-type alleles during recombinase polymerase amplification, allowing mutant alleles to undergo preferential exponential amplification to levels detectable by Sanger sequencing, highlighting the cost-effectiveness and translational potential of the PASEA platform (4).

Results: Beyond Cas9-based platforms, CRISPR-Cas13a has also been widely adopted for ctDNA detection due to its collateral single-stranded RNA cleavage activity. In regard of detecting rare mutations in ctDNAs, HiCASE was developed as a highly sensitive and specific approach based on CRISPR-Cas13a based detection. In this workflow, ctDNA fragments are first amplified to enrich target regions and the restriction enzymes selectively cut and delete wild-type sequences. T7 polymerase transcribed the Preserved mutant DNA into RNA, which is recognized by CRISPR-Cas13 and collateral cleavage of Cas13 degrades reporter RNA molecules, generating a robust fluorescent signal and enabling detection of extremely low-frequency variants such as EGFR T790M and C797S, with an exceptional limit of detection of 0.01% variant allele frequency with 88.1% sensitivity and 100% specificity, providing valuable guidance for targeted therapy and illustrating strong potential for clinical application (5).

Conclusion: CRISPR-based diagnostic technologies hold immense promise for revolutionizing cancer early detection and personalized therapies due to highly sensitivity, specificity, and rapid detection of genetic and epigenetic alterations.

keywords: ctDNA, cancer, CRISPR, diagnostics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-111

Correlation between Phenotype and Coagulation Factor Activity Level in Rare Bleeding Disorders: A Systematic Review

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Background and aim: Background Rare bleeding disorders (RBDs) represent 3 to 5% of congenital bleeding disorders and are primarily inherited in an autosomal recessive manner, with increased prevalence in consanguineous populations. Clinically, RBDs can be accompanied by mild to severe bleeding episodes. the study focused on RBD patients to explore the correlation between coagulation factor activity levels and bleeding severity.

Methods: This review adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was registered with the International Prospective Register for Systematic Reviews (PROSPERO). A comprehensive search was conducted across PubMed, Scopus, and Web of Science until April 1, 2024, with data extracted on bleeding severity, phenotype, and coagulation factor activity levels. our initial search yielded 944 articles. After removing 408 duplicate publications, 166 articles were excluded based on their titles and abstracts. Ultimately, after excluding rest of unrelated papers due to the rules 14 papers were included in the study.

Results: The analysis highlights complex and often inconsistent relationships between coagulation factor levels and the severity of bleeding. In cases of fibrinogen deficiency (FI), three out of four studies (n =73 of 111 cases, 66%) demonstrated a moderate to strong correlation between fibrinogen levels and bleeding severity. In prothrombin deficiency (FII), one of two studies (n= 16of 29 cases, 55%) found a strong correlation between FII levels and bleeding severity. Four of six studies (n = 106 of 139 cases, 76%) in FV deficiency found a weak or no correlation between factor activity and bleeding severity. In combined FV and FVIII deficiency, two of three studies (n = 26 of 60 cases, 43%) found a significant correlation between factor activity and bleeding severity. In FVII deficiency, four (of nine) studies with a study population of 325 patients (65%) found a weak correlation between factor activity and severity of bleeding.

Conclusion: The current analysis highlights the complex and sometimes contradictory relationships between coagulation factor levels and bleeding severity in RBDs.While lower factor activity levels generally correlate with increased bleeding severity, inconsistencies in this relationship suggest that additional factors, including genetic, phenotypic, and environmental influences, significantly impact bleeding tendencies. To address these complexities, future research should focus on clarifying these interactions through studies involving larger multicentric cohorts . Advanced molecular techniques, along with detailed clinical assessments through integrated bleeding scoring systems, may further our understanding of individual variability in bleeding manifestations

keywords: rare bleeding disorders, coagulation factor deficiencies, congenital bleeding disorders, bleeding

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-112

Molecular Resolution of ABO Discrepancies: A Case Series Involving Uncommon Weak B Subgroups

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Background and aim: ABO discrepancies arise when forward and reverse grouping mismatched results, necessitating resolution to prevent adverse outcomes from blood transfusion. A rare but significant cause of such discrepancies is the presence of weak B subgroups, characterized by markedly low B antigen expression. These subgroups are detected through the adsorption & elution method, which is very difficult and time -consuming. Molecular techniques offer a more accurate and efficient alternative for detecting these variants. This study presents three uncommon cases of weak B subgroups, in which ABO grouping failed using serological methods and was clarified by molecular methods.

Methods: ABO serological testing was performed using the conventional tube method with anti-A, anti-B, anti-AB, and anti-H reagents. Reverse grouping was carried out using A1, B, and O reagent red cells. Antibody screening was performed by the standard three-cell panel using the tube method at immediate spin, 37 °C incubation, and the antiglobulin (AHG) phase. ABO allele genotyping (O1, O2, A1, A2, and B) was performed using PCR SSP as described by Gassner et al.

Results: Three patients' samples were referred to the Immunohematology Reference Laboratory for ABO discrepancy analysis. The first case involved an 18-year-old female hospitalized for gastric surgery; the second, a 42-year-old female undergoing cesarean section. In both cases, the packed RBC were requested, and their mothers reported an O-positive blood group. The third case was a 15-year-old male with a mental disability whose sample was sent due to an unresolved ABO grouping result. ABO grouping was performed using both automated and tube methods. The results showed different discrepancies: forward grouping suggested weak B antigens, while the reverse grouping was consistent with group O. To resolve this incompatibility, Molecular testing was conducted using the PCR -SSP technique. The molecular results confirmed the presence of the B allele in all three cases. These molecular findings, integrated with serological results, support the classification of all patients as carriers of weak B subgroups.

Conclusion: The Molecular method s serves as valuable complements to serological methods in accurately determining ABO blood groups in both donors and patients. Notably, ABO genotyping plays a critical role in confirming weak expression of A or B antigens, especially in cases where serological results are inconclusive.

keywords: ABO Blood Group System, Blood Group ABO Incompatibility, Blood Transfusion

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-113

Determining the prevalence and type of alloantibodies in transfusion-dependent thalassemia patients in South Khorasan Province

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Background and aim: Patients with major thalassemia require regular blood transfusions, and one of the most important complications of repeated transfusions is the development of alloantibodies. This study aimed to investigate the prevalence and types of common alloantibodies in patients with thalassemia.

Methods: This study was conducted on 45 patients with thalassemia in Birjand city. Antibody screening tests were performed, followed by antibody identification. Demographic and clinical-laboratory data, including age, gender, and relevant clinical history, were extracted from patients' electronic medical records. Data were analyzed using SPSS software version 26.

Results: A total of 45 patients, including 21 males and 24 females aged between 1 and 36 years, were studied. Among them, 3 patients (6.6%) had positive antibody screening results. A total of 4 alloantibodies were identified, with the most common being anti-K (3 cases, 75%) and anti-E (1 case, 25%). The most frequent ABO phenotype was blood group O (42.2%), and the most prevalent Rh system antigens were c and e, present in 100% and 93.3% of patients, respectively. Four patients (8.8%) had undergone splenectomy. No significant association was found between alloimmunization and factors such as age, gender, blood group, number of transfused blood units, or splenectomy status.

Conclusion: Given the identification of alloantibodies against Kell and Rh (E) blood group systems in the studied thalassemia population, it is recommended to use blood units matched at least for Kell and Rh antigens to reduce the risk of alloimmunization.

keywords: Thalassemia, Alloimmunization, Alloantibody, Blood transfusion, Antibody screening, Antibody identification

PH-114

Evaluating Hemoglobin Measurement Agreement Above 18 g/dL in a Multi-Center National Study: Capillary vs. Venous Blood Analysis in Male Donors

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Background and aim: Accurate hemoglobin (Hb) measurement is crucial for blood donor screening to ensure donor safety. While automated cell counters serve as the gold standard, portable point-of-care devices that use capillary blood offer a convenient alternative, particularly in busy transfusion centers. However, their performance, especially at higher Hb levels (above 18 g/dL) which are less commonly evaluated, requires rigorous assessment. Notably, no previous study in Iran has conducted this specific comparison at elevated hemoglobin concentrations Our primary goal was to compare hemoglobin measurements from capillary blood (HemoCue Hb 301) with those from venous blood (automated cell counter)."

Methods: : This descriptive-analytical, cross-sectional study was conducted in 21 regional blood transfusion centers across Iran during September and November 2025. A total of 557 male donors, aged 17-70 years, with an initial capillary Hb level greater than 18 g/dL, were enrolled. Donors were selected via convenience sampling. Capillary blood was sampled using the HemoCue Hb 301. If the capillary reading exceeded 18 g/dL, venous blood was collected in EDTA tubes and analyzed by an automated cell counter (reference method). Data analysis included Pearson correlation coefficient, Intraclass Correlation Coefficient (ICC), and Bland-Altman analysis to evaluate agreement. The study protocol was approved by the relevant ethics committee, and informed consent was obtained from all participants.

Results: A total of 557 male donors were included, with a mean age of 39.9 ± 17 years. A significant portion, 304 donors (54.6%), were regular blood donors. The mean Hb levels showed no statistically significant difference between the HemoCue device (18.95 ± 0.86 g/dL) and the automated cell counter (19.02 ± 0.93 g/dL). Both Pearson correlation and ICC indicated a moderate level of agreement between the two methods (r = 0.50, ICC = 0.50). Bland-Altman analysis revealed a mean difference (bias) close to zero, with limits of agreement suggesting that most discrepancies were random rather than systematic. Notably, the agreement was strongest at higher hemoglobin concentrations (above 21 g/dL).

Conclusion: Our findings suggest that the HemoCue Hb 301 device exhibits acceptable agreement with automated cell counters for measuring hemoglobin in male blood donors with levels above 18 g/dL. This indicates its potential as a useful rapid screening tool for transfusion centers. Further research incorporating female donors would be beneficial to enhance the generalizability of these findings and refine screening protocols for optimal blood safety.

keywords: Hemoglobin measurement Capillary blood Venous blood HemoCue Hb 301 Blood

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July 20-23, 2026

PH-115

Investigation of the causes discovered discrepancies in blood group determination in blood transfusion in Khorasan Razavi Province

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Background and aim: The ABO blood group system is critical for safe transfusions, requiring consistent forward and reverse serological testing. Discrepancies between these methods necessitate investigation to identify causes and prevent transfusion errors. While vital, a comprehensive analysis of ABO grouping discrepancies among Iranian blood donors is lacking. This study investigated the frequency and underlying causes of ABO discrepancies over four years in Razavi Khorasan Province's blood transfusion centers. Findings will aid in establishing preventive strategies within Iran's blood banking system.

Methods: In this retrospective descriptive study, all cases of ABO blood group discrepancy between forward and reverse typing results, recorded for donors referred to the blood transfusion centers of Razavi Khorasan Province from 2021 to 2024, were reviewed. For each case, the pattern of mismatch was analyzed, the underlying cause was identified based on serological findings, and the frequency of each cause was subsequently calculated.

Results: Among 643,098 donors who presented to the blood transfusion centers of Razavi Khorasan Province during the study period, 184 cases (0.028%) exhibited ABO grouping discrepancies between forward and reverse typing results. The most common cause was ABO subgroup phenotypes, observed in 75 cases (40.76%). Within this category, the largest proportion was related to AB subgroups with 40 cases (53.33%), followed by A subgroups with 26 cases (34.66%), and B subgroups with 9 cases (12.00%). The second most frequent cause of discrepancy was the presence of additional cold and warm antibodies in the serum along with agglutination in the O-cell tube of the reverse typing, accounting for 63 cases (34.23%). The presence of weak Anti-A and Anti-B antibodies ranked as the third cause, identified in 43 cases (23.36%).

Conclusion: Investigating conflicting forward and reverse ABO blood grouping results is crucial in transfusion medicine. Accurate identification of discrepancies' causes dictates the fate of donated blood and donor eligibility. This study found ABO subgroups to be the predominant cause of discrepancies. Molecular investigation is recommended to precisely identify specific subgroup types. Developing targeted solutions for each identified cause will help manage future discrepancies, preserving valuable donors and blood products. This contributes to the overall safety and efficiency of blood transfusion services.

keywords: Blood group discrepancy, ABO blood typing , blood donors

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-116

AAV Vector-Mediated Gene Therapy for Severe Hemophilia A: Clinical Benefits, Limitations, and Future Directions

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Background and aim: Severe hemophilia A (HA) is a bleeding disorder caused by factor VIII (FVIII) deficiency, requiring lifelong prophylactic infusions that are costly, burdensome, and carry risks of inhibitor development. Adeno-associated virus (AAV) vector-mediated gene therapy, such as valoctocogene roxaparvovec, offers a paradigm shift by enabling sustained, endogenous FVIII production after a single administration. This review critically evaluates the therapeutic benefits and persistent limitations of AAV-based approaches for HA based on current clinical evidence.

Methods: A comprehensive literature search was conducted using PubMed and Google Scholar.

Results: AAV-based gene therapy consistently demonstrates significant reductions in annualized bleeding (ABR) and infusion rates (AIR). Treatment elevates FVIII activity, reducing spontaneous hemorrhages and improving quality of life per Haemo-QoL-A assessments, with no reported FVIII inhibitor development. However, this therapeutic success is tempered by notable limitations. FVIII expression exhibits significant inter-individual variability, and a gradual, non-linear decline over time raises questions about long-term durability, with current models estimating a median duration of 11-17 years. The most common adverse events are asymptomatic, reversible elevations in alanine aminotransferase (ALT, pooled incidence 0.50) and aspartate aminotransferase (AST, 0.29), indicating a predictable, immune-mediated hepatotoxicity targeting AAV capsid-loaded hepatocytes. While generally manageable with corticosteroids, this necessitates rigorous monitoring. Rare but serious adverse events, including thrombosis and atypical hemolytic uremic syndrome, have been reported, alongside theoretical concerns regarding vector integration, though not confirmed in biopsies.

Conclusion: AAV gene therapy for hemophilia A provides substantial clinical benefits, including profound bleed reduction, liberation from prophylaxis, and enhanced quality of life. Nevertheless, its widespread application is constrained by immunological barriers, variable and potentially non-durable FVIII expression, and safety concerns. Realizing its full curative potential requires standardizing vector production, pre-existing antibody assays, and long-term surveillance registries, as advocated by the ISTH. Future innovations, such as next-generation vectors with improved tropism and reduced immunogenicity, or CRISPR-based gene editing, are essential to overcome current hurdles and achieve a broadly accessible cure.

keywords: hemophilia A, AAV, gene therapy, factor VIII, valoctocogene roxaparvovec

PH-117

The Emerging Role of Innate Lymphoid Cells in Acute Leukemia: From Immune Regulation to Novel Immunotherapeutic Targets

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Background and aim: Acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) remain challenging hematologic malignancies due to immune evasion, relapse, and resistance to conventional therapies. Recent studies have highlighted the importance of innate lymphoid cells (ILCs) as key regulators of anti-leukemic immunity within the bone marrow microenvironment.This review aims to summarize current evidence regarding the biological functions of ILC subsets and their contribution to leukemia progression, immune escape, and emerging immunotherapeutic strategies in AML and ALL.

Methods: A comprehensive review of recent experimental, translational, and clinical studies investigating ILC subsets, including natural killer (NK) cells, ILC1s, ILC2s, ILC3s, and regulatory ILCs, in acute leukemia was performed.

Results: ILCs play critical roles in immune surveillance, cytokine regulation, and modulation of the leukemic niche. Leukemia-associated microenvironmental factors, including hypoxia, metabolic stress, checkpoint signaling, and inflammatory cytokines, profoundly alter ILC differentiation and function. NK cells and ILC1s demonstrate anti-leukemic activity through cytotoxicity and IFN-γ production, whereas dysregulated ILC2 and ILC3 responses may contribute to immune suppression and disease progression. Emerging evidence also highlights the importance of ILC plasticity and bidirectional interactions between leukemic cells and ILCs. Novel therapeutic approaches, including memory-like NK cells, engineered NK/ILC therapies, checkpoint blockade, and cytokine-based interventions, have shown promising preclinical and clinical results.

Conclusion: ILCs are central regulators of leukemia-associated immune responses and represent promising therapeutic and prognostic targets in acute leukemia. Improved understanding of ILC biology may facilitate the development of precision immunotherapies and biomarker-guided treatment strategies in AML and ALL.

keywords: Acute leukemia; AML; ALL; Innate lymphoid cells; Natural killer cells

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-118

Masked Polycythemia Vera in Patients with Concurrent Thalassemia Minor or Iron Deficiency Anemia: A Systematic Review

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Background and aim: Background: In regions with high prevalence of thalassemia minor and iron deficiency anemia (IDA), concurrent anemia can "mask" polycythemia vera (PV) by normalizing hemoglobin (Hb) and hematocrit (Hct), leading to diagnostic delay and increased thrombotic risk. The frequency of this "masked PV" phenomenon and its clinical consequences have never been systematically reviewed.

Methods: Methods: Systematic review following PRISMA guidelines. We searched PubMed, Scopus, and Web of Science (2000–2025) using MeSH terms: "Polycythemia Vera" AND ("thalassemia" OR "iron deficiency") AND ("masked" OR "diagnostic delay"). Inclusion criteria: confirmed PV with concurrent thalassemia minor (Hb electrophoresis) or IDA (ferritin 30 µg/L) AND Hb/Hct below conventional PV thresholds at presentation. Primary outcome: proportion with diagnostic delay 6 months. Secondary outcomes: thrombosis before diagnosis, associated factors.

Results: Results: Out of 847 records, 23 studies (147 patients) met criteria: 89 (60.5%) with thalassemia minor, 58 (39.5%) with IDA. Median Hb at presentation was 13.2 g/dL (males) and 11.8 g/dL (females) – below classic PV thresholds. JAK2V617F was positive in 94%. Mean diagnostic delay was 14.3 months. Before diagnosis, 34 patients (23.1%) experienced thrombosis (22 venous, 12 arterial), including 8 with Budd-Chiari syndrome. In 41 patients (27.9%), thalassemia or IDA had been diagnosed years earlier, but PV was never suspected because Hb/Hct were "normal."

Conclusion: Conclusion: Masked PV with concurrent thalassemia/IDA is not rare; nearly one-quarter present with thrombosis before diagnosis. Current guidelines fail to address this high-risk population. We propose screening any patient with microcytic anemia or IDA and persistently "normal" Hb (male 13–15, female 11.5–13.5 g/dL) plus unexplained splenomegaly, leukocytosis, thrombocytosis, or atypical thrombosis for JAK2V617F.

keywords: Polycythemia Vera - Anemia - beta-Thalassemia - JAK2V617F Mutation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-119

Prognostic Value of Neutrophil-to-Lymphocyte Ratio in Acute Kidney Injury and Chronic Kidney Disease: A Systematic Review and Meta-Analysis

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Background and aim: Background: Acute kidney injury (AKI) and chronic kidney disease (CKD) are associated with high morbidity and mortality. The neutrophil-to-lymphocyte ratio (NLR), an inexpensive and readily available inflammatory biomarker derived from complete blood count, has been proposed as a prognostic marker. However, the magnitude of its association with adverse outcomes in AKI and CKD remains unclear. This systematic review and meta-analysis aims to quantify the prognostic value of elevated NLR for all-cause mortality, major adverse kidney events (MAKE), and disease progression in patients with AKI or CKD.

Methods: Methods: We searched PubMed, Scopus, and Web of Science (inception to March 2025) using MeSH terms: "Neutrophil-to-Lymphocyte Ratio" AND ("Acute Kidney Injury" OR "Chronic Kidney Disease") AND ("prognosis" OR "mortality" OR "disease progression"). Inclusion criteria: (1) cohort studies (prospective/retrospective); (2) adult AKI or CKD (any stage); (3) baseline NLR; (4) adjusted HR/OR for all-cause mortality, MAKE, or ESRD progression; (5) follow-up ≥3 months. Exclusion: case reports, reviews, animal studies, or unadjusted analyses. Two reviewers screened, extracted data, and assessed quality (Newcastle-Ottawa Scale). Random-effects meta-analysis pooled adjusted HRs. Heterogeneity (I^2), subgroup analyses (AKI vs. CKD; NLR cutoffs), and publication bias (Egger's test) were evaluated.

Results: Results: Of 850 identified records, 18 cohort studies (total 4,700 patients) met inclusion criteria: 9 studies in AKI (n=2,300) and 9 in CKD (n=2,400). Median follow-up ranged from 6 to 48 months. Elevated NLR was significantly associated with increased risk of all-cause mortality in both AKI (pooled adjusted HR 1.65; 95% CI 1.39–1.96; I^2=52%, p0.001) and CKD (pooled adjusted HR 1.49; 95% CI 1.32–1.68; I^2=48%, p0.001). For MAKE in AKI, elevated NLR predicted higher risk (pooled adjusted OR 2.04; 95% CI 1.65–2.52; I^2=44%). In CKD, elevated NLR was associated with progression to ESRD (pooled adjusted HR 1.45; 95% CI 1.25–1.68; I^2=46%). Subgroup analysis showed that NLR cutoff values ≥3.0 had the strongest prognostic value (HR 1.79; 95% CI 1.48–2.16). Sensitivity analysis excluding low-quality studies did not change the direction or significance of results. No significant publication bias was detected (Egger's test p=0.30).

Conclusion: Conclusion: Elevated NLR is independently associated with higher all-cause mortality and adverse kidney outcomes in both AKI and CKD patients. The association is robust across different cutoff values and study populations. NLR, as a simple and cheap biomarker, may help risk stratify patients with kidney disease, particularly when advanced biomarkers are unavailable. Future studies should standardize NLR cutoff values and explore its integration into clinical decision rules. This meta-analysis provides quantitative evidence to support NLR as a prognostic tool in nephrology practice.

keywords: Biomarkers, Acute Kidney Injury, Renal Insufficiency, Chronic

PH-120

The role of platelet rich plasma (PRP) in Dental Pulp Regeneration: Diagnostic & Prognostic approach

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Background and aim: Dental pulp usually sustains damage due to cariogenic and periodontal infections, dental trauma, and dental surgical procedures. The common method for treating a damaged tooth pulp is root canal therapy (RCT), in which the necrotic pulp is removed but the tooth pulp is not restored using this method. Recently, Platelet-rich plasma (PRP), a rich source of cytokines and growth factors has emerged as a promising biomaterial for Dental pulp regeneration (DPR).Understanding the molecular mechanisms through which PRP influences cell proliferation, and apoptosis may contribute to the development of more effective regenerative therapy.

Methods: This review was conducted by PubMed, Scopus, Web of Science, and Google Scholar using relevant keywords. Studies including original research, in vitro, in vivo, and clinical investigatios published in English were selected and qualitatively analyzed.

Results: Evidence indicates that PRP exerts its regenerative effects primarily through the release of multiple growth factors and bioactive molecules that enhance cellular proliferation and migration of dental pulp stem cells(DPSCs). PRP also promotes odontogenic and osteogenic differentiation, contributing to the formation of dentin-pulp-like tissue. In addition, it significantly enhances angiogenesis by upregulating vascular-related signaling pathways, thereby improving tissue vascularization and survival. At the molecular level, PRP modulates several key pathways, including MAPK, PI3K/Akt, and ERK pathways involved in cell survival and angiogenesis, as well as Wnt/β-catenin, Smad1/5/8, and Notch signaling pathways regulating stem cell differentiation. Furthermore, apoptosis-related pathway such as JNK and Fas/FasL are influenced, suggesting a role in maintaining cellular balance during tissue regeneration.

Conclusion: Recent advances in tissue engineering have led to the improvement of treatment methods for damaged dental pulp through DPR. PRP may represent a promising regenerative strategy in endodontics by modulating critical molecular pathways involved in dental pulp repair and rgeneration.

keywords: Platelet Rich Plasma, Dental Pulp, Regeneration, Molecular pathway

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-121

GADD45G Expression as a Predictor of Induction Therapy Response in FLT3-ITD and KMT2A-Rearranged Acute Myeloid Leukemia.

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Background and aim: AML is a genetically heterogonous malignancy in which molecular abnormalities significantly treatment response and clinical outcome.FLT3-ITD mutations and KMT2A rearrangements represent important high risk genetic lesions associated with disease progression and inferior survival.GADD45G is a tumor suppressorgene involved in cell cycle regulation,apoptosis,and DNA damage response.Recent studies have demonstrated preferential silencing of GAAD45G in AML,particularly in FLT3-ITD muted and KMT2A rearranged cases,suggesting potential role in leukemogenesis and therapeutic resistance.accordingly, We aim to investigate the association between GADD45G expression and induction therapy response in AML patients harboring FLT3-ITD mutations and KMT2A rearrangements and to evaluate its potential value as a predictive biomarker.

Methods: Newly diagnosed AML patient were enrolle and were categorize according to FLT3-ITD and KMT2A status. Bone marrow or peripheral blood cells were collected before initiation of treatment. Total RNA extraction, cDNA synthesis, and quantitative real-time pcr were performed to determine relative GADD45G expression levels using 2-ΔΔct method. Expression profiles compared among molecular subgroups and healthy controls. Correlation between GADD45 expression and achievement of complete remission following induction chemotherapy were assessed.

Results: GADD45G expression significantly reduced in AML patient compared with healthy control, with the lowest expression levels observed in FLT3-ITD-positive and KMT2A rearranged subgroups. Reduced GADD45G expression may be associated with lower complete remission rates and poorer early treatment response.

Conclusion: GADD45G may represent a novel predictive biomarker for induction therapy response in AML. Intention of GADD45G expression with established molecular marker such as FLT3-ITD and KMT2A rearrangements may improve molecular risk stratification and facilitate individualized therapeutic decision-making in AML patient.

keywords: AML, GADD45G, FLT3-ITD mutation, KMT2A rearranged

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-122

Transcriptomic Profiling of Retinoic Acid Response in Acute Myeloid Leukemia Identifies GDF15 and PHLDB3 as Molecular Drivers of Differentiation

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Background and aim: Acute myeloid leukemia (AML) is the most frequent adult leukemia, characterized by maturation arrest and accelerated cell division in hematopoietic stem/progenitor cells. Retinoic acid (RA) is one of the most effective therapeutic agents in AML management, acting as a potent differentiation agent that overcomes this differentiation block and represses leukemogenesis. While RA triggers widespread transcriptional remodeling, isolating the dominant, high-impact downstream molecular drivers remains essential for identifying novel biomarkers and therapeutic targets. This study aimed to map the core transcriptomic engine responding to RA exposure in AML blasts using a comprehensive, multi-stage bioinformatics workflow.

Methods: Publicly available high-throughput bulk RNA-sequencing (RNA-seq) datasets evaluating RA-treated and untreated AML cell lines (OCI-AML-3) were retrieved from the Gene Expression Omnibus (GEO) database under the data series accession GSE298593. Sequencing was originally performed using Illumina NovaSeq 6000 platform. Quality control of the raw data was performed via FastQC within Galaxy server. Following strandedness identification, raw RNA-seq reads were mapped and quantified using the RNA-STAR and featureCounts algorithms, yielding an gene expression matrix for 8 independent samples. Downstream statistical analysis was performed using R software. Low-count genomic noise was removed and 12,829 high-confidence genes were leaved for further evaluations. Following library-size normalization and log2 variance stabilization, unsupervised sample clustering was evaluated via Principal Component Analysis (PCA). Differential Expression Analysis (DEA) was performed using the DESeq2 package. Selection criteria for differentially expressed genes (DEGs) were defined as a Bonferroni adjusted p-value 0.01 and an absolute Log2 Fold Change 2.

Results: Unsupervised PCA demonstrated distinct sample clustering based on biological gene expression profiles, with Principal Component 1 (PC1) alone capturing 51.8% of the total variance strictly according to treatment status. Under the defined selection criteria, the global transcriptomic landscape was successfully filtered to isolate exactly two core, highly significant DEGs: Growth Differentiation Factor 15 (GDF15) and Pleckstrin Homology Like Domain Family B Member 3 (PHLDB3). Both identified DEGs exhibited statistically profound upregulation in retinoic acid-treated cells compared to untreated controls.

Conclusion: This study pinpointed GDF15 and PHLDB3 as the primary molecular responders to RA exposure in AML cells. Given their established regulatory roles within the p53 tumor-suppressor signaling network and myeloid maturation pathways, these findings provide high-contrast transcriptomic evidence that retinoic acid directly orchestrates structural and anti-proliferative differentiation programs. These two genes represent highly reliable, robust biomarkers for tracking therapeutic response and differentiation success in acute myeloid leukemia models.

keywords: Acute myeloid leukemia, Retinoic acid, RNA sequencing, Gene expression analysis

PH-123

The Role of Leukemic Exosomes in Leukemia Pathogenesis and Microenvironment Remodeling

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Background and aim: Leukemic exosomes are small extracellular vesicles (30–100 nm) secreted by malignant hematopoietic cells that mediate intercellular communication within the tumor microenvironment. These vesicles carry a diverse cargo of proteins, lipids, nucleic acids, and microRNAs (miRNAs) capable of modulating the behavior of recipient cells. Emerging evidence suggests that leukemic exosomes contribute significantly to leukemia progression, angiogenesis, immune modulation, and therapeutic resistance.

Methods: A literature search was performed in PubMed, Scopus, and Web of Science databases to identify studies investigating the role of leukemic exosomes in hematological malignancies. Relevant articles addressing exosomal cargo, molecular pathways, biological functions, and clinical implications were reviewed and synthesized.

Results: Studies have demonstrated that AML-derived exosomes are enriched with leukemia-associated miRNAs, including let-7a, miR-9, miR-99b, miR-150, miR-155, miR-191, and miR-223, suggesting their potential as prognostic biomarkers. In B-cell precursor ALL, exosomal IL-15 contributes to blood–brain barrier disruption and central nervous system infiltration. CML-derived exosomes promote angiogenesis through endothelial cell activation, with miR-92a and miR-210 regulating integrin expression, Ephrin-A3 signaling, and VEGF-mediated pathways. In MM, exosomes released by bone marrow mesenchymal stem cells contain elevated levels of oncogenic factors, cytokines, adhesion molecules, and miRNAs such as miR-21 and miR-146a, enhancing tumor-supportive microenvironmental interactions. Similarly, CLL-derived exosomes exhibit increased expression of miR-150, miR-155, miR-29 family members, and miR-223, highlighting their role in disease pathogenesis.

Conclusion: Leukemic exosomes are key mediators of leukemia progression through the transfer of bioactive molecules that regulate angiogenesis, cellular proliferation, immune responses, and microenvironment remodeling. Their unique molecular cargo makes them promising candidates for diagnostic and prognostic biomarkers as well as potential therapeutic targets. Further studies are required to elucidate their mechanisms of action and facilitate their translation into clinical application.

keywords: Leukemic Exosomes, Extracellular Vesicles, miRNAs, Tumor Microenvironment

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-124

MicroRNA-Based Biomarkers in FLT3-Mutated Acute Myeloid Leukemia: Focus on miR-155 and the miR-29 family

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Background and aim: Acute myeloid leukemia (AML) is the most common acute leukemia in adults, characterized by disrupted myeloid differentiation and uncontrolled proliferation of leukemic blasts. Internal tandem duplication of FLT3 (FLT3-ITD), one of the most frequent molecular abnormalities in AML, is associated with poor prognosis and a higher risk of relapse. MicroRNAs (miRNAs), which are key players in epigenetics, play crucial regulatory roles in leukemogenesis and could potentially serve as valuable markers for disease monitoring and risk stratification. This review aims to assess the diagnostic value of miR-155 and the miR-29 family in AML patients with FLT3 mutations.

Methods: A narrative review of articles was conducted using databases such as PubMed, Scopus, and Google Scholar. Relevant studies published between 2009 and 2025 were identified using the keywords "AML," "FLT3-ITD," "microRNA," "miR-155," and "miR-29," and related articles were included in our review study. Additionally, other clinically relevant microRNAs, including miR-34a, miR-181, miR-125b, and miR-146a, were also discussed to provide a broader network of AML regulation mediated by microRNAs. Next, the methods for predicting microRNA target genes using computer algorithms like TargetScan, miRDB, and miRanda were explained. Furthermore, for AML treatment, downstream genes of these microRNAs were examined using targeted therapy. Finally, the potential clinical application of these microRNAs was discussed.

Results: Reviewed studies consistently demonstrated overexpression of miR-155 in FLT3-ITD AML, where activation of STAT5 and NF-κB signaling promotes leukemogenesis through suppression of differentiation-associated targets including PU.1 and SHIP1. In contrast, the miR-29 family exhibited tumor-suppressive functions through regulation of DNA methyltransferases, apoptosis, leukemic stem-cell maintenance, and cellular differentiation. Additional miRNAs including miR-34a and miR-181 showed potential prognostic and treatment-response value, whereas miR-125b and miR-146a displayed context-dependent regulatory effects. Integrative analyses revealed interconnected downstream regulatory cascades involving PI3K/AKT, NF-κB, JAK/STAT, Wnt/β-catenin, and epigenetic pathways. Computational target-prediction and network-based approaches further highlighted miRNAs as central regulatory hubs with potential applications in biomarker discovery, laboratory monitoring, risk stratification, and precision medicine. However, direct evidence regarding miR-29 function specifically in FLT3-mutated AML remains limited.

Conclusion: MicroRNAs constitute interconnected regulatory networks that influence leukemic proliferation, differentiation, epigenetic regulation, and therapeutic response in AML. Among them, miR-155 and the miR-29 family represent opposing functional hubs with potential diagnostic, prognostic, and therapeutic significance. Integration of miRNA profiling with molecular diagnostics may improve laboratory-based risk assessment and precision medicine strategies in AML. Nevertheless, further studies are required to clarify the role of miR-29 family members in FLT3-mutated disease and to validate their clinical utility.

keywords: Acute myeloid leukemia; FLT3-ITD; microRNA; miR-155; miR-29 family

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-125

Transcriptomic Profiling of ACSL4-Deficient Leukemia Models Identifies ITPKB as a Conserved Downstream Target Associated with Metabolic Remodeling

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Background and aim: Myeloid leukemias comprise a heterogeneous group of hematologic malignancies characterized by dysregulated proliferation and differentiation of myeloid progenitors. Acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) exhibit distinct molecular features but share metabolic adaptations that support disease progression. Beyond enhanced glycolysis, lipid metabolism has emerged as a central hallmark of leukemia progression and therapeutic resistance. ACSL4, an enzyme involved in fatty acid metabolism and membrane lipid remodeling, has emerged as a key regulator of leukemia-associated metabolic processes. This study aimed to identify transcriptional changes associated with ACSL4 knockdown across AML and CML cell lines.

Methods: Public RNA-sequencing (RNA-seq) datasets profiling ACSL4-knockdown and wild-type leukemia cell line models (K562 and NOMO-1 cell lines) were retrieved from the NCBI Gene Expression Omnibus (GEO; GSE274462). Raw reads were preprocessed on the Galaxy platform using FastQC, MultiQC, STAR, and featureCounts. Downstream statistical analyses were performed in R using the edgeR and limma packages. Lowly expressed genes were filtered prior to normalization, retaining 16,865 genes with ≥ 10 raw counts in at least three samples. Following TMM normalization and voom mean-variance transformation, linear modeling and empirical Bayes moderation (eBayes) were applied. Differentially expressed genes were identified using a dual-threshold strategy (raw P-value 0.005, |log2FC| ≥ 0.58). Gene Ontology (GO) Biological Process enrichment was assessed using Fast Gene Set Enrichment Analysis (fgsea).

Results: The dual-threshold transcriptomic screening identified two consistently downregulated genes across both independent cell lines. As expected, ACSL4 expression was reduced in both K562 (log2FC = -1.17, P = 2.92 × 〖10〗^(-7)) and NOMO-1 cells (log2FC = -4.25, P = 2.6 × 〖10〗^(-10)).Notably, Inositol-Trisphosphate 3-Kinase B (ITPKB) emerged as the only shared downstream gene, displaying reduced expression in K562 (log2FC = -2.44, P = 2.08× 〖10〗^(-4)) and NOMO-1 cells (log2FC = -0.62, P = 4.47 × 〖10〗^(-3)). Comparative Gene Set Enrichment Analysis (GSEA) revealed distinct but convergent pathway alterations following ACSL4 knockdown. NOMO-1 cells demonstrated enrichment of sterol biosynthesis, oxidative phosphorylation, and ER-stress pathways, alongside a marked activation of 'negative regulation of ferroptosis.' Conversely, K562 cells showed suppression of DNA repair and mitotic cell cycle programs. Collectively, these findings identify ITPKB as a conserved transcriptional target associated with ACSL4 deficiency and suggest broad metabolic remodeling across AML and CML cellular contexts.

Conclusion: Comparative transcriptomic analysis of ACSL4-deficient AML and CML models identified ITPKB as a conserved downstream target associated with lipid metabolic remodeling. The consistent downregulation of ITPKB across both leukemia cell lines, together with coordinated pathway alterations revealed by GSEA, suggests a functional connection between ACSL4-dependent lipid metabolism and intracellular signaling programs. These findings provide a foundation for future studies investigating the biological and therapeutic relevance of the ACSL4–ITPKB axis in myeloid leukemia.

keywords: Acute Myeloid Leukemia, ITPKB, RNA sequencing, Lipid metabolism, ACSL4

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-126

Ferroptosis-Related Biomarkers in Chronic Myeloid Leukemia: Potential Involvement of the miR-181/SLC7A11/GPX4 Axis in Tyrosine Kinase Inhibitor Resistance

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Background and aim: Chronic myeloid leukemia (CML) is characterized by abnormal tyrosine kinase signaling, and resistance to tyrosine kinase inhibitors (TKIs) remains a major clinical challenge. Ferroptosis, an iron-dependent form of regulated cell death, has emerged as a potential mechanism involved in cancer progression and therapeutic response. The SLC7A11/GPX4 pathway is a key regulator of ferroptosis and may be modulated by microRNAs. Therefore, this study aimed to investigate the role of the miR-181/SLC7A11/GPX4 axis in ferroptosis and its potential contribution to TKI resistance in CML.

Methods: A narrative review of the literature was conducted using PubMed, Scopus, Web of Science, and Google Scholar databases. Relevant English-language publications published between January 2024 and December 2026 were identified using combinations of the keywords “chronic myeloid leukemia,” “CML,” “ferroptosis,” “tyrosine kinase inhibitor resistance,” “miR-181,” “SLC7A11,” and “GPX4.” Original studies investigating ferroptosis-related mechanisms, biomarkers, and therapeutic targets in CML were prioritized. The retrieved literature was critically reviewed and qualitatively synthesized to evaluate the potential association between ferroptosis dysregulation and TKI resistance.

Results: Available evidence suggests that ferroptosis-related pathways are dysregulated in CML and may contribute to leukemic cell survival and therapeutic resistance. Increased activity of anti-ferroptotic regulators, particularly SLC7A11 and GPX4, has been associated with enhanced antioxidant defense, suppression of lipid peroxidation, and reduced susceptibility to ferroptotic cell death. Several experimental studies have demonstrated that pharmacological induction of ferroptosis can enhance the sensitivity of resistant leukemic cells to treatment, highlighting ferroptosis as a promising therapeutic target. Furthermore, emerging evidence from leukemia and other malignancies indicates that miR-181 may participate in the regulation of ferroptosis-associated signaling pathways, including components of the SLC7A11/GPX4 axis. Collectively, these findings suggest a potential role for ferroptosis-related biomarkers in predicting disease progression and treatment response in CML.

Conclusion: Ferroptosis appears to play a significant role in chronic myeloid leukemia and may affect sensitivity to tyrosine kinase inhibitors. Dysregulation of the miR-181/SLC7A11/GPX4 axis may contribute to ferroptosis suppression and the development of drug resistance. Modulation of this pathway could represent a promising strategy for overcoming TKI resistance and improving therapeutic outcomes in CML. Nevertheless, further experimental and clinical studies are required to confirm these findings and elucidate the underlying molecular mechanisms.

keywords: Chronic Myeloid Leukemia; Ferroptosis; Tyrosine Kinase Inhibitor Resistance; miR-181; SLC7A11

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-127

Investigating the effect of exosomes derived from cells treated with metformin and chloroquine on cell viability

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Background and aim: Exosomes are extracellular vesicles ranging from 30 to 150 nanometers in size that play a crucial role in intercellular communication. By transferring proteins, lipids, and RNAs, they can alter the behavior of target cells. The physiological conditions of producer cells, as well as pharmacological treatments, can influence the composition and function of exosomes. The aim of this study was to investigate the effect of exosomes derived from metformin- and chloroquine-treated cells on cellular viability.

Methods: In this study, cells were treated with metformin and chloroquine, and the exosomes released into the culture medium were subsequently collected. The isolated exosomes were then applied to target cells at various concentrations. To assess cell viability, the MTT assay was performed at 24 and 48 hours. The conversion of MTT into formazan crystals was considered an indicator of metabolic activity and the number of viable cells.

Results: The findings of this study suggest that the conditions of exosome-producing cells, particularly pharmacological treatment with metformin and chloroquine, can alter the biological function of exosomes and their effects on target cells. Exosomes derived from metformin-treated cells appear to exert protective effects on cellular viability. These findings warrant further attention for a better understanding of the role of exosomes in regulating cellular responses and for the development of exosome-based therapeutic approaches.

Conclusion: The results of this study demonstrated that pharmacological preconditioning of donor cells is a critical determinant in modulating the biological nature of secreted exosomes and, consequently, the response of target cells. Our findings confirmed that exosomes derived from metformin-treated cells, in contrast to control- and chloroquine-derived exosomes, possess a remarkable potential to enhance cell viability and promote the metabolic activity of target cells. These protective effects are likely attributable to alterations in the molecular cargo of exosomes (including proteins, miRNAs, or metabolites) in response to the activation of cell survival

keywords: Exosome, metformin, chloroquine, cell viability, MTT assay.

PH-128

The Effect of Metformin and Chloroquine Treatments on Alix mRNA Expression as a Key Marker of Exosome Biogenesis

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Background and aim: Alix protein is one of the key markers and major factors involved in the biogenesis and secretion of exosomes, and its expression is influenced by physiological conditions and pharmacological treatments. Considering the roles of metformin and chloroquine in regulating vesicular trafficking and autophagy pathways, this study aimed to investigate the effects of these two drugs on the expression level of the Alix gene. Materials and Methods: In this experimental study, cells were divided into three groups: control, chloroquine-treated group (CQ, 50 µM), and metformin-treated group (Met, 20 mM).

Methods: In this study, relevant articles on exosome production methods, including physical, chemical, and bioreactor-based approaches, were reviewed and analyzed through a search of reputable databases, including PubMed, Scopus, and Google Scholar, covering the period from 2015 to 2024.

Results: The review of literature revealed that while conventional physical methods (e.g., ultracentrifugation) remain common, they are limited by low yields and contamination. Advanced approaches, such as size-exclusion chromatography and microfluidics, offer superior purity and reproducibility. Chemical treatments enhance exosome release but may alter their biological content. Ultimately, bioreactor-based systems demonstrated the highest potential for large-scale, standardized production, suggesting that combining bioreactors with advanced purification methods is optimal for clinical and translational applications.

Conclusion: Large-scale production and standardization of isolation protocols remain the main bottlenecks in translating exosome-based therapy from the laboratory to the clinic. The integration of bioprocess engineering strategies with pharmacological manipulation of producer cells may provide a safe and cost-effective approach for generating pharmaceutical-grade exosomes. These advances hold great promise for a major transformation in personalized medicine and the treatment of refractory diseases in the near future.

keywords: Exosome, biogenesis, vesicle engineering, drug delivery, bioreactor, clinical laboratory.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-129

Effects of NRF2 inhibition in leukemic patients therapy: A literature review

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Background and aim: Leukemia refers to cancer affecting the blood-forming tissues, including bone marrow and the lymphatic system. Various types of leukemia occur in different age groups, with some prevalent in children and others in adults. Despite the availability of multiple chemotherapy agents for leukemia treatment, chemoresistance remains a challenge, partly due to the transcription factor NRF2. Elevated NRF2 expression in leukemic cells treated with chemotherapy agents can enhance cell survival. Therefore, inhibiting NRF2 alongside traditional chemotherapy may offer a promising approach to leukemia treatment. This study aims to investigate the role of NFR2 in chemotherapy as a target therapy for AML patients.

Methods: We searched several databases including PubMed, Google Scholar, Scopus, and Web of Science from 2017 December to 2024, for literature written in English or Persian. The search strategy was based on using the search term (in combination) including “Acute myeloid leukemia”, “AML”, “NRF2”, “Nuclear factor erythroid 2-Related Factor 2”, and “chemotherapy”, This study indicates the role of NFR2 as an effective target in the improvement of chemotherapy of AML patients.

Results: Nrf2, a redox-responsive transcription factor, orchestrates the expression of antioxidant and detoxifying genes, safeguarding cells from oxidative and electrophilic damage. In normal cells, NRF2 upregulates these proteins to maintain cellular homeostasis; however, its specific role in regulating endogenous ROS differs. Leukemia treatment strategies, including chemotherapy and radiation, rely on inducing apoptosis in malignant cells through cytotoxic stress. Certain chemotherapeutic agents generate high levels of reactive oxygen species (ROS), which damage DNA, mitochondrial inner membranes, and membrane phospholipids, effectively triggering apoptotic pathways. NRF2 has emerged as a promising therapeutic target in oncology. Ongoing research investigates both NRF2 inhibitors and inducers, as its activation is frequently linked to enhanced cell survival and chemotherapy resistance across various tumors. Consequently, understanding the dual role of NRF2 as a cytoprotective factor and a potential driver of drug resistance is critical for advancing leukemia therapies and sensitizing leukemic cells to treatment.

Conclusion: Nrf2 inhibition is actively explored in cultured cells, cancer tissues, and leukemia. Genetic and pharmaceutical NRF2-dependent antioxidant response inhibition holds promise for therapeutic benefits.

keywords: NRF2, Nuclear factor erythroid 2-Related Factor 2, Leukemia, chemotherapy, Oxidative

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-130

Deciphering the Molecular Landscape of LncRNA MALAT-1 in AML: Implications for Disease Progression and Patient Outcomes

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Background and aim: AML is a heterogeneous hematologic malignancy defined by clonal myeloid blast expansion in blood and bone marrow. Long non-coding RNAs (lncRNAs), molecules exceeding 200 nucleotides without protein-coding potential though some generate micro-peptides are crucial. They regulate gene transcription, post-transcriptional mechanisms, epigenetic modifications, DNA replication, chromosome stability, aging, and disease progression. LncRNAs exhibit aberrant expression across tissues, exerting oncogenic or tumor-suppressive functions. Given their regulatory roles in genomic activities, this study investigates the prognostic potential of MALAT-1 (Metastasis-associated lung adenocarcinoma transcript 1) as a clinical tool for assessing outcomes in AML patients, evaluating its significance in disease management and patient survival.

Methods: We searched several databases including PubMed, google scholar, Scopus, and web of science from 2017 December to 2023, for literature written in English or Persian. The search strategy was based on using the search term (in combination) including “Acute myeloid leukemia”, “AML”, “LncRNA”, “LncRNA MALAT-1”, and “prognostic significance”, This study indicates the application of LncRNAs as effective tools in the management of AML.

Results: This review evaluates the expression and functional significance of the long non-coding RNA MALAT-1 in acute myeloid leukemia (AML). Huang et al. analyzed 95 newly diagnosed AML patients (47 males, 48 females; median age 51) and discovered that MALAT-1 was significantly overexpressed in the M5 subtype compared to other subtypes and healthy controls. Elevated MALAT-1 correlated with higher white blood cell and platelet counts, though not with sex, age, hemoglobin, bone marrow blast percentage, or karyotype. Notably, high MALAT-1 expression linked to poorer overall survival (OS) in M5 patients, and multivariate analysis identified it as an independent prognostic factor. Furthermore, Jing Jin et al., studying 40 AML patients and 40 healthy controls, confirmed increased MALAT-1 expression in AML. Mechanistically, MALAT-1 interacts with METTL14 to enhance m6A modification of ZEB1, thereby significantly promoting AML cell survival and proliferation, highlighting MALAT-1 as a critical oncogenic regulator in leukemogenesis.

Conclusion: This study indicates the potential prognostic effects of LncRNA “MALAT-1” on AML patients in compare with healthy control group. Overexpression of MALAT-1 as an independent poor prognostic factor which is responsible for diminution of overall survival (OS) of AML patients. However; to clarify these subject future studies with higher sample size are required.

keywords: Acute myeloid leukemia, LncRNA MALAT-1, prognostic significance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-131

The Therapeutic Potential of Urolithin A in Multiple Myeloma: A Systematic Review

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Background and aim: Multiple myeloma (MM) is a hematologic malignancy characterized by clonal plasma cell proliferation, drug resistance, and immune dysregulation. Urolithin A (UA), a gut microbiota-derived metabolite, has recently emerged as a bioactive compound with potential anticancer and immunomodulatory properties. This systematic review aimed to evaluate and synthesize current evidence regarding the role of UA in modulating tumor progression, immune responses, and therapeutic sensitivity in multiple myeloma.

Methods: A systematic review was conducted based on PRISMA guidelines. Relevant studies were identified through a comprehensive literature search of PubMed, Scopus, Web of Science, and Google Scholar databases covering in vitro, in vivo, and translational studies evaluating the effects of urolithin A in multiple myeloma. The search focused on studies investigating UA's anticancer activity, immune modulation, and interaction with standard therapeutic agents. After screening and eligibility assessment, the most relevant experimental and translational studies were included for qualitative synthesis.

Results: The included studies consistently demonstrated that urolithin A exerts multifaceted anti-myeloma effects. UA inhibits proliferation and induces cytotoxicity in MM cell lines, including bortezomib-resistant models, through disruption of mitochondrial function, cell cycle arrest, and metabolic reprogramming. In vivo studies further confirmed its tumor-suppressive effects, showing reduced tumor burden and improved survival in xenograft models. Importantly, UA enhances the efficacy of conventional therapies, suggesting a synergistic effect that may help overcome drug resistance. In addition to direct tumor targeting, UA significantly modulates the immune microenvironment by enhancing CD8+ T cell function, promoting ERK1/2 signaling, autophagy, and metabolic fitness, thereby sustaining cytotoxic T cell activity. Furthermore, UA contributes to an anti-inflammatory tumor microenvironment by reducing pro-inflammatory cytokine activity and supporting tumor suppressor pathways. Clinical and microbiome-associated evidence also suggests that the presence of UA-producing gut microbiota correlates with improved patient outcomes and prolonged progression-free survival.

Conclusion: Urolithin A demonstrates promising anticancer and immunomodulatory effects in multiple myeloma through direct tumor suppression, enhancement of antitumor immunity, and potential synergy with existing therapies. However, further clinical studies are required to determine optimal dosing, safety profiles, and patient-specific microbiome influences to facilitate its translation into clinical practice as an adjunct therapeutic strategy.

keywords: Multiple myeloma; Urolithin A; Gut microbiome; Immunomodulation; Mitochondrial function

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-132

Investigation The Role of NF-κB in The Regulation of Apoptosis in Leukemia and Its Targeted Therapy

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Background and aim: Leukemia remains a major therapeutic challenge despite improvements in treatment. The Nuclear Factor-Kappa B (NF-κB) transcription factor is a regulator of many biological functions such as cell survival, inflammation, and hematopoiesis. NF-κB has been implicated in the pathology of some types of leukemias, with high levels of NF-κB associated with disease progression and drug resistance. This aberrant NF-κB activation can be caused by genetic mutations in the tumor cells and microenvironmental factors, which promote NF-κB signaling. The aim of this study is to explore how NF-κB signaling controls apoptosis in leukemia as well as NF-κB-based treatment strategies in leukemia.

Methods: The impact of NF-κB on leukemic cell apoptosis was examined across different leukemia types, including acute myeloid leukemia (AML), Chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL), and chronic lymphocytic leukemia (CLL). NF-κB expression patterns were analyzed, and the involvement of both canonical and non-canonical signaling pathways was evaluated. The regulation of various apoptosis-related genes by NF-κB was also investigated. In addition, therapeutic approaches targeting this pathway were reviewed based on evidence obtained from in vitro, and in vivo studies.

Results: NF-κB was continuously activated in a significant proportion of patients with AML, ALL, CML, and CLL. In this conditions, NF-κB supported survival signals and avoided apoptosis. IRAK1/4–NF-κB–PD-L1 signaling was critical for imatinib resistance. Inhibition of NF-κB lowered the expression of key anti-apoptotic genes such as BCL-2, BCL-xL, STAT-3, MCL-1, c-FLIP, cIAP, and XIAP. It also decreased the levels of proliferation-related genes like c-MYC and cyclin D1, D2, D3, and E, and also reduced the expression of pro-survival genes such as A1/BFL-1, thus reduced leukemic growth. Drugs that target the NF-κB pathway, such as bortezomib and carfilzomib, promoted apoptosis and improved sensitivity to chemotherapy. NF-κB inhibition strongly decreased BCL-2 and MCL-1 expression and induced apoptosis in AML. NF-κB inhibition reduced the expression of survival genes and IAPs, and enhanced apoptosis and therapeutic response in CLL. Similarly, in CML, NF-κB inhibition sensitized CML cells to TKI-induced apoptosis.

Conclusion: Abnormal activation of NF-κB is closely linked to reduced apoptosis, increased leukemic cell survival, and therapy resistance. Blocking NF-κB signaling consistently reduced leukemic cell survival and increased apoptosis in AML, ALL, CML, and CLL. Although NF-κB pathway is a promising therapeutic target, better results may require more selective inhibition and combination therapies. Further research is needed to improve NF-κB-based treatment strategies in leukemia.

keywords: Leukemia, NF-κB, Apoptosis, Targeted Therapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-133

Rare NK Cell Phenotype (CD3-Negative/CD8-Positive) in a Patient with Secondary Recurrent Miscarriage: A Flow Cytometry Case Report

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Background and aim: Recurrent pregnancy loss (RPL) occurs in approximately 5% of women, but the underlying cause remains unknown in a significant proportion of cases. The role of natural killer (NK) cells in shaping maternal-fetal immune tolerance has received much attention. While classical NK cells are defined as CD3-negative/CD56-positive and typically do not express CD8, we report a case of a woman with secondary RPL in whom an atypical CD3-negative/CD8-positive NK cell population was identified by flow cytometry.

Methods: The patient was a 41-year-old woman with a history of two successful pregnancies followed by three consecutive miscarriages. Peripheral blood was collected to evaluate lymphocyte subsets and analyzed using a Beckman Coulter Life Sciences CytoFLEX flow cytometer. Markers specific for T and B lymphocytes, including CD3, CD4, CD8, CD19, and CD20, and NK cell markers, including CD56 and CD16, were examined. NK cells were identified by first gating on CD3-negative lymphocytes, then analyzing CD56, CD16, and CD8 expression within this population. Reference ranges were adjusted for age and sex.

Results: The B lymphocyte population was within the normal range. While CD8-positive cytotoxic T cells were decreased (15.0%), the total number of CD3-negative/CD56-positive NK cells was increased (28.0%). NKT cells (CD3-positive/CD56-positive) were also slightly increased (10.7%). After gating on CD3-negative cells, a distinct subset of NK cells expressing CD56, CD16, and CD8 (dim) was identified. This CD3-negative/CD8-positive (dim) NK cell population is a rare finding, because classical NK cells typically do not express CD8.

Conclusion: We report a rare CD3-negative/CD8-positive NK cell subset identified by flow cytometry in a 41-year-old woman with secondary RPL, whose total NK cell count was also increased. Although increased NK cells have been associated with recurrent miscarriage, the clinical significance of this unusual CD8-positive NK phenotype remains unclear. This report highlights the value of precise flow cytometry gating in identifying rare cell subsets and serves as a basis for further investigation of this rare subset in normal individuals and patients with immunodeficiency or unexplained RPL.

keywords: Recurrent pregnancy loss; NK cells; flow cytometry; case report.

PH-134

Exosome-Mediated Effects of Doxorubicin in Hematologic Malignancies: Implications for Drug Resistance

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Background and aim: Exosomes are small extracellular vesicles that play a critical role in intercellular communication, tumor microenvironment modulation, and the transfer of regulatory biomolecules. In hematologic malignancies, emerging evidence suggests that chemotherapy, particularly doxorubicin, can alter exosome secretion, cargo composition, and biological function, thereby contributing to chemoresistance and disease relapse.

Methods: A literature review was conducted using relevant keywords including exosome, doxorubicin, chemoresistance, and hematologic malignancies. Experimental, animal, and clinical studies addressing exosome biogenesis, molecular cargo alterations, and resistance transmission were evaluated.

Results: The reviewed studies indicate that doxorubicin treatment is frequently associated with increased exosome release from malignant cells. In addition, changes in exosomal cargo, including resistance-associated miRNAs such as miR-21 and miR-155, have been reported. Exosomes derived from treated cells may transfer resistant phenotypes to neighboring sensitive cells, thereby promoting treatment failure. Pathways implicated in this process include p53, Rab27a, and the ceramide pathway.

Conclusion: Doxorubicin may influence treatment outcomes not only through direct cytotoxic effects, but also by modulating exosome biogenesis and cargo loading. Targeting exosome production and molecular trafficking pathways may represent a promising adjunct strategy to overcome drug resistance in hematologic malignancies. Future research should focus on exosomal biomarkers and pathway-specific inhibitors as potential therapeutic tools.

keywords: Exosome, Doxorubicin, Drug resistance, Hematologic malignancies, Extracellular vesicles

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-135

Dietary Modulation of Iron Metabolism and Its Role in Oxidative Stress-Mediated Vascular Dysfunction in Cardiovascular Disease: A Systematic Review

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Background and aim: Background: Cardiovascular disease (CVD) remains the leading cause of mortality worldwide, with growing evidence implicating disturbances in iron metabolism in its pathogenesis. This systematic review aimed to investigate and evaluate the association between dietary modulation of iron metabolism and oxidative stress-mediated vascular dysfunction in cardiovascular disease, emphasizing underlying pathophysiological and molecular mechanisms.

Methods: Methods: A comprehensive search of relevant literature was conducted across the PubMed, Scopus, and ScienceDirect databases following PRISMA guidelines, resulting in the identification of 24 studies that met the inclusion criteria, comprising 7 interventional and 17 observational studies.

Results: Results: Of the included studies, 21 (87.5%) demonstrated significant associations between dietary iron modulation and cardiovascular outcomes, vascular dysfunction, or oxidative stress-related biomarkers. The major mechanisms identified include heme iron-induced oxidative stress through Fenton chemistry, iron-catalyzed lipid peroxidation, reduced nitric oxide bioavailability leading to endothelial dysfunction, and ferroptosis-mediated cellular injury. Among observational studies, higher heme iron intake was associated with increased risks of cardiovascular events, myocardial infarction, arterial stiffness, and mortality (HRs ranging from 1.16 to 1.86). In contrast, non-heme iron generally showed weaker, neutral, or protective associations, with higher intakes linked to lower cardiometabolic multimorbidity risk (HR = 0.74) and reduced severe abdominal aortic calcification (OR = 0.40). Interventional studies demonstrated that bioactive compounds, including green tea extract, cherries, and hydroxytyrosol, reduced ferritin levels (up to 20.3%) and improved antioxidant capacity, while vitamin C-rich formulations showed mild improvements in endothelial markers. Conversely, three studies (12.5%) found no statistically significant

Conclusion: Conclusion: Dietary modulation of iron metabolism significantly influences cardiovascular risk through complex mechanisms involving oxidative stress, endothelial dysfunction, and ferroptosis. Heme iron appears to confer increased cardiovascular risk, whereas non-heme iron and polyphenol-rich dietary patterns may provide protective effects. Understanding these pathways may support future nutritional and therapeutic strategies aimed at reducing cardiovascular complications in at-risk populations.

keywords: Keywords: iron metabolism; dietary iron; oxidative stress; endothelial dysfunction; cardiovascular

PH-136

GATA2 Deficiency Presenting with a WHIM-Like Phenotype and Subsequent Development of Monosomy 7-Associated Myelodysplastic Syndrome in an Adolescent Female: A Case Report

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Background and aim: GATA2 (GATA-binding protein 2) deficiency is a germline predisposition syndrome associated with immunodeficiency, bone marrow failure (BMF), and an increased risk of myelodysplastic syndrome (MDS). Early diagnosis may be challenging because the clinical presentation is highly heterogeneous and can mimic other inherited hematologic or immunologic disorders. We report the case of an 18-year-old female with GATA2 deficiency and subsequent development of monosomy 7-associated MDS.

Methods: Clinical history, laboratory findings, bone marrow examinations, immunophenotyping, whole exome sequencing (WES), and cytogenetic evaluations were assessed during the patient's diagnostic workup and follow-up.

Results: The patient was born prematurely to consanguineous parents and initially presented at age 13 with growth retardation, anemia, thrombocytopenia, and leukopenia. Her history included congenital atrial septal defect requiring surgical repair, cochlear implantation for sensorineural hearing loss, visual impairment, numerous lower-extremity warts, recurrent oral aphthous ulcers, and hepatosplenomegaly. Laboratory evaluation demonstrated persistent pancytopenia with marked monocytopenia. Bone marrow examination revealed hypocellularity and erythroid hyperplasia without definitive morphologic evidence of MDS or increased blasts. Immunophenotyping showed profound and persistent $CD19^{+}$ B-cell depletion (1%) with relative T-cell predominance. WES identified a likely pathogenic GATA2 variant (c.1130dup; p.Tyr377*), while CXCR4 and CXCR2 variants were absent, arguing against WHIM syndrome. Subsequent cytogenetic studies demonstrated monosomy 7, an additional marker chromosome, and 7q22 deletion. Follow-up marrow evaluation showed dysplastic erythroid and myeloid changes consistent with progression to MDS. The patient received monthly azacitidine therapy and was referred for allogeneic hematopoietic stem cell transplantation.

Conclusion: This case highlights the progressive natural history of GATA2 deficiency from early multisystem manifestations to clonal cytogenetic evolution and development of monosomy 7-associated MDS by age 18, underscoring the importance of early genetic diagnosis and longitudinal hematologic surveillance in adolescents with unexplained cytopenias and syndromic features.

keywords: GATA2 deficiency; Myelodysplastic syndrome; Monosomy 7; Immunodeficiency; WHIM syndrome

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-137

Prognostic Value of Measurable Residual Disease Monitoring in TP53-Mutated Acute Myeloid Leukemia and Myelodysplastic Syndromes Treated with Ferroptosis-Inducing Therapy: A Systematic Review

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Background and aim: TP53-mutated acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) carry poor prognosis and treatment resistance. APR-246, a mutant p53 reactivator that induces ferroptosis via glutathione depletion, has shown promising early-phase efficacy. The prognostic value of measurable residual disease (MRD) monitoring during ferroptosis-inducing therapy remains undefined. This study evaluated this role.

Methods: PubMed, Scopus, and Web of Science were searched (January 2010–May 2026) for studies evaluating MRD monitoring in TP53-mutant AML/MDS patients treated with ferroptosis-inducing agents that reported overall survival (OS), event-free survival (EFS), or relapse-free survival (RFS). Data were narratively synthesized given limited eligible studies and methodological heterogeneity.

Results: Of 87 records screened, two studies (114 patients) met inclusion criteria. In 14 post-transplant patients treated with APR-246 plus azacitidine, MRD negativity by duplex sequencing (VAF 0.005%) after 12 cycles predicted superior OS (33.9 vs. 20.4 months; HR, 0.31; P=0.005), EFS (HR, 0.28; P=0.004), and RFS (HR, 0.33; P=0.018). In a 100-patient phase 2 trial, response with TP53 clearance (VAF 5%) improved OS (15.8 vs. 10.1 months; P=0.002); transplant recipients with NGS negativity did not reach median OS, versus 9.1 months without molecular response (P=0.01). Mechanistic data confirmed ferroptosis induction via glutathione depletion and GPX4 inactivation.

Conclusion: MRD monitoring, particularly by high-sensitivity NGS, appears prognostically valuable in TP53-mutated AML/MDS treated with ferroptosis-inducing therapy. MRD negativity was consistently associated with improved survival, with greatest benefit among patients achieving molecular clearance before transplantation, supporting its role in response assessment and treatment decisions. Larger, prospective trials with standardized MRD protocols are warranted.

keywords: Ferroptosis; Acute Myeloid Leukemia; Myelodysplastic Syndromes; Measurable Residual Disease; APR-246

PH-138

Dose- and Time-Dependent Cytotoxicity of Piperine in Multiple Myeloma Cells: An In Vitro Study

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Background and aim: Multiple myeloma (MM) is an aggressive hematologic malignancy characterized by abnormal plasma-cell proliferation in bone marrow. Although current therapies have improved outcomes, treatment-related toxicity remains a major challenge. Piperine, a bioactive alkaloid from black pepper, has been reported to enhance drug bioavailability and modulate cancer-related survival pathways. However, its direct cytotoxic effects on MM cells remain insufficiently defined. This study aimed to evaluate the effects of piperine on MM cell viability.

Methods: FT-IR analysis was performed to evaluate the spectral characteristics of piperine. MM suspension cells were cultured and treated with varying concentrations of piperine for 24 and 48 hours. Cell viability was assessed using an MTT assay, and statistical analyses were conducted to compare the viability of treated cells to untreated controls, establishing piperine's baseline cytotoxicity on MM cells.

Results: The FT-IR spectrum was consistent with published piperine spectra, showing characteristic bands corresponding to aliphatic/aromatic C–H stretching, conjugated amide C=O, aromatic C=C, and C–O–C vibrations. estimated IC50 values were 120 µM and 100 µM at 24 and 48 hours, respectively. ANOVA confirmed that piperine significantly reduced cell viability compared to untreated controls, with consistent dose- and time-dependent cytotoxic effects.

Conclusion: This study shows that piperine significantly reduces MM cell viability in a dose- and time-dependent manner, supporting its potential as a natural adjunct. Establishing baseline cytotoxicity provides a basis for further evaluation of piperine as a less toxic complementary option that may help improve treatment tolerability. Further studies should investigate its mechanisms, selectivity against healthy cells, and synergy with established MM therapies.

keywords: Multiple myeloma; Piperine; black pepper; Treatment

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-139

In Vitro Evaluation of Folate-Receptor-Targeted Chitosan–PLGA Nanoparticles for Drug Delivery of Sodium Butyrate against Leukemia cell

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Background and aim: Acute lymphoblastic leukemia (ALL) presents therapeutic challenges due to drug resistance, high relapse rates, and off-target toxicity of conventional therapies. Sodium butyrate (NB), a potent HDAC inhibitor with established anti-leukemic activity, suffers from rapid systemic clearance and non-selective cytotoxicity. This study aimed to develop folic acid (FA)-functionalized chitosan-PLGA (FA-CS-P) nanocarriers for selective, controlled delivery of NB to NALM6 leukemia cells.

Methods: FA-CS-P nanocarriers were synthesized via EDC/NHS-mediated conjugation and characterized using FT-IR spectroscopy, dynamic light scattering (DLS), zeta potential, TEM, and TGA. Drug release kinetics were assessed in PBS at pH 5.0, 6.0, and 7.4. Cytotoxicity against NALM6 and HDF normal cells was evaluated by MTT assay at 100–400 nM over 24 and 48 hours. Apoptosis induction was quantified using Annexin V-FITC/PI flow cytometry.

Results: FT-IR and TGA confirmed successful synthesis, with an NB encapsulation efficiency of 16.08%. TEM revealed uniform spherical morphology, with a core size of 40–60 nm and a zeta potential of +34.2 ± 0.12 mV. NB release was pH-sensitive, with accelerated release under acidic conditions. FA-CS-P-NB reduced NALM6 viability to 26% and 15% at 400 nM after 24 and 48 hours, respectively (IC_{50}: 300 nM/24h; 200 nM/48h), while preserving HDF cell viability above 70%. Flow cytometry showed 22% apoptosis in treated leukemia cells, compared with only 5% with free NB.

Conclusion: FA-CS-P-NB nanocarriers provide selective, pH-responsive NB delivery with superior apoptosis induction in leukemia cells and minimal toxicity to non-malignant cells, warranting further in vivo investigation and potential clinical translation.

keywords: Acute lymphoblastic leukemia; Chitosan; PLGA; Folic Acid; Sodium Butyrate

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PH-140

In Vivo chimeric antigen receptor (CAR)-T Cell Therapy for Hematologic malignancy and Autoimmune disease: A Systematic Review of Efficacy and Safety

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Background and aim: In vivo chimeric antigen receptor (CAR)-T cell therapy enables endogenous T-cell reprogramming without ex vivo manufacturing, leukapheresis, or lymphodepleting chemotherapy, potentially overcoming logistical and accessibility barriers of conventional CAR-T platforms. Clinical evidence for this approach is emerging, yet no systematic synthesis exists.

Methods: A systematic search of PubMed, ClinicalTrials.gov, and congresses (including ASH, ASCO, EHA) was conducted through June 2026. Studies were eligible if they enrolled patients receiving in vivo-generated CAR-T cells and reported efficacy or safety outcomes.

Results: Five studies were identified. Disease indications included relapsed/refractory multiple myeloma (MM; 2 studies, n=23), B-cell non-Hodgkin lymphoma (B-NHL; 2 studies, n=15), and refractory systemic lupus erythematosus (SLE; 1 study). Studies were conducted in China (3/5) and the USA (2/5). All were early-phase, single-arm, and without lymphodepleting chemotherapy. Delivery platforms comprised lentiviral vectors (3/5) and lipid nanoparticle–encapsulated CAR mRNA (2/5). CAR targets included BCMA (2 studies), CD19 (2 studies), and dual CD19/CD20 (1 study). In MM, ORR was 80–100%; 14/14 evaluable patients in the largest cohort achieved MRD negativity at 10^{-5}. In B-NHL, ORR ranged from 50–100% across dose levels. In SLE, complete peripheral B-cell depletion and SLEDAI reductions of up to 20 points were documented. CRS was reported in all studies and was predominantly grade 1–2; ICANS occurred in ≤2 patients per study and was generally low-grade.

Conclusion: In vivo CAR-T cell therapy demonstrates proof-of-concept efficacy across hematologic malignancies and autoimmune disease, with an encouraging preliminary safety profile. Standardized prospective trials with longer follow-up are warranted.

keywords: In vivo CAR-T cell therapy, Chimeric antigen receptor, Multiple Myeloma

PI-1

Association between MASP2 gene polymorphisms and susceptibility to Covid-19 in Iranian patients: a case-control study

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Background and aim: Coronavirus disease 2019 (Covid-19) has emerged as a significant public health concern and is widespread across numerous nations. Recent studies have shown that genetic and host immune factors can influence the severity of Covid-19 disease. For example, research has shown that gene polymorphisms in inflammatory pathways and the complement system can play an important role in susceptibility to the disease and its progression. In the current study, we investigated the association between several functional polymorphisms of mannan-binding lectin serine protease 2 (MASP2) and susceptibility to Covid-19 in Iranian patients.

Methods: In this case-control study, a total of 100 patients with COVID-19 and 100 healthy individuals without a history of COVID-19 infection were included. The rs56392418, rs61735600, rs72550870, rs2273346, and rs12711521 polymorphisms of the MASP2 gene were genotyped using the sequence-specific polymerase chain reaction (SSP-PCR) technique in patients with Covid-19 infection as well as healthy individuals without a history of Covid-19 infection.

Results: Our analysis of genotype frequencies revealed a significant association between the rs2273346 single-nucleotide polymorphism (SNP) and susceptibility to Covid-19. Specifically, individuals carrying the TC + CC genotype had a markedly lower risk of infection (P = 0.020, odds ratio = 0.304; 95% confidence interval = 0.151–1.004). In contrast, no significant differences were observed for the rs56392418, rs61735600, rs72550870, and rs12711521 polymorphisms, as allele distributions were comparable between Covid-19 patients and healthy individuals (P 0.05).

Conclusion: These findings provide novel insights into the immunogenetic factors influencing susceptibility and response to Covid-19. Our findings also support this role, especially the rs2273346 polymorphism of the MASP2 gene. In addition to being crucial for comprehending the pathophysiology of Covid-19, this discovery is also critical for identifying high-risk communities and creating effective, population-specific preventative strategies to stop the virus's spread.

keywords: COVID-19, MASP2, PCR-SSP, Mannose-binding lectin

PI-2

Investigation of CXCL-8 levels in bronchoalveolar fluids of Bronchiectasis patients with ventilator associated pneumonia (VAP)

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Background and aim: Bronchiectasis is a chronic lung disease characterized by permanent widening of the airways, often caused by recurrent infections and inflammation. CXCL-8 (IL-8) is a powerful chemoattractant chemokine for neutrophils and plays a crucial role in airway inflammation and tissue damage. The importance of neutrophils and CXCL-8 in lungs of bronchiectasis patients is not well understood. Thus, in this study we aimed to investigate the relationship between CXCL-8 levels in BAL and serum and the occurrence and outcome of VAP in patients with bronchiectasis

Methods: In this prospective cohort study, 60 ICU patients diagnosed with VAP from Masih Daneshgar hospital, Tehran, Iran (June 2024-june 2025) were enrolled, including 35 with bronchiectasis and 25 without. BAL samples were collected using fiberoptic bronchoscopy, in the tubes and the CXCL-8 levels was measured by ELISA methods. Disease severity and prognosis were assessed using the Clinical Pulmonary Infection Score (CPIS) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring systems.

Results: CXCL-8 levels were significantly elevated in both bronchoalveolar lavage fluid (BALF) and serum of bronchiectasis patients when compared to non-bronchiectasis controls (p=0.002 and p=0.001, respectively). The bronchiectasis cohort exhibited elevated APACHE II scores and a notably higher mortality rate (p=0.012). A significant positive correlation was found between CXCL-8 levels and CPIS scores (r=0.62, p=0.004), suggesting increased inflammatory severity.

Conclusion: In bronchiectasis patients with VAP, heightened CXCL-8 levels correlate with intensified inflammation, increased disease severity, and a higher risk of mortality. Tracking CXCL-8 could be an effective biomarker for forecasting results in critically ill patients with bronchiectasis.

keywords: BAL, CXCL-8, VAP

PI-3

Differential Expression of Th17-Related Cytokines in Patients of Chronic Kidney Disease with and Without Systemic Lupus Erythematosus

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Background and aim: Dysregulation of immune cells and cytokines, particularly T helper 17 (Th17) cells and their associated cytokines, is implicated in the pathogenesis of both systemic lupus erythematosus (SLE) and chronic kidney disease (CKD). This study aimed to investigate the serum levels of Th17-related cytokines (interleukin [IL]-17A, IL-21, IL-22, and IL-23) in CKD patients with and without SLE and explore their potential role in disease progression.

Methods: A total of 118 participants were included, comprising 78 patients with CKD (stages 3–5) and 40 healthy controls. Cytokine levels were measured using enzyme-linked immunosorbent assay kits.

Results: Patients with CKD exhibited significantly lower IL-21 levels and higher IL-22 and IL-17A levels compared with controls, while patients with end-stage renal disease showed elevated IL-21 and IL-23 levels. Among SLE-negative nephrotic patients, IL-23 and IL-17A were significantly upregulated, whereas SLE-positive nephrotic patients had increased IL-22 and IL-17A levels. In addition, IL-21 and IL-17A were significantly correlated in patients with CKD, suggesting a potential immunoregulatory interplay.

Conclusion: In conclusion, these findings indicate that Th17-related cytokines are differentially expressed depending on CKD stage and SLE status, potentially influencing immune responses, inflammation, and kidney fibrosis. Understanding alterations of these cytokines may aid in identifying targeted therapeutic approaches, particularly for patients with CKD at risk of SLE-related complications.

keywords: Th17 cytokines, chronic kidney disease (CKD), systemic lupus erythematosus (SLE).

PI-4

Glycosylation in Vaccine Design: Advancing Immunity and Pathogen Targeting

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Background and aim: Glycosylation establishes a complex "sugar code" that regulates immunological recognition, serving both as a barrier against pathogens and as a significant activator of innate immunity. Leveraging this dual nature presents a distinctive opportunity for systematic vaccine development. This paper examines the processes of glycan-mediated immune activation and assesses how "glycoengineering" can be utilized to create next-generation vaccines with improved immunogenicity and wider protective characteristics.

Methods: We performed a narrative review of literature published from January 2000 to May 2024, sourced from the PubMed and Google Scholar databases. The search method concentrated on research that elucidates glycan-mediated immune regulation, innovations in expression systems for glycoprotein synthesis, and translational obstacles in glyco-vaccinology. Relevant data were amalgamated to furnish a thorough overview of the present landscape of the sector.

Results: Our data indicate that the targeting of C-type lectin receptors (CLRs), including Dectin-1 and Mincle, with specific glycan motifs elicits strong Th1/Th17 immunological responses. Progress in glycoengineering has facilitated the synthesis of specific glycoconjugates through designed prokaryotic systems (e.g., E. coli pgl pathways) and the detection of sterically protected epitopes using MALDI-TOF mass spectrometry. Moreover, mannose metabolism is recognized as a pivotal regulator of CD8+ T-cell development and memory. The selection of carrier protein, particularly the comparison of Tetanus Toxoid (TT) and CRM197, along with the application of innovative zwitterionic polysaccharide-lipid nanoparticle conjugates, demonstrates considerable promise in enhancing vaccine immunogenicity.

Conclusion: Notwithstanding these scientific advancements, the clinical application of glycan-based vaccines encounters considerable obstacles. Significant challenges encompass the intrinsic heterogeneity of glycoforms in large-scale production, the inadequacy of traditional predictive markers in clinical trials (as demonstrated by the MVA85A tuberculosis vaccine), and the influence of host genetic polymorphisms, including FUT2 secretor status, on vaccine effectiveness. Future tactics must consider these biological characteristics to fulfill the potential of broad-spectrum, "pan-bacterial" vaccinations and precision immunotherapies.

keywords: Glycosylation, Vaccines, Conjugate, Glycoconjugates, Immunotherapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-5

Hematological Complications in Familial Mediterranean Fever: A Case Report and Literature Review

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Background and aim: Familial Mediterranean fever (FMF), caused by mutations in the MEFV gene, typically presents with fever and inflammatory markers such as leukocytosis. However, some FMF patients develop hematologic complications, including leukopenia and neutropenia. This study reports a unique FMF case characterized by periodic, synchronized cytopenias and includes a literature review to broaden the known spectrum of FMF's hematologic manifestations.

Methods: This study combines a retrospective case report with a literature review. Clinical, laboratory, and genetic data for a 29-year-old patient were collected, with the diagnosis of Familial Mediterranean Fever (FMF) confirmed by whole-exome sequencing (WES), identifying a heterozygous MEFV P.Val726Ala mutation; a comprehensive search across four databases—PubMed, Web of Science, Scopus, and ProQuest—was conducted using keywords related to FMF and hematological abnormalities, and seventeen studies describing FMF cases with hematologic complications were selected for analysis.

Results: This patient experienced four years of recurrent episodes (every 2–3 months) characterized by fever, fatigue, and synchronized, severe cytopenias, including leukopenia (WBC 0.881/mm³), an absolute neutrophil count (ANC 361/mm³), and thrombocytopenia (55 × 10^3/μL); initial suspicion favored aplastic anemia. Daily colchicine therapy successfully controlled symptoms and stabilized blood cell fluctuations, eliminating the need for G-CSF. The literature review of 34 patients revealed leukopenia as the most frequent hematologic complication, occurring in 61.8% of cases.

Conclusion: Hematological manifestations in FMF are diverse, extending beyond the typical inflammatory increases. They can include periodic, simultaneous decreases in blood cell counts, suggesting an exaggerated regulatory response. FMF should be considered in patients presenting with fever and unexplained periodic cytopenias. Early diagnosis and effective colchicine treatment are essential for long-term disease control and for achieving hematologic stability.

keywords: Familial Mediterranean Fever; Hematological Manifestations; MEFV Gene; Neutropenia

PI-6

Revolutionizing Vaccine Design: T-Cell-Targeted Strategies against Selective Intracellular Bacteria

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Background and aim: Intracellular bacterial pathogens, including Mycobacterium tuberculosis, Listeria monocytogenes, Salmonella enterica serovar Typhi, Chlamydia trachomatis, Legionella pneumophila, Brucella species, and Coxiella burnetii, pose significant global health challenges due to immune evasion and intracellular persistence, necessitating vaccines that enhance T-cell immunity.

Methods: A review of literature from 2020 to 2025 was conducted using PubMed, Embase, ClinicalTrials.gov, and Google Scholar. Search terms targeted T-cell responses (CD4+, CD8+, memory T cells) and vaccine designs (mRNA, viral vectors, multi-epitope, reverse vaccinology) for the specified pathogens, focusing on original research, clinical trials, and in silico studies.

Results: CD4+ Th1/Th17 cells drive IFN-γ/IL-17-mediated macrophage activation, while CD8+ T cells mediate cytotoxicity, but immune evasion via MHC suppression and T-cell exhaustion limits efficacy. Current vaccines (e.g., BCG for Mtb, Q-Vax for C. burnetii) show 50% adult efficacy or reactogenicity. Novel platforms include mRNA vaccines for Mtb and Chlamydia (60–70% preclinical efficacy), viral vectors like ChAdOx1 boosting BCG (45% clinical protection), and bioinformatics-driven multi-epitope vaccines. Challenges include prime-boost interference and poor mucosal delivery.

Conclusion: Advanced vaccine platforms show promise in overcoming T-cell evasion, but clinical trials for mRNA/multi-epitope vaccines against Mtb and Chlamydia, alongside AI-driven epitope optimization for Legionella and Coxiella, are critical. Combining novel vaccines with checkpoint inhibitors may enhance T-cell immunity and population coverage, addressing gaps in controlling intracellular bacterial pathogens.

keywords: Intracellular Pathogens, mRNA Vaccines, Multi-Epitope Vaccines, T-Cell Immunity

PI-7

The Effect of Gut Microbiome Modulation on Immune Response in IBD and the Identification of Therapeutic Opportunities through Probiotics: A Systematic Review

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Background and aim: Chronic Inflammatory Bowel Diseases (IBD), including Crohn's and Ulcerative Colitis, are characterized by severe immune dysregulation and uncontrolled inflammation. Recent evidence (2020-2025) suggests that gut dysbiosis is a primary, targetable pathogenic factor in IBD. The aim of this review is to systematically analyze new findings concerning the mechanisms of immunomodulation resulting from microbiome modification and to evaluate the therapeutic potential of probiotic strains.

Methods: This was a systematic and analytical review based on searches of accredited scientific sources (Open Access) from both Persian and English databases covering the period 2020 to 2025. Inclusion criteria focused on articles linking dysbiosis to chronic inflammation and the application of probiotics (such as Lactobacillus and Bifidobacterium) in regulating the immune axis (specifically Th17/Treg). Data related to key molecular mechanisms, including the production of Short-Chain Fatty Acids (SCFAs), were collected and analyzed.

Results: Findings confirm that microbiome modulation via probiotics is an effective immunogenic strategy. * Molecular Immune Regulation: The most critical mechanism is through the production of SCFAs (primarily butyrate). SCFAs activate GPR receptors on immune cells, boosting the differentiation of naïve T lymphocytes into Regulatory T cells (Treg). This enhances the production of anti-inflammatory cytokines (like IL-10) and diminishes Th17 inflammatory responses. * Barrier Restoration: Specific probiotic strains enhance the integrity of the epithelial barrier by strengthening Tight Junction proteins, thereby reducing intestinal permeability ("Leaky Gut"). * Clinical Efficacy: The use of probiotics as Adjuvant therapy in clinical trials has been associated with reduced inflammation severity and improved clinical indices during the remission phase of Ulcerative Colitis.

Conclusion: Probiotics function as potent immune modularity agents and offer a significant opportunity for complementary treatment in IBD. They target not only microbial composition but also directly regulate immune balance through bioactive metabolites (SCFAs). The development of Next-Generation Probiotics (NGPs) and postbiotics interventions are promising future approaches. Further precise clinical trials are essential to identify optimal strains and dosages for achieving maximum efficacy.

keywords: Gut Microbiome, IBD, Probiotics, SCFAs, Treg Cells.

PI-8

The application of mRNA vaccines in the treatment of non-infectious diseases: cancer and allergy

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Background and aim: mRNA-based vaccine technology has transformed molecular medicine by enabling rapid immune response programming. It effectively prevents infectious diseases and treats complex immune-mediated disorders like cancer and allergies. This study explores mRNA vaccines as a therapeutic platform for generating strong anti-tumor immunity while promoting immune tolerance in allergies. It also examines advancements in genetic carriers, such as lipid nanoparticles (LNPs) and DNA nanogels (DNGs), which enhance RNA delivery and improve immune responses.

Methods: We conducted a narrative review of literature published from January 2018 to May 2024, sourcing articles from the PubMed and Google Scholar databases. We combined relevant data to provide a comprehensive overview of the current landscape in the sector. The studies reviewed were analyzed for their mechanisms of dendritic cell activation, T-cell polarization, antigen presentation efficiency, and overall immunological outcomes.

Results: Preclinical findings show that mRNA vaccines, when delivered effectively to antigen-presenting cells, stimulate strong cellular immunity. This involves robust dendritic cell activation and the expansion of cytotoxic CD8+ T cells, leading to significant tumor growth suppression in animal models, underscoring their potential as cancer immunotherapeutics. The delivery system's quality is crucial, with advanced carriers like LNPs and dendrimers enhancing mRNA stability, minimizing degradation, and reducing excess innate activation. Notably, DNGs offer advantages with their structural rigidity and programmable architecture, leading to improved protection of mRNA, controlled release, and better endosomal escape. mRNA vaccines enhance antigen production and improve immune responses, leading to stronger T-cell memory and increased effector cell avidity. In allergic disease models, they promote Th1 pathways over Th2, expand regulatory T-cells, and foster long-term tolerance, showcasing their versatility in different immunological contexts.

Conclusion: mRNA vaccines are an adaptable platform for customized immune responses in cancer immunotherapy and allergy desensitization. Advances in delivery technologies, particularly DNA nanogels, have improved RNA stability and reduced excessive innate immune activation, enhancing mRNA vaccine efficacy. While preclinical results are promising, further clinical studies are needed to evaluate long-term safety and optimize treatment strategies. Overall, mRNA vaccines hold great potential in precision medicine for targeted immune system modulation.

keywords: mRNA vaccine, cancer immunotherapy, allergy tolerance, DNA nanogel, dendrimers

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-9

Update Considering the White Blood Cells Cross-Matching Staining Slides for Kidney Pre-Transplantation

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Background and aim: Background: Pre-transplantation cross-matching is critical for minimizing graft rejection in kidney transplantation. Traditional methods, such as complement-dependent cytotoxicity (CDC), face challenges in sensitivity and standardization. This study updates a staining-based cross-match protocol using peripheral blood mononuclear cells (PBMCs) from brain-dead donors, enhancing practicality for clinical decision-making. Aim: To evaluate a modified cross-matching technique that quantifies PBMC viability after exposure to recipient sera, rabbit complement, and eosin dye, providing a binary (yes/no) agreement for kidney selection.

Methods: Methods: PBMCs were isolated from 90 brain-dead donors via Ficoll gradient centrifugation in Khorshid University hospital, Transplantation Lab. Cells were incubated with recipient sera, rabbit complement, and eosin dye. Viability was assessed microscopically: dead cells (eosin-stained) and live cells (unstained) were counted to calculate percentage cytotoxicity. We assume a predefined threshold (e.g., 10% eosin-stained cells speculated incompatibility) determined transplantation suitability ("yes" for compatible, "no" for incompatible).

Results: Results: This PBMC-based staining assay offers a rapid, cost-effective alternative for pre-transplant cross-matching, particularly valuable in brain-dead donor scenarios. It balances sensitivity with operational simplicity, though threshold calibration may improve reliability.

Conclusion: Discussion: The method demonstrated high reproducibility, by comparing with other research in the world 85% of tests yielding clear yes/no agreements. Cytotoxicity percentages correlated strongly with clinical outcomes, reducing false negatives compared to standard CDC. Based on other studies discrepancies arose in 12% of cases, primarily due to low antibody titers, highlighting the need for optimized thresholds.

keywords: Transplantation; CDC; WBC cross-match;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-10

CD8+ T Cell–Derived Exosomes as Modulators of Tumor Progression and Antitumor Immunity: A Systematic Review

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Background and aim: Cancer progression is strongly influenced by the tumor microenvironment (TME), where immune cell–derived extracellular vesicles play a critical role in intercellular communication. Among these, exosomes released from CD8+ cytotoxic T lymphocytes have emerged as key regulators of antitumor immunity. While CD8+ T cells are well known for their direct cytotoxic activity, the functional significance of CD8+ T cell–derived exosomes (CD8+T-Exos) remains incompletely understood. This systematic review aimed to evaluate the cytotoxic and immune-regulatory roles of CD8+T-Exos in cancer, with particular emphasis on their molecular cargo, mechanisms of action, and therapeutic potential.

Methods: A systematic literature search was conducted in PubMed, Scopus, Embase, and Google Scholar according to PRISMA guidelines. Eligible studies included English-language animal and human investigations assessing CD8+T-Exos in cancer models. Reviews, in vitro-only studies, and articles lacking full text were excluded. Data extraction was independently performed by multiple reviewers, focusing on exosome isolation methods, molecular characterization, and biological effects on tumor cells and immune responses.

Results: From 1,057 identified records, seven studies met the inclusion criteria. Ultracentrifugation was the primary isolation technique, with transmission electron microscopy, flow cytometry, nanoparticle tracking analysis, and western blotting used for characterization. CD8+T-Exos consistently expressed canonical exosomal markers (CD9, CD63, CD81, TSG101) alongside T-cell–specific proteins (CD3, CD8, TCR). Functionally, most studies demonstrated that CD8+T-Exos exert antitumor effects by inhibiting cancer cell proliferation, migration, and metastasis through delivery of cytotoxic proteins (granzyme B, perforin) and regulatory microRNAs such as miR-298-5p and miR-765. Additionally, CD8+T-Exos enhanced antitumor immunity by promoting activation of low-affinity CD8+ T cells and increasing IFN-γ production. However, context-dependent pro-tumor effects were also reported, particularly via Fas/FasL signaling, which in certain models enhanced tumor invasion and immune evasion.

Conclusion: CD8+T cell–derived exosomes exhibit dual and context-dependent roles in cancer, functioning as potent mediators of cytotoxicity and immune modulation while occasionally facilitating tumor progression. Their ability to penetrate tumor tissue, carry bioactive cargo, and be engineered for targeted delivery highlights their promise as biomarkers and therapeutic agents. Further standardized and translational studies are required to optimize their clinical application and minimize adverse immune effects.

keywords: CD8+ T cells; Exosomes; Cancer immunotherapy; Tumor microenvironment; Immune regulation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-11

Immunomodulatory Effects of Neural Stem Cell Transplantation in Spinal Cord Injury: A Systematic Review of Preclinical Evidence

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Background and aim: Spinal cord injury (SCI) leads to persistent neurological deficits largely driven by secondary inflammatory responses. Although inflammation initially supports tissue repair, its prolonged activation exacerbates neuronal damage and impairs functional recovery. Neural stem cells (NSCs) have gained attention as a therapeutic strategy due to their capacity to modulate the inflammatory microenvironment in addition to their regenerative potential. This systematic review aimed to evaluate preclinical evidence on the immunomodulatory effects of NSC transplantation in SCI and to identify factors influencing therapeutic efficacy.

Methods: A systematic search of PubMed, Scopus, and Web of Science was conducted for studies published up to August 2025, following PRISMA guidelines. Eligible studies included in vivo preclinical investigations using rodent SCI models that evaluated inflammatory outcomes following NSC transplantation. Data were extracted on injury models, NSC source and delivery, timing of intervention, inflammatory markers, and functional outcomes. Study quality was assessed using standardized preclinical appraisal tools, and results were narratively synthesized due to methodological heterogeneity.

Results: Ten studies met the inclusion criteria, predominantly utilizing rat or mouse contusion or compression models at thoracic spinal levels. NSC transplantation consistently attenuated inflammatory responses, with approximately 70% of studies reporting significant reductions in pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Several studies demonstrated a shift in macrophage/microglia polarization toward an anti-inflammatory M2 phenotype, characterized by increased expression of markers including CD206 and arginase-1. These effects were most pronounced when NSCs were administered during the acute or subacute phases of injury. Enhanced immunomodulatory outcomes were observed when NSCs were genetically modified (e.g., Wnt4 or E-cadherin expression), preconditioned, or delivered using biomaterial scaffolds such as hydrogels. Importantly, reduced inflammation was frequently associated with improved histological repair and functional recovery, including better locomotor performance.

Conclusion: Preclinical evidence indicates that NSC transplantation effectively modulates neuroinflammation after SCI by suppressing pro-inflammatory pathways and promoting anti-inflammatory immune phenotypes. Optimization strategies, including timing of delivery, genetic enhancement, and biomaterial-assisted transplantation, substantially improve therapeutic outcomes. These findings support the translational potential of NSC-based immunomodulatory therapies for SCI, while highlighting the need for standardized models and further studies in chronic injury settings.

keywords: Spinal cord injury; Neural stem cells; Immunomodulation; Regenerative therapy

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PI-12

Pyrimethamine Enhances the Immune Responses of RAW264.7 Macrophages Against Leishmania major

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Background and aim: Background: Leishmania major, an intracellular protozoan, is the primary cause of cutaneous leishmaniasis (CL). Although polyvalent antimony compounds are commonly used to treat CL, treatment failure is frequent. Immunometabolic reprogramming of macrophages—the main host cells for L. major—toward the M1 phenotype may inhibit parasite growth. Pyrimethamine, an antimalarial antibiotic, inhibits dihydrofolate reductase (DHFR), affecting both host and parasite metabolism. Since pyrimethamine interferes with the folate pathway and phagocytosis in L. major, this study investigated its effect on key immunometabolites in infected macrophages.

Methods: Materials and Methods: RAW264.7 macrophages were divided into six groups: Sham, L. major infected, LPS-stimulated, pyrimethamine-treated (L. major+pyrimethamine, LPS+pyrimethamine), and pyrimethamine alone (5 µg/mL for 24 hours). Supernatants and cells were collected to measure lactate, nitric oxide (NO), reactive oxygen species (ROS), infection rate and index, as well as cytokine concentrations.

Results: Results: Pyrimethamine significantly increased intracellular ROS and NO levels in L. major-infected macrophages ($P \leq 0.05$), correlating with a significant reduction in infection rate and index ($P \leq 0.05$). TNF-α production was also significantly elevated in pyrimethamine-treated groups. However, no significant change in lactate concentration was observed.

Conclusion: Conclusion: Pyrimethamine enhances the immunometabolic response of macrophages against L. major by increasing ROS, NO, and TNF-α levels. These changes contribute to a reduced infection rate and lower macrophage infection index, suggesting pyrimethamine's potential as an immunomodulatory agent in leishmaniasis treatment.

keywords: Leishmania major, Macrophage, Immunometabolism, Pyrimethamine

PI-13

The Role of MicroRNAs in Regulating Human Immune and Inflammatory Responses During SARS-CoV-2 Infection

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Background and aim: Dysregulated immune and inflammatory responses play a significant role in the severity of COVID-19. Increased levels of cytokines like IL-6, IL-8, and TNF-α contribute to the cytokine storm and systemic inflammation associated with the disease. Recent research has shown that microRNAs (miRNAs)—small non-coding RNAs that regulate gene expression after transcription—are important modulators of these immune pathways during SARS-CoV-2 infection. This study aims to summarize and analyze the role of host miRNAs in modulating innate immune responses and inflammatory cytokine signaling, specifically the TNF-α and NF-κB pathways, during COVID-19.

Methods: A comprehensive literature review was performed using the PubMed, Scopus, and Web of Science databases to identify studies on changes in miRNA expression during SARS-CoV-2 infection and their effects on cytokine regulation and immune signaling pathways

Results: Several microRNAs (miRNAs) including miR-31-5p, miR-155, miR-146a, miR-21, miR-223, and miR-2392 have been found to significantly influence cytokine production and inflammatory signaling. MiR-31-5p and miR-27a-5p were upregulated in COVID-19 patients, suggesting that they play a role in the feedback regulation of TNF-α-induced inflammation. MiR-146a and miR-21 modulate the NF-κB and MAPK pathways, helping to maintain a balance between pro-inflammatory and anti-inflammatory cytokines. Conversely, a decrease in miR-766-3p expression was associated with increased levels of IL-6. These findings indicate that SARS-CoV-2 infection induces a distinct host miRNA signature that can influence immune dysregulation and the severity of the disease.

Conclusion: Host miRNAs are essential regulators of inflammatory and antiviral pathways in COVID-19. Their altered expression profiles may serve as predictive biomarkers and potential therapeutic targets for modulating the cytokine storm and improving patient outcomes.

keywords: microRNA, cytokine storm, TNF-α, NF-κB, inflammation, COVID-19, SARS-CoV-2, immune regulation

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July 20-23, 2026

PI-14

Chemokine CCL2 and its receptor CCR2 in different age groups of patients with COVID-19

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Background and aim: Despite the development of various antiviral drugs, most of them are not effective in the treatment of coronavirus disease 2019 (COVID-19) as a hyperinflammatory disorder. Chemokine (C-C motif) ligand 2 (CCL2) is one of the critical CC chemokines involved in the pathogenesis and severity of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. This study aimed to investigate the expression of CCL2 and CC chemokine receptor 2 (CCR2) in COVID-19 patients.

Methods: Peripheral blood samples were collected from 60 confirmed COVID-19 patients and 60 age-matched healthy subjects. The ages of the subjects were categorized as follows: up to 20 years, 20 to 40 years, 40 to 60 years, and more than 60 years. CCL2 serum levels were measured using the enzyme-linked immunosorbent assay (ELISA). CCR2 gene expression in peripheral blood mononuclear cells (PBMCs) was measured employing real-time polymerase chain reaction (PCR).

Results: In all age groups, CCL2 serum levels were significantly elevated in patients compared to healthy controls (P0.0001). CCL2 levels were higher in severe patients than in moderate patients. Moreover, CCR2 expression by PBMCs was higher in patients compared to control subjects. However, a significant difference between patients and controls over 60 years of age was identified (P=0.0353). There was no significant difference in CCR2 expression between moderate and severe COVID-19 patients.

Conclusion: Taken together, the findings demonstrate that CCL2 and CCR2 are upregulated in COVID-19 patients at protein and mRNA levels, respectively. Therefore, the CCL2/CCR2 axis may be a potential therapeutic target in order to improve patient outcomes.

keywords: CCL2, CCR2, COVID-19, SARS-CoV-2 infection, Chemokine

PI-15

Lack of Correlation Between the CCR5-D32 Mutation and Acute Myeloid Leukemia in Iranian Patients

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Background and aim: Chemokines and their receptors are crucially important in the pathogenesis of acute myeloblastic leukemia (AML). The CC chemokine receptor 5 (CCR5) is a specific chemokine receptor for CC chemokine ligand 3 (CCL3), CCL4 and CCL5 which all play key roles in identifying cancer properties and localization of leukemia cells. It has been demonstrated that the known mutation in CCR5 gene (CCR5-D32) leads to mal-expression of the receptor and affect its function. The aim of this study was to determine the rate of CCR5-D32 mutation within Iranian AML patients

Methods: In this study, blood samples were obtained from 60 AML patients and 300 healthy controls. The CCR5-D32 mutation was evaluated using Gap-PCR technique.

Results: Our results showed that CCR5-D32 mutation was not found in the patients, while three out of the controls had hetrozygotic form of this mutation. The rest of studied samples had the wild form of the gene. According to these findings, it can probably be concluded that the CCR5-D32 is not associated with susceptibility to AML in Iranian patients.

Conclusion: This study investigated the role of the CCR5-D32 mutation in the pathogenesis of acute myeloid leukemia (AML) among Iranian patients. While CCR5 and its ligands (CCL3, CCL4, CCL5) are known to influence leukocyte activation, proliferation, and AML progression, results showed no association between CCR5-D32 and AML susceptibility. The findings suggest that other genetic and epigenetic factors—such as polymorphisms, methylation, acetylation, or microRNA regulation—may contribute instead. This is the first report on CCR5-D32 in AML among Iranians, highlighting the need for broader studies in diverse ethnic groups to clarify its role.

keywords: CCR5-D32 mutation Acute myeloblastic leukemia Chemokine

PI-16

Thymoquinone improves experimental autoimmune encephalomyelitis by regulating both pro-inflammatory and anti-inflammatory cytokines

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Background and aim: Multiple sclerosis (MS) is an autoimmune condition marked by inflammation and the loss of myelin in the central nervous system (CNS). The aim of this research was to understand how Thymoquinone regulate the molecular and cellular processes involved in controlling experimental autoimmune encephalomyelitis (EAE), which is an animal model often used to study MS.

Methods: Female C57BL/6 mice were split into different groups receiving different doses (low, medium, and high) of Thymoquinone simultaneously with EAE induction. Clinical scores and other measurements were observed daily throughout the 25-day post immunization. We assessed lymphocyte infiltration and demyelination in the spinal cord through histological staining, analyzed T-cell profiles using ELISA, and quantified the expression levels of transcription factors in the CNS using Real-time PCR.

Results: Thymoquinone prevented the development of EAE. Histological experiments revealed only a small degree of leukocyte infiltration into the CNS. Thymoquinone resulted in a notable reduction in the generation of IFN-γ, IL-17, and IL-6, while simultaneously increasing the production of IL-4, IL-10, and TGF-β in Th2 and Treg cells. Results from Real-time PCR suggested Treatment with Thymoquinone decreased the expression of T-bet and ROR-γt while increasing the expression of Foxp3 and GATA3.

Conclusion: findings showed that Thymoquinone could decrease both disease incidence and severity.

keywords: Multiple sclerosis · Experimental autoimmune encephalomyelitis · Central nervous system

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PI-17

Dysregulation of Key Biological Processes in Endometriosis Pathophysiology

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Background and aim: Endometriosis is a disorder of the female reproductive system characterized by endometrium-like tissue outside the uterus. Although its etiology remains unclear, key contributing factors include dysregulation of cellular and molecular pathways, such as enzyme activity, exosome function, hormonal balance, apoptosis, angiogenesis, oxidative stress, epigenetics, and cytokine/chemokine signaling, which together influence disease onset and progression.This knowledge can provide a broader perspective on the onset and progression of endometriosis.

Methods: This narrative review is based on a comprehensive search of biomedical databases, including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar, covering studies published between 1976 and 2025. Keywords such as “endometriosis,” “pathophysiology,” “enzyme dysregulation,” “exosomes,” “hormonal imbalance,” “apoptosis,” “angiogenesis,” “oxidative stress,” “epigenetic dysregulation,” “cytokines,” and “chemokines” were used. Priority was given to original research articles, clinical trials, meta analyses, and molecular studies. Although no formal inclusion criteria were applied, studies were selected based on relevance and scientific quality to outline current insights into the dysregulated biological processes involved in endometriosis.

Results: This review demonstrated that the pathogenesis of endometriosis results from the dysregulation of a network of key signaling pathways, including NF-κB, MAPK, PI3K/Akt, TGF-β, and Wnt/β-catenin, leading to chronic inflammation, oxidative stress, immune dysfunction, abnormal angiogenesis, resistance to apoptosis, and fibrosis. In addition, hormonal imbalance and the induction of neuroangiogenesis contribute to increased cellular proliferation, survival, and invasiveness, ultimately resulting in chronic pain. Collectively, these findings indicate that endometriosis is a complex, multisystem molecular disease that requires targeted and multi-modal therapeutic strategies.

Conclusion: This review demonstrated that the pathogenesis of endometriosis results from the dysregulation of a network of key signaling pathways, including NF-κB, MAPK, PI3K/Akt, TGF-β, and Wnt/β-catenin, leading to chronic inflammation, oxidative stress, immune dysfunction, abnormal angiogenesis, resistance to apoptosis, and fibrosis. In addition, hormonal imbalance and the induction of neuroangiogenesis contribute to increased cellular proliferation, survival, and invasiveness, ultimately resulting in chronic pain. Collectively, these findings highlight endometriosis as a complex, multi-pathway disease that may benefit from AI-assisted targeted therapies.

keywords: Pathophysiology ; Endometriosis ; Therapeutic targets ; Dysregulation ; Etiology

PI-18

Dysregulation of Follicular Fluid Levels of BAX and BCL-2 in Infertile Women with Endometriosis

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Background and aim: Endometriosis is a chronic gynecological disorder affecting 10–20% of women of reproductive age and is a major cause of infertility. Impaired apoptosis and prolonged survival of ectopic endometrial cells are considered key mechanisms in disease progression. BAX and BCL-2 are major regulators of the intrinsic apoptotic pathway, and an imbalance between these markers may promote cell persistence, particularly in advanced stages. This study aimed to assess follicular fluid levels of BAX and BCL-2 in infertile women with endometriosis and evaluate their association with disease severity.

Methods: This case–control study included 80 infertile women (20–40 years) undergoing Intracytoplasmic Sperm Injection (ICSI). The participants comprised 40 women with endometriosis and 40 controls. Follicular fluid samples were obtained during oocyte retrieval, centrifuged, and stored at −80°C. BAX and BCL-2 concentrations were measured using ELISA.

Results: Endometriosis patients showed significantly lower BAX and higher BCL-2 concentrations in follicular fluid compared with controls (p 0.05). According to the American Society for Reproductive Medicine (ASRM) classification, 25 patients were in stages I–II and 15 in stages III–IV. Although not statistically significant, advanced-stage disease showed a trend toward higher BCL-2 expression and a reduced BAX/BCL-2 ratio, suggesting increased cellular survival.

Conclusion: Altered concentrations of apoptotic markers BAX and BCL-2 in follicular fluid may contribute to reduced apoptosis and enhanced cell survival in endometriosis. These changes, particularly in advanced stages, may influence disease progression and the microenvironment of oocyte maturation, contributing to infertility.

keywords: Endometriosis; Infertility; BAX Protein; BCL-2 Protein; Follicular Fluid

PI-19

The role of leukemia inhibitory factor in autoimmune disorders: insights into recovery and treatment

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Background and aim: Leukemia inhibitory factor (LIF) is a multifunctional cytokine involved in numerous physiological processes, including inflammation and immune response regulation. Recent studies have highlighted its potential role in the pathogenesis and treatment of autoimmune diseases such as rheumatoid arthritis (RA) and multiple sclerosis (MS). This review aims to investigate the role of LIF in various autoimmune disorders and its impact on the recovery and treatment of these diseases.

Methods: A comprehensive literature search was conducted using Google Scholar, PubMed, and Scopus databases. Relevant studies published up to December 2023 were identified using keywords such as “leukemia inhibitory factor”, “autoimmune diseases”, “rheumatoid arthritis” and “multiple sclerosis”.

Results: The literature indicates that LIF has a dual role in autoimmune diseases. In RA, LIF plays an important role in the progression of joint damage by increasing the inflammatory response. In MS, LIF has been shown to promote remyelination and neuroprotection, suggesting its potential as a therapeutic agent. However, the precise mechanisms by which LIF modulates immune responses in these conditions remain incompletely understood.

Conclusion: LIF represents a promising target for treating autoimmune diseases, particularly RA and MS. Further research is required to elucidate its mechanisms of action and develop targeted therapies that can control its beneficial effects while minimizing potential adverse outcomes.

keywords: leukemia inhibitory factor, autoimmune diseases, rheumatoid arthritis, multiple sclerosis.

PI-20

High Serum Levels of TGF-β in Iranians With Chronic HBV Infection

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Background and aim: The transforming growth factor-β (TGF-β) is an important cytokine with anti-inflammatory properties. The main purpose of this study was to compare the serum levels of TGF-β in a group of chronic HBV-infected (CHB) patients, as well as healthy individuals from South-East of Iran.

Methods: Sixty patients with CHB as well as sixty healthy individuals were enrolled in the study. ELISA technique was applied to measure the serum levels of TGF-β in both groups.

Results: Our results revealed that the serum levels of TGF-β were significantly increased in CHB patients in compare to healthy controls.

Conclusion: According to this result, it may be concluded that high serum levels of TGF-β may be a mechanism by which immune response against HBV is suppressed.

keywords: Hepatitis B, Chronic Transforming Growth Factor Beta

PI-21

The Role of Gut Microbiota in Modulating Immune Responses to Bacterial Infections: A Study on Escherichia coli and Host Immunity

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Background and aim: The human gut microbiota plays a crucial role in shaping the immune system, influencing both innate and adaptive responses to pathogens. Dysbiosis, or imbalance in microbial composition, has been linked to increased susceptibility to bacterial infections such as those caused by Escherichia coli (E. coli). This study investigates how specific gut bacteria modulate immune evasion mechanisms during E. coli infection, providing insights into potential therapeutic targets in bacteriology and immunology. Previous research indicates that commensal bacteria can enhance or suppress cytokine production, but the precise interactions remain underexplored in controlled models.

Methods: We utilized a murine model (C57BL/6 mice, n=30) divided into three groups: (1) control with normal microbiota, (2) antibiotic-treated to induce dysbiosis, and (3) probiotic-supplemented with Lactobacillus spp. Mice were infected intraperitoneally with a virulent strain of E. coli (O157:H7, 10^6 CFU). Immune responses were assessed via ELISA for cytokines (IL-6, TNF-α, IL-10), flow cytometry for T-cell activation (CD4+/CD8+ markers), and qPCR for gene expression of Toll-like receptors (TLRs). Bacterial load was quantified by colony-forming unit (CFU) assays in spleen and liver tissues. Data were analyzed using ANOVA with p0.05 considered significant.

Results: In the dysbiotic group, E. coli infection led to significantly higher bacterial loads (mean CFU: 5.2 × 10^7 in spleen) compared to controls (2.1 × 10^6, p=0.002). Cytokine levels showed elevated pro-inflammatory responses (IL-6: 450 pg/mL vs. 180 pg/mL in controls, p0.01), but reduced anti-inflammatory IL-10 (120 pg/mL vs. 320 pg/mL, p=0.005). Probiotic supplementation restored microbiota balance, reducing bacterial loads by 45% and normalizing T-cell activation (CD4+ increase from 15% to 28%, p=0.01). TLR-4 expression was upregulated in probiotic-treated mice, enhancing pathogen recognition.

Conclusion: This study demonstrates that gut microbiota composition critically influences immune responses to E. coli infections, with dysbiosis exacerbating bacterial persistence and inflammation. Probiotic interventions may offer a novel strategy to bolster host immunity against bacterial pathogens, highlighting the interplay between bacteriology and immunology for future clinical applications.

keywords: Gut microbiota, Escherichia coli, Immune response, Dysbiosis, Probiotics, Cytokines, Bacterial

PI-22

Exosome-Based Targeted Delivery of miR-145 Augments Therapeutic Outcomes in in Vitro NSCLC

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Background and aim: Exosomes have gained considerable attention as efficient nanoscale delivery systems for bioactive molecules, including microRNAs. Tumor-derived exosomes (Tex) not only function as natural carriers for miRNAs but also harbor tumor-associated proteins and antigens that can potentially elicit antitumor immune responses. The present study aimed to investigate the antitumor effects of miR-145–enriched Tex (Tex–miR-145) as a novel in vitro strategy to induce antitumor immune activity.

Methods: The expression level of miR-145 was evaluated in the human lung cancer cell line A549 and the normal lung epithelial cell line MRC-5. Both cell lines were cultured, and tumor-derived exosomes were isolated using a commercial extraction kit. Exosomes were subsequently loaded with miR-145 and delivery efficiency was confirmed by quantitative real-time PCR. Cell viability was assessed using the MTT assay following treatment with various concentrations of Tex–miR-145 and unloaded Tex at 24- and 48-hour time points. Apoptosis induction was analyzed using Annexin V/PI flow cytometry. Additionally, transwell assays were performed to evaluate the effects of Tex–miR-145 on tumor cell migration and invasion. The clonogenic potential of treated tumor cells was assessed using a colony formation assay.

Results: In vitro analysis revealed that miR-145 expression was significantly downregulated in A549 lung cancer cells compared with normal MRC-5 cells. Following exosome loading and treatment, real-time PCR confirmed successful delivery of miR-145 into tumor cells via Tex–miR-145. MTT assay results demonstrated a significant reduction in tumor cell proliferation in the Tex–miR-145–treated group compared with control and Tex-only groups, particularly at a concentration of 25 µg/mL after 48 hours. Flow cytometric analysis showed a marked increase in apoptotic cell populations in Tex–miR-145–treated cells relative to Tex and untreated controls. Furthermore, transwell assays revealed a significant decrease in tumor cell migration and invasion following Tex–miR-145 treatment. Consistently, colony formation assays indicated a substantial reduction in the clonogenic capacity of tumor cells exposed to Tex–miR-145 compared with control groups.

Conclusion: Tumor-derived exosomes effectively deliver miR-145 to lung cancer cells, significantly enhancing antitumor activity by inducing apoptosis and suppressing tumor growth and invasiveness in vitro, highlighting Tex–miR-145 as a promising therapeutic strategy for lung cancer.

keywords: Tumor-derived exosomes, miR-145, NSCLC, A-549 cell line, anti-tumor responses

PI-23

Contribution of Novel Inflammatory Markers to Predicting the Severity of Infectious Diseases

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Background and aim: Infections like COVID-19 and tuberculosis (TB) trigger strong immune responses and marked inflammation. Recent research emphasizes new biological markers for prognosis. Systemic inflammation markers include neutrophil/lymphocyte ratio (NLR), systemic immune-inflammation index (SII), prognostic nutritional index, and C-reactive protein. Emerging markers are the “molecular degree of perturbation” and specific pro-inflammatory cytokines such as interferon-alpha, interferon-beta, TNF-alpha, IL-17A, and IL-1 beta. These markers are promising for predicting the severity of TB and other infectious diseases, providing valuable insights into immune response and disease outcomes.

Methods: This study focused on the role of novel inflammatory markers in predicting the severity of infectious diseases, particularly COVID-19 and TB. A comprehensive search was conducted in databases such as PubMed, Scopus, SID, IranDoc, MagIran, and Google Scholar, using keywords including "inflammatory markers," "infectious diseases," "COVID-19," "tuberculosis," "NLR," "SII," "PNI," "cytokines," and "molecular degree of perturbation." Original research articles and review studies assessing systemic inflammatory indices, cytokine profiles, or molecular degree of perturbation in infected patients were included. Cross-sectional or cohort studies comparing patients with varying disease severities or healthy controls were eligible. Data were qualitatively synthesized regarding the diagnostic and prognostic relevance of these markers, with emphasis on their association with disease severity, immune dysregulation, and clinical outcomes.

Results: Several novel inflammatory markers—including NLR, SII, PNI, C-reactive protein–based ratios, and lymphocyte-to-HDL cholesterol ratio—are linked to disease severity and adverse outcomes in infectious diseases like COVID-19 and TB. Some outperform traditional indices in diagnostic accuracy. In TB, elevated proinflammatory cytokines correlate with severity, bacterial load, and delayed culture conversion. Network analyses identify IFN-α, IFN-β, IL-1 receptor I, and TNF-α as central to systemic inflammatory perturbation, highlighting their combined value as biomarkers.

Conclusion: Inflammatory biomarkers are valuable adjuncts for determining infection severity and progression. While NLR remains a useful biomarker, others such as cytokine profiles, lymphocyte-to-HDL ratio, and molecular degree of perturbation provide deeper insights into immune system imbalance and infection prognosis. These biomarkers may also become effective, cost-efficient alternatives to current infection indicators.

keywords: Novel inflammatory markers Predicting severity Infectious diseases Disease severity

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PI-24

Cytokine and Epigenetic Signatures of Immune Dysregulation in Mild and Severe Chronic Obstructive Pulmonary Disease

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Background and aim: Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory airway disorder characterized by persistent airflow limitation and systemic immune dysregulation. Beyond environmental risk factors, emerging evidence highlights the contribution of epigenetic mechanisms in sustaining chronic inflammation and disease progression. Cytokine imbalance plays a central role in COPD severity; however, the relationship between cytokine expression, secretion, and promoter methylation remains insufficiently defined. This study aimed to investigate immune and epigenetic alterations in mild and severe COPD by analyzing cytokine profiles and their promoter methylation status in peripheral blood mononuclear cells (PBMCs).

Methods: In this non-interventional applied-basic study, PBMCs were isolated from 90 participants, including patients with mild COPD (n=30), severe COPD (n=30), and healthy controls (n=30). Gene expression of pro- and anti-inflammatory cytokines was assessed using quantitative real-time PCR, with GAPDH as the internal control. Cytokine secretion levels were measured by ELISA. Promoter methylation status of selected cytokine genes was evaluated using bisulfite conversion followed by methylation-specific PCR. Statistical analyses were performed using GraphPad Prism, and group comparisons were considered significant at p 0.05.

Results: Compared with healthy controls, COPD patients exhibited significant upregulation of pro-inflammatory cytokines, including IL-1β, IL-6, IL-18, IFN-γ, and TNF-α, at both transcript and protein levels. These alterations were more pronounced in patients with severe COPD. In contrast, anti-inflammatory cytokines IL-10 and TGF-β showed reduced gene expression and secretion, with the greatest decline observed in severe disease. Promoter methylation analysis revealed a reciprocal epigenetic pattern: pro-inflammatory cytokine genes demonstrated significant hypomethylation, whereas anti-inflammatory cytokine genes exhibited hypermethylation in COPD patients. Importantly, the degree of methylation changes correlated with disease severity, distinguishing mild from severe COPD. These immune and epigenetic alterations collectively reflected a shift toward a hyper-inflammatory and hypo-regulatory immune phenotype.

Conclusion: The findings indicate that COPD progression is associated with coordinated immune and epigenetic dysregulation in circulating immune cells. A severity-dependent cytokine imbalance, reinforced by directional changes in promoter methylation, appears to perpetuate chronic inflammation in COPD. Integrating cytokine expression, secretion, and methylation signatures may enhance disease endotyping, prognostic stratification, and personalization of anti-inflammatory or epigenetic-based therapeutic strategies.

keywords: Chronic obstructive pulmonary disease; Cytokines; DNA methylation; Inflammation; Epigenetics

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PI-25

Clinical Significance of TIGIT Expression for Prognosis of Breast Cancer: A Systematic Review

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Background and aim: Breast cancer remains a leading cause of cancer-related mortality worldwide, with its prognosis heavily influenced by tumor subtype and immune microenvironment. Increasing evidence highlights immune checkpoint pathways as key regulators of tumor–immune interactions and clinical outcomes. Among these, TIGIT, an immune checkpoint receptor, has emerged as a critical regulator of immune responses in cancer. This study aimed to synthesize current evidence on the clinical and prognostic significance of TIGIT expression in breast cancer.

Methods: A systematic search of Web of Science, PubMed, Scopus, Embase, and Google Scholar was conducted up to December 2025. Eligible studies included human investigations assessing TIGIT expression in breast cancer and its associations with clinicopathological features and prognostic outcomes.

Results: Across 18 studies, TIGIT expression was consistently dysregulated in breast cancer, with significant associations to tumor aggressiveness, immune contexture, and clinical outcomes. Most transcriptomic and immunohistochemical analyses revealed upregulation of TIGIT in breast tumors, particularly in triple-negative, basal-like, and HER2-enriched subtypes, compared to normal tissue. High TIGIT expression correlated with adverse clinicopathological features, including advanced stage, high tumor grade, and elevated Ki-67 index. Immunologically, TIGIT expression aligned with immune-inflamed tumor microenvironments, characterized by increased infiltration of $CD8^+$ T cells, cytotoxic lymphocytes, NK cells, B cells, macrophages, and dendritic cells. TIGIT levels were also associated with other immune checkpoints such as PD-1, PD-L1, LAG-3, and TIM-3, indicating an exhausted yet active immune state. Prognostic associations were variable. Several studies linked high TIGIT expression to improved disease-free and overall survival, particularly in TNBC and luminal B subtypes. Conversely, other studies found neutral or adverse effects, influenced by tumor subtype and immune context.

Conclusion: The findings support the value of TIGIT as a complementary prognostic and predictive biomarker and provide a compelling rationale for its integration into immune-based stratification models and the development of precision immunotherapeutic strategies in breast cancer

keywords: TIGIT, T-cell immunoreceptor, Immune checkpoint, Breast cancer, Prognosis

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July 20-23, 2026

PI-26

Efficacy and Immunological Impact of Low-Dose Interleukin-2 on Treg Homeostasis in Steroid-Refractory Chronic Graft-versus-Host Disease: A Systematic Review

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Background and aim: Chronic graft-versus-host disease (cGVHD) is a leading cause of non-relapse morbidity, driven by a quantitative and functional deficiency in CD4+CD25+Foxp3+ regulatory T cells (Tregs). In steroid-refractory (SR) cases, a "functional IL-2 deficiency" impairs peripheral tolerance. Low-dose interleukin-2 (LD IL-2) selectively targets the high-affinity IL-2 receptor on Tregs to restore immune balance. This review synthesizes clinical and mechanistic data from 26 key studies regarding its therapeutic impact.

Methods: Following PRISMA guidelines, we systematically searched PubMed, Scopus, and Web of Science for studies on LD IL-2 and SR-cGVHD. Twenty-six papers were analyzed, including phase 1/2 clinical trials, pediatric-specific cohorts, and mechanistic laboratory investigations. Data extraction focused on objective clinical response rates (ORR), organ-specific success, and quantitative immunological markers—specifically absolute Treg counts, Treg:Tcon (conventional T-cell) ratios, and intracellular STAT5 phosphorylation. The synthesis also evaluated combination therapies involving extracorporeal photopheresis (ECP) and adoptive Treg infusions to determine synergistic effects on homeostatic restoration.

Results: Analysis reveals objective clinical response rates of 50–61% in adults and up to 82% in children. Organ-specific responses were highest in the liver (66.7%) and skin, while lung involvement (19.2%) was the most refractory. Immunologically, LD IL-2 restores the defective STAT5 signaling pathway, inducing a sustained 5-fold expansion of absolute Treg counts and normalizing the Treg:Tcon ratio. Mechanistic data highlight that IL-2 induces PD-1 expression on Tregs, which paradoxically maintains lineage stability and prevents exhaustion. Combination strategies, particularly with ECP, demonstrated enhanced efficacy and significant steroid-tapering potential. The therapy maintained a favorable safety profile, preserving "Graft-versus-Leukemia" (GVL) effects and natural killer (NK) cell activity. Long-term follow-up confirms that homeostatic expansion can be durably maintained for over two years with daily administration.

Conclusion: LD IL-2 represents a transformative, non-immunosuppressive approach for SR-cGVHD. By selectively restoring Treg homeostasis via the STAT5 pathway, it addresses the fundamental biological defect of the disease rather than providing broad immunosuppression. The therapy is safe, durable, and improves outcomes in liver and skin manifestations. These findings support its use in refractory settings and suggest potential for earlier prophylactic intervention.

keywords: Chronic Graft-versus-Host Disease, Interleukin-2, Regulatory T cells, Immune Homeostasis

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PI-27

Evaluation of circulating concentrations of CXCL1 (Gro-1), CXCL10 (IP-10) and CXCL12 (SDF-1) in ALL patients prior and post bone marrow transplantation

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Background and aim: The immune system plays an important role in the development of leukemia. CXC chemokines, as the molecular members of this system, are involved in the immune responses. Therefore, this study was designed to examine and compare the levels of CXCL1 (Gro-1), CXCL10 (IP-10) and CXCL12 (SDF-1) in ALL patients prior to and post bone marrow transplantation (BMT)

Methods: In this experimental study, samples were obtained from ALL patients and controls, and subjected to ELISA for detection of chemokines. Demographic data were also collected by a questionnaire. Data were analyzed using SPSS software.

Results: Our results showed that the serum levels of CXCL1 (Gro-1), CXCL10 (IP-10) and CXCL12 (SDF-1) were significantly increased in ALL patients compared to the controls. We also showed that the CXCL10 (IP-10) level was increased after BMT in ALL patients, while CXCL1 (Gro-1) and CXCL12 (SDF-1) were inversely decreased.

Conclusion: Our results allow for the conclusion that CXCL1 (Gro-1), CXCL10 (IP-10) and CXCL12 (SDF-1) are impor1tant for the pathogenesis of ALL. Notably, these chemokines might be used as pivotal biological markers in the diagnosis of leukemia. Recombinant CXCL1 (Gro-1), CXCL10 (IP-10) and CXCL12 (SDF-1) may be applied as a therapeutic approach in the treatment of leukemia patients.

keywords: ALL Leukemia Chemokine CXCL1 (Gro-1) CXCL10 (IP-10) and CXCL12

PI-28

Autoantibody investigation in patients with recurrent implantation failure classified according to endometrial immune profile

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Background and aim: Recurrent implantation failure (RIF) is one of the most complex challenges in infertility. While classifying patients by endometrial immune profile can aid in diagnosing immune-related RIF, current methods rely on invasive biopsies, limiting their practicality. The present study evaluates autoantibodies in subgroups of RIF patients. The use of peripheral blood markers instead of endometrial tissue sampling could lead to the development of less invasive methods for grouping RIF patients.

Methods: Study samples, consisting of endometrial tissue and peripheral blood, were collected during the mid-luteal phase from 80 RIF patients and 15 fertile controls. Immune profiling of the endometrium was performed using RT-qPCR to quantify transcripts of IL-18/TWEAK, IL-15/Fn-14 ratio, and CD56 mRNA expression, enabling the classification of RIF patients into three groups: balanced, low, and over-activated. In the next step, an autoantibody panel was assessed in peripheral blood via ELISA targeting anti-nuclear antibody (ANA), anti-double stranded DNA (anti-dsDNA), anti-cardiolipin, anti-β2-glycoprotein I, anti-phospholipid, anti-thyroglobulin (anti-TPO), anti-thyroglobulin (anti-TG), and anti-tissue transglutaminase (anti-TTG).

Results: Analysis of serum autoantibodies revealed distinct patterns among RIF patient subgroups (Balanced, Low, Over). The Over group exhibited significantly elevated levels of ANA, anti-phospholipid, Anti-β2-glycoprotein I, anti-TG, and anti-TPO antibodies relative to both the Balanced and Low groups. In contrast, no significant differences were observed for anti-cardiolipin, anti-dsDNA, or anti-TTG antibodies among any groups. Levels in the Balanced and Low groups were comparable for all antibodies tested.

Conclusion: It is possible that a minimally invasive blood test could be developed to replace the endometrial biopsy to classify RIF patients. This is indicated by the significant differences in peripheral blood markers that exist between RIF endotypes. The noteworthy point is that the lack of change in anti-cardiolipin, anti-dsDNA, and anti-tTG levels distinguishes RIF-associated immune activation from systemic autoimmunity, supporting a model of localized, tissue-specific immune dysfunction. Such methods can be used to improve personalized assisted reproductive technology (ART) protocols and targeted therapies.

keywords: Recurrent implantation failure, Infertility, assisted reproductive technology

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Tehran University of Medical Sciences (TUMS)
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PI-29

The potential role of herbal Medicine in Parkinson's Disease

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Background and aim: Parkinson's disease (PD) is a prevalent neurodegenerative disorder characterized by progressive loss of dopaminergic neurons, accumulation of α-synuclein, and chronic inflammatory infiltration. activation of the NF-κB signaling pathway in microglia and astrocytes, along with the production of inflammatory mediators, plays a critical role in PD pathology. Herbal medicines, containing natural anti-inflammatory compounds, have attracted attention as potential therapeutic agents to modulate this pathway.

Methods: We searched PubMed, Google Scholar, Clinical Trials and other Databases. We also reviewed these articles and collected the necessary information. Keywords used included “Parkinson's disease,” “NF-κB,” and “herbal medicine.”

Results: Many studies indicate that numerous herbal medicines and their bioactive compounds, such as polyphenols, flavonoids, terpenes, and alkaloids, exert antioxidant, anti-inflammatory, and anti-apoptotic effects. They inhibit NF-κB activation, reduce the expression of pro-inflammatory genes (TNF-α, IL-1β, IL-6) and enzymes (iNOS, COX-2), modulate related pathways such as MAPK, AKT, and NLRP3, and suppress microglial and astrocyte activation. These actions collectively reduce neuroinflammation and enhance neuronal protection. Furthermore, some herbal medicines prevent IκB phosphorylation and block NF-κB translocation to the nucleus, thereby limiting the exacerbation of inflammatory responses.

Conclusion: Herbal medicines targeting the NF-κB pathway may serve as complementary therapeutic strategies in PD management. Future clinical studies should focus on standardizing herbal compounds, determining optimal dosages, and evaluating NF-κB-dependent inflammatory markers, which could facilitate the development of herbal-based, multi-targeted therapies for PD.

keywords: Parkinson's disease, PD, NF-κB and Herbal medicine

17th International Congress of Lab. and Clinic
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PI-30

Evaluating Natural Killer Cell therapy as a Novel Immunotherapeutic Approach for Breast Cancer patients: A Systematic Review Study

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Background and aim: Breast cancer is the most prevalent malignancy among women and a leading cause of cancer-related death. Despite advances in conventional therapies, metastatic breast cancer remains difficult to treat. Natural killer (NK) cells, key components of the innate immune system, possess the ability to recognize and destroy tumor cells without prior sensitization. Their activity is influenced by the tumor microenvironment, including cytokines and immunosuppressive factors. These properties make NK cells attractive candidates for immunotherapy. This systematic review aims to evaluate emerging NK cell–based therapeutic strategies in breast cancer patients, focusing on clinical safety, efficacy, and treatment outcomes.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, and Google Scholar for articles published between January 2020 and December 2025. Search terms included ("NK Cell" OR "Natural Killer Cell" OR "CAR-NK" OR "Adoptive NK Cell Transfer") AND ("Breast Cancer" OR "Breast Neoplasm" OR "Triple-Negative Breast Cancer"). Inclusion criteria were limited to English-language Phase I/II clinical trials reporting safety, toxicity, and objective responses in human subjects. Animal studies and preclinical models were excluded. Two independent reviewers extracted clinical and outcome data, resolving discrepancies via a third. Data included patient cohorts, NK cell sources, and treatment combinations. Methodological quality was assessed using the Cochrane risk of bias tool for randomized trials. Statistical analyses were performed using R software version 4.2 to align clinical outcomes with reported data.

Results: The search identified 1802 records. After removal of duplicates, 857 studies citations remained. Title and abstract screening yielded 261 studies, of which 15 studies underwent full-text review. Ultimately 9 clinical trials involving 651 patients were evaluated. The objective response rate, defined as a response of partial response or better, was 38.4% (95% CI: 0.268-0.515), and the disease control rate, defined as stable disease or better, was 72.7% (95% CI: 0.648-0.794). Safety was favorable across all studies, with only mild (Grade 1/2) chills and fatigue reported. No severe cytokine release syndrome or neurotoxicity occurred, confirming acceptable tolerability and supporting NK cell therapy as a promising adjunct.

Conclusion: NK cell therapy demonstrates preliminary safety and promising efficacy in breast cancer and can be used as a complementary strategy alongside conventional therapies. Larger clinical studies with rigorous design are recommended to evaluate its long-term efficacy and safety.

keywords: NK cell, Breast cancer, Immunotherapy, Systematic review, Therapy.

PI-31

From Pathogen to Therapeutic Ally: A Historical Systematic Review of Herpes Simplex Virus (HSV-1) as an Oncolytic Immunotherapy for Solid Tumors

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Background and aim: Advanced solid tumor treatment remains a significant clinical challenge, necessitating innovative approaches like oncolytic virotherapy. Herpes Simplex Virus type 1 (HSV-1), due to its neurotropic tendencies and lytic capabilities, has emerged as a promising candidate. This systematic review aims to trace the historical evolution of HSV-1 from its initial concept as a simple oncolytic agent to its current status as a clinically approved, dual-mechanism immunotherapy platform for cancer treatment.

Methods: A systematic search was conducted across PubMed, Scopus, Web of Science, and Cochrane Library for articles published from inception to May 2025. Search terms included "Herpes Simplex Virus", "Oncolytic Virotherapy", "Cancer Immunotherapy", and "T-VEC". The review included studies detailing preclinical engineering, mechanisms of action, and clinical evaluations. Extracted data were synthesized chronologically to illustrate key developmental milestones, focusing on genetic modifications and clinical trial outcomes that defined the virus's therapeutic trajectory.

Results: The evolution of HSV-1 therapy is categorized into four distinct periods: 1) Inherent oncolysis (pre-1990s); 2) Attenuation and selectivity (1990s), featuring γ134.5 gene deletion to ensure safety; 3) Armed immunotherapy (2000s), incorporating GM-CSF expression to boost immune responses; and 4) Clinical validation (2010s–present), marked by the 2015 FDA approval of T-VEC. This progression transformed HSV-1 from a simple lytic agent into a platform that induces direct tumor cell death and systemic anti-tumor immunity, especially when combined with PD-1 inhibitors.

Conclusion: The history of oncolytic HSV-1 exemplifies sophisticated biomedical engineering, turning a pathogen into a powerful therapeutic. T-VEC's clinical success and regulatory approval solidify oncolytic HSV-1 as a fourth pillar in cancer treatment. Future research should focus on expanding its application to other solid tumors and engineering next-generation viruses for advanced immune modulation.

keywords: Herpes Simplex Virus, Oncolytic Virotherapy, Immunotherapy, Solid Tumors, T-VEC

PI-32

The Role of hTERT Promoter in Enhancing Tumor Selectivity and Reducing Immunogenicity in AAV-Mediated Cancer Gene Therapy: A Systematic Review and Meta-Analysis

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Background and aim: AAV-mediated cancer gene therapy faces challenges regarding tumor selectivity and immune evasion. Non-specific expression leads to toxicity and immune responses that reduce efficacy. The human telomerase reverse transcriptase (hTERT) promoter, active in over 85% of human tumors but quiescent in healthy tissues, offers a solution. This study aims to quantitatively synthesize hTERT's efficacy in enhancing selectivity and reducing immunogenicity in AAV-mediated therapy, addressing a gap in current comprehensive reviews.

Methods: A systematic review and meta-analysis were performed to address two questions: How precisely does the hTERT promoter restrict gene expression to tumors? and Does this selectivity reduce host immune responses? A comprehensive search of preclinical data was conducted to evaluate hTERT's performance in AAV vectors. Data were analyzed to assess the correlation between promoter specificity, reduction in off-target expression, and subsequent decrease in anti-vector and anti-transgene immunity.

Results: Preclinical evidence confirms the dual role of the hTERT promoter. First, it effectively restricts gene expression to tumor cells, minimizing off-target activity in healthy tissues. Second, this specific expression significantly decreases antigen presentation by non-tumor cells. Consequently, unwanted host immune responses against both the AAV capsid and the therapeutic transgene are reduced. This "immunological stealth" leads to improved vector persistence and sustained therapeutic efficacy compared to ubiquitous promoters.

Conclusion: The hTERT promoter is a highly effective tool for achieving tumor-specific gene expression in AAV-mediated cancer therapy. By concurrently enhancing therapeutic selectivity and significantly reducing vector immunogenicity, it addresses critical safety and efficacy barriers. These findings support the rational design of next-generation vectors with improved long-term outcomes and reduced systemic toxicity.

keywords: Telomerase, Gene therapy, Adeno-Associated Viruses, Neoplasms, Immunogenicity, hTERT

PI-33

Inducing Viral Mimicry in Colorectal Cancer through Epigenetic Reprogramming by Dietary Polyphenols: A Strategy to Overcome Immunotherapy Resistance

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Background and aim: Colorectal Cancer (CRC), particularly microsatellite stable (MSS) tumors, often resists immune checkpoint inhibitors (ICIs) due to a "cold" immunosuppressive microenvironment. Overcoming this resistance is a major priority. This study aims to explore the hypothesis that epigenetic reprogramming by dietary polyphenols can reactivate endogenous retroviruses (ERVs), inducing "viral mimicry" to convert cold MSS-CRCs into "hot," immunotherapy-responsive tumors.

Methods: A comprehensive analytical literature review was conducted using databases like PubMed and Web of Science. Keywords included "Colorectal Cancer", "Epigenetics", "Dietary Polyphenols", "Viral Mimicry", and "DNMT Inhibitors". The review critically synthesized data from in vitro, in vivo, and clinical studies to analyze the mechanistic link between polyphenol-induced DNA hypomethylation, ERV reactivation, and the subsequent activation of Type I Interferon (IFN-I) pathways in the context of ICI therapy.

Results: The review reveals that dietary polyphenols (e.g., EGCG, curcumin) inhibit DNA methyltransferases, causing DNA hypomethylation. This reactivates ERVs, producing double-stranded RNA (dsRNA) that triggers innate immune sensors. This "viral mimicry" induces a robust Type I IFN response, increasing MHC-I expression and cytotoxic T-cell infiltration. Consequently, the tumor microenvironment shifts from immunosuppressive to immunogenic. Preclinical data confirm that combining these epigenetic modulators with ICIs synergistically inhibits tumor growth and overcomes resistance in MSS-CRC models.

Conclusion: Epigenetic reprogramming via dietary polyphenols offers a promising strategy to induce viral mimicry and sensitize "cold" colorectal tumors to immunotherapy. This approach could provide a safer, accessible method to enhance ICI efficacy. Future research should prioritize clinical trials to validate this combination therapy and identify predictive biomarkers for patient selection.

keywords: Colorectal Cancer, Immunotherapy Resistance, Epigenetic Reprogramming, Dietary Polyphenols, Viral Mimicry

17th International Congress of Lab. and Clinic
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PI-34

Therapeutic Advances in Lung Cancer: A Systematic Review of Current Clinical Strategies

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Background and aim: Lung cancer continues to represent the primary cause of cancer-associated deaths globally. In recent years, substantial progress in molecular biology and translational research has markedly enhanced both diagnostic accuracy and therapeutic decision-making, particularly in non–small cell lung cancer (NSCLC). These scientific advancements have led to the first significant improvements in patient survival observed over the last decade. The present systematic review aims to summarize recent developments in curative, systemic, and palliative treatment modalities for lung cancer.

Methods: A comprehensive literature search was conducted across PubMed, Scopus, Web of Science, and Google Scholar databases to identify English-language clinical trial studies published between 2020 and November 2025. The search strategy incorporated keywords related to major treatment modalities, including surgery, targeted therapy, radiotherapy, chemotherapy, immunotherapy, cryotherapy, and phototherapy. Only peer-reviewed clinical trial articles were considered eligible for inclusion.

Results: Recent years have witnessed the introduction and clinical integration of numerous molecularly targeted agents for NSCLC, including inhibitors of EGFR, ALK, RET, MET, BRAF, NTRK/ROS1, and signaling pathways such as PI3K/AKT/mTOR and RAS–MAPK, in addition to immune checkpoint inhibitors targeting PD-1 and CTLA-4. Many of these therapies are now established as standard treatments for selected patient subgroups. Despite these advances, platinum-based chemotherapy, radiotherapy, and surgical intervention remain foundational components of NSCLC management, with technological innovations enhancing treatment precision and reducing procedure-related complications. Cryotherapy serves as a therapeutic alternative for patients unsuitable for surgery, whereas phototherapy is primarily applied in the palliative treatment of advanced centrally located tumors.

Conclusion: The therapeutic landscape of lung cancer is undergoing continuous transformation, driven by interdisciplinary collaboration and an increasing emphasis on personalized treatment strategies. Advances in targeted agents, immunotherapeutic approaches, surgical methodologies, and supportive interventions are collectively improving clinical outcomes and broadening available treatment options for individuals affected by lung cancer.

keywords: Lung cancer; Therapeutic strategies; Surgery; Chemotherapy; Radiotherapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-35

Advances in Breast Cancer Treatment: A Systematic Review of Emerging Clinical Approaches

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Background and aim: Advancements in breast cancer therapeutics have increasingly prompted a transition away from traditional treatment paradigms, including cytotoxic chemotherapy, endocrine-based approaches, and classical HER2-targeted regimens. Contemporary research efforts are now largely directed toward addressing fundamental barriers to effective treatment, such as acquired and intrinsic resistance mechanisms, biological heterogeneity within tumors, and the suppressive nature of the tumor immune microenvironment. Notably, reports published in 2024 have underscored substantial progress in immunotherapeutic strategies, antibody–drug conjugates (ADCs), and interventions targeting microenvironmental components, collectively indicating a strong potential for improving survival outcomes across diverse breast cancer subtypes.

Methods: An extensive and systematic literature search was undertaken using PubMed, Google Scholar, Scopus, Web of Science, and Embase to identify eligible clinical trial studies published from 2022 through November 2025. Studies were selected if they explored therapeutic mechanisms, evaluated biomarker relevance, or investigated the emerging role of cuproptosis in influencing treatment responsiveness. The extracted evidence was qualitatively integrated, with particular focus on mechanisms of action, principal clinical efficacy endpoints, resistance-driving pathways, and the development of novel combination-based treatment strategies

Results: Among current immunotherapeutic approaches, immune checkpoint inhibition—most prominently pembrolizumab administered in combination with chemotherapy—remains the sole strategy with confirmed overall survival benefit in PD-L1–positive early-stage and metastatic triple-negative breast cancer (TNBC). ADCs, including trastuzumab deruxtecan and sacituzumab govitecan, have yielded significant gains in progression-free and overall survival across HER2-positive, HER2-low, and TNBC populations and are progressively being incorporated into earlier therapeutic lines. Increasing evidence further delineates the central role of the immunosuppressive tumor microenvironment—comprising cancer-associated fibroblasts (CAFs), tumor-associated macrophages (TAMs), myeloid-derived suppressor cells (MDSCs), angiogenic signaling cascades, and cytokine-mediated networks—in fostering therapeutic resistance, thereby supporting the rationale for sophisticated combinatorial treatment approaches. In parallel, emerging platforms such as CAR-T and CAR-NK cell–based therapies, engineered exosome systems, and oncolytic virus–driven strategies have demonstrated compelling preclinical efficacy, although mature clinical survival data remain forthcoming.

Conclusion: Meaningful future advances in breast cancer treatment are likely to depend on rationally designed combination regimens that integrate tumor microenvironment–modulating agents with advanced cellular or viral immunotherapies, with the overarching goal of achieving more durable, sustained, and clinically impactful therapeutic responses.

keywords: Breast cancer; Immunotherapy; Antibody–drug conjugates

PI-36

ctDNA-based minimal residual disease assessment in the context of pembrolizumab-containing neoadjuvant regimens for early triple-negative breast cancer

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Background and aim: ctDNA-based minimal residual disease assessment in the context of pembrolizumab-containing neoadjuvant regimens for early triple-negative breast cancer

Methods: A systematic literature search following PRISMA principles was performed across PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar databases (January 2018 to October 2025). Search terms included early TNBC, pembrolizumab, KEYNOTE-522, circulating tumor DNA, and minimal residual disease. Randomized clinical trials and translational studies evaluating pCR, EFS, or the prognostic value of ctDNA-based MRD assessment were eligible for inclusion.

Results: Available data highlight two synergistic strategies for optimizing outcomes in early TNBC: pembrolizumab-based neoadjuvant chemo-immunotherapy to enhance tumor eradication, and ctDNA-based MRD monitoring to improve post-treatment risk stratification. Across multiple studies, detection of ctDNA following completion of curative therapy is consistently linked to a markedly increased probability of disease recurrence. Longitudinal ctDNA monitoring has also shown the ability to identify molecular relapse earlier than standard imaging or clinical follow-up.

Conclusion: An evolving treatment paradigm in early TNBC incorporates pembrolizumab-containing neoadjuvant therapy followed by structured ctDNA MRD surveillance after surgery and adjuvant treatment. This approach may enable risk-adapted surveillance strategies and facilitate early enrollment into clinical trials upon molecular relapse detection.

keywords: Breast cancer; Triple-negative breast cancer; ctDNA; Minimal residual disease; Pembrolizumab;

PI-37

Effect of Chitosan–Alginate Scaffolds and Zinc Oxide-Modified Scaffolds on the Viability of Mesenchymal Stem Cells

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Background and aim: Background Biomaterial scaffolds are widely used in tissue engineering, but their cytocompatibility is crucial for the success of cell-based therapies. This study aimed to evaluate the effect of chitosan–alginate scaffolds, with or without zinc oxide (ZnO) nanoparticles, on the viability and adhesion of mesenchymal stem cells (MSCs).

Methods: Methods MSCs were cultured on chitosan–alginate scaffolds and on scaffolds incorporated with ZnO nanoparticles. Cell viability was assessed using optical density (OD) readings from an ELISA reader. Data were analyzed using GraphPad software and one-way ANOVA. Cell adhesion to the scaffold surface was also quantified.

Results: Results The polymeric scaffold alone reduced MSC viability compared to cells cultured without scaffolds. Incorporation of ZnO partially mitigated this reduction, increasing viability to a mean. Despite this improvement, cell viability on ZnO-modified scaffolds did not reach the level observed in MSCs cultured alone. Additionally, MSC adhesion to the scaffold surface was approximately 68%.

Conclusion: Conclusion While chitosan–alginate scaffolds reduced MSC viability, the inclusion of ZnO nanoparticles enhanced cell survival and adhesion, suggesting that ZnO-modified scaffolds may offer improved cytocompatibility for MSC-based tissue engineering applications.

keywords: Chitosan–alginate scaffold, zinc oxide nanoparticles, mesenchymal stem cells, cell viability

PI-38

Neopterin as a Potential Biomarker for Gestational Diabetes Mellitus: A Systematic Review

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Background and aim: Gestational diabetes mellitus (GDM) occurs in approximately 8% of all pregnancies and represents one of the most common metabolic complications of pregnancy. The pathophysiology of GDM extends beyond hyperglycemia and is characterized by insulin resistance accompanied by chronic subclinical inflammation. Neopterin, a pteridine derivative produced by activated monocytes, macrophages, dendritic cells, and endothelial cells, serves as a sensitive marker of cellular immune activation. This systematic review aimed to synthesize available clinical evidence on the association between neopterin levels and GDM.

Methods: A systematic search was performed in PubMed, Web of Science, Embase, Scopus, and Google Scholar up to December 2025. Observational studies evaluating circulating or urinary neopterin levels in women with GDM compared with normoglycemic pregnancies were included.

Results: Across six included studies, neopterin levels were consistently elevated in pregnancies complicated by GDM compared with healthy pregnancies. Increased neopterin concentrations were observed in maternal serum, umbilical cord blood, and urine, with positive associations reported between neopterin and glycemic indices, including fasting glucose and HbA1c. Moreover, higher cord blood neopterin levels were linked to maternal insulin resistance and adverse neonatal indicators, such as lower Apgar scores, suggesting a potential role in fetal immune activation. At the molecular level, elevated neopterin was accompanied by disturbances in nitric oxide–related pathways, further supporting its involvement in GDM-associated metabolic and inflammatory dysregulation. Although GDM is recognized as a state of low-grade inflammation, inflammatory assessment using high-sensitivity C-reactive protein revealed no significant differences between GDM and control groups. In contrast, neopterin levels remained significantly higher in GDM, indicating that neopterin represent a more sensitive biomarker than conventional inflammatory markers.

Conclusion: The results collectively highlight the relevance of neopterin in GDM, suggesting its utility as a marker for early detection and clinical management. Future studies are needed to standardize its measurement and confirm its clinical application.

keywords: Neopterin, Gestational diabetes mellitus, Insulin resistance, Inflammation, Biomarker

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-39

Evaluating Chimeric Antigen Receptor T-cell therapy as a Novel Immunotherapeutic Approach for Breast Cancer patients: A Systematic Review Study

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Background and aim: Breast cancer is a major clinical burden and the second leading cause of cancer-related mortality in women. Its biological heterogeneity, particularly in aggressive subtypes such as HER2-positive and triple-negative disease, limits the effectiveness of conventional therapies. This therapeutic gap underscores the urgent need for advanced immunotherapeutic strategies. Chimeric antigen receptor (CAR) T-cell therapy, based on genetic reprogramming of autologous lymphocytes to recognize tumor-specific antigens, represents a promising approach. Building on success in hematologic malignancies, this study evaluates current evidence and explores CAR-T as a novel option for breast cancer patients.

Methods: A systematic search was conducted in Scopus, PubMed, Web of Science, and Google Scholar from inception until December 13, 2024. Two investigators independently applied the terms (“CAR T cell” OR “Chimeric Antigen Receptor T Cell”) AND (“Breast Cancer”), using controlled vocabularies and free text keywords. Inclusion criteria comprised clinical trials published in English that investigated CAR T interventions in breast cancer. Exclusion criteria included studies on other malignancies, non English publications, preclinical experiments, and article types such as case reports, reviews, and letters. Data extraction covered lead author, year, trial phase, patient demographics, sample size, intervention details, and outcomes. Discrepancies were resolved by consensus. Given the limited number of eligible studies, synthesis was descriptive rather than meta analytic.

Results: The search identified 1079 records. After removal of duplicates, 512 citations remained. Title and abstract screening yielded 164 studies, of which 6 clinical trials met inclusion criteria. Across these studies, 336 patients with triple negative or metastatic breast cancer were treated in phase I trials. Interventions included ROR1 specific CAR T (n=210), RNA electroporated cMET CAR T (n=84), and regionally delivered mesothelin targeted CAR T (n=42). Clinical activity was modest: 31 partial response, stable disease in 126 patients, and 42 complete metabolic responses. CAR T expansion and tumor infiltration were variable. Safety was acceptable, with mild cytokine release syndrome and no severe neurotoxicity.

Conclusion: CAR-T therapy, as a novel immunotherapeutic approach, holds significant potential in the management of breast cancer; however, further studies are needed to evaluate its safety and efficacy. This systematic review identifies future research directions and proposes strategies to enhance the effectiveness of this therapy.

keywords: CAR T cell therapy; Chimeric antigen receptor; Immunotherapy; Breast cancer.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-40

DNMT3A Mutations Promote TKI Resistance in CML via the IL-1β–NF-κB Axis

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Background and aim: Background Although tyrosine kinase inhibitors (TKIs) have dramatically improved outcomes in chronic myeloid leukemia (CML), a subset of patients develops therapeutic resistance. Mutations in epigenetic regulators such as DNMT3A are associated with poor prognosis, but the underlying mechanisms remain unclear.

Methods: Methods DNMT3A-mutant and wild-type CML cell lines were evaluated for TKI sensitivity. Transcriptomic profiling was performed to identify downstream signaling alterations. IL-1β expression was modulated genetically and pharmacologically, and NF-κB activation was assessed. The IL-1 receptor antagonist anakinra was used to disrupt IL-1β signaling, alone and in combination with TKIs.

Results: Results DNMT3A-mutant CML cells exhibited reduced sensitivity to TKIs and significant upregulation of IL-1β. Forced IL-1β expression induced TKI resistance, whereas IL-1β silencing or pathway inhibition restored TKI responsiveness. Pharmacologic blockade of IL-1 signaling suppressed NF-κB activation and synergistically enhanced TKI efficacy.

Conclusion: Conclusion DNMT3A mutations drive TKI resistance in CML through activation of an IL-1β–NF-κB signaling axis that promotes leukemic cell survival. Targeting IL-1β signaling represents a promising therapeutic strategy for overcoming resistance in DNMT3A-mutant CML.

keywords: DNMT3A; IL-1β; NF-κB; chronic myeloid leukemia; TKI resistance; anakinra.

PI-41

Modulating Inflammaging through Concurrent Exercise and Nutraceutical Supplementation: Effects of Alpha-Lipoic Acid and Royal Jelly on Macrophage Function in Aging

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Background and aim: Aging is a complex physiological process that progressively impairs cellular function and is accompanied by systemic consequences, notably a state of chronic, low-grade inflammation termed "inflammaging." Macrophages as key playe in the innate immune system, macrophages exhibit remarkable functional plasticity, primarily adopting either a pro-inflammatory (M1) or an anti-inflammatory (M2) phenotype. Accumulating evidence indicates that aging disrupts the balance between these phenotypes, lead to polarization toward the M1 state.

Methods: A literature review using web databases PubMed, Scopus, Google Scholar, and Embase from 2015 to 2025.

Results: Regular physical exercise, particularly aerobic modalities such as running and swimming, represents one of the most effective natural strategies for controlling inflammaging. These activities operate through defined cellular mechanisms: reduce the infiltration of pro-inflammatory (M1) macrophages into tissues, promote polarization toward the anti-inflammatory (M2) phenotype, enhance activation of the Nrf2 pathway to cellular defense against oxidative stress, and concurrently suppress the NF-κB pathway, thereby interrupting the inflammatory cycle. Royal jelly, a valuable natural substance, possesses notable anti-inflammatory properties attributed to its bioactive constituents, including 10-hydroxy-2-decenoic acid (10-HDA) and major royal jelly proteins (MRJPs). These compounds effectively mitigate inflammaging by downregulating the expression and secretion of key pro-inflammatory cytokines—such as TNF-α, IL-6, and IL-1β through inhibition of inflammatory signaling pathways (notably NF-κB and MAPK), as well as by reducing the production of reactive oxygen species (ROS). Alpha-lipoic acid (ALA), a potent antioxidant, plays a critical role in modulating aging-associated inflammatory responses.

Conclusion: Despite promising preclinical evidence, large-scale, well-controlled clinical trials are essential to confirm the efficacy, safety, and optimal dosing regimens of these strategies in humans, thereby establishing them as validated approaches for promoting healthy aging.

keywords: Aging, Inflammation, Macrophages, Exercise training, Royal jelly, Alpha-lipoic acid

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
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PI-42

Immunological innovations in early cancer detection: A review of emerging technologies and integrative approaches

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Background and aim: Early detection fundamentally improves cancer prognosis and treatment outcomes. The immune system's capacity to recognize molecular and cellular alterations during early tumorigenesis provides a powerful foundation for novel diagnostic strategies. This review critically evaluates current advances in immunology-based technologies for the identification of cancer at its pre-clinical and initial stages.

Methods: A comprehensive review of contemporary literature was conducted using data extracted from the Web of Science, Scopus, and Science Direct databases. The analysis focused on the principles and applications of next-generation immunological platforms, including advanced immunoassays (digital ELISA, multiplex systems), nanotechnology-enabled tools (nano-immunosensors, nanobodies), liquid biopsy techniques incorporating immune biomarkers, and the role of artificial intelligence (AI) in decoding complex immunomic data.

Results: Advanced immunological methods demonstrate superior sensitivity and specificity for early-stage malignancies. Nano-immunosensors and digital ELISA platforms can detect tumor-associated antigens and cytokines at sub-femtomolar concentrations, enabling the identification of molecular changes prior to anatomical tumor formation. Multiparametric immunoprofiling and liquid biopsy analyses of circulating tumor DNA (ctDNA) with immune markers provide multidimensional patient-specific signatures. The integration of machine learning for pattern recognition within these complex datasets has further enhanced diagnostic accuracy, with some AI models distinguishing early-stage cancer patients from healthy individuals with over 90% precision.

Conclusion: The convergence of immunology, nanotechnology, and data science is revolutionizing the paradigm of early cancer detection. These technologies offer a promising pathway toward minimally invasive, highly sensitive, and population-scalable screening. Future success hinges on overcoming challenges in standardization, cost reduction, and clinical translation. Ultimately, the integration of these immunodiagnostic tools into routine care is poised to become a cornerstone of predictive and preventive oncology.

keywords: Cancer, Nano immunosensor, Immune Profiling

PI-43

The application of laboratory markers in differentiating immunological causes of recurrent miscarriage

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Background and aim: Recurrent miscarriage is a complex reproductive disorder in which immunological abnormalities are considered a significant but debated cause. Differentiating recurrent miscarriage with immune origin from other etiologies remains challenging due to varied immune mechanisms and limited diagnostic agreement. Laboratory-based immunological markers have been suggested to assist in identifying immune dysfunction, including alterations in immune cell populations, cytokine profiles, and autoimmune parameters. Proper application of these markers may improve diagnostic accuracy and patient stratification.

Methods: A narrative review of recent literature was conducted focusing on immunological mechanisms and laboratory markers associated with recurrent miscarriage. These studies looked at both basic and specific immune cells, such as natural killer cells and regulatory T cells, as well as cytokines and autoantibodies. Laboratory techniques including immune cell phenotyping, cytokine measurement, and autoimmune marker assessment were reviewed. Studies addressing diagnostic limitations, variability in testing methods, and lack of standardization were also analyzed. Findings were qualitatively synthesized to assess the usefulness of laboratory markers in differentiating immunological causes of recurrent miscarriage.

Results: The reviewed evidence indicates that specific laboratory markers are frequently associated with immune-mediated recurrent miscarriage. Increased natural killer cell activity, reduced regulatory T cell function, imbalanced cytokine profiles, and the presence of autoantibodies have been commonly reported. However, significant variability in laboratory methodologies, reference ranges, and timing of testing limits their independent diagnostic value. Peripheral immune markers do not always reflect local uterine immune status, leading to contradictory interpretations. Combined immune profiling approaches appear more informative than individual markers in identifying immunological patterns linked to recurrent miscarriage.

Conclusion: Laboratory immunological markers can lead to identifying immune-related recurrent miscarriage, but their clinical application is limited by methodological dissimilarity. If we combine several immune measures within standard diagnostic approaches, we might better tell if immune problems are the cause and provide more individualized care. We need more research to confirm which immune marker panels are truly helpful in a medical setting.

keywords: Recurrent miscarriage, immunology, laboratory markers, autoimmunity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-44

Unraveling the Role of IL-17A Variants in Pulmonary Tuberculosis: Insights from a Case-Control Study

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Background and aim: The present study aimed to investigate the association between certain interleukin-17A (IL-17A) polymorphisms, specifically rs2275913 and rs8193036, and the susceptibility to pulmonary tuberculosis (PTB). Considering the function of IL-17A in regulating immunological responses, especially regarding bacterial infections, we sought to determine if variations in the IL-17A gene effect on PTB in the examined group.

Methods: We performed a case-control study with 100 individuals who were confirmed to have PTB and 100 control subjects. Genotyping for the IL-17A SNPs rs2275913 and rs8193036 was performed using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and Tetra-primer Amplification Refractory Mutation System (Tetra-ARMS PCR) methodologies. A statistical analysis encompassing odds ratios (OR) and 95% confidence intervals (CI) was conducted to assess the association between the polymorphisms and the risk of PTB.

Results: Our data indicated a significant connection between the rs2275913 polymorphism and elevated susceptibility to PTB (OR = 1.69, 95% CI: 1.09-2.61; p = 0.031). Also, a significant association between the rs8193036 polymorphism and increased susceptibility to PTB (OR=2.18, 95% CI: 1.46-3.27; p0.001).

Conclusion: The IL-17A polymorphisms rs2275913 and rs8193036 strongly correlate with increased susceptibility to PTB, according to this study. This suggests a potential genetic risk factor in the progression of the disease.

keywords: IL-17A, Pulmonary Tuberculosis, Polymorphism

PI-45

The Role of Laboratory Testing in the Detection of Acute and Delayed Hemolytic Transfusion Reactions

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Background and aim: Hemolytic transfusion reactions (HTRs) are serious and potentially life-threatening complications of blood transfusion caused by immune-mediated or non–immune-mediated destruction of red blood cells. These reactions may occur acutely within 24 hours of transfusion or present in a delayed manner up to 30 days post-transfusion. Despite advances in transfusion medicine, HTRs continue to contribute to morbidity and mortality, particularly when diagnosis is delayed. The objective of this systematic review was to evaluate the epidemiology, underlying mechanisms, clinical manifestations, diagnostic approaches, and outcomes of hemolytic transfusion reactions in transfusion-related settings.

Methods: A systematic search strategy was conducted in PubMed, Scopus, and Web of Science to identify relevant studies published between 2010 and 2025. Search terms included combinations of "hemolytic transfusion reaction," "blood transfusion," "immune-mediated hemolysis," "acute hemolytic transfusion reaction," "delayed hemolytic transfusion reaction," "ABO incompatibility," and "alloimmunization." Original research articles, clinical trials, cohort studies, and observational studies reporting clinical features, laboratory findings, management, or outcomes of hemolytic transfusion reactions were included. Review articles, conference abstracts, case reports, animal studies, and non-relevant publications were excluded. Titles and abstracts were screened, followed by full-text assessment of eligible studies. Duplicate records were identified and removed using reference management software

Results: transfusion reactions accounted for approximately 1–3% of all transfusion reactions. Acute HTRs were mainly associated with ABO incompatibility and typically occurred within the first hour of transfusion, presenting with fever, hypotension, flank pain, and hemoglobinuria. Delayed HTRs were primarily related to an anamnestic immune response to minor red blood cell antigens and developed days to weeks after transfusion, commonly presenting with unexplained anemia and jaundice. Laboratory findings consistently indicated hemolysis, including positive direct antiglobulin tests, elevated lactate dehydrogenase, decreased haptoglobin, and increased indirect bilirubin. Early recognition, prompt discontinuation of transfusion, and supportive management were associated with improved outcomes.

Conclusion: Although uncommon, hemolytic transfusion reactions remain clinically significant complications of blood transfusion. Acute reactions are most often caused by ABO incompatibility, while delayed reactions result from alloimmunization to minor antigens. Timely laboratory diagnosis, appropriate clinical management, and strict transfusion protocols are essential to reduce morbidity, prevent mortality, and enhance transfusion safety.

keywords: Hemolytic transfusion reaction ،Blood transfusion ،Immune-mediated hemolysis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-46

Advances in cancer immunotherapy: Strategies and innovations for adoptive immunotherapy of cancer

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Background and aim: Cancer immunotherapy has revolutionized modern oncology by harnessing the immune system to target malignant cells. Despite the progress achieved with conventional treatments such as chemotherapy, radiotherapy, and surgery, challenges, including treatment resistance, toxicity, and tumor immune evasion, persist. Recent advances in adoptive cell therapy (ACT), immune checkpoint inhibitors (ICIs), bispecific antibodies (BsAbs), and chimeric antigen receptor–based therapies have introduced new strategies to enhance antitumor immunity and improve clinical outcomes.

Methods: This narrative review summarizes and analyzes current preclinical and clinical evidence on modern cancer immunotherapeutic strategies. Relevant studies were identified through a comprehensive review of the literature focusing on ACT, CAR T-cell and CAR-NK cell therapies, monoclonal antibodies, bispecific antibodies, bispecific T-cell engagers (BiTEs), and immune checkpoint blockade. Emphasis was placed on mechanisms of action, therapeutic efficacy, resistance mechanisms, toxicity profiles, and emerging combination approaches.

Results: Adoptive cell-based therapies, particularly CAR T cells, have demonstrated remarkable efficacy in hematologic malignancies, while CAR-NK cells offer potential advantages in terms of safety and allogeneic applicability. Immune checkpoint inhibitors targeting PD-1/PD-L1 and CTLA-4 pathways have significantly improved survival in several solid tumors, although resistance and immune-related adverse events remain major limitations. Bispecific antibodies and BiTEs have emerged as powerful tools to redirect immune effector cells toward tumor cells, showing strong activity especially in hematologic cancers. However, issues such as cytokine release syndrome, neurotoxicity, antigen escape, and tumor microenvironment–mediated immunosuppression continue to challenge long-term efficacy.

Conclusion: Recent advances in cancer immunotherapy have substantially transformed the treatment landscape, offering durable responses in selected patient populations. Nonetheless, no single immunotherapeutic strategy is universally effective. Rational combination therapies, improved molecular design, modulation of the tumor microenvironment, and identification of predictive biomarkers are crucial for overcoming resistance and toxicity. A deeper mechanistic understanding of immune–tumor interactions will be critical for advancing personalized and more effective cancer immunotherapy.

keywords: Cancer immunotherapy; Adoptive cell therapy; CAR T-cells; Bispecific antibodies; Immune

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-47

Impact of Chronic Maternal Air Pollution Exposure (PM2.5) on Regulatory T cell Number, Proliferation, and Suppressive Activity in Neonatal Umbilical Cord Blood: A Case-Control Study

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Background and aim: Prenatal exposure to fine particulate matter (PM2.5) has been associated with various adverse health effects, yet its influence on neonatal immune tolerance remains unclear. Regulatory T cells ($CD4^+CD25^+FOXP3^+$) are critical for establishing immune balance during early life. This study examined how chronic maternal exposure to PM2.5 affects the frequency, function, and cytokine production of neonatal Tregs derived from umbilical cord blood.

Methods: In this case-control study, pregnant women from Tehran (n = 10), a highly polluted city, and Damavand (n = 10), a clean rural area, were recruited. Maternal exposure to air pollutants was estimated by measuring urinary levels of 6-hydroxy-nitropyrene and 8-hydroxy-pyrene using two-dimensional high-performance liquid chromatography coupled with tandem mass spectrometry (2D-HPLC-MS/MS). Umbilical cord blood mononuclear cells were isolated to analyze $CD4^+CD25^+FOXP3^+$ regulatory T cells by multicolor flow cytometry. Treg proliferation was assessed following IL-2 supplementation and anti-CD3/CD28 stimulation, while their suppressive function was determined in co-culture with effector T cells. IL-10 and TGF-β1 concentrations in culture supernatants were quantified by ELISA.

Results: Maternal urinary biomarkers of PM2.5 exposure were significantly higher in women from Tehran than in those from Damavand (p 0.0001). Although baseline frequencies of neonatal $CD4^+CD25^+FOXP3^+$ regulatory T cells did not differ between groups (p = 0.111), neonates from Tehran showed reduced FOXP3 expression, impaired Treg proliferation at days 7, 12, and 14 (p 0.05), and decreased suppressive function at a 1:1 effector-to-Treg ratio (61% vs. 72%, p = 0.017). Tregs from highly exposed infants exhibited lower IL-10 and TGF-β1 secretion, though nonsignificantly. Positive correlations between Treg frequency and IL-10 levels, and between suppressive function and FOXP3 expression, were evident only in neonates from low-pollution areas.

Conclusion: Chronic maternal exposure to PM2.5 during pregnancy compromises key functional properties of neonatal regulatory T cells—such as proliferation, cytokine secretion, and suppressive ability—without affecting their baseline frequency. These results suggest that sustained prenatal air pollution may impair neonatal immune tolerance and increase vulnerability to immune-related diseases, underscoring the need for strategies to reduce maternal PM2.5 exposure to protect early immune development.

keywords: $PM_{2.5}$; Maternal Air Pollution Exposure; Regulatory T cells; FOXP3; IL-10;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-48

Reproductive Immunomodulation in Goats: A Review of Anti-GnRH Approaches and the Potential of Anti-FSH Co-Targeting for Enhanced Immunocastration

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Background and aim: Raising intact male goats poses significant challenges due to testosterone-driven aggressive behaviors, heightened energy expenditure, and reduced feed efficiency, ultimately impairing growth performance. While surgical castration is commonly used to mitigate these issues, it entails welfare concerns such as pain, stress, infection, and mortality. Immunocastration has emerged as a promising alternative, leveraging the immune system to generate antibodies that neutralize critical reproductive hormones, offering an effective approach to reproductive management in male goats.

Methods: This review was conducted based on a comprehensive search of peer-reviewed, high-impact literature retrieved from reputable scientific databases and academic sources, including PubMed, Scopus, Web of Science, and Google Scholar.

Results: Research in immunocastration has predominantly targeted Gonadotropin-Releasing Hormone (GnRH). Studies in calves (Janet et al., 2012) and pigs (Han et al., 2017) demonstrate that anti-GnRH vaccination effectively suppresses testicular development, testosterone secretion, and reproductive axis activity, comparable to surgical castration. In pigs, immunocastration reduced both testicular and pituitary size, whereas surgical castration led to pituitary enlargement, likely due to loss of negative feedback. Both approaches decreased hypothalamic GnRH synthesis, confirming effective disruption of the hypothalamic-pituitary-gonadal (HPG) axis. Recent studies have demonstrated the efficacy of anti-GnRH immunocastration in male goats, with multiple research groups (Lents et al., 2018; Mandal et al., 2019; Ding et al., 2024; Pan et al., 2025) reporting significant reductions in testicular size, testosterone levels, and sperm production, often achieving azoospermia, while mimicking key physiological and behavioral traits of surgical castration. These approaches leverage DNA or peptide-based vaccines targeting gonadotropin-releasing hormone (GnRH), leading to suppressed hypothalamic-pituitary-testicular (HPT) axis

Conclusion: However, existing strategies predominantly focus on GnRH inhibition alone, despite evidence that follicle-stimulating hormone (FSH) plays a critical and partially independent role in spermatogenesis and may influence meat quality traits. This gap supports the hypothesis that a dual-target vaccine against both GnRH and FSH could produce synergistic effects, offering more comprehensive suppression of reproductive function, improved behavioral management, and enhanced carcass characteristics compared to single-antigen or surgical methods.

keywords: Immunocastration, GnRH vaccine, FSH vaccine, Reproductive suppression

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-49

Evaluation of Hyaluronic Acid-Conjugated PLGA Nanoparticles as a Targeted Curcumin Delivery System in Ulcerative Colitis

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Background and aim: Curcumin (CUR) is a natural component derived from the rhizomes of turmeric with significant anti-inflammatory properties. Despite its benefits for human health, CUR has limitations such as low water solubility and chemical instability. Nano-based drug delivery systems have recently been used to improve CUR's solubility, and they can be used in several inflammatory diseases, including Ulcerative Colitis. The available studies show that there are many known nanoformulations with curcumin. Our study proposes that formulating curcumin into hyaluronic acid-conjugated poly lactic-co-glycolic acid (PLGA) nanoparticles (Cur-HA-PLGA-NPs) could be a promising strategy for inflammatory colonic tissue and the potential treatment of ulcerative colitis.

Methods: Study selection and evaluation were performed using the PICO criteria and in accordance with the PRISMA checklist. A comprehensive search for relevant research was conducted on the PubMed, Scopus, Web of Science, and Google Scholar databases (2020-2025). MESH keywords were " Hyaluronic Acid ", "curcumin"," nano particle", and " Ulcerative Colitis ". Two reviewers extracted data independently. Only full-text articles published in English were considered, and studies were selected based on predefined inclusion and exclusion criteria.

Results: The database search identified 69 articles; after applying the inclusion criteria, 7 studies were finalized for our review. It was demonstrated that rectal delivery of Cur-HA-PLGA nanoparticles (Cur-HA-PLGA-NPs) resulted in significantly higher therapeutic efficacy than non-functionalized Cur-PLGA-NPs or untreated colitic controls. The HA-conjugated NPs showed selective accumulation in inflamed colonic tissue with minimal distribution in healthy colon, owing to HA–CD44 mediated targeting. There was also evidence of increased intestinal macrophage cellular uptake. Cur-HA-PLGA-NP therapy significantly decreased inflammatory cell infiltration and accelerated mucosal healing with re-epithelialization, according to histological examination. Pro-inflammatory cytokines, including TNF-α and IL-1, and IL-6, which are markers of decreased colonic inflammation, were also markedly reduced by therapy. Furthermore, treatment with Cur-HA-PLGA-NPs significantly improved disease activity indices, including body weight loss, colon length shortening, and histopathological scores, indicating a significant improvement in colitis-associated pathological characteristics.

Conclusion: In summary, hyaluronic acid-conjugated PLGA nanoparticles facilitated the efficient and selective transport of curcumin to inflamed colonic tissue, leading to increased cellular absorption, improved tissue localization, and superior therapeutic efficacy. This particular nanoformulation successfully reduced colonic inflammation, as shown by decreased inflammatory cell infiltration, faster mucosal repair, and lower pro-inflammatory cytokines. So, these data support Cur-HA-PLGA nanoparticles as a viable targeted nanotherapeutic method for ulcerative colitis.

keywords: ulcerative colitis; curcumin; nanoparticle; hyaluronic acid

PI-50

A Review of the Organ-Specific Effects of Cinnamon and Safflower Extract in Rodent Models: Scientific Basis and Research Gaps

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Background and aim: Medicinal plants such as Cinnamomum spp. (cinnamon) and Carthamus tinctorius (safflower) are rich in bioactive compounds, including cinnamaldehyde, eugenol, carthamin, and flavonoids with demonstrated antioxidant, anti-inflammatory, and metabolic-regulating properties. Despite their widespread use in traditional and preclinical medicine, systematic data on the safety and organ-specific effects of oral administration remain limited. This review aims to synthesize current evidence, justify the selection of rat and mouse models, and highlight knowledge gaps regarding chronic exposure and histopathological outcomes in vital organs.

Methods: A narrative review was conducted by analyzing peer-reviewed studies from major scientific databases (e.g., PubMed, Scopus, Web of Science). Emphasis was placed on in vivo studies involving oral gavage of cinnamon extract in rats and safflower extract in mice, with outcomes related to liver, kidney, cardiovascular, hematological, and inflammatory parameters. Only studies reporting dose, duration, extract type, and organ-level effects were included.

Results: Cinnamon gavage (100-200 mg/kg) in rats consistently showed hepatoprotective, nephroprotective, and hypoglycemic effects, alongside reduced oxidative stress and pro-inflammatory cytokines. Safflower extract (100-150 mg/kg) in mice improved hematological indices, attenuated liver and kidney damage, and suppressed systemic inflammation. Both extracts exhibited dose-dependent benefits, but long-term safety profiles and histopathological validation remain underexplored.

Conclusion: While existing data support the therapeutic potential of cinnamon and safflower, significant methodological inconsistencies such as variations in extract preparation, dosing regimens, and limited tissue-level analyses hinder definitive conclusions. Notably, potential risks (e.g., coumarin-induced hepatotoxicity in cinnamon) and organ-specific thresholds for safflower are poorly characterized. This review provides a scientific foundation for future controlled, histologically informed studies to establish safe and effective dosing protocols for preclinical and translational applications.

keywords: Cinnamon (Cinnamomum spp.); Safflower.(Carthamus tinctorius);bioactive compounds;antioxidant activity;anti_inflammatory effects;rodent models; preclinical

PI-51

Clinical and Laboratory Correlates of Cytokine Profiling in Sepsis: A Systematic Evaluation

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Background and aim: Sepsis remains a leading cause of mortality in intensive care units. Rapid identification of immune dysregulation is essential for guiding therapeutic decisions. Cytokine profiling—particularly IL-6, IL-10, and TNF-α—has gained attention as a potential diagnostic and prognostic tool. This systematic review investigates the clinical utility of cytokine signatures measured by modern laboratory technologies.

Methods: A systematic search of the literature (2013–2024) identified clinical studies evaluating cytokine levels in adult sepsis patients using ELISA, chemiluminescent assays, or multiplex immunoassay platforms. Extracted variables included cytokine concentration ranges, time kinetics, associations with SOFA and APACHE II scores, and relationships with mortality or organ dysfunction.

Results: Most studies demonstrated significantly elevated IL-6 levels at early presentation, correlating strongly with disease severity and 28-day mortality. IL-10 served as a marker of anti-inflammatory or immunosuppressive response and was consistently elevated in high-risk patients with poor outcomes. TNF-α exhibited rapid but short-lived increases, limiting its usefulness as a standalone marker. Multiplex cytokine panels provided higher predictive accuracy than single-marker approaches, especially when combined with lactate, CRP, and procalcitonin. However, inter-platform variability and lack of harmonized reference ranges limited cross-study comparisons.

Conclusion: Cytokine signatures—particularly IL-6 and IL-10—show strong potential as prognostic indicators in sepsis. Future multi-center studies with harmonized analytical methods are needed to validate cut-off values and integrate cytokine profiling into clinical decision-making pathways.

keywords: Sepsis,Cytokine Profiling,Interleukin-6 (IL-6),Interleukin-10 (IL-10),Biomarkers,Prognosis

PI-52

O58kkTherapeutic potential of polyclonal antibodies isolated from Aged Bovine serum: A review of methods, challenges, and applications in Veterinary Medicine

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Background and aim: Passive transfer of immunity via maternal colostrum rich in immunoglobulin G (IgG) is essential for protecting neonatal livestock against early-life infections. Multiparous and older cattle, due to repeated natural exposure to pathogens such as Escherichia coli, produce serum enriched with pathogen-specific polyclonal antibodies (PAbs). This serum represents a natural, accessible, and cost-effective source for developing passive immunization products in veterinary medicine. However, its systematic utilization remains underexplored.

Methods: This review was conducted through a systematic analysis of key scientific literature (from PubMed, Scopus, and Web of Science) published between 2002 and 2025. We evaluated and compared major IgG purification techniques from bovine serum, including ammonium sulfate precipitation, ion-exchange chromatography (IEX), and affinity chromatography (AC) using ligands such as Protein A.

Results: Polyclonal antibodies are ideal for passive immunization in livestock due to their broad epitope recognition, functional robustness, and scalability. Chromatographic methods, particularly AC and IEX, consistently yield higher purity and recovery than conventional precipitation techniques, though they pose cost and complexity challenges in veterinary settings. Evidence also supports the superior biological efficacy of IgG purified from multiparous cattle in neutralizing common neonatal pathogens.

Conclusion: Despite advances in human-grade antibody production, standardized, field-applicable protocols for veterinary IgG purification are still evolving. The optimal method must balance purity, functional integrity, cost, and scalability. Utilizing serum from experienced cattle is not only immunologically rational but also economically and ecologically advantageous, offering herd-relevant antibody profiles. Serum from multiparous cows is a valuable resource for veterinary passive immunization products. Developing simplified, efficient, and farm-compatible purification protocols, potentially integrating conventional and modern techniques, can significantly reduce neonatal mortality and improve herd health management.

keywords: Polyclonal antibodies, immunoglobulin G, passive immunity, antibody purification, ion-exchange chromatography,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-53

Prognostic and Diagnostic Significance of Survivin (BIRC5) Expression in Breast Cancer: A Systematic Review

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Background and aim: Breast cancer, representing approximately 30% of female malignancies with the highest global incidence and mortality, remains a critical health challenge despite therapeutic advances. A hallmark of its pathogenesis is resistance to apoptosis, allowing tumor cells to survive, proliferate, and evade treatments. Identifying reliable diagnostic and prognostic biomarkers is essential to predict therapeutic responses and patient outcomes. Survivin, or baculoviral inhibitor of apoptosis repeat-containing 5 (BIRC5), a multifunctional member of the inhibitor of apoptosis protein family, regulates caspase activity to inhibit apoptosis and promote proliferation. This systematic review critically examines Survivin's prognostic and diagnostic significance in breast cancer.

Methods: This systematic review, conducted per PICO and PRISMA guidelines, searched PubMed, SCOPUS, Web of Science, SID, Magiran, and Google Scholar (2021–2026) using MeSH terms "Breast cancer", "Survivin (BIRC5)", "Prognostic biomarker" and" Diagnostic biomarker" with Boolean operators. Two researchers independently screened articles based on inclusion criteria.

Results: After applying strict inclusion and exclusion criteria and critically evaluating study quality, only 6 articles were selected from an initial 354 records. Evidence synthesized from these studies highlights BIRC5 as a pivotal breast cancer biomarker. Diagnostically, BIRC5 shows consistent overexpression, with a 2.6-fold increase in tumor versus normal tissues (p0.0001), and the highest expression among BIRC genes in triple-negative breast cancer (0.684 logRQ). Prognostically, elevated BIRC5 independently predicts poor outcomes, with a pooled hazard ratio (HR) of 1.82 for overall survival. Its upregulation is strongly associated with aggressive features, including younger age (50 years; OR=2.0), high tumor grade, and basal-like and Luminal B subtypes. In ER-positive disease, it nearly triples recurrence risk (HR=2.7). Regulated via the TTP/HuR axis, high co-expression predicts the worst relapse-free survival (HR=2.34). Its higher prevalence in Black women (OR=1.9) also reflects demographic disparities, establishing BIRC5 as both a powerful diagnostic/prognostic marker and a promising therapeutic target.

Conclusion: Evidence indicates BIRC5 as a vital diagnostic and independent prognostic biomarker in breast cancer, strongly linked to aggressive disease and demographic disparities. Future research must focus on translating this knowledge into clinical utility by developing and testing targeted anti-BIRC5 therapies, particularly to address outcome inequities and improve survival in high-risk patient groups.

keywords: Breast cancer, Survivin (BIRC5), Prognostic biomarker, Diagnostic biomarker

PI-54

Laboratory diagnosis Complexities of Human Brucellosis: A Neglected Zoonotic Disease with Significant Impact on Public Health in Middle East

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Background and aim: Human brucellosis, a zoonotic disease caused by Brucella spp., is a neglected global health concern, particularly prevalent in the Middle East. Despite advancements, its diagnosis remains challenging due to overlapping symptoms with other infectious diseases and limitations in traditional diagnostic methods. This systematic review evaluates the performance of various laboratory diagnostic tests for human brucellosis in Middle Eastern countries.

Methods: A systematic review was conducted following PRISMA 2020 guidelines. A comprehensive literature searches of PubMed, Web of Science, and Scopus identified studies published between 2000 and 2024. Inclusion criteria focused on observational studies and randomized controlled trials assessing diagnostic methods for brucellosis with culture as the reference standard. Pooled sensitivity and specificity were calculated for each diagnostic test using a random-effects model.

Results: Out of 1,263 articles, 10 studies met the inclusion criteria. The Rose Bengal test and conventional PCR demonstrated the highest diagnostic accuracy, with pooled sensitivities of 100% and 90.4%, and specificities of 96.9% and 98.2%, respectively. IgG/IgM ELISA exhibited moderate performance, while the Standard Tube Agglutination Test showed lower sensitivity compared to other methods. Heterogeneity across studies was notable due to differences in protocols, populations, and disease stages.

Conclusion: The Rose Bengal test and qualitative PCR are highly effective for diagnosing human brucellosis in endemic regions, with the former being particularly valuable in resource limited settings. Despite their utility, serological and molecular tests require context-specific validation and standardization to improve diagnostic reliability. Integrating multiple diagnostic approaches and enhancing healthcare infrastructure are critical for better management of brucellosis in the Middle East.

keywords: brucellosis; zoonotic diseases; Middle East; diagnosis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-55

Prognostic Value of Progranulin (PGRN/GP88) in Breast Cancer: A Systematic Review

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Background and aim: Breast cancer (BC) is one of the most prevalent malignancies in women, with over one million confirmed diagnoses annually. Although targeted therapies have improved outcomes, there remains a critical need for reliable prognostic biomarkers to enhance personalized treatment strategies. Progranulin (PGRN/GP88), an 88-kDa secreted glycoprotein of the granulin/epithelin family, has gained attention as a regulator of tumor biology. PGRN modulates key cellular processes through signaling pathways involved in proliferation, tissue remodeling, and resistance to cellular stress. This systematic review aims to determine the prognostic relevance of PGRN expression in BC and its potential value in improving clinical decision-making.

Methods: This study was conducted in accordance with the PICO criteria, aligned with the research objective, and following the PRISMA checklist. A systematic review was performed with a comprehensive search of the PubMed, Scopus, Web of Science, SID, and Magiran databases, as well as the Google Scholar search engine. The search employed the MeSH keywords “Progranulin (PGRN/GP88),” “Breast Cancer,” and “Prognostic Biomarker,” combined using Boolean operators. Subsequently, two researchers independently reviewed and screened the retrieved articles based on the predefined inclusion criteria.

Results: Following the application of inclusion/exclusion criteria and quality assessment, 5 studies were selected from an initial pool of 226 articles. The synthesized evidence firmly establishes progranulin (PGRN/GP88) as a powerful prognostic biomarker in BC. Immunohistochemical data reveal its absence in benign tissue but frequent presence in malignancies, notably in 80% of invasive ductal carcinomas and 59% of triple-negative tumors. PGRN expression correlates strongly with aggressive features: high histologic grade, elevated Ki-67 index (48.8 vs. 30.3), and p53 positivity (44% vs. 25%). Critically, strong tumor expression (3+) confers a 5.9-fold higher recurrence risk and a 2.5-fold increased mortality hazard. Serum PGRN 55 ng/ml predicts a 4-fold reduction in overall survival. Furthermore, co-expression with its receptor sortilin identifies a highly aggressive subgroup with a 2.2-fold greater risk of BC-specific death. PGRN’s role in driving tumor progression underscores its dual utility as a robust prognostic indicator and a promising therapeutic target.

Conclusion: This systematic review confirms PGRN as a strong, independent prognostic biomarker in BC, linked to aggressive tumor biology and poorer outcomes. Its co-expression with sortilin defines a particularly high-risk subgroup. PGRN holds promise for inclusion in multi-marker panels to enhance risk stratification and personalize adjuvant therapy. Targeting the PGRN pathway also offers a potential therapeutic strategy for aggressive or resistant disease. Future work must prioritize standardizing PGRN assays and validating its clinical utility through prospective trials to effectively integrate this biomarker into patient care.

keywords: Progranulin (PGRN/GP88), Breast Cancer, Prognostic Biomarker

PI-56

Expanding Donor Identification Through Extended Familial HLA Screening: Clinical Experience From Shahid Sadoughi Hospital, Yazd

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Background and aim: Human leukocyte antigen (HLA) compatibility is the most critical factor influencing outcomes in hematopoietic stem cell transplantation (HSCT). In regions with limited access to large unrelated donor registries, systematic familial HLA screening remains essential. However, the clinical impact of extended family donor evaluation is often underreported.

Methods: This study analyzed real-world HLA typing data collected at Shahid Sadoughi Hospital, Yazd, from patients referred for HSCT due to malignant and non-malignant hematologic disorders, primary immunodeficiencies, and inherited metabolic diseases. Intermediate- and high-resolution HLA typing was performed for HLA-A, -B, -C, -DR, and -DQ loci. Patients were evaluated alongside first- and second-degree relatives to identify shared haplotypes and clinically relevant donor options.

Results: HLA-identical siblings represented the highest likelihood of full compatibility, consistent with classical Mendelian inheritance. Parents consistently shared one haplotype with the patient, providing haploidentical donor options. Notably, in multiple families, extended relatives—including uncles, aunts, and cousins—demonstrated partial or near-complete HLA matching, effectively expanding the donor pool beyond the nuclear family. In selected pedigrees, increased homozygosity at specific HLA loci was observed, particularly in consanguineous families, which further enhanced donor availability. Matching at class II loci, especially HLA-DR and HLA-DQ, played a significant role in donor prioritization due to its clinical relevance to graft-versus-host disease risk.

Conclusion: Our clinical experience demonstrates that extended familial HLA screening can substantially improve donor identification for HSCT. Incorporating broader family-based HLA evaluation into routine pre-transplant assessment may directly influence clinical decision-making and optimize donor selection strategies, particularly in resource-limited settings.

keywords: Hematopoietic Stem Cell Transplantation; Human Leukocyte Antigen; HLA Haplotypes;

PI-57

Current Trends and Concepts in CAR-NK Cell Therapy for Solid Tumors.

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Background and aim: Chimeric Antigen Receptor Natural Killer cell therapy is a novel and promising immunotherapy target for solid Tomor, as it corrects some of the shortcomings of CAR-T cell therapies. CAR-NK cells provide advantages in terms of reduced toxicities and simpler production techniques over CAR-T therapies, thus countering the issue of T cell infiltration in the case of solid tumors. In this study, we investigated the application of CAR-NK cell therapies in solid malignancies.

Methods: According to the articles that were surveyed from databases such as Google Scholar, PubMed and Scopus from February 2015 to April 2025, it was found that due to current trends, concepts, and challenges in CAR-NK cell therapy, Solid Tumors were explored. The keywords that we employed include Cellular immunotherapy, Natural killer (NK) cells, Solid tumors, and CAR-NK therapies.

Results: CAR-NK cells exhibit better safety compared to CAR-T cells, with reduced neurotoxicity, CRS, and GVHD risks. These cells are advantageous because of their distinct cytokine secretion characteristics, which qualify them for allogeneic usage. Therefore, these factors help promote the development of industrially acceptable modalities. CAR-NK cells demonstrate the ability to target various antigens expressed in solid malignancies, such as glioblastomas and colorectal carcinomas. By December 2025, over 40 clinical trials were registered for solid tumor indications, showing promising safety and early efficacy signs, such as tumor regression in certain patients with iPSC-derived therapies. Other factors are the inability to expand in vivo, inefficient tumor targeting, antigen escape, and exhaustion. Next-generation approaches focus on cytokine armoring, CRISPR-mediated receptor knockout, logic-gated CARs, metabolic reprogramming, and combined therapies with checkpoint inhibitors or nanoparticles. The development of off-the-shelf iPSC-NK products with suicide switches is enhancing manufacturability and safety.

Conclusion: In summary, CAR-NK therapy offers transformative potential as a safer, off-the-shelf, and universal immunotherapy for solid tumors. Clinical progress and engineering refinements through late 2025 are overcoming TME obstacles, improving durability, and fostering sustained responses, providing renewed optimism for refractory cancer patients.

keywords: Cellular immunotherapy, Natural killer (NK), Solid tumors, CAR-NK therapies

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-58

Uterine NK cells in RIF and RPL: quantitative and qualitative differences and association with IVF success: A systematic review and meta-analysis

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Background and aim: Uterine natural killer (uNK) cells have been identified as playing a pivotal role in decidual remodelling, angiogenesis, and trophoblast invasion. Dysregulated uNK density, which is frequently elevated, and altered function/receptor profiles contribute to defective placentation in recurrent pregnancy loss (RPL) and recurrent implantation failure (RIF). The present systematic review and meta-analysis aim to evaluate quantitative (density) and qualitative (subsets, receptors) alterations in uNK cells in patients with RPL/RIF in comparison with control groups. In addition, the study will examine the association of these alterations with outcomes, and the interplay with peripheral NK cells.

Methods: Databases (PubMed, MEDLINE, Embase, Scopus, Web of Science; inception to December 2025) were searched with terms "uterine natural killer cells", "uNK cells", "endometrial NK density", "CD56", "recurrent pregnancy loss", "RPL", "recurrent implantation failure", "RIF", "KIR receptors". Expert-refined syntax incorporated IHC/flow cytometry specifics. Reference lists of relevant articles were also screened. Inclusion criteria: studies quantifying uNK density/subsets/receptors in non-pregnant endometrium or decidua of RPL/RIF versus controls and Exclusion criteria include animal models, no controls, uncontrolled therapies, or sole peripheral focus. ROBINS-I use for assessing the risk of bias and dual review Done for selection of article. Furthermore PROSPERO-registered.

Results: Meta-analysis of 28 studies (20 density via IHC, 8 functional/receptor via flow/IHC; n=2,789 patients) showed markedly higher uNK density in RPL/RIF endometrium versus controls (SMD 1.29, 95% CI 0.94-1.64, p0.001), especially mid-secretory phase (SMD 1.52, p0.001). Elevated density (20% stromal cells) linked to lower live birth rates (OR 0.35, 95% CI 0.22-0.55, p0.001) and higher miscarriage (OR 3.68, p0.001). Subgroup: altered KIR profiles (reduced inhibitory KIRs) predominant in RPL (p=0.005); CD56bright dominance shifted in RIF. Weak correlation with pNK (r=0.18, p=0.04). Heterogeneity moderate-high (I^2=71%), reduced in secretory-phase subgroup (I^2=52%); sensitivity excluding older IHC studies amplified effects (SMD 1.48). Also, the funnel plot did not show bias.

Conclusion: Increased density and dysfunction of uterine NK cells are hallmarks of recurrent miscarriage and recurrent implantation failure, and their pivotal role in impaired angiogenesis and immune tolerance is confirmed. Analyses show that in recurrent miscarriage, destructive activity is higher, whereas in implantation failure, increased cell numbers predominate. The strengths of this study are its comprehensiveness and stage-based analyses, but the variability of testing methods and limited data from decidua are limitations. These quantitative and consistent findings support the use of uterine NK cell profiling as a clinical tool.

keywords: Uterine natural killer cells; Recurrent pregnancy; Recurrent implantation failure

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-59

The role of the vaginal/endometrial microbiome and cytokines/chemokines in RIF and implantation success; a systematic review meta-analysis

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Background and aim: The vaginal and endometrial microbiomes have been demonstrated to influence local immunity, with the prevalence of Lactobacillus species encouraging tolerance through the production of anti-inflammatory cytokines. Dysbiosis, defined as a disturbance in the balance of bacteria within the gut microbiota, characterised by a decrease in Lactobacillus and an increase in diversity and pathogens, has been demonstrated to elevate pro-inflammatory cytokines. This, in turn, has been shown to disrupt receptivity in cases of recurrent implantation failure (RIF) and recurrent pregnancy loss (RPL). This review meta-analyses the associations between dysbiosis and cytokines, and reproductive outcomes.

Methods: Searches (PubMed, MEDLINE, Embase, Scopus, Web of Science; inception to December 2025) used "vaginal microbiome", "endometrial microbiome", "dysbiosis", "Lactobacillus", "cytokines", "recurrent implantation failure", "RIF", "recurrent pregnancy loss", "RPL", "16S rRNA". Reference lists of relevant articles were also screened. Inclusion criteria: microbial profiling with cytokine quantification in RPL/RIF versus controls and Exclusion criteria include non-reproductive, no cytokines, uncontrolled antibiotics. ROBINS-I use for assessing the risk of bias and dual review Done for selection of article. Furthermore PROSPERO-registered.

Results: Pooled from 21 studies (12 vaginal, 9 endometrial; n=2,468 patients) revealed reduced Lactobacillus dominance in RPL/RIF (OR 0.29, 95% CI 0.19-0.44, p0.001), higher diversity (alpha index SMD 1.41, p0.001), and pathogens (e.g., Gardnerella/Prevotella OR 3.78, p0.001). Dysbiosis associated with elevated pro-inflammatory cytokines (IL-6/TNF-α SMD 1.48, 95% CI 1.12-1.84, p0.001; IL-1β SMD 1.09, p=0.001) and reduced IL-10/TGF-β. Severe dysbiosis predicted lower implantation (OR 0.41, p0.001) and live birth (OR 0.37, p0.001). Subgroup: stronger cytokine shifts in endometrial (SMD 1.62) versus vaginal; unexplained cases amplified effects. Low-moderate heterogeneity (I^2=58%) and sensitivity robust.

Conclusion: This analysis suggests that an imbalance of microbes in the reproductive tract increases inflammation and contributes directly to recurrent miscarriage and implantation failure. A decrease in protective bacteria, such as Lactobacillus, increases this risk. Examining the microbiome allows for targeted treatment. Overall, regulating the microbiome is an effective and novel strategy for treating this type of infertility.

keywords: Vaginal microbiome; Endometrial dysbiosis; Recurrent implantation failure; Recurrent pregnancy loss.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-60

The role of peripheral NK cells (pNK cells) and their toxic activity in recurrent pregnancy loss (RPL): systematic review and meta-analysis Levels and prognosis

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Background and aim: There is a well-established association between recurrent miscarriage and implantation failure, which is characterised by increased destructive activity of natural killer cells in the blood. This inflammatory state impairs both embryo implantation and placental formation. Increased activity reduces maternal-foetal immune tolerance by exacerbating inflammatory responses and damaging placental cells. This systematic review analyses the available data on differences in this activity between women with fertility issues and those who are fertile. It also examines the predictive significance of this activity for miscarriage and implantation outcomes, as well as the possible underlying mechanisms.

Methods: A comprehensive search was conducted across PubMed, MEDLINE, Embase, Scopus, and Web of Science (from inception to December 2025) using terms including "peripheral natural killer cells", "pNK cytotoxicity", "NK cell activity", "recurrent pregnancy loss", "RPL", "recurrent implantation failure", "RIF", "K562 assay", and synonyms. Expert consultation refined the syntax to include assay-specific terms (e.g., 51Cr-release, flow cytometry). Included studies were observational/cohort or RCTs reporting pNK cytotoxicity levels (preconception or early pregnancy) in RPL/RIF versus controls, or predictive outcomes. Exclusions: non-English publications, absent quantitative cytotoxicity data, animal studies, or confounding immunomodulatory interventions. Risk of bias was assessed using ROBINS-I; two independent reviewers screened with third-party arbitration. Sensitivity analyses addressed assay heterogeneity; protocol registered in PROSPERO.

Results: Pooled analysis of 23 studies (16 preconception, 7 early pregnancies; total n=3,142 patients) confirmed significantly elevated pNK cytotoxicity in RPL/RIF women compared to controls (standardized mean difference [SMD] 1.64, 95% CI 1.32-1.96, p0.001 preconceptionally; SMD 1.48, 95% CI 1.10-1.86, p0.001 in early pregnancy). High cytotoxicity (25% lysis at 50:1 effector:target ratio) strongly predicted miscarriage risk (odds ratio [OR] 4.12, 95% CI 2.89-5.87, p0.001) and reduced live birth rates post-IVF (OR 0.31, 95% CI 0.19-0.51, p0.001). Subgroup analyses revealed stronger associations in unexplained RPL (SMD 1.89, p0.001) versus secondary RPL, and with flow cytometry assays versus chromium-release (p=0.02 for heterogeneity). Cytotoxicity correlated positively with pro-inflammatory cytokines (e.g., TNF-α, IFN-γ; r=0.45-0.62) and inversely with Treg levels. Moderate heterogeneity (I^2=65%) was partially explained by timing and assay type; sensitivity analysis excluding high-bias studies strengthened effects (SMD 1.78). No significant publication bias (Egger's test p=0.12).

Conclusion: This comprehensive analysis shows that increased destructive natural killer (NK) cell activity in the blood is a strong marker of recurrent miscarriage and recurrent implantation failure, particularly in cases where the cause is unknown. The findings support the use of this test for risk assessment and guiding immunomodulatory therapies. Standardisation of testing methods and their combination with other markers for personalised therapy are recommended for the future. Overall, targeting this excessive activity is a promising strategy for improving pregnancy success rates.

keywords: Peripheral natural killer cells; pNK cytotoxicity; Recurrent pregnancy loss.

PI-61

Treg cells and immune balance in the endometrium of women with RPL or RIF: levels and role in fetal tolerance.

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Background and aim: Regulatory T cells (Tregs) are pivotal in maintaining maternal-fetal tolerance by suppressing inflammation and promoting a Th2 bias. A decrease in Tregs, coupled with an imbalance between Tregs and Th17 cells, gives rise to pro-inflammatory conditions that exert a detrimental effect on implantation in cases of recurrent pregnancy loss (RPL) and recurrent implantation failure (RIF). The present review conducts a meta-analysis of Treg levels, subsets and ratios in the peripheral and decidual environments of patients experiencing recurrent pregnancy loss and recurrent implantation failure, in comparison to control groups.

Methods: Comprehensive searches (PubMed, MEDLINE, Embase, Scopus, Web of Science; inception to December 2025) with "regulatory T cells", "Treg", "FoxP3", "Treg/Th17 ratio", "Th17", "recurrent pregnancy loss", "RPL", "recurrent implantation failure", "RIF". Expert-optimized for flow/IHC. Included: Treg/Th17 quantification in RPL/RIF versus controls. Exclusions: non-human, no ratios, mixed therapies. ROBINS-I; dual screening; subgroup for site/timing; PROSPERO-registered.

Results: Analysis of 25 studies (16 peripheral, 9 decidual/endometrial; n=2,935 patients) showed significantly reduced Treg proportions in RPL/RIF (SMD -1.38, 95% CI -1.68 to -1.08, p0.001), elevated Th17 (SMD 1.21, p0.001), and inverted Treg/Th17 ratios (Th17 dominance OR 5.04, 95% CI 3.42-7.43, p0.001). Low Tregs predicted poorer live birth (OR 0.28, p0.001) and higher miscarriage (OR 4.19, p0.001). Subgroup: decidual deficits stronger (SMD -1.59); unexplained RPL most pronounced. Inverse Treg-Th17 correlation (r=-0.56). Heterogeneity moderate (I^2=63%); sensitivity confirmed robustness.

Conclusion: Dysregulation of Treg and Th17 cells is a key feature of recurrent miscarriage and implantation failure, which suggests an immune tolerance defect. Focusing on uterine tissue will clarify the local mechanism. In this context, the role of Th17 cells is more important than that of classical inflammatory pathways. Profiling these cells could help to categorise patients. Treg-boosting therapies, such as vitamin D, have shown promising results, and novel approaches, such as IL-2, are under investigation. Targeting the Treg system is a promising therapeutic strategy for immune-mediated infertility.

keywords: Regulatory T cells; Treg/Th17 balance; Recurrent pregnancy loss.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-62

Improved Cytotoxicity and Apoptosis in Breast Cancer Cells via Peptide-Targeted Liposomal 5FU and Berberine Delivery

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Background and aim: Breast cancer is a major cause of cancer-related deaths among women globally, and current treatments are often hindered by poor targeting and systemic toxicity. This study developed RGD-functionalized liposomes co-loaded with 5-fluorouracil and berberine as a targeted nanocarrier for breast cancer therapy. The liposomes were prepared via thin-film hydration and characterized for physicochemical properties. Their anticancer activity was assessed in MCF-7 cells using cytotoxicity and apoptosis assays. The RGD-modified formulation showed significantly enhanced cytotoxicity and apoptosis compared to free drugs and non-targeted liposomes, indicating improved cellular uptake through integrin-mediated targeting and superior therapeutic potential.

Methods: Preparation of nanoformulation , Characterization of nanoliposomes (Using dynamic light scattering (DLS) analysis). cell culture, Apoptosis assay (Apoptosis assay was performed by using Annexin V/propidium iodide (PI) assay kit)

Results: Dynamic light scattering (DLS) analysis revealed that the Lip-BRB-5FU-RGD nanoparticles had an average particle size of 173.1 nm and a zeta potential of −4.4 mV, as shown in Figures 2a and 2b. The cytotoxic effects of the formulations were evaluated using the MTT assay. As illustrated in Figure 5, Lip-5FU-BRB-RGD exhibited the strongest cytotoxic activity across all tested concentrations, reducing cell viability by approximately 75% compared to free 5FU-BRB and non-targeted Lip-5FU-BRB at the highest concentration. Furthermore, apoptosis analysis demonstrated that Lip-BRB-RGD induced the highest levels of cell death, with Annexin V+/PI+ populations reaching 1.86% and 66.6%, respectively.

Conclusion: This study describes the development of RGD-functionalized liposomal nanoparticles co-encapsulating berberine and 5-fluorouracil for targeted cancer therapy. TEM confirmed a core–shell structure, while zeta potential analysis showed suitable negative charge for colloidal stability. In vitro assays demonstrated significantly higher cytotoxicity of Lip-BRB-5FU-RGD against MCF-7 cells compared to free drugs and non-targeted formulations. RGD modification enhanced cellular uptake and apoptosis induction, indicating effective integrin-mediated targeting. Overall, these findings highlight the strong anticancer potential of this nanocarrier system and support further in vivo evaluation.

keywords: Liposomes, 5-fluorouracil, Berberine, Breast cancer, RGD peptide.

PI-63

Immunotherapy Approaches of CAR-T and CAR-Natural Killer Cell-Based Therapies in Hematologic Malignancies: Where Are We?

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Background and aim: Hematologic neoplasms remain a critical global health concern. Conventional treatments such as chemotherapy, radiotherapy, and transplantation are effective but burdened with significant risks. Recent advances have focused on immunotherapy, particularly chimeric antigen receptor (CAR)-based strategies that reprogram immune cells to target malignancies. CAR-T cell therapies have demonstrated encouraging outcomes against blood cancers. Building on these successes, researchers are exploring CAR-engineered natural killer (CAR-NK) cells, which possess intrinsic tumor-targeting capabilities and offer a potentially safer, more efficient therapeutic platform for hematologic malignancies.

Methods: Starting from a broad inquiry, one key step involved building a precise search method to locate recent studies on the topic within PubMed. Following that effort, additional sources emerged through queries in Google Scholar and Scopus, capturing papers missing from the initial pool. A total of 251 articles made the cut, each examined thoroughly before integrating findings into the report. Ethics Committee Approval No.: IR.ABADANUMS.REC.1405.027

Results: Results from the published studies revealed engineered T cells performed well against specific forms of acute lymphoblastic leukemia (ALL) and multiple myeloma (MM). Research teams now explore natural killer cells as an alternative approach to attack malignant growths. While modified T cell treatments typically eliminate tumor cells more effectively, their use can lead to severe issues such as widespread inflammatory responses or neurological side effects, raising safety concerns. In contrast, NK cells generally pose fewer risks since they identify damaged or invaded cells through built-in mechanisms, rarely provoking intense damage. Still, researchers struggle to identify suitable markers that help CAR-NK cells eliminate tumors effectively. Improvements have emerged through engineered receptor approaches, though challenges remain.

Conclusion: Though promising, CAR-cell therapy needs more study before its full capabilities become clear. This review gathers data from up-to-date research to highlight current progress in the field. Because obstacles remain, ongoing work will be essential moving forward. Insights shared here may guide scientists toward solutions yet to be tested.

keywords: Chimeric Antigen Receptors, Natural Killer Cell, T-Lymphocyte, Hematologic Neoplasm

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-64

Quercetin Against Breast Cancer: A Narrative Review of Its Antiproliferative Mechanisms and Therapeutic Potential

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Background and aim: Breast cancer remains one of the leading causes of cancer-related mortality among women worldwide, with treatment resistance and tumor heterogeneity limiting long-term therapeutic success. Natural compounds such as quercetin, a dietary flavonoid with antioxidant and anti-inflammatory properties, have gained increasing attention for their potential anticancer effects. This narrative review aims to summarize current preclinical and emerging clinical evidence on the antiproliferative, pro-apoptotic, and metabolic regulatory mechanisms of quercetin in breast cancer.

Methods: A comprehensive literature search was conducted in PubMed, Scopus, and Web of Science databases for studies published between 1975 and 2024. Keywords included “quercetin,” “breast cancer,” “apoptosis,” “cell cycle arrest,” and “signaling pathways,” using appropriate Boolean operators. Peer-reviewed English and Persian articles focusing on in vitro, in vivo, and early clinical studies were included. A total of 65 relevant studies were selected and analyzed in this narrative review.

Results: Quercetin exhibited significant antiproliferative effects in multiple breast cancer cell lines in a dose-dependent manner. It induced cell cycle arrest, predominantly at the G_2/M phase, and promoted apoptosis through both intrinsic and extrinsic pathways. Quercetin modulated key survival and stress-related signaling pathways, including PI3K/Akt/mTOR and JNK, by upregulating PTEN and downregulating phosphorylated Akt and mTOR. Epigenetic regulation was also observed through modulation of microRNAs, notably upregulation of miR-146a and downregulation of miR-21, contributing to apoptosis and growth inhibition. In addition, quercetin suppressed tumor metabolism by inhibiting glycolysis via downregulation of PKM2, LDHA, and GLUT1, leading to reduced lactate production. Preclinical in vivo studies, particularly using quercetin-loaded nanoparticles, demonstrated enhanced antitumor efficacy, reduced metastasis, and improved chemosensitivity compared to free quercetin.

Conclusion: Quercetin exhibits significant potential as a multitargeted adjunctive agent in breast cancer therapy through its combined effects on cell proliferation, apoptosis, signaling pathways, and tumor metabolism. Despite strong preclinical evidence, challenges such as low bioavailability and limited clinical data remain. Future studies should focus on optimized delivery systems and well-designed clinical trials to facilitate its translation into clinical practice, particularly for aggressive breast cancer subtypes.

keywords: Quercetin; Breast cancer; Apoptosis; Cell cycle arrest; PI3K/Akt signaling

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PI-65

Lipid Nanoparticle-Based mRNA Vaccines for Cancer Immunotherapy

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Background and aim: Cancer comprises a heterogeneous group of disorders characterized by dysregulated cell growth, uncontrolled proliferation, and the ability to invade surrounding tissues. Global epidemiological reports indicate that cancer is among the leading causes of mortality worldwide. Therefore, research increasingly focuses on prevention, early diagnosis, and the development of innovative targeted therapies. Recently, mRNA vaccines formulated in lipid nanoparticles (LNPs) have attracted substantial interest due to their specificity, adaptability, and capacity to elicit robust immune responses. This study investigates the therapeutic potential of LNP–mRNA vaccines in cancer immunotherapy, emphasizing their mechanisms of action and clinical relevance for future treatment strategies.

Methods: In this review, we searched PubMed, the Scientific Information Database (SID, Iran), and Google Scholar for articles published from 2021 to 2025. The search strategy included the keywords “cancer,” “vaccine,” and “LNP–mRNA.” More than 60 articles were initially identified, of which 22 met the inclusion criteria and were selected for final analysis.

Results: Studies indicate that mRNA vaccines can induce the expression of tumor-associated antigens (TAAs) and tumor-specific antigens (TSAs) by activating dendritic cells, leading to robust activation and proliferation of CD8+ T cells, CD4+ T cells, and natural killer cells. This promotes tumor-specific immune responses and targeted cytotoxicity without major HLA restrictions, enabling broader T-cell activation. However, challenges such as mRNA instability, immune response regulation, and efficient in vivo delivery remain significant limitations. Advances in nanomedicine have expanded the use of nanomaterials in cancer immunotherapy, particularly biomimetic nanoparticles with high loading efficiency and controlled release properties. The FDA-approved lipid-based nanoparticles (LNPs) provide structural stability, protection, and targeted delivery for mRNA formulations. By adjusting lipid composition and surface modifications with ligands, peptides, or monoclonal antibodies, LNPs can enhance intracellular uptake and tumor specificity. Furthermore, combining LNP–mRNA vaccines with immunotherapies such as CAR T-cell therapy may yield synergistic and sustained antitumor outcomes.

Conclusion: The application of mRNA vaccines in oncology remains in its early stages; however, the rising global cancer burden and limitations of conventional therapies underscore the demand for novel strategies. Lipid nanoparticle (LNP) delivery systems show promising clinical utility by stabilizing mRNA, improving biodistribution, enhancing cellular uptake, and facilitating targeted delivery. LNP–mRNA vaccines, with high potency, low toxicity, rapid development potential, and cost-effective manufacturing, represent a viable alternative to traditional treatments. Continued research and optimization are required to fully translate their therapeutic potential into clinical practice.

keywords: LNP-mRNA Vaccine Cancer

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-66

Development of a Novel Chimeric Multi-Epitope Vaccine Against Leishmania major Based on LmSTI Antigen: An Integrated Immunoinformatic and Molecular Dynamics Study

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Background and aim: Cutaneous Leishmaniasis (CL), mainly caused by Leishmania major, remains a global health challenge due to drug resistance and toxicity. With no licensed vaccine available, designing a potent subunit vaccine is critical. This study aimed to design a multi-epitope vaccine construct utilizing the immunogenic Stress-Inducible Protein 1 (LmSTI) combined with a potent adjuvant.

Methods: High-affinity CTL, HTL, and B-cell epitopes were predicted from LmSTI using IEDB and NetMHC servers. Selected epitopes were fused using EAAAK, GPGPG, and KK linkers. To enhance immunogenicity, the Resuscitation-promoting factor E (RpfE) was added as a TLR4 agonist adjuvant at the N-terminus. The construct's physicochemical properties, allergenicity, and 3D structure were modeled. Finally, molecular docking and 100 ns molecular dynamics (MD) simulations were performed to assess interaction with Toll-like receptor 4 (TLR4).

Results: The final construct was characterized as stable (Instability Index 40), soluble, and non-allergenic. Molecular docking demonstrated a strong binding affinity between the vaccine and TLR4. MD simulation analysis confirmed the stability of the complex, indicating robust interaction under physiological conditions. Immune simulation predicted significant production of IFN-γ and antibodies.

Conclusion: The proposed LmSTI-based multi-epitope vaccine demonstrates high potential for inducing specific cellular and humoral immunity against L. major. While in silico results are promising, in vivo experimental validation is required to confirm safety and efficacy.

keywords: Leishmania major, multi-epitope vaccine, LmSTI, Immunoinformatic, Molecular Dynamics

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-67

Evaluation of TIM-3 Gene Expression as Blood-Based Biomarker in Patients with Gastric Cancer Resistant to Chemotherapy and Treated with Immunotherapy

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Background and aim: Gastric cancer is one of the most aggressive malignancies of the gastrointestinal tract.In recent years, immune checkpoint inhibitors, particularly programmed cell death protein-1 inhibitors such as pembrolizumab, have emerged as a novel treatment option for patients with advanced gastric cancer. However, clinical responses to these therapies are highly heterogeneous.Increasing evidence suggests that complementary inhibitory pathways, including TIM-3 play important roles in immune regulation and may contribute to immune resistance.The aim of this study was to evaluate changes in the expression of TIM-3 genes in PBMC of patients with gastric cancer before and after treatment with pembrolizumab.

Methods: In this study, blood samples were collected from 30 patients who met the inclusion criteria, including a confirmed diagnosis of gastric cancer by a physician, resistance to standard chemotherapy, and age over 18 years. After isolating peripheral blood mononuclear cells (PBMCs), the expression of Tim-3 gene was evaluated using Real-time PCR. Beta-actin was used as the reference gene for data normalization. Statistical analysis of the data was performed using SPSS software version 26. Patients meeting exclusion criteria (including serious side effects, unwillingness to continue cooperation, death during treatment, incomplete treatment courses) were excluded from the study.

Results: The results demonstrated a statistically significant decrease in the expression of TIM-3 following pembrolizumab treatment,These findings indicate systemic immune alterations in PBMCs after PD-1 blockade and suggest that the expression of these inhibitory immune checkpoints may be modulated by immunotherapy.

Conclusion: This study highlights the value of PBMCs as a non-invasive and accessible source for assessing immune-related changes in patients with gastric cancer. Monitoring the dynamic expression of TIM-3 in peripheral blood may contribute to a better understanding of immune modulation during pembrolizumab treatment and provide a foundation for future studies investigating immune mechanisms associated with cancer immunotherapy.

keywords: Gastric cancer, Pembrolizumab, PBMC, TIM-3,Immunotherapy

PI-68

The influence of occupational heat stress on serum inflammatory cytokines among traditional bakery workers in Iran

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Background and aim: Heat exposure exceeding the ISO7243:1989 standard limit can contribute to health problems among employees in a variety of workplaces. Ignoring heat standard requirements in hot working conditions such as bakeries results in physiologic and health problems, as well as an elevated risk of later illnesses.

Methods: In this analytical case-control study, the serum levels of four inflammatory factors (interleukin-1 beta, interleukin-6, tumor necrosis factor-α, and Creactive protein) were assessed using an enzyme-linked immunosorbent assay. 105 male artisan bakers (in four job classifications in bakeries and staff) were compared based on demographic characteristics and inflammatory factors.

Results: The findings of the study showed correlations between serum interleukin-1β, interleukin-6, and C-reactive protein levels and thermal exposure in the occupational environment and employment type. Moreover, some differences in serum level of interleukin-1β and job type were observed. Heat overexposure affected the increase of interleukin-1β and C-reactive protein secretion.

Conclusion: As a result of years of working in high-temperature conditions, inflammation can lead to subsequent diseases in workers. To protect their health from this occupational hazard, additional safeguards are needed. Our recommendations could also be applied to overly hot work environments that may cause heat stress in workers.

keywords: Inflammation , Thermal stresses, Inflammatory Cytokine

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-69

High-dose vitamin D3 supplementation improves the clinical manifestations of chronic urticaria patients

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Background and aim: Chronic spontaneous urticaria (CSU) is a debilitating inflammatory skin condition marked by recurrent wheals, pruritus, and angioedema lasting over six weeks. Their pathophysiology is predominantly immune-mediated, with mast cell and basophil activation playing an essential role. New research suggests that vitamin D3, by altering the function of innate and adaptive immune cells, may affect disease activity. Several studies have shown lower serum vitamin D3 levels in CSU patients compared with healthy controls. This systematic review aimed to examine the evidence on the effects of vitamin D3 supplementation on CSU disease severity and the quality of life (QOL) of CSU patients.

Methods: PubMed, Scopus, Web of Science (WOS), and Google Scholar were searched by the medical librarian and information specialist. The initial search yielded 52 records; after screening titles and abstracts, only 30 were relevant. By studying the full text, only 5 articles were relevant to the purpose of this study and were included in our review. There were no language or date restrictions on our search strategy. The reference lists of the retrieved articles were also hand-searched to ensure no relevant articles were missed. Inclusion criteria were all types of human studies (clinical trials, uncontrolled trials, observational studies, and case series). All studies that included CU patients to evaluate the effects of vitamin D3 supplementation on alleviation of disease symptoms and patients' QOL were included.

Results: The PRISMA flowchart provides an overview of the search process. The study selection adhered to PRISMA guidelines, yielding five studies that met the inclusion criteria for qualitative synthesis. These studies included 208 CSU patients (156 women and 52 men). One study was a double-blind, randomized controlled trial, while the others were observational. In all studies, vitamin D3 was administered as an adjunct treatment, although doses and treatment durations varied. Three studies using validated scoring systems such as USS, UAS7, and UAS4 reported that vitamin D3 supplementation reduced CSU severity. Additionally, three studies using the DLQI and CU-Q2oL questionnaires showed improvements in quality of life. Two studies evaluated immunological markers and reported changes in cytokine profiles, including reductions in IL-10, IL-17, TGF-β1, erythrocyte sedimentation rate, and IgE levels, along with increased FOXP3 expression following supplementation. Overall, vitamin D3 supplementation was associated with improved symptoms and quality of life in CSU patients.

Conclusion: Evidence indicates that vitamin D3 supplementation may serve as a beneficial, safe, and cost-effective adjunctive therapy for CSU individuals. Supplementation was associated with less severe disease, improved QOL, and changes in immune system markers thought to play a role in CSU pathogenesis. However, more trials with larger sample sizes are needed to confirm the results. Additionally, meticulously designed, large-scale clinical trials are necessary to validate the therapeutic efficacy of vitamin D3 and to determine optimal dosing strategies in the management of CSU.

keywords: Chronic spontaneous urticaria, Vitamin D3 supplementation, Immune modulation

PI-70

Therapeutic Impact of Single-Chain Variable Fragments (scFvs) in Cancer Treatment: A Systematic Review

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Background and aim: Single-chain variable fragments (scFvs) are engineered antibody fragments composed of variable heavy and light chains connected by a flexible linker. Due to their small size, high specificity, and improved tumor penetration, scFvs have emerged as promising tools in cancer therapy. This systematic review aims to evaluate the therapeutic impact of scFv-based strategies in cancer treatment, focusing on immunotoxins, drug and gene delivery systems, and cellular immunotherapies such as CAR-T cells.

Methods: A systematic literature search was conducted using electronic databases including PubMed, Google Scholar, and publisher platforms. Studies published between 2012 and 2025 investigating scFv-based therapeutic approaches in cancer were included. Both preclinical and review studies were analyzed following PRISMA guidelines.

Results: Six relevant articles were included. scFv-based immunotoxins demonstrated selective cytotoxicity against HER2-positive cancer cells in vitro and acceptable safety profiles in vivo. Advanced delivery platforms using scFv-functionalized nanoparticles showed enhanced targeting efficiency. Furthermore, scFv-engineered CAR-T cells exhibited significant anti-tumor activity in preclinical cancer models.

Conclusion: scFv-based therapeutic strategies represent a versatile and effective approach in cancer treatment. Despite existing limitations such as stability and immunogenicity, recent advances highlight the growing potential of scFvs in precision oncology.

keywords: scFv, cancer therapy, immunotoxin, CAR-T, targeted delivery

PI-71

Immuno-Inflammatory Significance of Monocyte-Platelet Aggregates and β2 Integrin LFA-1 in Acute Coronary Syndrome

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Background and aim: Objective: Atherosclerosis is an inflammatory disease driven by complex interactions between platelets and immune cells. Monocyte-Platelet aggregates (MPA) and β2 integrins such as lymphocyte function-associated antigen 1 (LFA-1) play pivotal roles in leukocyte recruitment and vascular inflammation. This study investigated PMA formation and LFA-1 expression in patients with acute coronary syndrome (ACS).

Methods: Materials and Methods: Thirty ACS patients and thirty age-matched healthy individuals were analyzed. MPA frequency and LFA-1 expression levels were measured by flow cytometry. Dot plot analysis and Pearson correlation coefficient were used to explore associations between PMA and LFA-1. Multilevel statistical modeling assessed the influence of LFA-1 on PMA formation. Diagnostic relevance was evaluated using ROC curve analysis.

Results: Results: ACS patients exhibited significantly increased MPA levels and LFA-1 expression compared with healthy subjects. Despite their concurrent elevation, no significant linear correlation was detected between MPA and LFA-1. ROC analysis supported the potential diagnostic relevance of both parameters in ACS.

Conclusion: Enhanced monocyte-platelet interaction and increased LFA-1 expression highlight the immuno-inflammatory landscape of ACS. Elevated MPA and LFA-1 expression may serve as valuable diagnostic and risk stratification biomarkers in patients with ACS.

keywords: Keywords: Atherosclerosis; Leukocyte-Platelet Interaction; β2 Integrins; LFA-1; Acute Coronary Syndrome

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-72

Tocilizumab-Induced IL-6R Blockade in Juvenile vs. Adult Rheumatoid Arthritis: Systematic Review of Th17/Treg Balance and Synovial Biomarker Responses

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Background and aim: Rheumatoid arthritis (RA) is predominantly driven by interleukin-6 (IL-6), which fosters osteoclastogenesis, suppresses regulatory T cells (Tregs), and activates Th17 cells, thereby instigating synovial inflammation. In both adult rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA), tocilizumab, a monoclonal antibody that targets the IL-6 receptor (IL-6R), has demonstrated effectiveness in blocking this inflammatory cascade. Age-related changes in immune modulation, particularly changes in Th17/Treg dynamics, synovial biomarker expression, and IL-6 signaling pathways, may have an impact on these patients' treatment outcomes. Juvenile rheumatoid arthritis often presents with more significant systemic inflammation, but adult rheumatoid arthritis is marked by chronic synovial remodeling.

Methods: A comprehensive search of PubMed, MEDLINE, Embase, Scopus, and WOS (from inception to June 2025) was conducted using terms including "tocilizumab", "IL-6 inhibition", "juvenile idiopathic arthritis", "rheumatoid arthritis", "Th17", "Treg", and "synovial biomarkers" and their synonyms. Expert input was also sought to design the search syntax for this study. Included studies were clinical trials that reported Th17/Treg ratios, synovial histopathology, or cytokine profiles (e.g., IL-17, IL-23, RANKL) before and after tocilizumab/placebo. Studies other than RCTs, studies with only a published protocol version without an article, and studies in which the intervention/control group received additional treatments were exclusion criteria for articles from the screening process. Also, two referees independently screened the articles and their differences of opinion were resolved by the third referee.

Results: A pooled analysis of data from 14 studies (8 pediatric, 6 adult; n=1,522 patients) shows that tocilizumab more effectively normalized Th17/Treg ratios in JIA than in adult RA (68% vs. 52%, p=0.03). Pediatric patients showed a more marked reduction in synovial IL-17A and RANKL; this was linked to a faster clinical remission. Adults had lower MMP-3 and VEGF levels, which suggests stronger effects on stromal remodeling. JIA had higher relapse rates (23% vs. 12% in adults, p=0.04), maybe resulting from rebound IL-6 generation following therapy termination. While JIA patients showed faster suppression of IL-1β (−54% vs. −29% in adults at week 4, p=0.01), adults showed longer-lasting declines in GM-CSF and IL-8. Flow cytometry data from three studies (n=213) show that although their numerical increase was transient (peaking at week 8 and declining by week 24), young Tregs restored suppressive activity more rapidly (FoxP3+Helios+ cells: +82% vs. +43% in adults, p=0.005).

Conclusion: Tocilizumab's immunomodulatory effects are age-dependent, with superior Th17/Treg modulation in JIA but more sustained synovial biomarker responses in adults. These findings highlight the need for age-specific therapeutic monitoring strategies.

keywords: Tocilizumab; IL-6; JIA; Rheumatoid arthritis; Th17; Treg; Synovial biomarkers.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-73

Potential applications of nanotechnology to improve the safety and efficacy of CAR-T cell therapy

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Background and aim: In the past decade, Chimeric antigen receptor (CAR)-T cell therapy has become one of the most successful anticancer modalities, as evidenced by the U.S. FDA approval of seven different CAR-T products. Nonetheless, CAR-T cell therapy faces significant challenges, including complex and customized manufacturing processes, potentially severe side effects (including cytokine release syndrome, neurotoxicity, leukemic transformation, and on-target off-tumor toxicities), and limited efficacy in solid tumors. This review aims to synthesize and categorize the potential applications of nanotechnology to augment CAR-T therapy, spanning cell engineering, safety control, and efficacy enhancement.

Methods: We conducted a comprehensive literature review to establish a structured classification of how nanotechnology interfaces with and enhances the CAR-T therapeutic workflow. We identify and characterize five distinct, synergistic application classes: I) Non-viral manufacturing of CAR-T cells: Utilizing nanocarriers (e.g., lipid and polymeric nanoparticles or exosomes) for the efficient, scalable, and safe delivery of nucleic acids (mRNA, plasmid DNA) to engineer T cells ex vivo, overcoming high cost and safety concerns regarding the use of viral vectors. II) In vivo engineering of CAR-T cells: Biocompatibility and low immunogenicity of nanoparticles make them reliable candidates to deliver CAR-encoding genes directly to endogenous T cells within the patient's body, aiming to create a streamlined, off-the-shelf therapeutic approach that bypasses complex ex vivo manufacturing. III) Improving the safety profile of CAR-T cell therapy: Deploying nanotechnology to control toxicity, including cytokine-capturing nanosponges to mitigate cytokine release syndrome and neurotoxicity.

Results: Furthermore, CAR-T cells can be labeled with nanoscale imaging agents, such as iron oxide nanoparticles, enabling real-time, non-invasive tracking of their in vivo biodistribution. This capacity can also be leveraged to guide CAR-T cells to tumor sites, thereby optimizing dosing regimens and potentially reducing off-tumor toxicities by correlating cell trafficking patterns with clinical outcomes. IV) enhancing the in vivo function of CAR-T cells: Applying multifunctional nanosystems to enhance in vivo proliferation and persistence of CAR-T cells, increase tumor infiltration of CAR-T cells, and overcome immunosuppressive tumor microenvironment. V) cell-free CAR-based immunotherapy: CAR-T cell-derived exosomes encapsulate key cytotoxic and signaling molecules from parent cells but lack a nucleus. This offers major advantages: reduced risk of severe cytokine release syndrome and neurotoxicity, enhanced ability to penetrate the solid tumor stroma, and the potential for an off-the-shelf, allogeneic therapy without the risk of graft-versus-host disease (GvHD).

Conclusion: In conclusion, nanotechnology offers a versatile toolkit to refine CAR-T cell therapy and address its major limitations in safety, efficacy, and scalability. Nonetheless, nano-tailored CAR-T cell therapy remains largely preclinical. Significant translational challenges, including complex biocompatibility, scalable production in compliance with current good manufacturing practice (cGMP), and long-term in vivo fate of nanomaterials, must be rigorously addressed before advancing nano-tailored CAR-T cell therapy to clinical settings.

keywords: CAR-T cell therapy; Immunotherapy; Nanotechnology

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-74

Hypoxia and Its Impact on CAR T-Cell Therapy: A Systematic Review

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Background and aim: Hypoxia is characteristic of the solid tumor environment and is one of the obstacles to chimeric antigen receptor T (CAR T) cell therapy. While these achievements in hematological malignancies, however, CAR T cells mostly face metabolic limitation, immune suppression, and exhaustion in the hypoxic solid tumor microenvironment, which limits their efficacy. In this review, we aim to briefly explain how low oxygen levels affect the function of CAR T-cells and to suggest ways to boost the effectiveness of anti-tumor CAR T-cells in low-oxygen environments, as well as future research directions.

Methods: We conducted a comprehensive search of PubMed, Scopus, Web of Science, and clinical trial registries (ClinicalTrials.gov) using keywords such as "hypoxia AND CAR T-cell," "HIF-1α AND immunotherapy," and "tumor microenvironment AND T-cell exhaustion." Included studies were categorized based on in vitro, in vivo, and clinical evidence. Two independent reviewers initially evaluated the titles and abstracts of studies, and then the full texts of potentially relevant studies were evaluated. To identify additional publications, a manual search of reference lists of included articles was conducted.

Results: Studies show that Treg cells in the steady state rely on oxidative metabolism (OXPHOS) and extensive mitochondrial networks for their inhibitory function. However, in inflammatory environments, these cells switch to glycolysis, which is associated with FoxP3 instability and a tendency toward Th17-like phenotypes. In fact, it is a situation-dependent double standard: OXPHOS is the basis of immune tolerance, while glycolysis is generally associated with reduced suppressive function. Hypoxia impairs CAR T-cell function primarily through stabilization of HIF-1α, which leads to a metabolic shift to inefficient glycolysis, reduced energy production (ATP/NAD+), and impaired cytotoxicity. Hypoxia also reduces the efficacy of CAR T-cells by creating an immunosuppressive environment (through increased PD-L1 and secretion of inhibitory factors from the tumor stroma) and inducing terminal fatigue in cells. However, targeted interventions such as inhibiting HIF-1α or supporting oxidative metabolism could offer promising strategies to improve CAR T-cell function in solid tumors.

Conclusion: Hypoxia is a key challenge for CAR T-cells in solid tumors, as it creates a complex immune suppression network. Promising strategies include designing hypoxia-resistant CARs, metabolic engineering of cells, and the use of targeted drug compounds (such as HIF or CD39 inhibitors). The ultimate efficacy of these strategies needs to be confirmed in future clinical trials.

keywords: Hypoxia; CAR T-cell; T-Cell Exhaustion; Immunosuppression; Tumor Microenvironment.

PI-75

Mitochondrial Dynamics in Treg Function: A Systematic Review of Oxidative Phosphorylation vs. Glycolysis in Immune Suppression

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Background and aim: The preservation of immunological tolerance relies on Tregs, whose suppressive function is closely associated with metabolic reprogramming. Recent findings demonstrate the significance of mitochondrial dynamics—encompassing fusion, fission, and metabolic transitions between OXPHOS and glycolysis—in regulating Treg stability, proliferation, and function. Conventional T cells depend on glycolysis for activation, whereas Tregs OXPHOS and FAO to maintain their suppressive function. The metabolic flexibility of Tregs in various inflammatory settings remains a subject of ongoing controversy. This systematic review assesses the impact of mitochondrial dynamics on Treg function by comparative analysis of OXPHOS-dependent suppression in stable contexts versus glycolysis-driven adaptation in pro-inflammatory situations.

Methods: The PubMed/MEDLINE, Embase, and Web of Science databases were searched thoroughly and methodically between 2010 and 2025. Important terms like "regulatory T cells," "Treg," "mitochondrial dynamics," "oxidative phosphorylation," "glycolysis," and "immune suppression" were used in the process. Search terms were combined using the Boolean operators AND and OR. Two independent reviewers initially evaluated the titles and abstracts of studies, and then the full texts of potentially relevant studies were evaluated. To identify additional publications, a manual search of reference lists of included articles was conducted. The inclusion criteria for the studies included the investigation of mitochondrial metabolism in Treg function, utilizing either human samples or animal models.

Results: The findings are based on a comprehensive analysis of 1,450 experimental data sets and 32 distinct research projects. The findings indicate that Tregs fundamentally rely on fatty acid oxidation and oxidative phosphorylation under stable conditions, supported by extensive, interconnected mitochondrial networks facilitated by specific proteins. Under inflammatory conditions such as hypoxia or the presence of certain cytokines, the metabolic pathway of these cells shifts towards glycolysis. This shift can be detected by markers such as increased HK2 expression. The shift towards glycolysis is associated with FoxP3 instability, reduced inhibitory function, and increased production of mitochondrial reactive oxygen species. Increased production of these reactive species, in turn, makes Tregs more malleable and prone to develop into Th17-like cells, which are associated with the production of interleukin-17. These observations highlight the complex relationship between metabolic malleability and Treg cell stability.

Conclusion: Studies show that Treg cells, in the steady state, rely on oxidative metabolism (OXPHOS) and extensive mitochondrial networks for their suppressive function. However, in inflammatory environments, these cells switch to glycolysis, which is associated with FoxP3 destabilization and a tendency toward Th17-like phenotypes. In effect, this is a situation-dependent double standard: OXPHOS is the basis of immune tolerance, while glycolysis is generally associated with reduced suppressive function.

keywords: Regulatory T cells; mitochondrial dynamics; oxidative phosphorylation; glycolysis; immune suppression.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-76

Combining MSC-Derived Exosomes with Immune Checkpoint Inhibitors (Anti-PD-1/PD-L1) in AML Therapy: Mechanisms and Therapeutic Potential

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Background and aim: In AML, mesenchymal stem cell exosomes (MSC-exo) play a dual role. Their molecular content (including miR-155, miR-34a, TGF-β and PD-L1) is crucial. On the one hand, these vesicles contribute to leukemia progression and the establishment of a tumor-promoting microenvironment by transmitting immunosuppressive signals such as PD-L1 and TGF-β. On the other hand, due to their targeting nature and immunomodulatory capabilities, they have great potential as smart carriers for targeted drug delivery or immunotherapy. In simple terms, exosomes can be either an ally of the tumor or a weapon against it, depending on their content.

Methods: The following keywords were used in a systematic literature search conducted in PubMed, Embase, Web of Science, and the Cochrane Library (January 2010–June 2025): ("MSC exosomes" OR "mesenchymal stromal cell extracellular vesicles") AND ("acute myeloid leukemia" OR "AML") AND ("PD-1" OR "PD-L1" OR "immune checkpoint blockade"). Requirements for inclusion were original studies examining MSC-Exos in AML models or patients, results on the interactions between exosomes and PD-1/PD-L1 signaling, and results on immune modulation or tumor response. Exclusion rules included studies of hematologic malignancies other than AML, non-English publications, and reviews lacking primary data. Two independent reviewers initially evaluated the titles and abstracts of studies, and then the full texts of potentially relevant studies were evaluated. To identify additional publications, a manual search of reference lists of included articles was conducted.

Results: Preclinical research (n=29) indicates that MSC-Exos have dual effects on the advancement of AML and the immune system's reaction to tumors. Specifically, UC-MSC-Exos downregulate PD-L1 expression on leukemia cells by delivering tumor suppressor miRNAs such as miR-34a and, in combination with anti-PD-1, significantly increase cytotoxic T cell proliferation and IFN-γ production, leading to a 52–67% reduction in tumor burden in animal models. In contrast, BM-MSC-Exos have donor-dependent effects and in some cases facilitate leukemia progression by increasing PD-L1-expressing MDSCs and delivering TGF-β1. Proteomic analysis has also identified two functionally contrasting subgroups: proinflammatory exosomes (rich in HLA-DR and CD40) are associated with improved survival, whereas immunosuppressive exosomes (containing CD73 and TGF-β) accelerate leukemogenesis. Available clinical data support the safety of this approach, and subgroup analyses suggest that the outcome of the treatment is strongly dependent on three factors: cell source, culture conditions and separation method.

Conclusion: Mesenchymal exosomes have a dual role in acute myeloid leukemia, and their ultimate effect (immune enhancement or tumor escape) depends crucially on three factors: cellular source (cord-derived), tumor microenvironment, and production techniques. For therapeutic use, these exosomes must be engineered, selected in appropriate patients with biomarkers, and tested in clinical trials in combination with existing immunotherapies. The main challenge is the transition from non-standard preclinical research to precision personalized medicine.

keywords: Mesenchymal stromal cell-derived exosomes; Acute myeloid leukemia; PD-1/PD-L1 blockade

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-77

Comparative Efficacy of Bivalent, Quadrivalent, and Nonavalent HPV Vaccines in Preventing Infection, Precancerous Lesions, and Genital Warts: A Systematic Review of Clinical Trials

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Background and aim: Human papillomavirus (HPV) causes approximately 690,000 cases of cancer each year. Since 2006, three preventive vaccines with different strengths have been developed: dual (against HPV-16/18), quadrivalent (against HPV-6/11/16/18), and nine-valent (against 9 types). This systematic review compares vaccines based on four key criteria: 1) immune response (neutralizing antibody titer or GMT), 2) clinical efficacy in preventing infection, precancerous lesions (CIN2+), and genital warts, 3) cross-protection against non-vaccine-related types, and 4) duration of protection (persistence of antibody and clinical effect). The aim is to provide evidence for informed policy and clinical choice.

Methods: We will systematically search several databases include (including PubMed, Scopus, and Web of Science) and Google Scholar search engine were searched by the authors for randomized controlled trials and observational studies with comparator arms. We used the keywords "Human papillomavirus vaccine" and "Immune response" and their synonym using Medical Subject Headings (MeSH) and free-text method to develop the search strategy. Standardized data extraction will focus on immunogenicity outcomes (GMTs), clinical efficacy against virological and histological endpoints, and safety profiles. Risk of bias will be assessed using Cochrane tools, and we will perform meta-analyses where appropriate. Two reviewers independently screened records, extracted data, and assessed risk of bias using the Cochrane Risk of Bias Tool. Discrepancies were resolved by consensus.

Results: Based on data, the dual vaccine (Cervarix) elicited the strongest and most persistent antibody response against HPV-16/18 (primary GMT: 5400 and 3200; after 5 years: 2200 and 1300) with the lowest annual decline rate (10-12%). The quadruple vaccine (Gardasil) had a lower initial response (1800 and 900) and a more rapid decline (15-20% per year). The nine-valent vaccine (Gardasil-9) showed a moderate response to HPV-16/18 (2100 and 1100), but extended coverage to five additional carcinogens, with GMTs of 300-550 after 5 years. vaccines maintained protective levels (200 for HPV-16 and 100 for HPV-18) and were more than 90% effective in preventing infection and precancerous lesions. The strength of the dual vaccine is the outstanding cross-protection (46-60%) against related types, while the nine-valent vaccine, with 97% coverage against 9 types, offers the broadest oncogenic protection and can prevent about 90% of HPV-related cancers.

Conclusion: The current study highlights a key trade-off in HPV vaccine choice: the Gardasil-9 provides broader protection by adding five additional cancer-causing types, while the Cervarix produces a stronger and more sustained antibody response against HPV-16/18. Although direct coverage of Gardasil-9 results in better overall cancer prevention, Cervarix shows significant cross-protection against related types. These findings support the WHO recommendation to prioritize Gardasil-9 whenever possible, while recognizing the continued importance of Cervarix in specific situations, such as when cervical cancer prevention is an absolute priority and there are economic constraints.

keywords: Human papillomavirus vaccine; immunogenicity; antibody response.

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July 20-23, 2026

PI-78

StudyongeneexpressionofIL-17Aineutopicandectopictissue sample of endometriosis patients and comparison with control group

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Background and aim: The growth of endometrial tissue beyond the uterine cavity characterizes en dometriosis, a chronic inflammatory disease. IL-17A, along with other immune mediators and a myriad of immune cells including Th17 lymphocytes and macrophages, are more prevalent in the peritoneal fluid of patients with endometriosis. IL–17A facilitates the implantation of endometrial tissue in ectopic locations by inducing growth factors and inflammatory cytokines from other im munecells. ThisworkfocusesonthelevelsofIL-17Ageneexpressionintissuesamplesfrompatient and control groups, as prior research has not extensively covered the gene expression of inflam matory mediators in tissue samples.

Methods: This study is both experimental and case-control in nature. Tissue samples were collected from 32 women undergoing laparoscopy at Yazd Shahid SadoughiHospital. Thesamplesweredividedintotwogroups: 16patientswithendometriosisand 16 healthy individuals. Within the patient group, there were two types of samples: eutopic and ec topic. The expression of IL-17A was assessed with RT-qPCR.

Results: RT-qPCR results showed a significant difference in IL-17A gene expression betweenectopiclesions andeutopicsamplesfrom endometriosis patients (P value 0.0001). Additionally, there was a significant increase in gene expression in eutopic samples from endometriosis patients compared to control samples (P value = 0.0176).

Conclusion: This study confirms the crucial involvement of inflammatory mediators like IL-17A in endometriosis through molecular findings in tissue samples, reflecting the elevated IL-17A content in the eutopic endometrium and ectopic lesions of endometriosis patients.

keywords: endometriosis, IL-17A, Th17 lymphocytes, inflammatory

PI-79

The Role of Exosomes in Breast Cancer Progression: Mechanisms of Communication Between Tumor Cells and the Microenvironmenta

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Background and aim: Exosomes are small extracellular vesicles that play a vital role in intercellular communication by transporting proteins, lipids, and genetic material between cells. In the context of breast cancer, exosomes have gained attention for their involvement in tumor progression, metastasis, and modulation of the tumor microenvironment (TME). These vesicles enable communication between tumor cells and various components of the TME, including immune, stromal, and endothelial cells. Understanding how exosomes influence breast cancer progression can offer new therapeutic opportunities to target tumor cell interactions and metastasis.

Methods: A thorough literature search was conducted across PubMed, Scopus, and Web of Science to identify studies published up to March 2025 that explored the role of exosomes in breast cancer. The studies included focused on how exosomes contribute to communication between tumor cells and the TME, immune system regulation, and overall tumor dynamics. Data on the molecular composition of exosomes, their impact on cancer progression, and potential therapeutic approaches were extracted and analyzed.

Results: The review identified 30 studies that examined the role of exosomes in breast cancer progression. Findings consistently demonstrated that exosomes support tumor progression by promoting angiogenesis, immune suppression, and the formation of pre-metastatic niches. Exosomes carry various oncogenic molecules such as microRNAs, proteins, and signaling factors, which modulate the behavior of surrounding stromal and immune cells, thus enhancing tumor growth and spread. Additionally, exosomes have been shown to contribute to drug resistance by transferring molecules that influence the efficacy of chemotherapy and other treatments.

Conclusion: Exosomes are integral to breast cancer progression by facilitating communication between tumor cells and the TME. Their capacity to transfer bioactive molecules that foster tumor growth, metastasis, and drug resistance positions them as potential targets for therapeutic intervention. However, challenges remain in targeting exosomes effectively due to issues with specificity and delivery. Future research should aim to develop exosome-based diagnostic and therapeutic strategies to improve breast cancer treatment outcomes.

keywords: Breast Cancer, Exosomes, Microenvironment.

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-80

Molecular Neutrophil-to-Lymphocyte Ratio (NLR) in Pediatric Appendicitis: A Systematic Review of Diagnostic Accuracy

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Background and aim: Although acute appendicitis is still the most common pediatric surgical emergency, accurate diagnosis is still difficult because of atypical presentations and constraints of current biomarkers. An emerging inflammatory index, the neutrophil-to- lymphocyte ratio (NLR) shows the balance between adaptive (lymphocyte-mediated) and innate (neuraphil-driven) immune responses in abdominal inflammation. By capturing both systemic inflammation (neutrophilia) and stress response (lymphopenia), NLR provides possible advantages over conventional markers like WBC count or C-reactive protein (CRP) in pediatric populations where radiation-free diagnostics are prioritized. While investigating its immunological basis in the pathophysiology of appendiceal inflammation, this systematic review assesses NLR's diagnosis accuracy in pediatric

Methods: Between 2010 and 2025, the subsequent search phrases were employed to query PubMed/MEDLINE, Embase, and the Cochrane Library: The terms that require definition include: "neutrophil-to-lymphocyte ratio," "NLR," "pediatric appendicitis," "diagnostic accuracy," and "inflammatory biomarkers." The studies reviewed provided cut-off points, AUC values, and NLR sensitivity and specificity for appendicitis in individuals under 18 years of age. Case reports and research studies without a control group were excluded from the analysis. Two independent reviewers initially evaluated the titles and abstracts of studies, and then the full texts of potentially relevant studies were evaluated. To identify additional publications, a manual search of reference lists of included articles was conducted.

Results: Pooled analysis of 22 studies (n=9,357 children) revealed that the NLR demonstrated superior diagnostic performance for pediatric appendicitis compared to conventional biomarkers, with an overall AUC of 0.89 (95% CI 0.85-0.92) versus 0.76 for WBC count and 0.82 for CRP. The optimal diagnostic NLR cut-off ranged between 4.5-6.2, showing 84% sensitivity and 88% specificity for detecting appendicitis, while values ≥7.0 significantly predicted perforation (OR 3.4, 95% CI 2.1-5.5). Performance varied by age group, with adolescents (AUC 0.91) showing better discrimination than younger children (AUC 0.83), likely reflecting developmental differences in immune responses. NLR maintained diagnostic accuracy across different clinical settings, with 78% positive predictive value in emergency departments and 85% in surgical evaluations, suggesting its utility as both a screening tool and severity marker in pediatric appendicitis.

Conclusion: This systematic review confirms the dual role of NLR as an effective biomarker for both diagnosis and prognosis of appendicitis in children. Its diagnostic accuracy (with an optimal cutoff of 4.5 to 6.2) (84% sensitivity, 88% specificity) is higher than conventional markers, and values ≥7 reliably indicate risk of rupture. Although the determination of age-related reference ranges and standard measurement times requires future research, NLR is currently considered an accessible and cost-effective tool to improve initial assessment in pediatric emergency care.

keywords: “Neutrophil-to-lymphocyte ratio”, “pediatric appendicitis”, “diagnostic accuracy”, “inflammatory biomarkers”

PI-81

Comprehensive Overview of Pro-Inflammatory and Pro-Survival Mechanisms in Neuroinflammatory Pathways and Neurodegeneration

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Background and aim: Neuroinflammation plays a pivotal role in the pathophysiology of neurodegenerative disorders, mediated by a complex network of signaling pathways that are both pro-inflammatory and pro-survival. These pathways can either exacerbate neuronal damage or offer protective effects, depending on the context. A comprehensive understanding of the intricate interactions between these pathways is vital for identifying potential therapeutic targets for conditions such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis.

Methods: This review study involved a systematic search of scientific databases, including Scopus, PubMed, and Embase, from 2016 to 2025. Using relevant keywords such as Neurodegeneration, Neuroinflammation, Pro-Inflammatory, and Pro-Survival, a total of 74 articles meeting the inclusion criteria were selected for analysis.

Results: Pro-inflammatory mediators, including TNF-α, IL-1β, and IFN-γ, were found to activate glial cells, which contribute to sustained inflammation and neuronal death. In contrast, pro-survival pathways such as PI3K/Akt and NF-κB were shown to support neuronal survival under stress, often mitigating inflammatory damage. Dysregulation of these pathways in several neurodegenerative diseases results in an imbalance that favors inflammation, thus accelerating neurodegeneration. Notably, microglial activation can be both neurotoxic and neuroprotective, with its effects contingent on the disease context and stage.

Conclusion: : The interaction between pro-inflammatory and pro-survival signaling pathways is a key determinant of neurodegenerative disease progression. Therapeutic strategies should focus on modulating these pathways to mitigate inflammation while promoting neuroprotection. Given the dual nature of immune responses in the brain, targeted interventions are critical. Further investigation is needed to identify key regulatory factors that can shift the balance towards neuroprotection without compromising vital immune functions. Targeting both pro-inflammatory and pro-survival pathways holds promise as a therapeutic approach for neuroinflammatory diseases, though careful consideration of their dynamic roles is essential

keywords: Neurodegeneration, Neuroinflammatory, Pro-Inflammatory, Pro-Survival.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-82

Modulation of Transforming Growth Factor-β (TGF-β) gene expression by Flutamide and its sulfonamide-Modified Derivative in a Murine Colon Carcinoma Allograft Model

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Background and aim: Colorectal cancer is the third most commonly diagnosed cancer worldwide and the fourth leading cause of cancer-related mortality. The Organic Chemistry Research Group at Bu-Ali Sina University has synthesized a structural derivative of flutamide featuring a sulfonamide functional group. Notably, flutamide is an anti-androgen primarily used in the treatment of prostate cancer and is not conventionally recognized as a standard therapeutic agent for colorectal cancer. The newly modified compound was designed to potentially enhance anticancer activity. In this study, we evaluated the expression of the TGF-β gene in an allograft model using the CT26 cell line following treatment with formulations.

Methods: Female BALB/c mice (n = 5 per group) were divided into seven experimental groups: (1–2) tumor-bearing mice treated with unmodified flutamide via intraperitoneal (IP) or intratumoral (IT) routes, (3–4) tumor-bearing mice treated with the modified flutamide via IP or IT administration, (5) tumor-bearing untreated controls, and (6–7) healthy treated with the unmodified or modified flutamide via IP administration. Treatments were administered daily for 15 days. At the end of the treatment period, tumor tissue (not skin surrounding the tumor) was harvested, and TGF-β mRNA expression was quantified using real-time quantitative PCR (qRT-PCR).

Results: TGF-β expression was significantly upregulated in tumor tissue from mice receiving the modified flutamide via intratumoral injection compared to the untreated tumor-bearing control group (P = 0.016). Conversely, a significant downregulation of TGF-β was observed in the group treated with unmodified flutamide via the intraperitoneal route (P = 0.012). No statistically significant changes in TGF-β expression were detected in the remaining treatment groups (P 0.05).

Conclusion: These findings suggest that both the chemical modification of flutamide and the route of administration critically influence TGF-β expression in the tumor microenvironment. While TGF-β exhibits a well-documented dual role acting as a tumor suppressor in early stages and promoting immunosuppression and metastasis in advanced disease. The observed upregulation following intratumoral delivery of the modified compound may reflect a context-dependent modulation of the tumor immune milieu.

keywords: Colon carcinoma; Modified Flutamide; TGF-β gene expression; BALB/C mouse

PI-83

Application of Artificial Intelligence in Flow Cytometry for the Diagnosis of Autoimmune and Immunodeficiency Disorders

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Background and aim: Flow cytometry is a fundamental technique in clinical immunology for the evaluation of immune cell phenotypes in autoimmune and immunodeficiency disorders. However, conventional manual analysis of flow cytometry data is time-consuming, operator-dependent, and limited in its ability to interpret high-dimensional datasets. The aim of this review is to summarize recent advances in the application of artificial intelligence (AI) for the automated interpretation of flow cytometry data in the diagnosis and monitoring of autoimmune and immunodeficiency diseases.

Methods: A comprehensive review of the current literature was conducted focusing on the use of artificial intelligence, including machine learning and deep learning techniques, in flow cytometry data analysis. Relevant studies addressing AI-based algorithms, automated gating strategies, immune cell classification, and clinical applications in autoimmune and immunodeficiency disorders were analyzed and synthesized.

Results: AI-based approaches demonstrated improved accuracy and reproducibility in flow cytometry data interpretation compared to conventional manual gating. Machine learning algorithms enabled efficient classification of immune cell populations and identification of disease-specific immunophenotypic patterns, while deep learning models facilitated automated gating and detection of subtle immune alterations. These methods showed significant potential in enhancing early diagnosis, disease stratification, prognostic assessment, and therapeutic monitoring in both autoimmune and immunodeficiency disorders.

Conclusion: The integration of artificial intelligence into flow cytometry analysis represents a transformative advancement in clinical immunology. AI-driven approaches enhance diagnostic precision, reduce operator-dependent variability, and support personalized immune profiling. With further standardization and clinical validation, AI-assisted flow cytometry is expected to play an increasingly important role in the diagnosis and management of autoimmune and immunodeficiency diseases.

keywords: Flow Cytometry; Artificial Intelligence; Autoimmune Diseases; Immunodeficiency; Machine Learning;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-84

Clinical association of the anti-Phosphatidylserine antibodies with CagA-positive Helicobacter pylori infection in peptic ulcer patients

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Background and aim: Infection with Helicobacter pylori, particularly cytotoxin-associated gene A (CagA)–positive strains, is strongly associated with the development of peptic ulcer (PU) disease. Emerging evidence suggests that autoimmune responses against phospholipid antigens may contribute to disease pathogenesis. This study aimed to evaluate serum levels of anti-phosphatidylserine (anti-PS) antibodies in H. pylori–infected PU patients compared with asymptomatic (AS) carriers and uninfected controls, and to determine their association with CagA status.

Methods: The study included 100 H. pylori–infected PU patients, 65 H. pylori–infected AS carriers, and 30 H. pylori–negative healthy controls. Anti-CagA seropositivity was detected in 80 PU patients and 40 AS carriers. Serum anti-PS antibody concentrations were quantified using enzyme-linked immunosorbent assay (ELISA). Comparisons between groups and correlations with CagA status were statistically analyzed.

Results: PU patients exhibited significantly elevated serum anti-PS levels compared with AS carriers (P0.001) and uninfected controls (P 0.001). No significant difference was observed between AS carriers and controls. Within the PU group, anti-PS levels were markedly higher in anti-CagA–positive patients compared with anti-CagA–negative patients (P 0.01).

Conclusion: Elevated circulating anti-PS antibodies are strongly associated with PU disease, particularly in patients infected with CagA-positive H. pylori strains. These findings support a potential role for phospholipid-directed autoimmune responses in PU pathogenesis.

keywords: Peptic ulcer; Helicobacter pylori; Virulence factor, anti-phosphatidylserine antibodies

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-85

Modulatory Effects of Hyaluronic Acid on Hydrogen Peroxide-Induced Cytotoxicity in Breast Cancer Cells: Implications for Enhanced Therapeutic Strategies

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Background and aim: Cancer represents one of the most significant global health challenges, necessitating the development of effective treatment strategies. Hydrogen peroxide (H_2O_2) has garnered attention as a potent oxidizing agent in cancer therapy; however, its application may be difficult to control. In this study, we investigated the potential of hyaluronic acid (HA) as a protective agent that can modulate the oxidative effects of H_2O_2.

Methods: The effects of H_2O_2 and HA on the viability and apoptosis of breast cancer cells were examined. Cells were treated with varying concentrations of H_2O_2 (0-1000 µM) for 24 hours, followed by assessments of cell viability and apoptosis.

Results: The findings indicated that increasing concentrations of H_2O_2 led to a dose-dependent decrease in the viability of cancer cells, accompanied by an increase in apoptosis. Notably, when H_2O_2 was combined with HA, the IC50 value shifted from 100 µM to 200 µM, indicating a change in cellular sensitivity to treatment. Similar trends were observed in apoptosis levels.

Conclusion: The results demonstrate that hyaluronic acid can mitigate the toxic effects of hydrogen peroxide, rendering its application more controllable. These findings may contribute to the design of novel therapeutic strategies for breast cancer.

keywords: Hydrogen peroxide, hyaluronic acid, cancer cells, viability, apoptosis.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-86

Tumor Microenvironment Mediated Immune Suppression as a Barrier to Dendritic Cell-Based Immunotherapy in Hematologic Malignancies

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Background and aim: Dendritic cell (DC)-based immunotherapy represents a cornerstone of cancer immunology due to the central role of DCs in antigen uptake, processing, and initiation of adaptive immune responses. In hematologic malignancies, however, the clinical efficacy of DC-centered approaches remains limited. A major contributor to this limitation is the tumor microenvironment (TME), which is characterized by complex immunosuppressive networks that disrupt DC development, maturation, migration, and antigen-presenting capacity. These alterations ultimately impair effective T-cell priming and antitumor immunity.

Methods: This narrative immunology-focused review synthesizes current experimental and translational evidence investigating the impact of the hematologic tumor microenvironment on DC biology and function. Relevant studies were identified through a targeted literature survey of peer-reviewed preclinical and clinical research addressing DC-TME interactions, immune suppression mechanisms, and immune-modulatory intervention strategies.

Results: The hematologic TME was found to impair DC function through multiple interconnected mechanisms, including expansion of regulatory immune cell populations, secretion of inhibitory cytokines, metabolic reprogramming, and upregulation of immune checkpoint pathways. These factors collectively suppress DC maturation, reduce antigen presentation efficiency, and limit DC migration to lymphoid organs. Emerging immunological strategies such as Toll-like receptor agonists, immune checkpoint inhibitors, metabolic modulation, and advanced antigen delivery platforms have demonstrated the capacity to partially restore DC functionality and enhance downstream T-cell-mediated immune responses under suppressive microenvironmental conditions.

Conclusion: Tumour microenvironment-mediated immune suppression is a key barrier to the effectiveness of dendritic cell-based immunotherapy in hematologic malignancies. Suppressive cells, inhibitory cytokines, and metabolic constraints impair DC differentiation, maturation, migration, and antigen presentation, limiting T-cell-mediated antitumor responses. Future strategies integrating DC vaccination with immune checkpoint modulation, metabolic targeting, and advanced antigen delivery may enhance DC functionality and improve clinical outcomes.

keywords: Dendritic cell immunotherapy, Tumor microenvironment, Immune suppression, Hematologic malignancies

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-87

Investigation of the Effects of Lawson on the Expression of MMP7, IL-6, and TNF-α Genes in Human HaCaT Keratinocyte Cells Under High-Glucose Conditions

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Background and aim: Diabetes is one of the chronic metabolic diseases characterized by elevated blood glucose levels and the development of complications such as diabetic foot ulcers (DFU). In these patients, increased environmental glucose induces oxidative stress, chronic inflammation, and impaired function of keratinocyte cells. These alterations are associated with increased expression of inflammatory genes such as IL-6 and TNF-α, as well as changes in the levels of matrix metalloproteinase enzymes, including MMP7. Lawsone, the active compound of the henna plant (Lawsonia inermis), is known for its antioxidant and anti-inflammatory properties. The aim of this study was to investigate the effect of lawsone

Methods: Human keratinocyte (HaCaT) cells were cultured in DMEM medium and, after reaching appropriate confluence, were treated with specified concentrations of glucose and lawsone. After 24 hours, total RNA was extracted and cDNA synthesis was performed. The expression levels of IL-6, TNF-α, and MMP7 genes were evaluated using real-time PCR and the $2^{-}\Delta\Delta CT$ method, normalized to the reference gene GAPDH.

Results: Exposure of HaCaT cells to high glucose resulted in a significant increase in TNF-α gene expression and a decrease in MMP7 expression within the first 24 hours, while no significant change was observed in IL-6 expression. Treatment of the cells with lawsone led to a significant reduction in the expression of the inflammatory genes TNF-α and IL-6, along with a gradual increase in MMP7 expression compared to the glucose-treated group.

Conclusion: The findings of this study indicate that lawsone can attenuate the harmful effects of high glucose on keratinocytes by inhibiting inflammatory pathways and reducing TNF-α expression. Moreover, the increased expression of MMP7 following lawsone treatment suggests a potential role of this compound in activating matrix remodeling pathways and promoting wound repair. Therefore, lawsone may be considered a natural compound with therapeutic potential for improving the healing process of diabetic wounds.

keywords: Diabetes, Lawsone, Keratinocyte, Diabetic foot ulcer, MMP7

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-88

Effect of Progesterone on the Expression of TGF-β and IL-6 Genes in Human Dermal Fibroblasts (HDFs)

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Background and aim: Wound healing is a multistep biological process involving hemostasis, inflammation, cell proliferation, and tissue remodeling. Fibroblast activation and extracellular matrix production are essential for effective tissue repair. Transforming growth factor beta (TGF-β) plays a central role in wound healing by promoting fibroblast proliferation and migration while exerting anti-inflammatory effects. In contrast, interleukin-6 (IL-6) is a pro-inflammatory cytokine whose excessive expression may lead to chronic inflammation and impaired healing. Therefore, balanced regulation of TGF-β and IL-6 is critical for optimal wound repair. This study investigated the effect of progesterone on TGF-β and IL-6 gene expression in human dermal fibroblast (HDF) cells.

Methods: After the cells reached an appropriate confluency, they were treated with progesterone at a low concentration, and after 24 hours, RNA was extracted and synthesized into cDNA. Gene expression was assessed using Real-Time PCR relative to the reference gene GAPDH, and relative changes in gene expression were calculated using the ΔΔCt-2 method.

Results: The results showed that progesterone significantly increased TGF-β gene expression and decreased IL-6 gene expression ($P \leq 0.05$).

Conclusion: These findings indicate that a low concentration of progesterone may exert anti-inflammatory effects and also facilitate wound healing by increasing TGF-β and decreasing IL-6, thereby promoting fibroblast proliferation and extracellular matrix remodeling. In other words, Progesterone may reduce cutaneous inflammation and improve tissue repair. This study provides an initial basis for investigating the application of progesterone in the treatment of inflammatory skin disorders and in enhancing the wound healing process, and it can serve as a foundation for future research on hormonal factors in tissue regeneration.

keywords: Wound healing, Progesterone, TGF-β, IL-6, Human dermal fibroblasts

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-89

A Comprehensive Evaluation of the Prognostic Potential of Amyloid Precursor Protein (APP) and Its Metabolites in Breast Cancer

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Background and aim: Background : Amyloid Precursor Protein (APP), best known for its role in Alzheimer's disease pathogenesis, has recently gained attention as a multifaceted molecule with potential functions in oncogenesis. However, the clinical value and prognostic power of APP and its proteolytic products (e.g., sAPPα, sAPPβ, Aβ) in breast cancer remain systematically undefined. This systematic review aims to integrate existing evidence and clarify the association of these molecules with clinical outcomes in breast cancer patients.

Methods: Materials and Methods: For this review article, an extensive and systematic search was conducted in PubMed/MEDLINE, Scopus, and Web of Science databases up to the end of December 2025. The main keywords used included "Amyloid Precursor Protein," "APP," "Breast Neoplasms," "Prognosis," "Biomarker," "sAPPalpha," "sAPPbeta," and "Amyloid-beta." Human studies investigating the quantitative association of APP or its fragment levels (in tissue, serum, or plasma) with pathological features or clinical outcomes of breast cancer were selected. Their methodological quality was assessed using the standardized Newcastle-Ottawa Scale tool.

Results: Findings: Out of 325 initially identified studies, 18 studies ultimately met the inclusion criteria for this review. Data analysis revealed that the expression patterns of APP and the ratios of its proteolytic fragments (particularly an increased sAPPβ/sAPPα ratio) vary across different breast cancer subtypes. In 11 studies (61%), higher levels of full-length APP or an increased sAPPβ/sAPPα ratio were significantly associated with aggressive tumor features, including higher grade, estrogen receptor-negative status, the presence of lymphatic metastasis, as well as reduced overall survival and disease-free survival. Three studies (17%) reported no significant association, and four studies (22%) suggested a contradictory or even protective role for certain isoforms. Significant heterogeneity was observed among studies regarding sampling methods, assay techniques (ELISA, Western blot, immunohistochemistry), and cutoff points.

Conclusion: Conclusion: Based on current evidence, APP and its processing pathway appear to play a role in breast cancer progression, particularly in more aggressive subtypes. Although these molecules have not yet been established as standard prognostic biomarkers in clinical practice, the findings indicate their high potential as part of a multivariable panel to aid in more accurate risk stratification and treatment personalization. Prospective, multicenter studies with large sample sizes and standardized assay protocols are essential for the definitive confirmation of these findings and for determining their added value compared to current

keywords: Keywords: Amyloid Precursor Protein, Breast Cancer, Prognosis, Biomarker, sAPPα, sAPPβ.

PI-90

Lactate in Sepsis: Clinical Value and Comparison with CRP and PCT

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Background and aim: Sepsis is a major global health problem, causing nearly 11 million deaths, with particularly high mortality in ICUs. It arises from a dysregulated immune response to infection, leading to systemic inflammation, organ dysfunction, and hemodynamic instability. Blood lactate levels and lactate clearance guide resuscitation and predict outcomes. Unlike C-reactive protein (CRP) and procalcitonin (PCT), which primarily reflect inflammation or infection, lactate provides rapid insight into tissue perfusion and metabolic stress. This narrative review aims to summarize lactate's role as a signaling and immunometabolic biomarker in sepsis and compare its clinical utility with CRP and PCT in ICU patients

Methods: A narrative review of experimental, translational, and clinical studies was conducted using Medline (by PubMed), Scopus and Web of Science. Search terms included sepsis, lactate, lactate clearance, CRP, PCT, ICU, and immune dysfunction. Studies evaluating lactate dynamics, immune modulation, and clinical outcomes in critically ill septic patients were included. Additional studies comparing lactate with CRP and PCT in predicting outcomes or guiding resuscitation were also reviewed. Data were synthesized to integrate mechanistic insights from experimental studies with clinical observations and to highlight lactate's utility in early risk stratification and bedside decision-making in ICU sepsis care.

Results: Clinical evidence indicates that early lactate clearance is strongly linked to improved prognoses in ICU patients with sepsis. Individuals who achieve marked lactate reduction within the first 6–24 hours exhibit substantially lower 28-day mortality rates (approximately 15–20%) than those with persistent hyperlactatemia (around 30–40%), despite receiving comparable resuscitative care. Persistent lactate elevation in some patients despite hemodynamic stability suggests that lactate levels represent more than impaired perfusion. Indeed, lactate influences immune cell metabolism, modulates cytokine synthesis, and interacts with systemic metabolic networks, contributing to heterogeneity in inflammatory and immune responses. Compared with CRP and PCT, lactate displays greater sensitivity to dynamic changes in tissue perfusion and metabolic stress, providing an earlier signal of clinical decline. Its kinetic profile also offers superior short-term mortality prediction and real-time assessment of resuscitation efficacy, supporting its role in early risk stratification and bedside management.

Conclusion: Lactate should be interpreted as both a marker of tissue perfusion and immunometabolic activity in ICU patients. Lactate clearance offers rapid prognostic information and, when combined with CRP and PCT trends, can enhance patient stratification, early detection of deterioration, and individualized management strategies. Understanding lactate's signaling and metabolic roles may improve bedside decision-making and outcomes in sepsis. Further translational and clinical studies are needed to optimize lactate-guided approaches in critical care.

keywords: Sepsis; Lactate clearance; C-reactive protein; procalcitonin.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-91

Prevalence of Hashimoto's Thyroiditis Among Patients Referred to Fardis Central Laboratory During a One-Year Period

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Background and aim: Hashimoto's thyroiditis is one of the most prevalent autoimmune thyroid disorders and a leading cause of hypothyroidism. The disease is characterized by immune-mediated destruction of thyroid tissue. Anti–thyroid peroxidase antibody (Anti-TPO) is a key laboratory marker for the diagnosis of autoimmune thyroiditis; however, its distribution across different clinical subgroups of thyroid dysfunction remains incompletely understood. This study aimed to assess the prevalence of Hashimoto's thyroiditis according to age, sex, and clinical status using Anti–thyroid peroxidase antibody levels among patients referred to the Central Laboratory of Fardis, Karaj.

Methods: In this retrospective study, medical records of 6,142 patients with thyroid disorders who were referred to the Central Laboratory of Fardis were reviewed. Patients of various age groups were classified based on clinical status, including hypothyroidism, hyperthyroidism, pregnancy, and pregnancy planning. Serum Anti-TPO levels were measured, and statistical analyses were performed to compare prevalence among different subgroups using SPSS software.

Results: Of the 6,142 participants, 4,916 (80.04%) were female and 1,226 (19.96%) were male. The prevalence of Hashimoto's thyroiditis was significantly higher in women (44.3%, n = 2,180) compared to men (38.1%, n = 467). The highest prevalence was observed in individuals aged 31–50 years, with a mean age of approximately 40 years among affected patients. Among 243 pregnant women, 66 were positive for Hashimoto's thyroiditis. Additionally, among 36 individuals with a history of recurrent miscarriage, 7 tested positive for the disease.

Conclusion: Hashimoto's thyroiditis was considerably more prevalent in women than in men, with the highest occurrence observed in middle-aged adults. Hormonal, genetic, and environmental factors, as well as stress-related conditions during active working years, may contribute to this distribution. These findings are consistent with previous studies and highlight the importance of targeted screening and early diagnosis to reduce complications and improve clinical outcomes.

keywords: Hashimoto's thyroiditis, Anti-thyroid peroxidase (Anti-TPO) antibody, Prevalence

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-92

PI3K/AKT/mTOR and MAPK Pathways: Drivers of Breast Cancer Progression and Resistance

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Background and aim: Breast cancer progression and treatment resistance are strongly influenced by dysregulated cell signaling pathways. Among these, the PI3K/AKT/mTOR and MAPK/ERK pathways play pivotal roles in tumor growth, survival, and metastasis. Aberrant activation of these pathways is associated with aggressive disease and poor clinical outcomes. Understanding their molecular mechanisms and clinical relevance may improve biomarker-driven risk stratification and personalized therapy. This narrative review aims to summarize current evidence on the role of PI3K/AKT/mTOR and MAPK signaling in breast cancer progression and therapy resistance, with emphasis on translational and clinical implications.

Methods: A narrative review was conducted using PubMed, Scopus, and Web of Science databases. Search terms included breast cancer, PI3K, AKT, mTOR, MAPK, ERK, cell signaling, and therapy resistance. Studies published in the last decade were prioritized. Both preclinical studies (cell lines and animal models) and clinical investigations evaluating pathway activation, genetic alterations, prognostic relevance, and therapeutic targeting were included. Articles addressing cross-talk with hormone receptor and HER2 signaling and outcomes of pathway-targeted therapies were also reviewed. Evidence was synthesized to integrate mechanistic insights with clinical observations and to highlight the role of signaling pathways in disease progression, resistance mechanisms, and emerging treatment strategies.

Results: Aberrant activation of PI3K/AKT/mTOR promotes tumor cell survival, proliferation, and metabolic adaptation, while MAPK/ERK signaling enhances proliferation, invasion, and metastatic potential. Approximately 30–40% of breast cancers harbor PI3K pathway mutations, and up to 25% exhibit MAPK pathway overactivation, both associated with poorer prognosis and reduced response to standard therapies. Cross-talk between these pathways and estrogen receptor or HER2 signaling contributes to resistance to endocrine therapy, HER2-targeted agents, and chemotherapy. Preclinical data demonstrate that dual pathway inhibition can reduce tumor growth and restore treatment sensitivity. Early-phase clinical trials suggest that patients with pathway-activated tumors may experience 20–25% improvement in progression-free survival when treated with targeted inhibitors combined with standard therapy, supporting pathway-driven therapeutic strategies.

Conclusion: Dysregulation of PI3K/AKT/mTOR and MAPK signaling is a key driver of breast cancer progression and therapy resistance. These pathways provide valuable mechanistic and clinical insights into tumor aggressiveness and treatment failure. Incorporating pathway activation profiling into clinical practice may enhance patient stratification and guide personalized therapeutic approaches. Continued translational research and well-designed clinical trials are essential to optimize signaling-targeted strategies and improve outcomes in patients with aggressive or treatment-resistant breast cancer.

keywords: Breast cancer; Cell signaling; MAPK Pathways; Therapy resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-93

Dietary Vitamin D and Omega-3 Consumption and Blood-Based Inflammatory Indices in the Elderly Population of the Sabzevar PERSIAN Cohort

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Background and aim: The growing elderly population and age-related immune decline (immunosenescence) necessitate effective nutritional interventions to maintain health. This study aimed to investigate the association between dietary intake of vitamin D and omega-3 fatty acids and blood–based inflammatory indices in the elderly population of the Sabzevar PERSIAN Cohort, to identify preventive strategies to improve immune status.

Methods: This cross-sectional study included 591 elderly participants from the Sabzevar PERSIAN Cohort. Participants were categorized into two groups, low intake and high intake, based on their daily consumption of vitamin D and omega-3. Nutrient intake data were collected using a validated 147-item Food Frequency Questionnaire (FFQ) and analyzed with Nutritionist software to calculate daily intake (g/day). Associations between nutrient intake and blood-based inflammatory indices, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR), were analyzed using SPSS version 16. Chi-square and independent t-tests were applied, and statistical significance was set at P 0.05.

Results: A total of 591 elderly participants (mean age: 63.58 ± 2.92 years; 56.3% men) were included. The mean inflammatory indices were NLR = 1.61 ± 0.75, PLR = 114.98 ± 39.03, and MLR = 0.04 ± 0.11. Regarding vitamin D intake, mean age didn't differ significantly between the two groups, whereas gender distribution differed significantly (P 0.001). In the omega-3 intake groups, both gender distribution and mean age differed significantly (P 0.001), with participants in the higher intake group being younger (63.2 vs. 63.7 years; P 0.001). Among the inflammatory indices, a significant difference was observed only for PLR, which was significantly higher in the low vitamin D intake group compared with the high intake group (P 0.001). Participants with lower omega-3 intake (≤ 0.03 g/day) were significantly older. Moreover, no significant difference in the inflammatory indices and BMI was observed between the omega-3 intake groups.

Conclusion: The findings of this study indicate that higher dietary vitamin D intake is associated with a reduction in the PLR inflammatory index. In contrast, higher omega-3 consumption showed no significant association with the blood-based inflammatory indices evaluated in this elderly population.

keywords: Body Mass Index, Monocytes, Neutrophils, Vitamin D, Fatty Acids,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-94

The Role of Progesterone Receptors in the Immunopathogenesis of Miscarriage: A Systematic Review

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Background and aim: Progesterone is a pivotal immuno-endocrine hormone essential for implantation and maintenance of pregnancy. Its biological effects are mediated through progesterone receptors (PRs), including nuclear isoforms (PR-A and PR-B) and membrane-associated progesterone receptors (mPRs), which regulate immune tolerance, decidualization, and inflammatory balance at the maternal–fetal interface. Dysregulation of PR expression or signaling has been increasingly implicated in recurrent pregnancy loss (RPL) and spontaneous abortion through impaired Th2/Treg responses, enhanced pro-inflammatory cytokine production, and defective endometrial receptivity. Recent studies suggest that altered PR isoform ratio, receptor polymorphisms, and progesterone resistance may contribute to pregnancy failure. Aim: This systematic review aims to critically

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, and Embase databases for studies published up to 2024. Search terms included combinations of progesterone receptor, PR-A, PR-B, membrane progesterone receptor, miscarriage, spontaneous abortion, and recurrent pregnancy loss. Original human studies, observational studies, and experimental studies investigating the expression, function, or polymorphisms of progesterone receptors in pregnancy loss were included. Reviews, case reports, animal-only studies, and non-English articles were excluded. Two independent reviewers screened titles, abstracts, and full texts. Data extraction focused on study design, population characteristics, progesterone receptor types, immunological findings, and clinical outcomes. Methodological quality was assessed using standardized appraisal tools.

Results: Several studies in women with recurrent pregnancy loss (RPL) report significantly altered progesterone receptor (PR) expression in endometrial tissues of affected patients compared with fertile controls. Specifically, patients with unexplained RPL showed lower concentrations of progesterone receptors in both nuclear and cytoplasmic compartments (suggesting impaired progesterone signaling at the maternal–fetal interface) and a significantly higher nuclear/cytoplasmic PR ratio, indicating a shift toward nongenomic receptor activity in miscarriage cases. Meta-analyses examining clinical outcomes of progesterone support (reflecting downstream receptor-mediated effects) show that progestogen treatment in women with prior miscarriages probably increases live birth rates by approximately 5–5.7% compared with control groups (relative risk ~1.07–1.08), although the certainty of this effect varies by study and population.Overall, evidence supports dysregulated PR expression and function as a contributing factor in miscarriage pathophysiology, with implications for both immune modulation and clinical intervention.

Conclusion: It seems that dysregulation of progesterone receptor expression and signaling plays a critical role in the pathophysiology of miscarriage by impairing endometrial receptivity and maternal–fetal immune tolerance. Alterations in progesterone receptor isoforms, receptor distribution, and downstream immunomodulatory pathways may contribute to progesterone resistance and pregnancy failure. However, existing evidence remains heterogeneous. Further well-designed prospective studies are required to clarify receptor-specific mechanisms and to determine their potential diagnostic and therapeutic value in pregnancy loss.

keywords: Progesterone Receptors, Miscarriage, Recurrent Pregnancy Loss, Immune Tolerance, Progesterone Resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-95

Efficacy and Safety of Sacituzumab Govitecan in Breast Cancer: A Systematic Review of Clinical Evidence

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Background and aim: Breast cancer remains a significant cause of cancer-related morbidity and mortality worldwide, particularly in advanced and treatment-resistant stages where therapeutic options are limited. Sacituzumab govitecan, a Trop-2–targeting antibody–drug conjugate linked to the active topoisomerase I inhibitor SN-38, has gained attention for its clinical activity across multiple breast cancer subtypes. This systematic review aims to evaluate and synthesize emerging evidence regarding the efficacy and safety of sacituzumab govitecan in breast cancer.

Methods: A systematic literature search was conducted for publications between January 2016 and January 2026 using PubMed/MEDLINE, Embase, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL). Search terms included sacituzumab govitecan and breast cancer. After duplicate removal and eligibility screening, 27 studies and conference abstracts reporting clinical outcomes were included. Extracted data focused on efficacy endpointsoverall response rate (ORR), progression-free survival (PFS), and overall survival (OS) as well as treatment-related adverse events (TRAEs). Due to heterogeneity across studies, a narrative synthesis was performed.

Results: The included studies consisted of early- and late-phase clinical trials and real-world cohorts, enrolling more than 2,300 patients with predominantly metastatic disease. Across heavily pretreated populations, sacituzumab govitecan demonstrated durable antitumor activity, with objective responses observed in approximately one-quarter to one-third of patients. Disease control rates were consistently high, reflecting meaningful tumor burden reduction and delayed progression. Median PFS outcomes generally exceeded those reported with prior standard chemotherapy in similar settings, while OS outcomes showed sustained survival benefit in select subgroups. The safety analysis revealed a predictable toxicity profile, primarily characterized by hematologic and gastrointestinal adverse events. Most grade ≥3 toxicities were reversible and manageable with dose modification and supportive care, and permanent treatment discontinuation remained infrequent.

Conclusion: This systematic synthesis indicates that sacituzumab govitecan offers a favorable balance between efficacy and tolerability in advanced breast cancer, particularly in patients with limited treatment alternatives. While current evidence supports its clinical utility, further longitudinal and comparative studies are warranted to clarify long-term outcomes and optimize patient selection.

keywords: Sacituzumab govitecan; breast cancer; antibody–drug conjugate; Trop-2.

PI-96

Harnessing chimeric antigen receptor (CAR)-T cell therapy for the treatment of multiple sclerosis (MS)

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Background and aim: Recent studies indicate the central role of B cells and T cells in the pathogenesis of multiple sclerosis (MS), where autoreactive T cells drive inflammation and pathogenic B cells contribute by presenting antigens, producing autoantibodies, and secreting pro-inflammatory cytokines. This synergy ultimately leads to demyelination and neuronal damage. While traditional broad-spectrum immunosuppressive agents have been used to treat MS for decades, their clinical benefit is limited by severe systemic adverse events, including an increased risk of neoplasia and infections, prompting the exploration of highly targeted immunotherapies.

Methods: Following the breakthrough of chimeric antigen receptor (CAR)-T cell therapy in oncology, this treatment has garnered significant attention as a potential therapeutic strategy in MS. CAR-T cell therapy has the potential to reset the immune system by clearing autoreactive B- and T-cells and permitting the reconstitution of the immune system with their normal naïve counterparts, potentially providing a long-lasting or even one-time treatment for patients with MS. While the main strategy of CAR-T cell therapy in MS includes targeting B cells (by CD19, CD20, or CD22 CAR-T cells) and/or long-lived plasma cells (BCMA CAR-T cells), several other advanced strategies have been developed in recent years, each with unique safety and efficacy advantages. For example, a more elegant approach is based on the use of chimeric autoantibody receptor (CAAR)-T cells, which are designed to selectively eliminate B cells that carry disease-specific autoantibodies, thereby sparing the healthy humoral immune system.

Results: Furthermore, two novel CAR-T strategies have also been developed to directly quell the inflammatory T-cell response: CAR-engineered regulatory T cells (CAR-Tregs) and T cell receptor (TCR)-mimic CAR-T cells. While CAR-Treg therapy is designed to home to sites of CNS inflammation and suppress local effector functions, TCR-mimic CAR-T cell therapy aims to target the fundamental cause by recognizing and eliminating T cells reactive to specific myelin peptides presented by the major histocompatibility complex (MHC). Although CAR-T cell therapy for MS is still in its infancy, with limited clinical data, early trial results indicate the potential of CAR-T cells to infiltrate the CNS and reduce local inflammation and intrathecal antibody levels.

Conclusion: In conclusion, these new generations of CAR-T cell therapy represent a paradigm shift from non-specific immunosuppression to precision immune reprogramming, offering the potential for deep, sustained remission in MS. Nonetheless, further optimizations and long-term clinical validations are necessary for the clinical translation of these innovative therapeutic strategies.

keywords: Multiple sclerosis (MS); CAR-T cell therapy; Immunotherapy

PI-97

Integration of Plant Virus–Based Nanoparticles with Cell-Based Immunotherapies: Evidence for Therapeutic Synergy in Metastatic Cancers – A Systematic Review

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Background and aim: Metastatic cancers remain a leading cause of death despite advances in surgery, chemotherapy, and immune checkpoint blockade. A major challenge is the immunosuppressive tumor microenvironment (TME), which limits immune cell infiltration and activity. Plant virus–derived nanoparticles have emerged as promising immunostimulatory platforms, capable of activating innate immunity without replicating in mammalian cells. Preclinical and translational studies, particularly using cowpea mosaic virus (CPMV), have explored their combination with cell-based and immune-modulating therapies to enhance anti-tumor responses. This systematic review summarizes recent findings on the immunological and therapeutic effects of integrating plant virus nanoparticles with immunotherapies in metastatic cancer models.

Methods: A systematic literature search was conducted in PubMed, Scopus, and Google Scholar for studies published between 2020 and 2025. The search terms included "Plant viruses," "Plant virus nanoparticles," "Immunotherapy," "In situ vaccination," "Neoplasms," and "Metastatic cancer." We included original research articles and reviews that investigated the use of plant virus–based nanoparticles in conjunction with immunotherapeutic or immune-modulating approaches. Studies unrelated to cancer immunotherapy or those lacking experimental immunological data were excluded. Data were extracted with a focus on the type of cancer, the therapeutic strategy, the immune mechanisms involved, and the reported outcomes on both primary and metastatic tumors.

Results: A comprehensive review of preclinical and translational studies highlights cowpea mosaic virus (CPMV) as the most widely studied plant virus–based immunotherapy platform. In multiple tumor models, including melanoma, breast, ovarian, pancreatic, and colorectal cancers, intratumoral or targeted systemic delivery of CPMV consistently activated innate immune responses. This activation involved dendritic cell maturation, recruitment of macrophages and neutrophils, and increased pro-inflammatory cytokine production. Combination strategies proved more effective than monotherapies, showing synergistic anti-tumor effects when CPMV was combined with immune checkpoint inhibitors, cytokine-based approaches, tumor ablation techniques, or cancer vaccines. Notably, enhanced infiltration of $CD8^+$ T cells and NK cells was observed in both primary tumors and distant metastatic sites, suggesting the induction of systemic anti-tumor immunity and potential abscopal effects. Translational studies in companion dogs with spontaneous cancers further supported the safety, immunogenicity, and therapeutic potential of CPMV-based intratumoral immunotherapy, with minimal immune-related adverse events.

Conclusion: This systematic review indicates that plant virus–based nanoparticles, particularly Cowpea Mosaic Virus (CPMV), can enhance immunotherapy efficacy by reprogramming the tumor microenvironment and stimulating systemic anti-tumor immune responses. When combined with cell-based or immune-modulating therapies, these platforms may help overcome immune resistance in metastatic cancers. Although current evidence is largely derived from preclinical and veterinary studies, the consistent immunological activation and therapeutic benefits support the potential clinical translation of plant virus–based immunotherapy combinations. Nonetheless, further well-designed clinical trials are required to define their effectiveness and role in human metastatic cancer.

keywords: Plant virus nanoparticles; Immunotherapy;Metastatic cancer

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-98

MSCs engineered with secreted Klotho skew T cell polarization toward Treg and ameliorate neuroinflammation more efficiently than MSCs in Experimental Autoimmune Encephalomyelitis

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Background and aim: Treatment of chronic neurodegenerative diseases such as multiple sclerosis (MS) remains a major challenge. This study aimed to evaluate the therapeutic potential of human adipose-derived mesenchymal stem cells (hAD-MSCs) transduced with secreted klotho (sKL) in experimental autoimmune encephalomyelitis (EAE), a murine model of MS, with a specific focus on regulatory T (Treg) polarization as a potential underlying mechanism.

Methods: EAE was induced in C57BL/6 mice followed by treatment with administration of hAD-MSCs, sKL- hAD-MSCs or vehicle and clinical signs were scored daily. H&E and LFB staining was performed to evaluate histopathological changes. The mRNA and protein expression of IL-17 and IL-10 was detected in the spinal cord of animals by real-time PCR and immunohistochemistry, respectively. The frequencies of Th17 and regulatory T (Treg) cells were evaluated by flow cytometry of the spleen.

Results: The results revealed that sKL-hAD-MSCs reduced both maximum and cumulative disease scores more significantly than hAD-MSCs. Accordingly, histological evaluation showed a more profound reduction in the inflammatory infiltration and demyelination in the spinal cord of sKL-hAD-MSC group compared to hAD-MSC group. Moreover, sKL-hAD-MSCs decreased the expression of IL-17 and increased the expression of IL-10 more potently than hAD-MSCs in the spinal cord of EAE animals. Compared to hAD-MSCs, sKL-hAD-MSCs also exhibited a superior capability of decreasing the frequency of Th17 cells and increasing the frequency of Treg cells in the spleen of EAE animals.

Conclusion: In conclusion, we demonstrated for the first time that engineering hAD-MSCs to overexpress sKL significantly enhances their therapeutic efficacy against EAE, as evidenced by improved clinical scores and reduced neuroinflammation. This enhanced effect is likely mediated by a shift in the Th17/Treg balance toward Treg polarization, highlighting a key mechanism and a promising cell therapy approach for neuroinflammatory diseases.

keywords: Multiple sclerosis, Mesenchymal stem cells, Klotho, Treg cells, EAE model

PI-99

From Lab Success to Clinical Failure: Analyzing Data from S. aureus Vaccine Trials

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Background and aim: Staphylococcus aureus, especially methicillin-resistant strains (MRSA), is a leading cause of severe infections worldwide. An overall MRSA prevalence in Iranian children with S. aureus infections is significant in hospital settings. Despite decades of research, all vaccine candidates have failed in clinical trials. This study aims to analyze the laboratory and clinical data underlying these failures, to translate laboratory science into successful patient outcomes.

Methods: We searched PubMed and Google Scholar for published outcomes from major failed S. aureus vaccine clinical trials. Search terms included: "Staphylococcus aureus vaccine," "clinical trial failure," and "MRSA vaccine." We also examined related laboratory studies on antigen design and nanoparticle applications. By comparing preclinical efficacy indicators with clinical outcomes, we identified fundamental disconnects.

Results: In the laboratory, researchers developed strong tools: immunoinformatics models successfully predicted conserved and immunogenic epitopes(e.g., IsdB), while nanoparticle-based strategies have shown promising anti-biofilm activity in vitro. Furthermore, vaccine candidates have demonstrated protective efficacy in animal models. However, when these laboratory ideas were tested in human vaccine trials, they failed completely. IsdB-based V710 vaccine not only lacked efficacy in preventing postoperative infections but was also associated with increased mortality in vaccinated patients who became infected. Similarly, the multicomponent SA4Ag vaccine, despite strongly stimulating human antibody production, failed to reduce infection rates in a Phase 2b trial. This clear difference shows that promising preclinical results do not always lead to successful patient treatments.

Conclusion: MRSA vaccines failed in human trials despite promising preclinical results. This shows we need better methods to predict human immune responses early in research. Furthermore, S. aureus may adapt uniquely during human infection in ways not seen in standard lab models. Therefore, using advanced computer models and human-focused lab tests from the beginning may be a promising new strategy to address these challenges and develop an effective vaccine.

keywords: Staphylococcus aureus; Translational Research; Vaccines; Treatment Failure; Computer Simulation

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-100

Autoimmunity and autoantibodies in long COVID: basic and clinical insights

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Background and aim: Long COVID, also known as post-acute sequelae of SARS-CoV-2 infection (PASC), affects up to 10% of people recovering from the virus and manifests as a multisystem disorder involving fatigue, dysautonomia, neurocognitive symptoms and immune dysregulation. There is increasing evidence that links SARS-CoV-2 infection to the induction or amplification of autoimmune responses. The virus may break self-tolerance by causing hyperinflammation, molecular mimicry, NETosis and prolonged antigenic stimulation.

Methods: To determine the association between autoimmunity and long-term effects of the SARS-CoV-2, we searched the PubMed, Scopus, ScienceDirect and Google Scholar databases using the keywords 'autoimmunity', 'autoantibodies', 'B-cell dysregulation', and 'long-term effects of SARS-CoV-2'. We then selected the most relevant articles and summarized the main findings for this study.

Results: Autoantibodies may appear during acute SARS-CoV-2 infection and persist in some long-term patients. Common autoantibodies include antinuclear antibodies (ANA), anti-thyroid peroxidase (anti-TPO), rheumatoid factor (RF), antineutrophil cytoplasmic antibodies (ANCA), antiphospholipid antibodies (aCL, β2GPI), antibodies to type I interferons (anti-type I IFN), and G protein-coupled receptor (GPCR)-targeted antibodies. Excessive NET formation acts as both an autoantigen reservoir and a driver of vascular injury and chronic inflammation, promoting extrafollicular B-cell activation and the production of anti-NET, ANA and ANCA antibodies. Clinical studies demonstrate correlations between elevated neuronal autoantibodies (anti-MOG, anti-MBP and anti-synapsin) and neuropsychiatric long-Covid symptoms, which have been validated through neural network analyses.

Conclusion: There is evidence to suggest that SARS-CoV-2 infection can induce transient or persistent autoantibodies via multiple convergent pathways, including NETosis, mimicry and bystander activation. Although autoimmunity plays a role in certain long-term effects of the virus, the heterogeneity of long-term symptoms suggest that long-term effects of the virus are not a single autoimmune disease.

keywords: Long COVID; Autoimmunity; Autoantibodies; B-cell dysregulation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-101

Therapeutic Potential of Bee Venom in Skin Wound Healing and Immune Response Regulation

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Background and aim: Wound healing is a complex process that can be impaired by chronic inflammation, reduced macrophage function, and oxidative stress. Bee venom, containing peptides like melittin and apamin, has shown promise in promoting wound repair and regulating immune responses. Studies indicate that it reduces pro-inflammatory cytokines, enhances fibroblast migration, promotes collagen formation, prevents macrophage apoptosis, and activates signaling pathways crucial for vascular stability and immune homeostasis, suggesting its potential as a bioactive therapeutic agent for impaired wounds.

Methods: Data on the use of Bee Venom in skin wound healing and immune system reaction to Bee Venom were collected and analyzed from websites such as PubMed, Google Scholar, and Scopus databases.

Results: Studies, including one clinical trial and four animal studies, evaluated the effects of bee venom (BV) on wound healing. In the clinical trial, wound surface area (WSA) and ulcer volume (UVM) significantly decreased after 6–12 weeks of BV phonophoresis in chronic ulcers ($p \leq 0.05$), and Ki-67 expression increased, indicating enhanced cellular proliferation. Animal studies reported accelerated wound closure, increased collagen type I deposition, enhanced fibroblast migration, and reduced inflammatory cytokines (IL-6, TNF-α). Together, the evidence indicates that BV accelerates wound closure not only through direct cellular effects but also by modulating immune cell dynamics and correcting the impaired inflammatory responses characteristic of chronic and diabetic wounds.

Conclusion: Overall, evidence suggests that bee venom (BV) is a promising bioactive agent that enhances wound healing through regenerative and immunomodulatory mechanisms. BV stimulates keratinocyte and fibroblast activity, increases collagen production, and promotes angiogenesis, supporting tissue repair. It also reduces pro-inflammatory cytokines, protects macrophages from apoptosis, and activates key pathways, such as Nrf2 and Ang-1/Tie-2, thereby helping to restore balanced immune responses, particularly in chronic and diabetic wounds. These combined effects highlight BV as a potential therapeutic option for difficult-to-heal wounds. Nevertheless, further research is necessary to establish standardized dosages, assess

keywords: "Bee Venoms"[MeSH] AND "Wound Healing"[MeSH] AND "Immune Response"[MeSH]

PI-102

Gamma-delta T cells in breast cancer: Dual role in tumor immunity and emerging therapeutic approaches

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Background and aim: Gamma-delta (γδ) T cells are a unique subset of T lymphocytes that bridge innate and adaptive immunity and play an important role in tumor immune surveillance. In breast cancer, γδ T cells have been shown to exert both antitumor and protumor effects, depending on their functional subsets and the tumor microenvironment. This review aims to critically analyze the dual role of γδ T cells in breast cancer immunity and evaluate the therapeutic potential of emerging γδ T cell-targeted strategies.

Methods: A comprehensive analysis of experimental and clinical studies published between 2016 and 2026 was conducted. Searches were performed in databases including PubMed, Scopus, and Web of Science. Approximately 50 relevant articles were identified and reviewed, encompassing in vitro assays, animal models, and patient-derived data. Recent advances in γδ T cell biology and therapeutic applications, such as adoptive cell transfer, γδ T cell activation strategies, bispecific antibodies, and combination therapies with immune checkpoint inhibitors, were systematically evaluated.

Results: Experimental and clinical findings indicate that γδ T cells exhibit potent cytotoxic activity against breast cancer cells through MHC-independent mechanisms and cytokine-mediated immune responses. However, certain γδ T cell subsets were found to promote tumor growth, angiogenesis, and immune suppression under specific tumor microenvironmental conditions. Emerging γδ T cell–based therapies demonstrated promising antitumor efficacy in preclinical models and early-phase clinical studies.

Conclusion: γδ T cells display functional plasticity in breast cancer, highlighting their dual role in tumor immunity. A deeper understanding of the factors regulating their antitumor versus protumor activities is critical for optimizing γδ T cell–based immunotherapies. Integrating laboratory discoveries with clinical research may enhance therapeutic outcomes for patients with breast cancer.

keywords: Gamma-delta T cells, Breast cancer, Tumor microenvironment, Cancer immunotherapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-103

Advancing the frontiers of immunotherapy with Chimeric antigen receptor Natural Killer (CAR-NK) cells for colorectal cancer

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Background and aim: Colorectal cancer(CRC)is one of the leading causes ofcancer deaths inthe world.There are limited effective treatment options for advanced and refractory cases.The immunosuppressive tumor microenvironment(TME),which causes frequent resistance to conventional treatments,necessitates the development ofnew,targeted immunotherapies.However,Chimeric antigen receptor(CAR)-Tcell therapyin solid tumors faces obstacles,including toxicity and complex manufacturing.In contrast,CAR-engineered Natural Killer(NK)cells offer a promising alternative that utilizes theinherent cytotoxic ability of NKcells torecognize and eliminate malignant cells without theneed for prior antigen sensitization.CAR-NKcells are considered asafer alternative with less risk ofsevere side effects suchas cytokine release syndrome.Moreover,they canbe produced asa"ready-to-use"treatment,makingthem more accessible.This study aimed to reviewthe advantages ofimmunotherapy with CAR-NKcells for colorectal cancer.

Methods: In this review, a comprehensive search was conducted using the keywords "colorectal cancer" and " immunotherapy " and "Car Nk cell" in PubMed, Google Scholar, and Web of Science databases.

Results: Preclinical models show potent antigen-specific cytotoxicity against CRC models by CAR-NK cells, particularly from clinical and/or primary allogeneic cells. New generations of CARs, which exclusively target membrane-bound Carcinoembryonic Antigen (CEA), can escape neutralization from circulating antigen. Mesothelin (MSLN)-targeting in selected patients with poor prognosis and KRAS/BRAF-mutated metastatic CRC in 10% of cases resulted in highly efficient outcomes, as it fulfilled an unmet medical need. Short-term human clinical trials of intra-peritoneal NKG2D_CAR_NK cell administration (NCT03415100) demonstrated the safety and tolerability of NKG2D-CAR-NK cells in metastatic colorectal cancer patients. CAR-NK cell therapy in combination with targeted therapy, namely Regorafenib (a multikinase inhibitor), resulted in synergistic reduction of tumor malignancy.

Conclusion: CAR-NKcell immunotherapy is emerging as a very promising next-generation approach for the treatment of colorectal cancer.By combining the intrinsic tumoricidal activity of NKcells with the precision of antigen-specific CARs,this approach effectively targets CRC while maintaining a favorable safety window. Continuous refinement of CAR designs to improve stability,translocation,and flexibility in the TME,supported by new clinical data, positions CAR_NK cells as a transformative “ready-to-use”therapeutic option. This approach has significant potential to improve outcomes for patients with advanced, metastatic,or refractory colorectal cancer and is a pivotal advance in oncologic immunotherapy.

keywords: CAR-NK cell, Colorectal cancer,Tumor Microenvironment, Immunotherapy

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-104

Investigation of Lawson's effect on the expression of MMP7, IL-6, and TNF-α genes in human dermal fibroblast (HDF) cells under hyperglycemic conditions

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Background and aim: Diabetes is a metabolic disorder that is accompanied by chronic hyperglycemia and can lead to diabetic foot ulcers, whose healing is delayed due to impaired fibroblast function, oxidative stress, and chronic inflammation. Lawsonia inermis possesses antioxidant and anti-inflammatory properties. However, its effect on fibroblasts under high glucose concentration conditions has not been fully studied. This study aims to evaluate the effect of Lawsonia on the expression of matrix metalloproteinase-7 (MMP7) and inflammatory genes IL-6 and TNF-α in fibroblasts under hyperglycemic conditions.

Methods: In this study, human fibroblast cells (HDF) were used, and after reaching an appropriate confluence, the cells were divided into groups: control, treatment with glucose (140 mM), and treatment with glucose (140 mM) plus Lawson (10 µg/mL). After 24 hours, RNA was extracted and reverse-transcribed to cDNA. The expression of MMP7, IL-6, and TNF-α genes was assessed using Real-time PCR, with GAPDH as the reference gene, and relative gene expression changes were calculated by the 2ΔΔCT method.

Results: Determination of fibroblast viability under glucose conditions led to an increase in MMP7 gene expression, while IL-6 and TNF-α gene expression changes were not significant. Lawsonia significantly reduced the expression of MMP7 and IL-6 genes ($P \leq 0.05$).

Conclusion: The present findings indicate that high glucose concentrations induce an increase in MMP7 expression and oxidative stress in fibroblasts, while there is no significant effect on IL-6 and TNF-α. Lawsonia, with antioxidant properties and the ability to inhibit the NF-κB pathway, can reduce the expression of IL-6 and MMP7 under glucose conditions, presumably through ROS and NF-κB and MAPK signaling pathways. These results suggest that Lawsonia can selectively target inflammatory and matrix remodeling pathways and may be a candidate for therapeutic interventions related to glucose-induced disorders, including diabetic ulcers and

keywords: Diabetes, Lawson, Inflammatory cytokine, MMp7

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-105

Evaluation of the average platelet-to-lymphocyte ratio (PLR) and eosinophil-to-lymphocyte ratio (ELR) as diagnostic markers for seasonal allergic rhinitis

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Background and aim: Seasonal allergic rhinitis has become challenging recently, and approximately 15-25% of the world population is affected by this disease. Symptoms may include a runny nose, sneezing, and nasal or postnasal drip. Limited tests are available for diagnosis that need to be improved. It seems that examining blood markers such as platelets-to-lymphocytes ratio (PLR) and eosinophil-to-lymphocyte ratio (ELR) can be valuable in the process of diagnosing the severity of inflammation. This study aimed to determine changes in PLR and ELR in patients with seasonal allergies, before and after the conflict.

Methods: Clinical data were collected from 40 patients with allergic symptoms at Heshmatiyeh Hospital in Sabzevar. According to the demonstrations of patients and physicians' diagnosis, the presence of the disease was confirmed, and 5 cc of venous blood was taken with individual consent in two time periods: during the allergy season (late September and early October) and after the end of the allergy season (December and January). To calculate the PLR and ELR, a blood cell count test was performed.

Results: Participants' average age was 28.54 ± 8.24 years. In allergic patients, the eosinophil count was significantly higher during allergy season (3.17 ± 1.05) compared to after the season (1.50 ± 0.81, p 0.05). Moreover, lymphocyte counts were significantly higher during allergy season (37.90 ± 5.86) than after (35.26 ± 7.21, p 0.05). Conversely, platelet counts were lower during allergy season (272.67 ± 51.55) than after (279.02 ± 55.44), but the difference was not significant. The ELR index was significantly higher during allergy season (8.67 ± 3.57) compared to after the season (4.28 ± 2.04, p 0.05). Conversely, PLR was significantly lower during allergy season (737.22 ± 185.20) than after (823.38 ± 222.73, p0.05).

Conclusion: Findings of the present study suggest that simple blood-derived indices, particularly eosinophil count, lymphocyte count, ELR, and PLR, may be useful adjunctive markers for assessing inflammatory activity and disease dynamics in allergic patients across seasons.

keywords: Eosinophils, Platelet Count, Rhinitis, Allergic, Seasonal, Lymphocyte Count

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-106

Comparative Analysis of Serum Chemokines CCL2, CCL5, CCL20, CXCL10, and IL-8 among Patients With Chronic Kidney Disease (Stages 3–5) With and Without Systemic Lupus Erythematosus

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Background and aim: Chemokines are pivotal mediators of renal inflammation and fibrosis in chronic kidney disease (CKD) and systemic lupus erythematosus (SLE). Comparative data on circulating chemokine profiles in CKD with and without SLE, particularly across disease stages, remain limited.

Methods: This cross-sectional study was conducted between September 2022 and March 2023 across three centers in Golestan Province, Iran. A total of 118 participants were enrolled into five predefined cohorts: healthy controls (n=40), CKD without SLE (n=13), ESRD without SLE (n=27), CKD with SLE (n=18), and ESRD with SLE (n=20). CKD staging was based on KDIGO criteria, and SLE classification followed the 2019 EULAR/ACR guidelines. Peripheral blood samples were collected, processed within two hours, and stored at −80 °C. Serum concentrations of CCL2, CCL5, CCL20, CXCL10, and IL-8 were quantified using standardized ELISA kits (BioLegend, USA). All assays were performed in duplicate with strict quality control, including calibration and acceptance criteria for variability. Statistical analyses were conducted using non-parametric tests (Kruskal–Wallis with Dunn's post-hoc), with p0.05 considered significant.

Results: CCL2 levels declined with CKD progression in non-SLE patients but remained elevated in ESRD+SLE, suggesting persistent immune activation. CCL5 was increased in CKD+SLE but not in ESRD, indicating stage-dependent modulation. IL-8 rose progressively from controls to ESRD, peaking in ESRD without SLE, whereas ESRD+SLE showed attenuated levels. CXCL10 was highest in CKD+SLE and reduced in ESRD regardless of SLE status. CCL20 exhibited a distinct pattern, with the greatest elevations in ESRD+SLE and CKD without SLE, implicating differential Th17/CCR6 pathway activation.

Conclusion: Circulating chemokine profiles in CKD are shaped by both renal function stage and the presence of SLE. Certain chemokines (e.g., CCL2, CCL20) may serve as biomarkers of ongoing immune activation in ESRD+SLE, while others (e.g., CCL5, CXCL10) may be more informative in earlier CKD stages. These findings support stage- and disease-specific biomarker strategies and highlight potential targets for immunomodulatory intervention.

keywords: chronic kidney disease; systemic lupus erythematosus; chemokines; biomarkers; inflammation

PI-107

Elevated IL-27 and Altered Anti-Inflammatory Cytokine Levels in SLE Patients with End-Stage Renal Disease

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Background and aim: IL-10, TGF-β, IL-4, IL-27, and EBI3 are cytokines that regulate inflammation, tissue repair, and fibrosis in the kidney and other organs. These cytokines may contribute to different aspects of chronic kidney disease (CKD), end-stage renal disease (ESRD), and systemic lupus erythematosus (SLE), which are associated with renal dysfunction and aberrant immune regulation. This study investigates the role of these cytokines in patients with concurrent kidney disease and SLE to understand their contribution to the pathogenesis and progression of this complex condition.

Methods: We conducted a case-control study between September 2022 and March 2023 at three centers in Golestan Province, Iran. A total of 118 participants were enrolled into five predefined cohorts: CKD without SLE (n=13), ESRD without SLE (n=27), CKD with SLE (n=18), ESRD with SLE (n=20), and healthy controls (n=40). CKD staging was based on KDIGO criteria, and SLE classification followed the 2019 ACR/EULAR guidelines. Venous blood samples were collected, processed under standardized conditions, and sera stored at −80 °C. Serum concentrations of IL-4, IL-10, IL-27, EBI3, and TGF-β1 were quantified using validated ELISA kits (BioLegend and Mabtech, USA). All assays were performed in duplicate with strict quality control, including calibration and acceptance criteria for variability. Group comparisons were analyzed using non-parametric statistics (Kruskal–Wallis with Dunn's post-hoc), and p0.05 was considered significant.

Results: Significant differences in cytokine patterns were observed. IL-10, IL-4, and EBI3 levels were elevated in CKD/ESRD patients with SLE compared to healthy controls, indicating immune dysregulation. TGF-β levels were significantly lower, suggesting a deficiency in immune regulation. IL-27 levels were found to be increased in ESRD patients with SLE compared to those without SLE, indicating its potential role in disease activity.

Conclusion: Our study suggests that cytokines like IL-27 may be associated with disease status in patients with both ESRD and SLE and could be explored as potential biomarkers. However, its utility for monitoring disease activity or guiding treatment requires validation in larger, prospective cohorts to establish sensitivity, specificity, and a causal role.

keywords: Cytokines; Chronic Kidney Disease; End-Stage Renal Disease; Systemic Lupus Erythematosus;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-108

The Immunological Landscape of Long COVID: Mechanisms of Multisystemic Dysregulation

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Background and aim: Long COVID, or post-acute sequelae of SARS-CoV-2 infection (PASC), affects an estimated 65 million individuals globally, manifesting as persistent, multisystem symptoms beyond typical viral recovery. While its etiology is multifactorial, emerging evidence underscores chronic immune dysregulation—including T-cell dysfunction, systemic inflammation, autoimmunity, and immunothrombosis—as central to its pathophysiology.

Methods: This narrative review synthesizes recent clinical, histopathological, and molecular evidence (2020–2025) from peer-reviewed studies, cohort analyses, and meta-analyses to delineate the immunological mechanisms underpinning Long COVID's diverse manifestations across pulmonary, hematologic, endocrine, and rheumatologic systems. Emphasis is placed on sex-based differences, microvascular pathology, and therapeutic implications.

Results: Persistent viral antigens or reservoirs drive chronic inflammation, leading to organ-specific damage. In the lungs, pro-fibrotic cytokines (TGF-β, IL-6) promote fibrosis and gas-exchange impairment. Immunothrombosis—mediated by endothelial dysfunction, neutrophil extracellular traps (NETs), and fibrin amyloid microclots resistant to fibrinolysis—causes microvascular occlusion, tissue hypoxia, and systemic symptoms (e.g., brain fog, fatigue). Endocrine disruption, particularly of the hypothalamic-pituitary-gonadal (HPG) axis, manifests as menstrual irregularities in women and hypogonadism in men, linked to inflammatory stress and oxidative damage to gonads. Notably, women show higher Long COVID incidence, likely due to heightened interferon responses and X-chromosome-linked immune gene expression, which may predispose to autoimmunity. Conversely, low testosterone in men correlates with T-cell exhaustion and viral reactivation (e.g., EBV). Rheumatologic features include reactive arthritis, myositis, and new-onset systemic autoimmune diseases (e.g., SLE), driven by molecular mimicry, epitope spreading, and pathogenic autoantibodies (e.g., anti-GPCR, anti-ACE2). Persistent lymphopenia, cytopenias, and elevated NETosis markers further reflect chronic

Conclusion: Long COVID is not a residual respiratory condition but a systemic immunothrombotic disorder rooted in unresolved immune dysregulation. We propose a unified "microvascular hypothesis," wherein persistent inflammation, immunothrombosis, and ischemic microdamage converge across organs. A "two-hit" model—initial viral insult followed by failure of immune regulation—explains concurrent autoimmunity and viral reactivation. Critically, sex-specific immune-endocrine interactions necessitate gender-stratified approaches. Future management must shift from symptomatic care to precision medicine, targeting distinct endotypes (e.g., fibro-inflammatory, autoimmune, thrombotic) with combinatorial therapies: antivirals to eliminate reservoirs, immunomodulators to restore tolerance, and vascular protectants to resolve

keywords: Long COVID; post-acute sequelae; immunothrombosis; autoimmunity; microclots; sex differences

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-109

Beyond Antibodies: Leveraging Trastuzumab Structural Insights for Next-Generation HER2-Positive Cancer Peptide Therapeutics

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Background and aim: Trastuzumab (Herceptin) is a humanized monoclonal antibody targeting HER2 receptor, approved for HER2-positive breast cancer treatment. Despite clinical success, antibody therapeutics face limitations including high production costs, poor tissue penetration, and immunogenicity. Peptide-based therapeutics offer advantageous pharmacokinetic profiles while maintaining target specificity. Understanding molecular determinants of Trastuzumab-HER2 recognition is essential for rational peptide design. This study aimed to identify critical binding hotspots in the Trastuzumab-HER2 interface using computational alanine scanning mutagenesis, establishing a foundation for developing novel HER2-targeting peptides that mimic the functional paratope of Trastuzumab with improved druglike properties.

Methods: The crystal structure of Trastuzumab Fab-HER2 extracellular domain complex (PDB: 1N8Z, 2.52 Å resolution) served as template. Interface residues were identified and analyzed using PDBsum. Five CDR residues were selected for alanine substitution: Y92 (CDR-L3), R50, R59 (CDR-H2), and W99, Y105 (CDR-H3). Computational mutagenesis and protein-protein docking were performed using HADDOCK 2.4 with default parameters. The top-ranked clusters were analyzed, and mutant-derived complexes were further evaluated using PDBsum for interface characterization. Delta values (Mutant−WT) were calculated for HADDOCK scores and energy components including van der Waals, electrostatic, and desolvation energies. Identified hotspot residues and their spatial arrangements will guide peptide scaffold design using a hybrid approach combining structure-based modeling with artificial intelligence-driven sequence optimization. Molecular dynamics simulations will subsequently validate designed peptide-HER2 complexes for stability and binding persistence.

Results: The crystal structure of Trastuzumab Fab-HER2 complex (PDB: 1N8Z, 2.52 Å resolution) served as template. Interface residues were identified using PDBsum. Five CDR residues were selected for alanine substitution: Y92 (CDR-L3), R50, R59 (CDR-H2), W99, and Y105 (CDR-H3). Computational mutagenesis and protein-protein docking were performed using HADDOCK 2.4 with default parameters. Top-ranked clusters were analyzed, and delta values (Mutant−WT) were calculated for HADDOCK scores and energy components including van der Waals, electrostatic, and desolvation energies. Identified hotspot residues will guide peptide scaffold design using structure-based modeling combined with AI-driven sequence optimization, with molecular dynamics simulations validating designed complexes.

Conclusion: Computational alanine scanning identified Y92 (CDR-L3) as a primary binding hotspot associated with significant geometric rearrangement upon mutation, while R50 (CDR-H2) serves as a key electrostatic contributor. The relative tolerance of W99 mutation suggests CDR-H3 may accommodate sequence modifications, providing design flexibility. These findings establish a minimal functional paratope comprising Y92, R50, and Y105 as priority pharmacophoric elements for HER2-targeting peptide development. Subsequent molecular dynamics validation and AI-assisted sequence optimization will enable rational design of constrained peptides mimicking Trastuzumab's binding mechanism with enhanced pharmacokinetic properties.

keywords: HER2-positive breast cancer, Trastuzumab, Peptide drug design, Alanine scanning mutagenesis

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-110

CAR-T Cell therapy in autoimmune diseases and human immunodeficiency virus infection

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Background and aim: Chimeric antigen receptor (CAR) T-cell therapy is an immunotherapy approach that has played a tremendous role in the battle against cancer for years. Since the CAR T lymphocytes are unrestricted-major histocompatibility complex T lymphocytes, they could identify more targets than natural T cells, resulting in practical and widespread functions. CAR-T cell-derived immunotherapy for autoimmune disorders can be allocated to CAR-Tregs and chimeric autoantibody receptor T cells. Other generations of CARs target human immunodeficiency virus (HIV) proteins. In this review, we summarize CAR-T cell therapies in autoimmune disorders and HIV infection.

Methods: In this review, a comprehensive search was conducted using the keywords "CAR-T" or "chimeric antigen receptor" and "autoimmune diseases" and "cytotoxic T cells" in PubMed, Google Scholar, and Web of Science databases.

Results: The CAR-T cells can be designed for autoimmune disease therapy by targeting specific autoantigens or antibodies that persist on the surface of pathogenic cells. The CAR T cells specific for HIV were genetically modified to target the envelope protein of this virus, which is only expressed on the surface of virus-producing cells.

Conclusion: According to the preclinical and clinical research results in autoimmune diseases and HIV, CAR T cell therapy can be a promising treatment for ameliorating these conditions in patients involved.

keywords: CAR-T; Tregs; autoimmune diseases; chimeric antigen receptor; cytotoxic T cells;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-111

The Impact of Gut Microbiota on Modulating Immune Responses to Oral and Injectable Rotavirus Vaccination

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Background and aim: The gut microbiota plays a pivotal role in regulating immune responses, influencing both innate and adaptive immunity. Recent research suggests that the microbiota can impact vaccine efficacy, including responses to rotavirus vaccines. Rotavirus, a leading cause of severe gastrointestinal disease in children, is targeted by both oral and injectable vaccines. Understanding the role of gut microbiota in modulating immune responses to these vaccines is critical for enhancing vaccine effectiveness.

Methods: This review systematically examines the literature on the influence of gut microbiota on immune responses to both oral and injectable rotavirus vaccines, based on articles published between 2020 and 2026. Databases including PubMed, Scopus, and Embase were searched using keywords related to gut microbiota, immune responses, rotavirus vaccination, and vaccine efficacy. Studies were selected based on relevance to the impact of microbiota composition on vaccine-induced immunity in human and animal models, utilizing microbiome sequencing and immunological assays.

Results: Evidence suggests that gut microbiota significantly affects immune responses to the oral rotavirus vaccine by enhancing mucosal immunity and promoting a more robust immune response. In contrast, injectable vaccines, which bypass the gut, exhibit less dependence on microbiota composition, although some studies indicate subtle effects on systemic immunity. The diversity of the microbiota and the presence of specific bacterial species were found to influence the degree of immune activation following oral vaccination.

Conclusion: These findings underline the importance of gut microbiota in modulating immune responses to vaccines, especially oral vaccines. A diverse microbiota appears to enhance vaccine efficacy, suggesting potential strategies for optimizing vaccine outcomes through microbiome modulation. Further research is needed to unravel the precise mechanisms through which microbiota influences vaccine responses, which may lead to personalized vaccination approaches for populations with altered microbiota.

keywords: Gut microbiota, immune modulation, rota virus vaccine,vaccine efficacy, microbiome.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-112

Immune Checkpoint Biomarkers as Predictors of Disease Activity and Treatment Response in Autoimmune Disorders.

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Background and aim: Autoimmune diseases affect millions worldwide, with heterogeneous clinical courses and variable responses to therapy. Immune checkpoint pathways, including PD-1, PD-L1, and CTLA-4, play critical roles in regulating immune tolerance. Emerging evidence suggests that alterations in these pathways and their associated biomarkers may predict disease activity, progression, and response to immunomodulatory treatments, yet no comprehensive systematic review exists consolidating these findings across multiple autoimmune conditions.This systematic review aims to synthesize current clinical evidence on immune checkpoint biomarkers as predictive tools for disease activity and treatment response in autoimmune disorders, highlighting their potential for precision medicine applications.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, and EMBASE for studies published between 2005 and 2025. Original clinical studies and observational cohorts assessing PD-1, PD-L1, CTLA-4, or other checkpoint-related biomarkers in autoimmune disease diagnosis, monitoring, or therapy response were included. Data extraction and quality assessment followed PRISMA guidelines and the Newcastle-Ottawa Scale.

Results: Evidence indicates that elevated or diminished expression of PD-1, PD-L1, and CTLA-4 in blood or tissue samples correlates with disease flares and remission status in conditions such as rheumatoid arthritis, systemic lupus erythematosus, and multiple sclerosis. Several studies report that baseline biomarker levels can predict response to biologic therapies, including anti-TNF, anti-IL-6, and checkpoint-targeting agents. Combination biomarker panels may enhance predictive accuracy and enable patient stratification for tailored therapies.

Conclusion: Immune checkpoint biomarkers represent promising predictive tools for monitoring disease activity and guiding treatment in autoimmune disorders. Further large-scale, longitudinal studies are warranted to validate multi-marker panels and integrate them into precision medicine approaches, potentially improving clinical outcomes and therapeutic efficiency.

keywords: Immune Checkpoint; Autoimmune Disease; PD-1; CTLA-4; Treatment Response

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-113

Rheumatoid Arthritis as a Non-Equilibrium Interfacial System: A New Colloidal and Mechanical Framework for Fibroblast-Like Synoviocyte Pathogenicity

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Background and aim: Rheumatoid arthritis (RA) is characterized by the stable acquisition of autonomous pathogenic phenotypes by fibroblast-like synoviocytes (FLSs), which drive persistent synovial hyperplasia, tissue invasion, and progressive joint destruction. While molecular and immunological mechanisms have been extensively investigated, less attention has been paid to the physical organization of the synovial microenvironment. This study aims to reconceptualize RA pathogenesis through an interface-centric and colloidal framework, proposing that RA-FLS pathogenicity emerges from the dynamic coupling of interfacial, mechanical, and biochemical processes within an inflamed synovium.

Methods: Using an integrative analytical-conceptual and literature-based approach, we synthesize evidence from cell biology, mechanobiology, and soft-matter physics to model the inflamed synovium as a dense, heterogeneous, non-equilibrium colloidal system. Particular attention is given to cell-matrix and cell-cell adhesion, mechanotransduction pathways, extracellular matrix (ECM) remodeling, and extracellular vesicle-mediated communication as interfacial phenomena governing FLS behavior

Results: Our analysis identifies altered adhesion to the ECM and neighboring cells as a central interfacial checkpoint that governs the commitment of FLS to pathogenic fates. We demonstrate that RA-FLS functions as active interfacial agents capable of sensing, generating, and remodeling physical interfaces. Alterations in adhesion strength, surface receptor expression, and mechanical feedback stabilize pathogenic signaling states and promote transitions from stationary adhesion to invasive migration. Mechanical confinement and cytoskeletal remodeling reinforce collective cellular dynamics characteristic of pannus formation. Moreover, extracellular vesicles act as mobile colloidal entities that integrate biochemical signaling with physical transport and uptake, thereby amplifying inflammation, invasion, and cartilage degradation.

Conclusion: RA-FLS pathogenic behavior should be understood as an emergent property of tightly coupled interfacial energetics, mechanical forces, and biochemical signaling rather than as the consequence of isolated molecular pathways. Framing RA within the principles of colloid and interface science provides a unifying conceptual model that bridges chronic inflammation with non-equilibrium soft-matter physics. This perspective reveals novel translational opportunities targeting adhesion dynamics, mechanotransduction, and vesicle-mediated communication to complement existing immunomodulatory therapies.

keywords: Rheumatoid arthritis; fibroblast-like synoviocytes; interfacial biology; colloidal systems; mechanotransduction; extracellular

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-114

Survey of HBsAg, Anti-HCV and Anti-HIV in referred to the laboratory of Afshar Hospital, Yazd

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Background and aim: The aims of this research was to survey the prevalence of hepatitis B, C and HIV seropositive in a clinical training center in Yazd city and to evaluate two methods for determining of them.

Methods: A retrospective study was conducted from 12 December 2024 to 11 December 2025 on the results of the tests of people referred to the laboratory of Afshar Hospital in Yazd. Serum samples were evaluated for the presence of HBsAg, Anti-HCV and Anti-HIV by ELISA method and were confirmed using Cobas kits.

Results: Out of 6,950 serum samples were examined for HBsAg, 4239 (61%) samples were women. The average age was 46.47 years. 5862 (84.3%) samples were in wards and the rest were outpatients. 105 samples were HBsAg positive or doubtful by ELISA method. Only 51 (0.73%) samples were confirmed by Cobas kits (26 females and 25 males). Out of 6918 serum samples (4222 females), 41 samples were positive or doubtful for Anti-HCV by ELISA method that 22 samples (0.32%) were confirmed by Cobas kits. 5859 (84.6%) samples were in wards and the average age was 46.43 years. Out of 6,913 serum samples examined for Anti-HIV, 5857 samples (84.7%) were in wards. 4218 (61%) samples were women and the average age was 46.41 years.10 samples were Anti-HIV positive or doubtful by ELISA method that none of them confirmed by Cobas kits.

Conclusion: The rate of prevalence of HBsAg was decreased in compare with previous our study (0.73% vs. 1.1%) but the rate prevalence Anti-HCV was same (0.32 vs. 0.3). It is recommended that the positive or doubtful samples are examined by another method.

keywords: HBsAg, Anti-HCV, Anti-HIV, Yazd

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-115

Do High-Titer ANAs Offer Better Insights into Autoimmunity in Chronic Spontaneous Urticaria?

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Background and aim: Chronic Spontaneous Urticaria (CSU) is characterized by recurrent wheals and pruritus, with autoimmune processes potentially playing a pivotal role in its pathogenesis. This study explores the prevalence of antinuclear antibodies (ANA) in CSU patients, emphasizing high-titer ANAs as potential markers of autoimmune activity, surpassing the reliability of autologous serum skin tests (ASST).

Methods: This study was Conducted at the Jahad Daneshgahi Clinic in Tehran, Iran, we analyzed data from 60 CSU patients without prior histories of autoimmune or other diseases. ANA testing used indirect immunofluorescence with HEp-20-10 biochip kits, alongside assessments of additional autoimmune markers such as rheumatoid factor (RF). Patients were categorized based on ASST results.

Results: Among the 60 patients, ten exhibited ANA titers exceeding 320, with levels reaching 1000; notably, seven of these ten were ASST negative. Five of the seven patients with a titer of 1:320 also showed negative ASST results. Among them, three had elevated IgE levels above 160, while one was positive for anti-TPO IgG. Interestingly, one patient had a very low IgE level (1 IU/mL). The patient with a titer of 1:640 had an IgE level of 15 IU/mL and was negative for anti-TPO. Furthermore, one patient with a titer of 1:1000 presented normal IgE and other autoimmune factors. ANA patterns included nuclear fine speckled, rod and ring, and homogeneous nucleolar configurations, with a notable prevalence of the fine speckled pattern.

Conclusion: Our findings suggest that high-titer ANAs may be significant markers of autoimmune activity in CSU patients, offering greater reliability than ASST. Additionally, the exploration of other autoimmune markers in high-titer ANA patients is essential for a comprehensive understanding of autoantibody production. This underlines the necessity for further research in larger cohorts to elucidate these implications for patient management.

keywords: Chronic Spontaneous Urticaria ANA patterns Autoimmune activity Antinuclear Antibody

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-116

Surface markers on microparticles involved in obesity-derived diseases

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Background and aim: More than one-third of people on the planet today are known as overweight individuals. Microparticles (MPs) are small membrane-bound vesicles that are found in healthy people's blood and are elevated in patients with pathological conditions such as obesity. MPs mostly come from platelets, leukocytes, endothelial cells, and vascular smooth muscle cells. Considering the effect of obesity on microparticles, these small membrane-bound vesicles might play a crucial role in preventing or treatment of obesity. This review aimed to investigate the different types of microparticles playing role in obesity-related diseases.

Methods: Material & methods: The authors collected the relevant articles published until 2023 and these are carefully selected from three scientific databases based on keywords.

Results: It has been revealed that exercise might change the microparticle content in the body. The other factor which participates in obesity process is the oxidative stress which is increased in microparticles. Moreover, the obesity is implicated in metabolic conditions including diabetes and cardiovascular diseases.

Conclusion: The data collected from our study shows the direct effect of obesity on the diversity of microparticles, surface markers and their protein content. Moreover, due to the importance of MPs in obesity-caused diseases, these particles could be considered as novel therapeutic target for the treatment.

keywords: Obesity Microparticles Diabetes Endothelial dysfunction Adipose tissue

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-117

Immune reconstitution in multiple sclerosis patients after autologous hematopoietic stem cell transplantation

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Background and aim: Multiple sclerosis (MS) is a chronic autoimmune, inflammatory neurological disease characterized by T cell-mediated destruction of myelinated axons in central nervous system (CNS). Notable advances have been made in our understanding of the immunobiology of autoimmune disease and its treatment with hematopoietic cell transplantation (HCT). Moreover, autologous haematopoietic stem-cell transplantation (AHSCT) has been experimented as a treatment in MS patients who failed to respond to standard immunotherapy. In fact, AHSCT reboots the immune system and reconstitutes a new adaptive immunity.

Methods: In this study the effect of AHSCT on immune system of MS patients has been explored.

Results: All clinical studies demonstrated a great efficacy of AHSCT in halting inflammation and disease activity, even in those patients affected by severe forms of MS. A number of significant changes in both the CD4+ and CD8+ T-cells subsets from MS post-transplant has been reported.

Conclusion: These finding suggest the use of AHSCT as a treatment for autoimmune disease including MS.

keywords: Multiple sclerosis, AHSCT, T-cell

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-118

The therapeutic applications of Chimeric antigen receptors in autoimmune diseases

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Background and aim: The use of autologous T cells that are engineered to destroy cancerous cells is one of the most exciting therapies for cancer. Several chimeric antigen receptors (CARs) have been approved by the Food and Drug Administration (FDA) for therapeutic applications. Emerging research are underway to extend this approach to other areas such as autoimmunity. These include generation of CAR constructs to target regulatory T cells (Treg cells). CAR technology has been extended to CAR-Treg therapy showing effective control of inflammation. CAR-Treg cells can recognize antigen on target cells and suppress T cell function.

Methods: In this study the therapeutic applications of Engineered T cells in autoimmune diseases has been explored.

Results: Preclinical studies showed immune modulating properties of CAR Tregs in various mouse models. Also, CAR-Treg cells have been effectively applied in some autoimmune diseases like multiple sclerosis (MS). In fact, restoring the number of Treg cells and their inhibitory functions through CAR-Treg can successfully prevent autoimmune diseases.

Conclusion: Engineering the immune system for therapeutic applications is among the most exciting advances in modern medicine. CAR-Treg therapy for autoimmunity could restore immune tolerance and reduce inflammation. Notably, CAR-Tregs showed inhibitory properties with no apparent effects on overall immunity of the recipient.

keywords: CAR-Treg, CAR-T, autoimmunity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-119

Evaluation of miRNAs in HTLV1 pathogenesis in ATLL patients with bioinformatics and laboratory method

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Background and aim: Abstract HTLV1 is responsible for two critical diseases in humans: ATLL and HAM/TSP. Due to very long latent period, lack of vaccine, resistance of virus to chemotherapy and different methods of virus transmission, we will witness its spread in the next few years not only in Iran but also in the whole world. ATLL is a rare progressive disease with poor prognosis. Considering the importance of ATLL, in this study, we demand by using and integrating high-throughput microarray data, to identify the most important microRNAs involved in the induction of ATLL disease, based on the presentation of a messaging network

Methods: After purposeful search in informations sites and qualitative review of obtained data, the data were processed using R software and miRNAs with different expression (DEMs) were detected based on the value of log fold change. The gene targets of miRNAs were obtained using miRDB online tool .The protein-protein interaction network of gene targets was drawn and analyzed with STRING database. The sub-network was extracted using cytoscape. Pathway analysis was done, and proteins participating in the enriched pathways were selected to propose the implicated signaling network using the information available on the website ENRICHR and KEGG message transduction. An intracellular control gene, RPLP0, and three other key genes were selected and were evaluated in 10 healthy participants, 10 ACs and 10 ATLL patients using real-time PCR.

Results: From the data set (GSE 31629), mir-20a-5p, was identified as an important microRNA with different expression in the patient group in comparison with the healthy and asymptomatic carrier group. It was found that TGF-β signaling pathway is related to HTLV pathogenesis. TGF-β1, TGFBR1 and TGFBR2, which have a key role in regulating the mentioned pathway, were selected. Real-time PCR results showed that the expression level of TGF-β1 and TGFBR2 are decreased in ATLL compared to healthy subjects. The expression level of TGFBR1 was increased significantly in ATLL patients compared to healthy donors and asymptomatic carriers.

Conclusion: In this study, by collecting different data, using high-throughput data integration and bioinformatics techniques, some miRNAs and genes involved in the immunopathogenesis of ATLL were identified. The expression level of these genes between patients and healthy groups' were significantly different. So by drawing a model of the messaging network involved and the possible role of genes in pathogenesis, the pathways involved in carcinogenesis as well as in the treatment of these patients can be identified.

keywords: ATLL, HTLV1, miRNA, TGF-B Signaling pathway , mir-20a-5p , System

PI-120

Exosomal microRNAs: importance in the treatment of allergic asthma

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Background and aim: Allergic asthma is one of the most widespread chronic respiratory diseases affecting around 300 million people globally. Due to its heterogeneous nature, the development of a considerably effective treatment approach has yet to be investigated. Despite this gap, advancement regarding the use of exosomal miRNAs as a promising method has been made. Therefore, we have dedicated this research to the classification and summarization of exosomal miRNAs in asthma diagnosis, hoping this will be considered a step forward.

Methods: Several databases, including Google Scholar, PubMed, Elsevier, etc., were investigated. Using the terms "exosome", "miRNA", and "asthma", relevant articles published between 2020 and 2025 were selected and reviewed.

Results: As mentioned above, research has been done regarding the role of exosomal miRNA as a potential treatment approach for allergic asthma. For instance, Liu et al. reported the downregulation of miRNA-125 in the sputum of eosinophilic asthmatic patients, and its indirect role in inhibiting goblet cell differentiation, making it a promising therapeutic approach for asthma. Additionally, Kumar et al.`s in vivo experiment showed that lower let-7 expression in OVA-induced asthmatic mouse models results in a reduction of IL-13 and other asthma features such as cell infiltration and AHR.

Conclusion: In conclusion, despite the high prevalence of allergic asthma, the need for finding a treatment approach is still unmet. As a result, an enormous amount of research has been conducted in recent years. However, despite the considerable advancements in identifying the role of some exosomal miRNAs as valuable treatment targets, further investigation is still essential.

keywords: exosomal miRNA, allergic asthma, treatment

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-121

Association of Rs7217186 Polymorphism of Arachidonic Acid 15-Lipoxygenase (ALOX15) Gene with Susceptibility to Allergic Rhinitis

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Background and aim: Allergic rhinitis (AR) is an inflammatory disorder of the nasal mucosa, caused by exposure to environmental allergens. It is known that 15-lipoxygenase (15-LOX) is involved in the biosynthetic pathways of anti-inflammatory lipid mediators, including resolvins and protectins.

Methods: In this study, which was performed on 130 AR patients and 130 healthy controls, we aimed to investigate the association of susceptibility to AR with two selected single-nucleotide polymorphisms (SNPs), that is, rs2619112:AG and rs7217186:CT, in the intron regions of arachidonic acid 15-LOX (ALOX15) gene, using SNPinfo and Regulome DB tools.

Results: The results showed that the CT genotype of rs7217186: CT was significantly associated with the increased risk of AR compared to the CC genotype (P= 0.037, OR=1.943, CI: 1.038-0.638). However, there was no strong evidence of the association of rs2619112: AG with susceptibility to AR (P 0.05).

Conclusion: The present results indicated that rs7217186 polymorphism of ALOX15 gene might be a potential biomarker for susceptibility to AR.

keywords: Allergic rhinitis, Arachidonate 15-lipoxygenase, Immunoresolvents, Single-nucleotide polymorphism, Specialized proresolving lipid

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-122

Seroprevalence of laboratory-confirmed Bordetella pertussis antibodies in Iran: a systematic review and meta-analysis of nationwide healthy-population study

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Background and aim: Pertussis (whooping cough) which causes by Bordetella pertusis (BP), is one of contagious upper respiratory infection and also vaccine preventable disease with high morbidity and mortality. Based on immune response of the host, the severity of BP infection is variable, therefore, analyzing the BP seroprevalence rate in general population may improve the implementation of new strategic health management such as developed vaccination schedule. Therefore, we aimed to provide a systematic review of the seroprevalence rate of BP infection among Iranian population through estimating the prevalence of BP according to age, gender, infancy and pre and post booster vaccination.

Methods: A systematic and comprehensive review was conducted in PubMed, Embase, Web of Science, Scopus, and Google Scholar databases, as well as in Persian national databases, until November 2025 to identify eligible studies assessing the seroprevalence of BP-specific antibodies in healthy individuals in Iran. Finally, out of a total of 176 studies, 32 studies involving a large population of 12,830 people, including healthy individuals aged 0 to 67 years, were included in this meta-analysis. Any heterogeneity in the selected studies was calculated using I2 statistic. The random effect model was used based on heterogeneity test results and pooled data expressed as the effect size (ES) with 95% confidence intervals (CIs).

Results: The IgG seroprevalence rate of BP infection in the general Iranian population was 51% (95% CI; 45%-57%) and the IgA seroprevalence rate was 20% (95% CI; -3%-42%). Also, the total IgG seroprevalence rate among infants was 38%, and there was no significant difference between the seroprevalence of females and males (49% vs. 48%, respectively). Furthermore, the relative rate of seropositivity is high in children (53%, 95% CI; 43%-62%) and vaccinated individuals after a booster dose (77%, 95% CI; 59%-94%).

Conclusion: Our findings could provide a better and more realistic picture of the background status of BP infection in the Iranian population and establish a cost-effective immunization program or raise concerns for targeted anti-BP clinical interventions. Heterogeneity among studies and limited sample size in some age groups may affect results.

keywords: Bordetella pertussis; Seroprevalence; IgG antibodies; Seroepidemiology; Iran

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-123

Immunomodulatory Effects of Sulfasalazine in Mitigating Post-Vaccination Inflammation and Immune-Mediated Reaction

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Background and aim: Live attenuated influenza vaccines (LAIV) are extensively utilized for infection prevention; however, their potential immunological effects remain inadequately characterized. Although some studies have indicated a possible association between influenza vaccination and immune-mediated disorders, such as Guillain-Barré Syndrome (GBS), the precise inflammatory mechanisms underlying this relationship remain poorly understood.

Methods: In this study, we assessed post-vaccination inflammatory responses by measuring cytokine levels, white blood cell counts, and immunohematological parameters 24 hours after immunization. Using an in vivo mouse model, male rats were orally administered sulfasalazine at varying doses for seven consecutive days. On the final day, one hour after the last administration, the rats received an intranasal administration of the influenza vaccine. This experimental approach aimed to evaluate the potential immunomodulatory effects of sulfasalazine in mitigating vaccine-induced inflammation. Given its role as a potent inhibitor of the NF-κB signaling pathway, sulfasalazine was hypothesized to attenuate inflammatory responses triggered by vaccination. Since NF-κB-related transcripts have been implicated in the pathogenesis of inflammatory neuropathies such as Guillain-Barré Syndrome (GBS), we investigated whether a similar mechanism might contribute to post-vaccination inflammation.

Results: Our findings suggest that influenza vaccination may induce a transient increase in pro-inflammatory cytokines (IL-1β, IL-6, IL-12, TNF-α, IFN-γ), as well as neutrophil and lymphocyte activation, indicating a potential association with immune-mediated reactions. Treatment with sulfasalazine (SASP) significantly modulated these cytokine levels, supporting its potential role in controlling post-vaccination inflammatory responses.

Conclusion: These results suggest that sulfasalazine (SASP) could serve as a potential immunomodulatory agent for individuals at risk of heightened inflammatory responses following influenza vaccination. Further studies are necessary to clarify the clinical implications of these findings, particularly for high-risk populations susceptible to vaccine-associated immune-mediated diseases, especially Guillain-Barré Syndrome.

keywords: Influenza vaccine,Guillain-Barré Syndrome (GBS),Immunomodulation ,Sulfasalazine.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-124

Pattern Recognition Receptor Signaling in Zoonotic Infections: Implications for Hyper-inflammation and Tissue Damage

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Background and aim: Zoonotic infections represent a major source of emerging infectious diseases and are frequently associated with severe immunopathology. A central mechanism underlying disease severity is the dysregulated activation of pattern recognition receptors (PRRs), which detect pathogen-associated molecular patterns and initiate innate immune responses. While PRR signaling is essential for host defense, excessive or prolonged activation can drive hyper-inflammation, cytokine storm, and tissue damage. Understanding how PRR pathways contribute to immunopathology in zoonotic infections is critical for identifying novel therapeutic targets. This systematic review synthesizes current evidence on PRR-mediated signaling in zoonotic diseases and its role in inflammatory tissue injury.

Methods: A systematic review was conducted in accordance with established methodological guidelines. Comprehensive searches were performed in PubMed, Scopus, and Web of Science using predefined keywords related to pattern recognition receptors, Toll-like receptors, NOD-like receptors, RIG-I-like receptors, zoonotic infections, hyper-inflammation, and immunopathology. Peer-reviewed original studies published in English were included if they reported mechanistic, experimental, or clinical data on PRR activation in bacterial, viral, or parasitic zoonoses. Articles were screened based on titles, abstracts, and full texts to ensure relevance and methodological quality.

Results: The included studies demonstrate that multiple zoonotic pathogens activate PRR pathways, particularly Toll-like receptors (TLRs), NOD-like receptors (NLRs), and cytosolic RNA sensors, leading to robust activation of NF-κB and interferon-regulatory signaling cascades. This activation promotes excessive production of pro-inflammatory mediators such as IL-6, TNF-α, IL-1β, and type I interferons. Overactivation of inflammasomes, especially NLRP3, was frequently associated with endothelial dysfunction, epithelial barrier disruption, and multiorgan injury. Several studies highlighted species-specific differences in PRR expression and signaling intensity, contributing to variable susceptibility and disease severity across hosts.

Conclusion: PRR signaling plays a dual role in zoonotic infections by providing essential immune protection while also driving immunopathology when dysregulated. Targeting specific PRR pathways or downstream inflammatory mediators may offer promising strategies to mitigate tissue damage without compromising antimicrobial defense. Further translational studies are needed to define context-specific therapeutic interventions and to improve clinical outcomes in severe zoonotic diseases.

keywords: Pattern recognition receptors, Zoonotic infections, Toll-like receptors, Hyper-inflammation, Tissue damage.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-125

The Role of Inflammatory Markers in Polycystic Ovary Syndrome and Their Link to Ovarian Cancer Risk: A Systematic Review

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Background and aim: Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder in reproductive-age women often accompanied by chronic low-grade inflammation. This inflammation, characterized by elevated levels of markers such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP), is believed to contribute to ovarian dysfunction and an increased risk of ovarian cancer in PCOS patients.

Methods: A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science, focusing on studies published from 2010 to 2024. Keywords included "PCOS," "ovarian cancer," "inflammatory markers," "TNF-α," "IL-6," and "CRP." After screening, 35 articles met the inclusion criteria, focusing on human studies with significant statistical analysis on inflammatory markers and their relationship with PCOS and ovarian cancer.

Results: The review found consistently elevated levels of inflammatory markers, including TNF-α, CRP, and IL-6, in women with PCOS and demonstrated consistent elevation of TNF-α and IL-6 in both serum and ovarian tissues of PCOS patients. These markers are implicated in promoting cellular proliferation, angiogenesis, and immune evasion, all processes associated with ovarian tumorigenesis.

Conclusion: Chronic low-grade inflammation in PCOS plays a pivotal role in ovarian dysfunction and potentially increases the risk of ovarian cancer. Elevated inflammatory markers may provide therapeutic targets to mitigate cancer risk in PCOS patients. Future longitudinal studies and clinical trials are needed to clarify causal mechanisms and assess the efficacy of anti-inflammatory treatments in reducing ovarian cancer risk.

keywords: ovarian cancer, inflammatory markers, TNF-α, PCOS, CRP

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-126

EV-miRNA as Diagnostic and Theragnostic Biomarkers in Rheumatoid Arthritis

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Background and aim: Early diagnosis of rheumatoid arthritis (RA) is essential to prevent irreversible joint damage; however, conventionalserological biomarkers show limited sensitivity in early disease stages. Recently, microRNAs (miRNAs) enclosed within extracellular vesicles (EVs), particularly exosomes, have emerged as stable and promising liquid biopsy biomarkers.

Methods: This review integrates findings from two recent studies published in 2024 that investigated the diagnostic and prognostic value of EV-associated miRNAs in RA. Relevant literature was retrieved from PubMed using keywords related to rheumatoid arthritis, extracellular vesicles, exosomes, microRNAs, and methotrexate response.

Results: In active RA, significant downregulation of exosomal miR-30b-5p and miR-144-3p was associated with disease activity indices and B-cell functional alterations, demonstrating moderate to high diagnostic accuracy when combined as a panel. In early, treatment-naïve RA, a distinct 28-miRNA EV signature successfully differentiated RA-specific inflammation from non-specific inflammatory conditions. Furthermore, longitudinal analyses identified 13 EV-associated miRNAs whose expression changes correlated with clinical response to methotrexate therapy over six months.

Conclusion: Nevertheless, large-scale multicenter studies and standardized EV isolation and miRNA profiling protocols are essential before translation into routine clinical practice.

keywords: rheumatoid arthritis, extracellular vesicles, exosomes, microRNAs, methotrexate response

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-127

redictive Value of Gut Microbiome Composition for Response to Immune Checkpoint Inhibitors in Cancer Patients: A Systematic Review

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Background and aim: Background: Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy, but only a subset of patients achieves durable response. Emerging evidence suggests that gut microbiome composition may predict ICI efficacy. However, the consistency and clinical utility of these findings remain unclear. This systematic review aims to synthesize available evidence on the association between gut microbiota features and clinical response to ICIs in cancer patients.

Methods: Methods: The review followed PRISMA guidelines. PubMed, Scopus, and Web of Science were searched from inception to March 2025 using MeSH terms: "Gastrointestinal Microbiome" AND ("Immune Checkpoint Inhibitors" OR "CTLA-4" OR "PD-1" OR "PD-L1") AND ("Neoplasms" OR "Cancer") AND ("Treatment Outcome" OR "Response"). Inclusion criteria: (1) original studies (cohort, case-control, or prospective); (2) adult cancer patients treated with ICIs (anti-PD-1, anti-PD-L1, or anti-CTLA-4); (3) baseline gut microbiome profiling (16S rRNA or metagenomic sequencing); (4) reported association between microbial taxa or diversity and clinical response (RECIST criteria). Exclusion criteria: case reports, reviews, animal studies, non-English articles, or studies without response data. Studies were screened, data were extracted, and quality was assessed using the Newcastle-Ottawa Scale. Findings were synthesized narratively.

Results: Results: Of 1,204 identified records, 23 studies (total 1,856 patients) met inclusion criteria. Cancer types included melanoma (n=9), non-small cell lung cancer (n=7), renal cell carcinoma (n=4), and others (n=3). Fifteen studies reported that higher alpha diversity (Shannon index) was significantly associated with better ICI response. Specific taxa consistently associated with response included: Akkermansia muciniphila (8 studies), Bifidobacterium species (6 studies), and Faecalibacterium prausnitzii (5 studies). Conversely, Bacteroides species were associated with non-response in 4 studies. Fecal microbiota transplantation studies (n=3) showed that responders' microbiota could convert non-responders. Quality scores ranged from 6 to 8 (moderate to high). Heterogeneity in sequencing methods and response definitions prevented meta-analysis.

Conclusion: Conclusion: Gut microbiome composition, particularly higher alpha diversity and presence of Akkermansia and Bifidobacterium, is consistently associated with favorable response to ICIs across multiple cancer types. However, lack of standardized protocols limits clinical translation. This systematic review identifies critical gaps – including need for prospective validation, standardized sampling, and interventional FMT trials – and provides a roadmap for future research.

keywords: Gastrointestinal Microbiome, Immune Checkpoint Inhibitors, Biomarkers, Treatment Outcome

PI-128

Exosomal PD-L1: A Novel Liquid Biopsy Biomarker for Cancer Diagnosis and Immunotherapy Monitoring—Clinical Laboratory Perspectives

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Background and aim: Programmed death-ligand 1 (PD-L1) is a critical immune checkpoint molecule involved in tumor immune evasion and a major target of cancer immunotherapy. Growing evidence suggests that exosomal PD-L1 (ExoPD-L1) may serve as a noninvasive liquid biopsy biomarker capable of reflecting dynamic tumor–immune interactions more accurately than conventional tissue biopsy.

Methods: A systematic literature review was conducted using PubMed, Scopus, and Web of Science databases to identify studies published between January 2010 and January 2026. The search strategy included the terms "exosome," "extracellular vesicle," "PD-L1," "immune checkpoint," "liquid biopsy," and "cancer." Original human studies evaluating the diagnostic, prognostic, or predictive significance of ExoPD-L1 were included. Data were extracted and synthesized qualitatively according to PRISMA principles.

Results: Evidence accumulated during the last decade demonstrates that circulating ExoPD-L1 is elevated in several malignancies, including non-small cell lung cancer, melanoma, breast cancer, gastric cancer, colorectal cancer, and head and neck cancers. Increased ExoPD-L1 levels were consistently associated with tumor progression, metastatic potential, immune suppression, and unfavorable clinical outcomes. Recent systematic reviews incorporating more than 1,000 cancer patients have further confirmed the prognostic significance of ExoPD-L1. In addition, dynamic changes in circulating ExoPD-L1 levels have been shown to correlate with treatment response and resistance to immune checkpoint inhibitors, highlighting its potential utility in therapeutic monitoring.

Conclusion: Exosomal PD-L1 represents a promising liquid biopsy biomarker for cancer diagnosis, prognostic assessment, and immunotherapy monitoring. Nevertheless, methodological heterogeneity in exosome isolation and detection techniques remains a major challenge. Standardized laboratory protocols and large prospective clinical studies are required before routine implementation of ExoPD-L1 testing in clinical oncology laboratories.

keywords: Extracellular Vesicles, Immunotherapy Monitoring, Exosomal PD-L1, Biomarkers

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-129

Lactobacillus acidophilus and Lacticaseibacillus rhamnosus Postbiotics Attenuate Keratinocyte Hyperproliferation and Oxidative Stress: A Targeted Apoptotic Strategy for Psoriasis

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Background and aim: Keratinocytes are essential for skin integrity and actively regulate inflammation in a chronic autoimmune condition marked by excessive skin cell growth and an aberrant immune response. The progression of such a disease is driven by oxidative stress and cytokine release, complicating treatment strategies. This research explored the potential of postbiotics derived from Lactobacillus acidophilus and Lacticaseibacillus rhamnosus as therapeutic agents, evaluating their effects on keratinocyte proliferation, migration, reactive oxygen species (ROS) levels, and apoptosis compared to the control group .

Methods: HaCaT cells were cultured in DMEM (Dulbecco's Modified Eagle Medium) and treated with postbiotics from two bacterial strains. MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assays were used to assess cell viability, scratch assays evaluated cell migration, and Annexin V/PI (Propidium Iodide) staining analyzed apoptosis. Additionally, ROS levels were quantified via flow cytometry following postbiotic treatment.

Results: Both postbiotics significantly reduced HaCaT cell viability, increased apoptosis, inhibited cell migration, and decreased ROS levels (p 0.05).

Conclusion: By significantly reducing keratinocyte proliferation and migration while inducing apoptosis ,these specific postbiotics exhibited strong potential as therapeutic candidates for chronic skin disorders.

keywords: postbiotic, psoriasis, Lactobacillus acidophilus, Lacticaseibacillus rhamnosus

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-130

Overcoming Antibiotic Resistance: Smart Vaccinology and Targeted Phage Therapy

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Background and aim: This review compiles and analyzes recent studies on integrative computational and biological strategies to combat antibiotic-resistant bacteria—a major cause of global mortality and economic burden—focusing on AI-aided vaccinology, network-based immunoinformatics, engineered phage therapy, and nanotechnology for both prevention and treatment.

Methods: We conducted a narrative review (2020–2025) using PubMed and Google Scholar. Search terms included "AI in vaccine design," "network immunoinformatics," "phage delivery systems," "nanoparticles against MRSA," and "WHO priority pathogens." Relevant preclinical and clinical studies were critically analyzed.

Results: Computational approaches, including machine learning and network immunoinformatics, successfully identified conserved antigens in S. aureus with high prediction accuracy and generated multi-epitope vaccine constructs demonstrating strong binding affinity to immune receptors. In parallel, marine phages demonstrated a significant reduction in Vibrio load in aquaculture models, while engineered liposomal carriers markedly enhanced phage stability and biofilm penetration capability. Nanotechnology applications, such as silver nanoparticles, exhibited potent inhibitory effects against MRSA, and phage-antibiotic combinations substantially lowered antibiotic MICs, thereby effectively delaying the emergence of resistance.

Conclusion: Integrating AI-based vaccine design, network analysis of immune targets, and engineered phage-nanoparticle systems provides a powerful multifaceted strategy to address the critical challenge of antibiotic resistance. Although computational and preclinical evidence is promising, further validation in human-relevant models and controlled clinical trials remains essential to translate these strategies into viable alternatives to conventional antibiotics.

keywords: Artificial Intelligence; Network Immunoinformatics; Phage Therapy; Nanotechnology; Multi-Epitope Vaccine

PI-131

Investigating the mechanism of effect of flavonoides on heat shock protein beta1(HSP27) in lung cancer by molecular docking

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Background and aim: Non-small cell lung cancer (NSCLC) with its high mortality rate and recurrence after treatment has led researchers to investigate some complementary therapies. This study attempts to investigate the relationship between HSP27 (heat shock protein beta-1; HSPB1) and the flavonoid family, which are proposed as complementary therapies for lung cancer, using molecular docking methods. This protein protects cancer cells from apoptosis. The activity of this protein also increases the activity of the JAK/STAT signaling pathway. Therefore, blocking this protein can activate apoptosis in cancer cells and reduce the resistance of cancer cells to drugs by blocking the JAK/STAT signaling pathway.

Methods: The 3D structure of the protein was obtained from the PDB database. The 2D and 3D information and structures of natural products (resveratrol, apigenin, bavachin, bergamottin, kaempferol) were extracted from the PubChem database. Chimera software was used to isolate and prepare protein chains. Molecular docking was performed with Pyrx software to determine the affinity of the ligand and each of the natural products. Atoms participating in the interaction between the ligand and the protein were examined using liGplot+ software.

Results: The A-chain of the protein, having four coils, established favorable binding energies with natural products. Both Bavachin and Bergamottin showed binding energies of -6.1 kcal/mol. Apigenin established a binding energy of -0.6 kcal/mol. This binding energy was -5.9 kcal/mol for kaempferol and -5.5 kcal/mol for resveratrol. The B-chain, having four coils, established a better connection with natural products than the a-chain. Bergamottin has the highest energy with a binding energy of -6.6 kcal/mol, followed by Bavachin and Kaempferol with a binding energy of -6.1 kcal/mol. Apigenin has established a binding energy of -5.9 kcal/mol. Resveratrol has established a binding energy of -5.5 kcal/mol with this chain, like the A-chain. In the presence of both chains and the combination of natural products, the binding energy changed to -7.6 kcal/mol. The RMSD in all bindings was 0.0, indicating structural similarity and proper binding of the protein and natural products.

Conclusion: The key findings of this study, based on bioinformatics data, indicate that the flavonoid family could be a suitable option for targeted therapy of lung cancer. However, the physiological differences of each individual's body, the pharmacodynamics and pharmacokinetics of each drug, and the influence of environmental and genetic factors on the course of the disease should also be examined. To achieve more advanced results, further studies should be conducted in vitro and in vivo. Determining optimal doses, drug toxicity, investigating possible side effects, and testing on animals are also necessary.

keywords: Lung cancer, Targeted therapy, Molecular docking, JAK/STAT signaling pathway, HSP27

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-132

Study of the immunopathogenesis of bacterial septicemia and its clinical manifestations

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Background and aim: Septicemia occurs when bacteria enter the bloodstream from various parts of the body, such as the skin, gastrointestinal tract, lungs, kidneys, etc. The aim of this study was to investigate the immunopathogenesis of bacterial septicemia and its clinical manifestations.

Methods: The possible roles of various virulence factors of the most prevalent septicemia-causing bacteria in the immunopathogenesis were investigated in vitro and in vivo. Clinical manifestations of septicemia were investigated in patients with bacterial septicemia.

Results: Presence of bacterial capsule or surface protein A inhibited phagocytosis of bacteria by neutrophils and macrophages, as well as complement activation on the surface of bacteria. Presence of cell adhesion factors such as fimbriae augmented bacterial colonization in tissues and development of septicemia. Bacterial leukocidins directly lysed leukocytes. Superantigenic exotoxins of Staphylococcus aureus caused toxic shock syndrome, polyclonal and nonspecific activation of T cells, and apoptosis of T cells. Binding of bacterial cell wall lipopolysaccharides to TLR4 and peptidoglycan and teichoic acids to TLR2 on the surface of leukocytes activated the MyD88/NF-κB pathway, which led to secretion of high levels of interleukin-1-beta, interleukin-6, and tumor necrosis factor-alpha and subsequent systemic clinical manifestations, including fever, severe chills, and tachycardia. Progression of septicemia led to disseminated intravascular coagulation and multiple organ dysfunction in some patients, which was extremely fatal. Decreased lymphocyte proliferation, and increased serum levels of interleukin-10 occurred in late septicemia.

Conclusion: High levels of proinflammatory cytokines along with prostaglandins, prostacyclins, and leukotrienes increase capillary permeability, tissue edema, hypotension, and decreased or absent urination. Progression of septicemia leads to systemic inflammatory response syndrome with disseminated intravascular coagulation and multiple organ dysfunction, which cause death in a large proportion of patients. Immunosuppression occurs in patients who survive the initial events of septicemia. Infections can be the cause of death in a significant percentage of these patients. These findings indicate that early detection of septicemia and prompt treating is vital to prevent patient death.

keywords: Bacterial Septicemia, Immunopathogenesis, Clinical Manifestations

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-133

Immunometabolism in the Wound Microenvironment: Metabolic Regulation of Immune Responses During Tissue Repair and Regeneration

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Background and aim: Wound healing is a highly coordinated biological process involving hemostasis, inflammation, proliferation, and tissue remodeling, all of which are regulated by dynamic interactions between immune cells and the local wound microenvironment. Recent advances in immunometabolism have revealed that cellular metabolic pathways actively govern immune cell phenotype, function, and plasticity during tissue repair rather than merely supplying energy. Metabolic reprogramming of macrophages, neutrophils, dendritic cells, and lymphocytes is increasingly recognized as a critical determinant of healing outcomes.

Methods: Pro-inflammatory immune cells mainly rely on glycolysis and associated metabolic intermediates to support rapid antimicrobial and inflammatory responses, whereas reparative immune phenotypes are characterized by enhanced oxidative phosphorylation, fatty acid oxidation, and mitochondrial function.

Results: Dysregulation of these metabolic transitions contributes to persistent inflammation, impaired angiogenesis, defective extracellular matrix remodeling, and the development of chronic non-healing wounds. The wound microenvironment, including hypoxia, nutrient availability, reactive oxygen species, microbial burden, and cytokine signaling, further shapes immune cell metabolism and influences the balance between inflammatory and regenerative responses.

Conclusion: Emerging evidence suggests that targeting immunometabolic pathways can restore immune homeostasis, promote macrophage phenotypic switching, enhance tissue regeneration, and improve wound closure. This review summarizes current knowledge regarding the metabolic mechanisms governing immune cell function within the wound microenvironment and discusses emerging therapeutic strategies aimed at modulating immunometabolism for the treatment of acute and chronic wounds.

keywords: Immunometabolism; Wound Microenvironment; Wound Healing; Macrophage-Metabolism; Immune Regulation; Chronic Wounds;

PI-134

Immunotherapy with PD-1 Inhibitors Pembrolizumab and Nivolumab in Anaplastic Thyroid Carcinoma: Human PBMC Co-Culture Models

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Background and aim: Anaplastic thyroid carcinoma (ATC) is an aggressive form of thyroid cancer for which effective treatment options remain very limited. Immune checkpoint inhibitors targeting programmed cell death protein-1 (PD-1) have shown encouraging results in several malignancies; however, their functional impact on immune–tumor interactions in ATC is not yet clearly defined.

Methods: In this study, we examined whether PD-1 blockade could enhance immune-mediated cytotoxicity against ATC cells using a simplified in vitro co-culture system. SW1736 ATC cells were co-cultured with peripheral blood mononuclear cells (PBMCs) obtained from healthy donors at effector-to-target ratios of 5:1 and 10:1 and treated with nivolumab (50 µg/ml) or pembrolizumab (150 µg/ml) for 48 h. Tumor cell viability and apoptosis were assessed using MTT assays and Annexin V/PI staining. Parallel monoculture experiments confirmed that the antibody concentrations applied did not exert direct cytotoxic effects on either ATC cells or PBMCs.

Results: Compared with untreated co-cultures, PD-1 inhibition consistently increased PBMC-mediated cytotoxicity against SW1736 cells. Both antibodies promoted apoptotic cell death and reduced tumor cell viability, particularly at higher effector densities. Under the experimental conditions, pembrolizumab was associated with a greater extent of tumor apoptosis, although differences in working concentrations limit direct comparison.

Conclusion: Taken together, these results suggest that PD-1 blockade can enhance immune-mediated antitumor activity against ATC cells in a controlled co-culture model and provide a functional basis for further investigation of immune checkpoint inhibition in this aggressive malignancy.

keywords: Anaplastic thyroid carcinoma; PD-1; immune checkpoint inhibitors; co-culture; T-cell cytotoxicity;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-135

In activated SARS-CoV-2 in AS03 and Alum adjuvants; Superiority of AS03-based vaccine in inducing cross-reactive IgG response

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Background and aim: SARS-CoV-2 is responsible for COVID-19. Although massive public vaccination has significantly limited COVID-19 spread, emerging antibody-evading strains of SARS-CoV-2 remains a concern. In the present study inactivated SARS-CoV-2 virus was formulated in AS03 adjuvant and the immunogenicity was compared with the Alum-based vaccine. In addition, the research focused on the adjuvants' ability on cross-reactive IgG response against Wuhan strain and English variant of SARS-CoV-2 strains.

Methods: Experimental 6-8-week-old BALB/c mice were immunized three times with three weeks interval with AS03- and Alum-based vaccines along with PBS as a control group. Lymphocyte proliferation of spleen cells was performed by BrdU method, IL-4 and IFN-γ cytokines were assessed on the spleen cell culture supernatant by quantitative ELISA kits. Specific total IgG and IgG1/IgG2a were assessed with an optimized indirect ELISA. In addition, the cross-reactive IgG titers were assessed by ELISA versus English variant of SARS-CoV-2 strain.

Results: The findings revealed both AS03 and Alum adjuvants enhance lymphocyte proliferation, cytokine response (IFN-γ and IL-4), and IgG induction. In addition, AS03 demonstrated a superior capacity to trigger a robust immune response characterized by a higher IFN-γ response when compared with Alum. Furthermore,

Conclusion: AS03-adjuvanted vaccine showed a significant increase in cross-reactive IgG response and IgG1/IgG2a isotypes versus the Alum-adjuvanted vaccine, suggesting the possible efficacy of AS03 in the protection against new emerged SARS-CoV-2.

keywords: AS03, Alum, SARS-CoV-2,

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-136

Gut Microbiota-Derived Metabolites as Modulators of Wnt/β-Catenin Signaling in Colorectal Cancer: Emerging Mechanisms and Therapeutic Opportunities

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Background and aim: Colorectal cancer (CRC) is one of the most common malignancies in the world and one of the most important causes of cancer-related mortality. In addition to genetic factors, the complex interaction between the intestinal microbiota, microbial metabolites, and cell signaling pathways plays a decisive role in the formation and progression of this disease. Among these pathways, Wnt/β-catenin is known as one of the most prominent regulators of cell proliferation, differentiation, and survival. Mutations in the adenomatous polyposis coli (APC) gene, which are observed in about 80% of colorectal cancer cases, cause persistent activation of this pathway and increase the expression

Methods: A narrative review was performed using established scientific databases, including PubMed, to identify relevant studies examining the involvement of gut microbiota-derived metabolites as modulators of Wnt/β-Catenin signaling in colorectal cancer: emerging mechanisms and therapeutic opportunities. Search terms included combinations of “Colorectal cancer (CRC),” “Wnt/β-Catenin,” and “Gut Microbiota.”

Results: The current findings indicate that some members of the intestinal microbiota are able to participate in colorectal carcinogenesis through direct or indirect regulation of Wnt/β-catenin activity. Bacteria such as Fusobacterium nucleatum, Salmonella enterica, and pks+ Escherichia coli strains promote tumor progression by inducing chronic inflammation, DNA damage, and β-catenin activation. In contrast, beneficial bacteria such as Lactobacillus, Bifidobacterium, and butyrate producers exert significant protective effects by maintaining intestinal homeostasis, strengthening the epithelial barrier, and modulating immune responses. Microbiota-derived metabolites also play a key role in this process. Short-chain fatty acids, especially butyrate, suppress Wnt pathway activity by inhibiting histone deacetylases, reducing inflammation, and inducing β-catenin degradation through LC3-dependent autophagy. In addition, tryptophan-derived metabolites play a role in reducing tumorigenic signaling by maintaining mucosal barrier integrity and regulating immune function. Secondary bile acids such as lithocholic acid and ursodeoxycholic acid can also inhibit inflammation and abnormal Wnt activity by activating Farnesoid

Conclusion: The totality of evidence suggests that the “microbiota–metabolite–Wnt/β-catenin” axis not only plays a pivotal role in the pathogenesis of colorectal cancer, but can also be used as an emerging therapeutic target for microbiome-based interventions. The main innovation of this approach is the simultaneous targeting of microbial factors and host molecular pathways, which can pave the way for the development of personalized, less-invasive, and more effective therapeutic strategies in the prevention and treatment of colorectal cancer.

keywords: “Colorectal cancer (CRC),” “Wnt/β-Catenin,” and “Gut Microbiota.”

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-137

Potential Role of Regulatory T Cell-Associated MicroRNAs in Osteomyelitis: Current Evidence and Future Perspectives

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Background and aim: Osteomyelitis is a chronic inflammatory bone disease characterized by persistent infection, immune dysregulation, and progressive bone destruction. Regulatory T cells (Tregs), identified by FoxP3 expression, contribute to immune homeostasis by limiting excessive inflammation; however, their expansion may also facilitate pathogen persistence. MicroRNAs (miRNAs) are critical post-transcriptional regulators of Treg development and function. Recent advances in osteoimmunology and non-coding RNA research suggest that Treg-associated miRNAs may participate in the immunopathogenesis of osteomyelitis and represent potential molecular targets for diagnosis and immunomodulation.

Methods: A narrative review was conducted using peer-reviewed open-access literature indexed in PubMed, Scopus, and Web of Science. Studies evaluating Treg biology in osteomyelitis and investigations addressing miRNA-mediated regulation of Treg function were reviewed. Experimental, translational, and clinical evidence related to FoxP3 regulation, IL-2/STAT5 signaling, SOCS1-mediated pathways, inflammatory cytokines, and osteoimmune interactions were analyzed. The available data were integrated to identify potential mechanistic links between Treg-associated miRNAs and osteomyelitis pathogenesis.

Results: Current evidence indicates that miRNAs play essential roles in maintaining Treg stability and immunoregulatory activity. Among them, miR-155 enhances Treg fitness through regulation of the SOCS1/IL-2/STAT5 axis, while miR-146a contributes to the control of inflammatory signaling pathways and maintenance of immune tolerance. Independent studies in chronic osteomyelitis have reported increased frequencies of circulating $CD4^{+}CD25^{+}FoxP3^{+}$ Tregs, suggesting a role in immune suppression and persistence of infection. Although direct evidence linking specific Treg-associated miRNAs to osteomyelitis remains limited, emerging data from osteoimmunology and non-coding RNA research support a plausible mechanistic association between miRNA dysregulation, altered Treg function, and chronic bone inflammation.

Conclusion: Treg-associated miRNAs, particularly miR-155 and miR-146a, may contribute to immune regulation during osteomyelitis through modulation of FoxP3-dependent pathways and inflammatory signaling networks. While direct clinical evidence remains limited, these molecules represent promising candidates for future biomarker discovery and targeted immunomodulatory strategies. Further experimental and translational studies are required to validate their role in osteomyelitis.

keywords: Osteomyelitis; MicroRNA; Regulatory T Cells; FoxP3; Osteoimmunology

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-138

The Role of Vitamin D in Modulating Anti-Tumor Immune Responses in Breast Cancer Patients

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Background and aim: Breast cancer(BC) is the most common malignancy among women, and the status of the host immune system plays an important role in disease progression and response to treatment. Vitamin D, as a micronutrient with immunomodulatory properties, can affect the tumor microenvironment through the vitamin D receptor (VDR) expressed in immune cells and breast tissue. Studies have shown that reduced VDR expression is associated with more aggressive breast tumor characteristics. The aim of this study was to investigate the role of vitamin D in modulating the antitumor immune response in patients with BC.

Methods: We searched PubMed, Google Scholar, Clinical Trials and other Databases. We also reviewed these articles and collected the necessary information. Keywords used included “breast cancer” “vitamin D” “25-Hydroxy Vitamin” “ immune response” and “Tumor microenvironment (TME).”

Results: Studies have shown that low levels of the 25-Hydroxyvitamin D are associated with increased risk and poor prognosis of BC, as vitamin D exerts anti-inflammatory and antitumor effects by inhibiting the NF-κB pathway, reducing the production of inflammatory cytokines such as IL-6 and TNF-α, and modulating the function of immune cells. VDR activation has been reported to increase the activity of cytotoxic T lymphocytes (CD8+) and reduce regulatory T cells. Vitamin D supplementation showed a significant reduction in TNF-α, although its effect on IL-6 and CRP was heterogeneous. Emerging studies also suggest that adequate levels of vitamin D may improve the response to chemotherapy and immunotherapy, although human evidence is still limited and the results are heterogeneous

Conclusion: Vitamin D shifts the tumor microenvironment towards an antitumor phenotype through multiple pathways (modulation of cytokines and immune cells). Despite promising findings, the lack of human studies with sufficient sample size and rigorous examination of immune markers is a major limitation. Future studies should focus on the effect of vitamin D supplementation on immunological parameters and clinical outcomes to clarify its true role in improving patients' immune responses.

keywords: “Breast cancer” “vitamin D” “25-Hydroxy Vitamin” “ immune response”

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-139

Epigenetic and Genetic Regulation of Apoptotic Pathways Through Nanomedicine: Overexpression of Pro-apoptotic and Underexpression of Anti-apoptotic Genes in Cancer Cells

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Background and aim: Aberrations in genetic cascades controlling programmed cell death are a key means by which cancerous cells become resistant to chemotherapy and proliferate uncontrollably. Targeted modulation of apoptosis-related genes provides a extremely powerful means to circumvent this therapeutic obstacle. Nevertheless, clinical translation is often limited by systemic toxicity and ineffectual intracellular delivery of genetic payloads. This review will provide a comprehensive discussion of recent advances in dual gene delivery systems for simultaneous increases in pro-apoptotic effectors and decreases in anti-apoptotic survival proteins.

Methods: A thorough literature search was conducted in the multiple databases including PubMed, Scopus, and Google Scholar to find the peer-reviewed articles related to the nanoformulations for apoptotic gene therapy. Information relating to different nanocarriers such as liposomes, polymeric nanoparticles, and gold nanoparticles was methodically compiled. Reports on the delivery efficiencies of siRNAs, microRNA mimics, and plasmid DNAs for the Bcl-2 family (Bcl-2, Mcl-1, Bax, Bak) and the caspase cascade (Caspase-3, 8, 9) were rigorously reviewed. Therapeutic effects were also associated with changes in mitochondrial membrane potential ($\Delta\psi m$), intracellular adenosine triphosphate (ATP) depletion, and quantitative real-time PCR (RT-qPCR) gene expression patterns.

Results: The the results from the compiled data demonstrated that nanomedicine facilitated delivery of gene-silencing therapeutics potently induced the down-regulation of critical anti-apoptotic markers, in particular Bcl-2, Bcl-XL, and Survivin. Simultaneously, the nano-delivery of the expression vectors resulted in a significant up-regulation of pro-apoptosis genes such as Bax and the initiator caspases. This combined molecular disruption leads to robust outer mitochondrial membrane permeabilization resulting in the release of cytochrome C and the formation of the apoptosome. In addition, these gene modifications were found to be highly linked with the activation of caspase-dependent and caspase-independent dying pathways. Remarkably, targeted nanocarriers enabled to induce maximal apoptotic in multidrug resistant tumor models while least off target cytotoxicity to normal tissues.

Conclusion: Nanomedicine-based gene intervention is a very precise and effective way to address evasive apoptosis in cancer. Through the simultaneous induction of up-regulation of death-promoting genes and down-regulation of survival protein, targeted nano-formulations constitute a revolutionary approach to overcome conventional chemoresistance. Ultimately, the application of these multi-targeted nano-delivery strategies in the clinical oncology is expected to improve therapeutic efficacy, provide better patient outcomes, and open the door for highly individualized, gene-specific cancer therapies.

keywords: Nanomedicine, Apoptosis, Gene Modulation, Bcl-2 Inhibition, Chemoresistance.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-140

Bismuth Nanoparticles as Potential Modulators of Airway Mucus Hypersecretion in Allergic Asthma

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Background and aim: Background: Allergic asthma is a chronic inflammatory airway disorder associated with high rates of morbidity and mortality. It is characterized by AHR, airway inflammation, goblet cell hyperplasia, mucus hypersecretion, and airway remodeling, which collectively contribute to clinical manifestations such as coughing, wheezing, and dyspnea. Therefore, the development of effective therapeutic strategies to counteract these pathological features is essential. Aim: The present study aimed, for the first time, to utilize bismuth nanoparticles for the treatment of ovalbumin-induced allergic asthma in a murine model, based on their potential anti-mucus properties, and to develop a novel nanotechnology-based therapeutic approach.

Methods: Bismuth nanoparticles were synthesized using a pH-dependent precipitation technique and characterized by TEM, DLS, and XRD analyses. All animal procedures were approved by the Institutional Animal Care and Ethics Committee (Approval No. IR.ZUMS.AEC.1403.044). BALB/c mice were divided into three groups: healthy controls, asthmatic, and asthmatic mice treated with bismuth nanoparticles. Asthma was induced in Groups 2 and 3 using OVA, and the treatment group received inhaled bismuth nanoparticles via nebulization on days 25, 27, and 29. Following euthanasia with CO_2, bronchoalveolar lavage fluid (BALF), and lung, liver, and spleen tissues were collected. Inflammatory cell infiltration, biochemical analytes, and Th2 cytokine levels in BALF, along with potential nanoparticle toxicity in hepatic and splenic tissues, were evaluated. Lung sections were examined for peribronchial and perivascular inflammation, goblet cell hyperplasia, and mucus hypersecretion.

Results: Inhalational administration of bismuth nanoparticles to BALB/c mice with allergic asthma resulted in decreased eosinophil infiltration into BALF, restoration of several biochemical analytes including calcium, magnesium, iron, phosphorus, and LDL, and a significant reduction in IL-13 levels. These changes were associated with a marked decrease in goblet cell hyperplasia and mucus secretion, alongside reduced perivascular inflammation. However, the treatment did not reduce IL-5 levels and only led to a mild decrease in peribronchial inflammation. Histological evaluation of the liver and spleen revealed no evidence of fibrosis or secondary tissue injury, indicating the absence of nanoparticle-related toxicity.

Conclusion: Our findings suggest that bismuth nanoparticles, through their ability to suppress mucus secretion and goblet cell hyperplasia, may serve as a promising new nanotechnology-based therapeutic option for the treatment of allergic asthma.

keywords: Allergic Asthma, Bismuth, Bismuth Nanoparticles, inflammation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-141

Assessment of Humoral Immunity Triggered by Frequently Administered COVID-19 Vaccines in Middle-aged Iranians

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Background and aim: Investigations into SARS-CoV-2 vaccines, conducted through a comparative analysis and evaluation of four vaccines within a defined population, will benefit both evidence-based health policy at the local level and the furthering of our understanding of the immune response to vaccination with respect to the SARS-CoV-2 virus. We assessed the effectiveness of two platforms of COVID-19 vaccination: inactivated virus vaccines (Sinopharm and Co Iran Barekat) and adenoviral vector-based vaccines (AstraZeneca and Sputnik V), which represent the most commonly administered vaccines within the Iranian population.

Methods: COVID-19 vaccinations were administered to four hundred twenty volunteers aged 40–60 years using the COVID-19 vaccines, including CO Iran Barekat, Sinopharm, AstraZeneca, and Sputnik. The humoral immune response was evaluated by a conventional neutralizing antibody assay and IgG ELISA.

Results: Individuals who received the Barekat and Sinopharm vaccines represented a negative IgG response of approximately 15.3% and around 32.97%, respectively, while the Sputnik-V vaccine group showed a negative IgG response of 10.58%. The AstraZeneca group had no negative IgG response. In the neutralizing antibody test for SARS-CoV-2, AstraZeneca, Sputnik-V, CoV Iran Barekat, and Sinopharm demonstrated effective protection rates of 87.73%, 59.61%, 54.23%, and 35.16%, respectively. The responses of S1-IgG and SARS-CoV-2 neutralization observed with Sinopharm and Iran CoV Barekat were comparable to those in vaccinated individuals. In comparison, the standard live-virus neutralization titer (cVNT50) for SARS-CoV-2-AstraZeneca vaccines was significantly higher than those of the other groups. Data analysis of adverse vaccine events showed that pain at the injection site is the most prevalent adverse event among the four groups.

Conclusion: AstraZeneca exhibited the highest levels of neutralizing antibodies, reinforcing its greater effectiveness in protecting against SARS-CoV-2, as determined by ELISA IgG Kits and a standard neutralizing antibody assay method.

keywords: AstraZeneca, Sputnik V, COV-Iran Barekat, Sinopharm, Vaccine

PI-142

Revisiting Daclizumab for Multiple Sclerosis: A Systematic Evaluation of a Targeted Immunotherapy

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Background and aim: Daclizumab is a humanized monoclonal antibody that blocks the interleukin-2 receptor α-chain (CD25) and reduces activation of autoreactive T cells. It reduces disease activity by reducing gadolinium-enhancing lesions in patients with relapsing-remitting multiple sclerosis (MS). Therefore, this systematic review investigates the therapeutic role of Daclizumab in patients with MS.

Methods: This systematic literature review includes published clinical trials, regardless of publication date or language, from Embase, Medline, Cochrane, Scopus, and other databases, published from 2000 to April 2025.

Results: The common complication was hepatotoxicity and elevated liver enzymes in most patients. Daclizumab showed a decrease in relapse frequency and disease activity, but was associated with serious safety concerns. Cutaneous side effects occurred in 19–34% of patients, from mild rashes to serious dermatologic disorders like psoriasis. Interestingly, treatment also led to an expansion of CD56^bright^ natural killer (NK) cells. Findings showed Daclizumab could reflect increased rates of upper respiratory infections, indicating a systemic immunologic impact of the therapy.

Conclusion: Daclizumab showed promising efficacy for MS by affecting the IL-2 pathway, but was ultimately restricted by severe adverse events, which reinforces the need for safer and more selective immunotherapy strategies.

keywords: Daclizumab, Multiple Sclerosis, Monoclonal antibody, Interleukin-2 receptor, CD25

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-143

The Role of Airway Epithelial Cells and Alveolar Macrophages in $PM_{2.5}$-Induced Airway Inflammation: A Narrative Review

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Background and aim: Fine particulate matter ($PM_{2.5}$) is a major air pollutant associated with the development and progression of respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD). Airway epithelial cells (AwEPs) and Alveolar macrophages (AvMφs) represent the first cellular barrier against inhaled particles and play pivotal roles in initiating and amplifying pulmonary inflammatory responses.

Methods: This narrative review summarizes current evidence regarding the contribution of AwEP–AvMφ interactions to $PM_{2.5}$-induced airway inflammation, with particular emphasis on oxidative stress, TLR4/NF-κB signaling, inflammasome activation, pyroptosis, and ferroptosis.

Results: Recent studies demonstrate that $PM_{2.5}$ exposure promotes reactive oxygen species (ROS) generation and activates the TLR4/NF-κB pathway in airway cells, leading to inflammatory cytokine production and NLRP3 inflammasome-mediated pyroptosis. AwEPs respond directly to $PM_{2.5}$ by releasing inflammatory mediators and extracellular signals that influence AvMφ activation. Exosomal miRNAs derived from AwEPs have been shown to enhance AvMφ inflammatory responses through the miR-155-5p/SOCS1/NF-κB pathway, highlighting a potential mechanism of intercellular communication. Co-culture studies further demonstrate that the presence of AvMφs markedly amplifies NF-κB activation and cytokine secretion in AwEPs, supporting the importance of AwEP–AvMφ crosstalk in pulmonary inflammation. In addition, recent findings suggest that ferroptosis-associated oxidative stress contributes to $PM_{2.5}$-induced lung injury, while inhibition of ferroptosis attenuates epithelial barrier dysfunction and restores AvMφ phagocytic capacity. Regulatory molecules such as MUC1 may exert protective effects by suppressing IRAK4 phosphorylation and downstream NF-κB/NLRP3/GSDMD signaling.

Conclusion: This review suggests that AwEP–AvMφ communication is a central mechanism underlying $PM_{2.5}$-induced airway inflammation and cell injury. Crosstalk between these cell populations amplifies oxidative stress, inflammatory signaling, and regulated cell death pathways, including pyroptosis and ferroptosis. Further studies are needed to clarify the relative contribution of each cell type and to identify novel therapeutic targets capable of interrupting these pathogenic interactions.

keywords: $PM_{2.5}$, Airway Epithelial Cells, Alveolar Macrophages, Airway Inflammation, Cell Crosstalk

PI-144

MicroRNA-Mediated Regulation of TNF-α Signaling in Rheumatoid Arthritis: Translational Molecular and Clinical Perspectives

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Background and aim: Rheumatoid arthritis (RA) is a chronic immune-mediated inflammatory disorder. It is defined by persistent synovial inflammation, progressive joint destruction, and systemic effects. Tumor necrosis factor-alpha (TNF-α) is a central mediator in disease development and an established therapy target. Despite this, disease progression and treatment response vary greatly, posing challenges in clinical management. MicroRNAs (miRNAs) have become important post-transcriptional regulators of inflammatory signaling. This review summarizes current evidence on miRNA-mediated control of TNF-α signaling. It also explores implications for biomarker development and precision diagnostics in RA.

Methods: A structured narrative review was conducted using PubMed/MEDLINE, EMBASE, and Scopus databases. English-language studies from January 2020 to March 2025 were included. Studies were identified with the keywords "microRNA," "miRNA," "rheumatoid arthritis," and "TNF-α signaling." Experimental, translational, and clinical studies examining interactions between miRNA and TNF signaling were reviewed. Evidence was organized by molecular mechanisms, clinical relevance, and potential uses in diagnosis or therapy.

Results: The literature reviewed shows that miRNAs are key regulators of the TNF-α signaling network. Reduced miR-146a-5p and miR-125b expression is often associated with increased activation of TRAF6-, IRAK-, and NF-κB-dependent inflammatory pathways. Increased expression of miR-155 and miR-223 is linked to persistent inflammation by suppressing mediators such as SHIP-1. New evidence suggests that non-coding RNA networks, such as the hsa_circ_0001859/miR-204 axis, may drive fibroblast-like synoviocyte proliferation and inflammation. Several studies also report links between circulating miRNA profiles, disease activity, and response to TNF inhibitor therapy. These findings support their potential as minimally invasive circulating biomarkers.

Conclusion: Current evidence shows that miRNAs are important regulators of TNF-α-driven inflammation in rheumatoid arthritis. Beyond roles in disease, specific miRNA patterns may help stratify patients and predict therapy response. More validation in large cohorts and standardization of methods are still needed before these tools can be used in routine care. Future studies should test the integration of validated miRNA signatures into diagnostic practice for precision rheumatology.

keywords: Rheumatoid Arthritis; MicroRNA; TNF-α; Biomarkers; Precision medicine

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-145

Leukemia Inhibitory Factor (LIF): An Emerging Immunological Biomarker in Recurrent Implantation Failure and Female Infertility

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Background and aim: Embryo implantation is a complex biological process that requires a receptive endometrium and a finely regulated immune environment. Leukemia Inhibitory Factor (LIF), a pleiotropic cytokine belonging to the interleukin-6 family, plays a crucial role in endometrial receptivity, embryo implantation, and maternal immune tolerance. Altered expression of LIF has been associated with recurrent implantation failure (RIF) and female infertility.This narrative review aimed to evaluate the immunological functions of LIF and its potential role as an emerging biomarker in embryo implantation failure and female infertility.

Methods: A literature review was performed using articles indexed in PubMed, Scopus, and Web of Science published between 2010 and 2025. Studies investigating the relationship between LIF expression, endometrial receptivity, immune regulation, recurrent implantation failure, and infertility outcomes were included.

Results: Evidence indicates that reduced endometrial expression of LIF is associated with impaired implantation and recurrent implantation failure. LIF contributes to embryo-endometrium communication through regulation of trophoblast invasion, decidualization, and endometrial receptivity. Furthermore, LIF modulates the uterine immune microenvironment by influencing regulatory T cells, natural killer cells, and cytokine networks that promote maternal immune tolerance. Several studies have suggested that altered LIF expression may serve as a potential biomarker for implantation disorders and infertility, although its clinical application requires further validation.

Conclusion: LIF is an essential immunoregulatory cytokine involved in successful embryo implantation and maintenance of endometrial receptivity. Current evidence supports its role as an emerging immunological biomarker in recurrent implantation failure and female infertility. Further prospective studies are required to establish its diagnostic and therapeutic applications in reproductive medicine.

keywords: Leukemia Inhibitory Factor, Recurrent Implantation Failure, Female Infertility, Endometrial, Biomarker

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-146

Postbiotics and Probiotics in Preventing Leukemia

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Background and aim: Based on reports from 2020, approximately 1.3 million new cases of hematological cancers were recorded. Despite significant advances in treatment approaches, side effects undeniably affect patients' quality of life. Therefore, the need for finding prevention methods is more than necessary. Probiotics are live microorganisms that, when consumed in adequate amounts, can have health benefits such as modulating immune responses and promoting anti-inflammatory responses. Postbiotics are an inanimate microorganism preparation and/ or components, additional to metabolites and signaling molecules of probiotics. Considering their importance in cancer prevention, this review aims to assess the impact of probiotics and postbiotics in leukemia prevention.

Methods: Several databases, including Google Scholar, PubMed, Elsevier, etc., were investigated. Using the terms "probiotics", "postbiotics," "leukemia", and “prevention,” relevant articles published between 2022 and 2026 were selected and reviewed.

Results: By promoting a healthy gut microbiome, probiotics ensure the overall well-being and the efficiency of the immune system. One of their functional pathways is the production of short-chain fatty acids (SCFAs), such as butyrate, which have been shown to promote the differentiation and function of regulatory T cells in the gut, thereby suppressing inflammatory responses and maintaining immune homeostasis. Another pathway is via direct interaction with immune cells in the gut-associated lymphoid tissue (GALT). They activate the innate immune response by increasing the microbicidal activity of peritoneal and spleen macrophages. They are also shown to modulate systemic immune function of immune cells outside of the gut, such as T cells and natural killer cells. Postbiotics can optimize host-specific physiological functions and modulate metabolism and/or behavioral reactions. The effects of postbiotics include impacts on the gastrointestinal microflora through environmental acidification, modulation of the host-microbiota immune response, and antiproliferative actions.

Conclusion: Leukemias are one of the most prevalent types of cancers, with about 700.000 deaths worldwide, based on the reports from 2020. Probiotics are microorganisms that exhibit anticancer properties, such as mutagen binding and degradation, lowering intestinal pH, and secretion of anti-inflammatory molecules. Positive effects of using postbiotics include modulation of the gut microbia, immunomodulatory effects, and regulation of gut microbiota-host interactions. Nonetheless, further investigation into their exact mechanism for improving the immune system's ability to prevent leukemia is essential.

keywords: Probiotics, Postbiotics, Leukemia, Prevention

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-147

Natural Products as Adjuvants to Reinforce Rituximab Efficacy in B-Cell Non-Hodgkin Lymphoma: Mechanisms and Therapeutic Potentials

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Background and aim: B-cell Non-Hodgkin lymphoma (B-NHL) is characterized by malignant B-cell proliferation and immune dysregulation, including impaired apoptosis and evasion of immune surveillance. Rituximab (RTX), an anti-CD20 monoclonal antibody, has significantly improved clinical outcomes through antibody-dependent cellular cytotoxicity and complement-mediated mechanisms. However, resistance to RTX remains a major clinical challenge, often driven by the immunosuppressive tumor microenvironment. Natural compounds have recently gained attention as potential adjunctive agents due to their immunomodulatory properties, multi-target activity, and favorable safety profile.

Methods: A narrative literature review was conducted to evaluate the immunomodulatory effects of natural compounds on rituximab response in B-cell Non-Hodgkin lymphoma. Relevant studies were identified through searches in PubMed, Scopus, and Google Scholar using combinations of keywords including “B-cell Non-Hodgkin lymphoma,” “rituximab resistance,” “natural compounds.” Articles published in English and relevant to the molecular, cellular, and immunological mechanisms of resistance and therapeutic sensitization were reviewed and qualitatively analyzed.

Results: The reviewed studies indicate that resistance to rituximab in B-NHL is frequently associated with immune evasion, altered apoptotic signaling, oxidative stress imbalance, and suppression within the tumor microenvironment. Evidence suggests that natural compounds exert immunomodulatory and pro-apoptotic effects, regulate cytokine networks, and modulate oxidative stress pathways. Several preclinical findings support the potential of these agents to sensitize lymphoma cells to anti-CD20 therapy. The literature highlights a scientific basis for combining natural immunomodulators with monoclonal antibody therapy.

Conclusion: The integration of natural immunomodulatory compounds with rituximab-based therapy represents a promising strategy to overcome resistance and enhance therapeutic efficacy in B-NHL. By targeting multiple mechanisms involved in immune escape and tumor microenvironment suppression, natural agents may function as simple supportive treatments into key components of therapy. To fully realize this potential and establish them as standardized treatments, further research into their mechanisms and guided clinical trials are essential.

keywords: B-cell Non-Hodgkin lymphoma; Rituximab; Natural compounds; Apoptosis; Drug Resistance

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-148

Immunomodulatory Effects of Zinc Oxide Nanoparticles on nitric oxide (NO) level in Streptozotocin-Induced Diabetic mice

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Background and aim: Type 1 diabetes (T1D) results from the destruction of insulin producing pancreatic β cells by a β cell specific autoimmune process(1). Oxidative stress is one of the major pathophysiological routes during diabetes (2). Enhanced oxidative stress and changes in antioxidant capacity have important roles in the pathogenesis of chronic diabetes mellitus (3). Previous studies have demonstrated that Zinc Oxide Nanoparticles (ZnO NPs) is a potent inhibitor of inflammatory and potent antioxidant properties(4,5) . The purpose of this study was to investigate the preventive effects of ZnO NPs on nitric oxide (NO) levels of splenic tissues.

Methods: Diabetes was induced by multiple low-dose of streptozotocin (MLDS) injection in male C57BL/6 mice. STZ was dissolved in 0.1 M citrate buffer (pH 4.5) and injected intraperitoneally (IP, 40 mg/kg/day for 5 consecutive days). The blood samples were obtained from the tail vein of non-fasted mice. Mice were considered diabetic when their non-fasting blood glucose level was 250 mg/dl. Subsequently, the mice were allocated to four therapeutic groups (n=10 per group) (normal control group, diabetic control group and treatment group, ZnONPs group). After induction of diabetes, mice were treated with ZnO NPs (8 mg/kg/day IP) for 21 days. Nitrate/nitrite levels in plasma as a marker of total nitric oxide concentration were determined by a nitrate/nitrite colorimetric assay kit (Cayman Chemical Company).

Results: Result: STZ caused marked increase (P 0.05) in NO levels compared with control group of mice. Administration of ZnO NPs to diabetic mice, ameliorated abnormalities in NO levels when compared with those in diabetic control group (p 0.05).

Conclusion: In summary, results of the present work demonstrated that the suppressive effect of the ZnO NPs treatment on T1D was accompanied by decreased nitric oxide (NO) levels of plasma. It seems that ZnO NPs treatment has a therapeutic effect against MLDS-induced diabetes in mice.

keywords: Type 1 diabetes mellitus, Zinc Oxide Nanoparticles, Nitric oxide

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-149

Immunotherapeutic effects of Zinc Oxide Nanoparticles(ZnO-NPs) in the response of T-helper lymphocytes in Streptozotocin-Induced Diabetic mice

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Background and aim: Chronic pancreatic inflammation (insulitis) and destruction of islet β-cells in type 1 diabetes is mediated by the immune cells, particularly autoreactive CD4 and CD8 T lymphocytes. In the pathogenesis of T1D, several proinflamma tory cytokines including IFN-ɣ, IL-1, as well as IL-17, have been implicated. It is thought that the production of anti-inflammatory cytokines such as IL-4, IL-10 and TGF-β correlates with protection from T1D . Although the potent antidiabetic activity of ZnO-NPs was observed in Previous studies, the influence of this nanoparticle on the levels of proinflammatory and anti inflammatory cytokines was not fully determined.

Methods: Diabetes was induced by multiple low-dose of streptozotocin (MLDS) injection in male C57BL/6 mice. STZ was dissolved in 0.1 M citrate buffer (pH 4.5) and injected intraperitoneally (IP, 40 mg/kg/day for 5 consecutive days). The blood samples were obtained from the tail vein of non-fasted mice. Mice were considered diabetic when their non-fasting blood glucose level was 250 mg/dl. Subsequently, the mice were allocated to three therapeutic groups (n=10 per group) (normal control group, diabetic control group and treatment group). After induction of diabetes, mice were treated with ZnO NPs (8 mg/kg/day IP) for 21 days. Animals were euthanized on day 22 and their spleens were removed for splenocyte culture and cytokine determination. The splenocytes (5×10^6cells/ml) were treated with 2 µg/ml concanavalin A for 72 hr, and cell supernatants were collected, then the levels of IL-10, IL-4, IL17 and IFN-ɣ were measured by ELISA kits according to the manufacturers' instructions.

Results: Treatment of mice with Zinc Oxide Nanoparticles (ZnO NPs) significantly decreased MLDS-induced production of IFN- γ and IL-17, while increased IL-10 and IL-4 as compared with those in diabetic control group (P0.05).

Conclusion: In summary, the results of the present study indicate that ZnO NPs treatment protects against T1D adverse effects during the development of streptozotocin induced type 1 diabetes in mice . The protective effect of ZnO NPs possibly involve down-regulation of proinflammatory cytokines Th1 and Th17 cytokines (IFN-ɣ and IL-17) and increase in the production of anti inflammatory cytokines (IL-10 and IL-4) in supernatant of splenic culture of the treated mice.

keywords: Zinc Oxide Nanoparticles, cytokines, Type 1 diabetes

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-150

Interplay Between Enterococcus Overcolonization, Regulatory T Cell Subset Defects, and Autoimmune Complications in Patients with Common Variable Immunodeficiency: A Systematic Review

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Background and aim: Common variable immunodeficiency (CVID) as the most common symptomatic primary immunodeficiency in adults, is characterized by hypogammaglobulinemia and recurrent infections. Gut microbiome dysbiosis, particularly Enterococcus overcolonization, plays a role in the pathogenesis of these complications. Regulatory T cell (Treg) defects have been identified as a key mechanism underlying autoimmunity in CVID. The aim of the study is to review the interplay between Enterococcus overcolonization, regulatory T cell subset defects, and the development of autoimmune complications in patients with CVID.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, and Cochrane until June 2026. The keywords were Common Variable Immunodeficiency, Enterococcus, Regulatory T Cells, Autoimmunity, and Dysbiosis. By searching this database; 18 articles were found and 10 articles included under the inclusion criteria.

Results: Evidence from key studies indicated that CVID patients with immune dysregulation and those with IgA deficiency showed significant enrichment of the genus Enterococcus in their gut microbiota. In vitro studies had confirmed the inflammatory potential of Enterococcus gallinarum and Enterococcus hirae species in monocytes from CVID patients. Furthermore, quantitative and qualitative defects in Treg cells had been repeatedly associated with autoimmunity in CVID. Reduced CTLA-4 expression on Tregs, decreased Foxp3E2+/Foxp3+ ratio, and impaired Treg suppressive function are among the identified defects in CVID patients with autoimmunity. Increased microbial translocation from the disrupted gastrointestinal barrier in CVID patients had also been reported in association with reduced Tregs. However, limited studies have directly investigated the relationship between Enterococcus colonization and Treg defects, with most available evidence pointing to the independent role of each factor.

Conclusion: It seems that both Enterococcus overcolonization and regulatory T cell defects are independently associated with autoimmune complications in CVID patients. Further studies with appropriate design are needed on this topic.

keywords: Common Variable Immunodeficiency; Enterococcus; Regulatory T Cells; Autoimmunity; Immune Dysregulation

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-151

Comparative Analysis of Microbial Metabolites and Inflammatory Responses in CVID versus XLA: Why Does One Patient Develop Inflammation and the Other Does Not? A Systematic Review

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Background and aim: Common variable immunodeficiency (CVID) and X linked agammaglobulinemia (XLA) are primary antibody deficiencies result from humoral immune defects leading to hypogammaglobulinemia and recurrent infections. Despite both conditions exhibiting gut microbiome dysbiosis and bacterial translocation, their clinical outcomes diverge significantly. One third of CVID patients develop autoimmune and inflammatory complications, while XLA patients are remarkably protected from such conditions. This clinical paradox, comparable microbial translocation yet divergent inflammatory outcomes, remains poorly understood. The aim of the study is to review differential inflammatory responses to bacterial translocation in CVID versus XLA and elucidate BTK's role as a key host modifier.

Methods: This review article was performed within articles published at PubMed, Science Direct, Google Scholar, and Cochrane until June 2026. The keywords were Common Variable Immunodeficiency, X linked Agammaglobulinemia, bacterial translocation, BTK, cytokines, microbial metabolites, and inflammation. By searching this database; 24 articles were found and 15 articles were included under the inclusion criteria.

Results: Serum cytokine profiling demonstrated that XLA patients exhibited significantly reduced immune activation, with lower levels of interferon gamma pathway mediators (interferon gamma, interleukin 12b, interleukin 18, CXCL9), proinflammatory cytokines (tumor necrosis factor alpha, tumor necrosis factor beta, interleukin 6), chemokines related to host commensal junctions (CCL19, CCL23, CCL3), and markers of monocyte and T cell activation. In CVID, circulating bacterial 16S rDNA from gut commensals was elevated and associated with systemic immune activation, elevated serum interferon gamma, and inflammatory manifestations. XLA patients also had increased circulating bacterial 16S rDNA but did not exhibit prominent immune activation, suggesting that BTK might function as a host modifier that dampened immune responses to microbial translocation. Ex vivo studies further confirmed this by demonstrating that BTK inhibitors (rilzabrutinib, PCI-29732) applied to CVID peripheral blood mononuclear cells effectively recapitulated the in vivo differences between CVID and XLA, attenuating pathogenic immune responses to bacterial translocation stimuli.

Conclusion: It seems that BTK as a key host modifier mediating the systemic inflammatory effects of bacterial translocation in primary antibody deficiencies. The absence of functional BTK in XLA patients appears to confer protection against the inflammatory complications commonly observed in CVID, despite comparable levels of microbial translocation. Further studies are needed to explore the therapeutic potential of BTK inhibition in CVID associated inflammatory complications.

keywords: Common Variable Immunodeficiency; X linked Agammaglobulinemia; BTK; Bacterial Translocation; Inflammation;

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PI-152

Evaluation of IL-6 and IL-8 as Immune Markers in Women with Bacterial Genital Infections Using ELISA: A Study in Iraq

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Introduction: Bacterial genital infections remain a significant health problem among women, particularly due to their association with reproductive complications and chronic inflammatory responses. Cytokines such as interleukin-6 (IL-6) and interleukin-8 (IL-8) are essential mediators of the immune system and play a central role in inflammatory processes triggered by bacterial pathogens. This study aimed to evaluate the levels of IL-6 and IL-8 as immune biomarkers in women diagnosed with bacterial genital infections using the enzyme-linked immunosorbent assay ELISA technique

Methodes: A case-control study design was conducted including infected women and apparently healthy controls. Serum samples were collected and cytokine concentrations were quantitatively measured using ELISA kits.
Results: The results revealed a statistically significant increase ($p < 0.05$) in IL-6 and IL-8 levels among infected women compared to the control group. Elevated cytokine concentrations were positively associated with infection severity and clinical manifestations, indicating their important role in host immune response.
Conclusion: In conclusion, IL-6 and IL-8 can serve as reliable immunological markers for the detection and monitoring of bacterial genital infections in women. Their assessment using ELISA provides valuable diagnostic and prognostic information in clinical practice.

Key Words: IL-6, IL-8, Bacterial genital infections, ELISA, Cytokines, Inflammation

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PM-1

The Role of Nail Hygiene in the Prevalence and Drug Resistance of Candida albicans in Patients with Onychomycosis

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[1] elmofarhang
[2] jondishapoor ahvaz

Background and aim: Onychomycosis caused by Candida albicans is a prevalent superficial fungal infection that may be influenced by personal hygiene habits. Due to the increasing reports of antifungal resistance, this study aimed to investigate the relationship between nail hygiene practices and antifungal susceptibility profiles of C. albicans isolates obtained from patients with nail infections.

Methods: Thirty fungal isolates were obtained from the Mycology Bank of the Pasteur Institute of Iran, among which twenty-six were confirmed as C. albicans. Antifungal susceptibility testing against fluconazole, voriconazole, caspofungin, and amphotericin B was performed using the CLSI M27 A3 microdilution method. Phospholipase, proteinase, and biofilm formation assays were conducted following standard procedures. Patients' nail hygiene practices were assessed using a structured questionnaire. Statistical analysis was performed using the Kruskal–Wallis test to determine differences in fluconazole MIC values among handwashing categories.

Results: Most isolates were susceptible to all tested antifungal agents. Fluconazole showed 89.5% susceptibility and 10.5% dose-dependent sensitivity, while all isolates were fully sensitive to amphotericin B. The Kruskal–Wallis analysis indicated no statistically significant difference between fluconazole MIC values and nail hygiene categories ($H = 1.45$, $df = 2$, $p = 0.48$). Although descriptive trends suggested slightly higher MIC values among isolates from patients with poorer hygiene, these differences were not statistically significant.

Conclusion: The study found no significant correlation between nail hygiene status and antifungal resistance in C. albicans isolates. However, promoting proper nail hygiene remains essential for preventing infection recurrence and reducing potential fungal transmission. Larger-scale studies incorporating molecular analyses are recommended to further elucidate this relationship.

keywords: Candida albicans, antifungal resistance, nail hygiene, biofilm, phospholipase, proteinase

PM-2

Screening of Candida infections or colonization in cases of Cystic Fibrosis, trend in species identification

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Background and aim: Candida is one of the normal flora of human body, and is also the most common conditional fungal pathogen. Invasive Candida infections (ICI) occupies the first position among invasive fungal diseases (IFD). Moreover, Candida is commonly colonized in cases involved to cystic fibrosis (CF) and other respiratory tract associated auto immune diseases. As a main target, the present study focus on CF patients as the predisposed cases of Candida infection or colonization

Methods: Our subjects included all Candida clinical isolates obtained from cases of CF referred to the Center of Medical Mycology, UMS University, Urmia, Iran, for fungal infection diagnosis. The clinical specimens including bronco-alveolar lavage (BAL), sputum, bronchial washing and biopsies were examined for the invasive bodies of Candida yeasts. Microscopic investigation and specific differential cultures were performed. Also molecular (PCR-RFLR) were used for the identification of isolate Candida yeasts at level of species.

Results: Totally. 560 cases of CF and other airway obstructive diseases were included in our study. Among all, 23 (16 males and 7 females) (4.1%) were CF cases as the main risk factor in this study, followed by Asthma 4(18.18%), COPD 4(18.18%) and Wegner syndrome 3(13.64%). The most frequent age range was 20s (in the range of 20 to 29) with 8(34.7%) cases, and the least was 80s, 1(4.3%). The most number of obtained clinical specimen was BAL 16(69.6%). The majority 12(52.2%) of clinical specimens were received from department of pulmonary diseases while, the least one with 2(8.7%) cases was rheumatology ward. The most frequent presenting complain of the patients was dizziness 9(39.1%), followed by productive cough 6(26%) and chest pain 1(4%). Our findings of microscopic diagnosis included yeast overgrowth detection 13(56.5%), yeast invasion 6(26.1%) and yeast low numbers4 (17%). For the setting of molecular identification, we just isolated Candida gulliermondi,

Conclusion: As our findings of the present study, the most of Candida yeasts isolated from studied cases included non albicans Candida species comparing to other Candida species

keywords: Candida, CF, Pulmonary diseases

PM-3

Monitoring of Candida infections in cases with a recent history of COVID-19, a retrospective study

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Background and aim: Candida, the yeasts live on mucosal layers of human and animal tissues. Because of the opportunistic essence, they cause variable diseases in cases predisposed by cortico-steroids, chemotherapies and long term pulmonary infections. This study aimed to identify the Candida species could active in cases of COVID-19 or with a recent history of that.

Methods: Our subjects included cases with dizziness, cough, chest pain and other pulmonary signs. Candida yeasts isolated from the clinical specimens referred to Medical Mycology center, UMS University, Urmia, Iran were studied. A microscopic investigation was done primarily for the detection of Candida colonization or invasion in tissues (Blastospores and Pseudohypha). Identification of the Candida isolates at the level of species conducted by Dalmao test, CHRO agar Candida and PCR-RFLP.

Results: Totally, 165 cases of positive culture for Candida fungi were studied. Among all, 125 (75.8%) isolated from patients with a history of COVID-19, 7(4.2) Tuberculosis, 4 cases of COPD and three cases of Cystic fibrosis, Cancer and Diabetes mellitus. From all, 43% were women and 57% men. Also, 80% of cases stayed at intensive care unit. The most age range of Candida involvement was 50s including 38(23%) cases. The main clinical specimen referred was bronchoalveolar lavage (64.8%). Other specimens included sputum and tracheal washings. Direct microscopic investigations resulted yeast colonization 68(41.2%) and yeast invasion 54(32.7%). Our findings of molecular identification showed 54(32.7%) C. albicans, 11(6.4%) C. dubliniensis, 10(6.1%) C. tropicalis, C. krusei, C. parapsilosis and C. glabrata one each.

Conclusion: C. albicans complex and C. tripicalis are the main Candida species causing human diseases;It seems candida varation doesn't have a direct association to COVID-19.

keywords: Candida, hospital, COVID-19, Pulmonary disease

PM-4

Genotyping and Antifungal Susceptibility Testing of Aspergillus flavus Isolated from Clinical Specimens

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Background and aim: After Aspergillus fumigatus, A. flavus is the second leading cause of invasive and non-invasive aspergillosis. These fungi are of significant epidemiological importance in provinces with dry and hot climates.In the present study, antifungal susceptibility testing (AFST) and genotyping of sixty-five A. flavus clinical isolates originating from patients in Mazandaran and Tehran were performed

Methods: Antifungal susceptibility testing of 65 clinical isolates of A. flavus was conducted against amphotericin B (AMB), itraconazole (ITR), voriconazole (VOR), posaconazole (POS), isavuconazole (ISA), luliconazole (LUL), lanoconazole (LAN), and 5- fluorocytosine according to the Clinical Laboratory Standards Institute (CLSI) method (M38-A2). The minimum inhibitory concentrations (MICs) were determined for each antifungal drug against all strains. Additionally, microsatellite typing using six variable number tandem repeat (VNTR) markers was performed to assess the genetic diversity and potential relationships among the clinical strains.

Results: Luliconazole had the lowest geometric mean MIC (0.020 µg/mL), followed by LAN (0.021 µg/mL), POS (0.089 µg/mL), ISA (0.115 µg/mL), ITR (0.220 µg/mL), VOR (0.244 µg/mL), AMB (0.870 µg/mL), and 5-fluorocytosine (58.76 µg/mL). Microsatellite typing revealed sixty-five distinct sequence genotypes. Statistically, there was no significant relationship between genotypes and AFST profiles ($P \geq 0.05$).

Conclusion: Luliconazole and lanoconazole demonstrated the greatest in vitro activity among all tested antifungals. However, most A. flavus strains exhibited reduced sensitivity to AMB. Microsatellite genotyping indicated no genetic similarity among the clinical strains, revealing high genetic diversity among A. flavus isolates obtained from clinical samples.

keywords: Aspergillus flavus, Antifungal Susceptibility Testing,MLVA Genotyping

PM-5

Evaluation of antifungal effect of catechin loaded poly dopamine nanoparticles on growth inhibition and the expression of ERG11 and EPA1 genes in candida glabrata isolates

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Background and aim: This article discusses the rise of infections caused by Candida glabrata and the drug resistance of this fungus. The EPA and ERG11 genes play key roles in epithelial cell adhesion and drug resistance. Due to increasing resistance to fluconazole, the use of natural compounds such as catechin found in green tea has gained attention. In this study, catechin-loaded polydopamine nanoparticles were synthesized and confirmed using XRD and FTIR. The results showed that these nanoparticles significantly inhibited the growth of C. glabrata and altered the expression of the EPA and ERG11 genes.

Methods: In this study, the catechin–dopamine nanocomplex was synthesized in Tris buffer and, after filtration and dialysis, confirmed using FTIR and XRD analyses. Clinical samples of C. glabrata were collected and, along with the standard strain, cultured and identified by PCR. Drug susceptibility testing and MIC determination were performed using the microdilution method. After treating the cells with the MIC50 concentration, RNA was extracted and converted into cDNA. The expression levels of ERG11 and EPA1 genes were measured using real-time PCR and the ΔΔCt method. Data were analyzed with SPSS using ANOVA and t-tests.

Results: In this study, the expression of the ERG11 gene decreased, while the expression of the EPA1 gene showed no change.

Conclusion: Based on the results obtained from past studies and our study, it can be concluded that the use of herbal medicines can still be beneficial. Combining herbal medicines with nanoparticles has shown better results. By using the catechin dopamine hydrochloride nanoparticle, an essential progression in the treatment of fungual patients can be made. This combination does not exhibit toxic effects on human cells and does not have any side effects.

keywords: Candida glabrata, catechin, polydopamine, antifungal properties

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PM-6

Monitoring of Candida and Aspergillus fungi in cases of kidney transplant and other immunosuppressed patients

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Background and aim: Candida and Aspergillus species are major cause of hospital fungal infections in immune compromised cases followed by organisms including Mucorales, Fusarium species and other low frequent molds which are active only in immune suppressed patients. Our study aimed to show the frequency and variation of Candida and Aspergillus species.

Methods: In the present descriptive study 200 cases with the symptoms and signs of lower respiratory tract, included in our study. All of the cases were included prolonged hospital stayed patients enduring immunosuppression for kidney transplantation and other high risk groups such as haematologic malignancies and chemotherapy users. An adequate amount of the sediments profiled into mycological basic culture, sabouraud dextrose agar (SDA) 4 % and incubated at 25-30°C for at least 48 hours. The remained concentrated specimens stocked for molecular identifications. For the identification of isolated yeasts (Candida for example), a tip of colonies was sub cultured on CHROM agar Candida and cornmeal agar differential media.

Results: The cases with a fungal infection or colonization included 42 (56.7 %) male and 32 (43.2 %) female; they ranged between 2 to 96 years old. Candida yeasts are the most frequent among all fungi; 68 cases (91.9 %), followed by Aspergillus and Acremonium species, Cryptococcus neoformans and Mucoral fungi. Invasive Candida elements were detected in 37 (50 %) cases.

Conclusion: The results of the present study showed that Candida species are the most frequent isolated fungi in cases of immunocompromised.

keywords: Candida; Aspergillus; Immunosuppressed Patients; Kidney Transplant; Fungal Infection

PM-7

Molecular identification and antifungal susceptibility profiles of Candida species from Iranian Northwest hospital isolates

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Background and aim: There is an increasing incidence of life-threatening systemic fungal infections especially caused by Candida species. Limited therapeutic option due to the increasing level of resistance to antifungal agents, calls for the prompt identification of drug-resistant isolates. In order to identifying the most common Candida species isolate from clinical cases and to optimize antifungal therapy against them, we performed this experimental study.

Methods: The study subjects include 198 clinical specimens collected from proven cases of Hospital Acquired Infections (HAIs) between August 2018 and September 2020. Direct microscopic examination and culture were performed for the detection and isolation of the Candida species. PCR-RFLP and real-time PCR were performed to confirm the molecular typing of Candida isolates. Antifungal susceptibility testing using CLSI BMD MIC (M27-A2) guidelines was performed on the isolated Candida species.

Results: The results of molecular identifications showed that, 54(58%) had a fungal infection. Total of the isolates of HAIs, 66.6% belong to Candida species. including C. albicans, C. dubliniensis, C. tropicalis, C. globata, C. krusei, C. guilliermondii and C. parapsilosis. Our results of antifungal susceptibility testing revealed that 5 out of 15 isolated C. albicans and 1 out of 3 C. dubliniensis were resistant to itraconazole in-vitro (MIC 24h) and only case of C. tropicalis was resistant after 48 hours.

Conclusion: As our findings, C. albicans and C. dubliniensis were the most frequent isolated yeasts of hospital acquired infections. We showed decreased susceptibility to itraconazole (a routinely used antifungal drug). Molecular identification of Candida species and their resistance patterns is essential for optimized patients' management and reduction in unnecessary drug overuse.

keywords: Candida identification, Drug sensitivity, Hospital, Antifungal Agents

PM-8

Exploring the Antifungal Potential of Nano-Formulated Lawsonia inermis Against Candida albicans and Candida glabrata: Growth Inhibition and Biofilm Disruption

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Background and aim: Candida albicans(C. albicans) and Candida glabrata(C. glabrata) are two most prevalent etiologic agents of candidiasis worldwide. The rise of drug-resistant Candida species is a growing global concern, prompting the need for novel antifungal strategies. This study aimed to investigate antifungal effects of Lowsonia inermis (LAW) - medicinal plants and LAW-loaded mesoporous silica nanoparticles (LAW-MSNs) on Candida albicans and Candida glabrata and biofilm formation. Additionally, ALS1 and EPA1 genes in C. albicans and C. glabrata isolates was evaluated before and after exposure to these compounds respectively.

Methods: Twenty C. albicans and 20 C. glabrata include 10 fluconazole -resistant and 10 fluconazole-sensitive strains were examined. Lawsone-loaded mesoporous silica nanoparticles was prepared and characterized using transmission electron microscopy (TEM) and X-ray diffraction (XRD). The anti-fungal activity of LAW and LAW-MSN and biofilm inhibition was determined. ALS1 and EPA1 genes expression was evaluated using q RT-PCR; the cytotoxicity effect of LAW and LAW-MSNs on keratinocyte cell line (HacaT) investigated using the MTT assay.

Results: Findings of study indicated that the LAW-MSNs inhibited Candida Spp. in lower MIC than LAW and significantly decreased biofilm formation of drug -resistant and -sensitive isolates. Moreover, both LAW and LAW-MSNs down regulated the expression of adhesion genes ALS1 and EPA1 in C. albicans and C. glabrata isolates; however, this effect was not detected in fluconazole-resistant C. glabrata exposured to LAW.

Conclusion: As a result, LAW as a natural component extracted from herbal medicine considered a promising anti-fungal candidate with minimum cytotoxicity effect against host cells, however this activity boosted in nano-based LAW that confirmed nano formulation enhanced antifungal properties. More in vitro and in vivo studies are required to evaluate the effectiveness of these compounds as a therapeutic strategy to address novel anti-fungal therapy in the future.

keywords: antifungal activity; biofilm formation; Candida albicans; Candida glabrata; lawsone; mesoporous

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PM-9

Evaluation of antifungal effect of pure thymoquinone and thymoquinone-encapsulated chitosan nanoparticles on standard Candida strains and cytotoxicity in vitro

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Background and aim: Background: The present study was designed to investigate the antifungal effect and compare different concentrations of thymoquinone on standard Candida strains, including Candida albicans, Candida glabrata, Candida parapsilopsis, and Candida tropicalis, and to investigate the toxicity of thymoquinone on fibroblastic cell lines in laboratory conditions.

Methods: The present experimental study was designed to determine the minimum inhibitory concentration (MIC) and minimal fungicidal concentration (MFC) of thymoquinone in dilutions of 70-0.13 µg/ml was investigated on four yeast strains of Candida including Candida albicans (ATCC 10231), Candida glabrata (ATCC2001), Candida tropicalis (ATCC 200956), and Candida parapsilosis (ATCC22019) by broth microdilution method. MTT test were used to evaluate the cytotoxicity of thymoquinone and fibroblast cell line.

Results: The results of MIC and MFC examinations of thymoquinone showed that Candida albicans is less sensitive than other strains to thymoquinone (MIC: 2.18 µg/ml, MFC: 4.37 µg/ml) and cytotoxicity of thymoquinone on fibroblast cell line showed that the lowest toxicity was in 31.72 µg/ml and the highest toxicity was in 13.07 µg/ml. As a result, according to the MIC and MFC, these concentrations were non-toxic on the fibroblast cell line.

Conclusion: As the results of the present study have shown, thymoquinone in specified concentrations has an inhibitory and fungicidal effect on Candida strains with the least toxicity on the fibroblastic cell line.

keywords: Candida spp, Thymoquinone, Cytotoxicity

PM-10

Diabetes Mellitus, a critical risk factor of Candida infections, trends in species identification

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Background and aim: Diabetes mellitus (DM) is an important risk factor for fungal infections, especially candidiasis, due to immune down regulation and chronic (persistent) hyperglycemia. This study investigates the prevalence, clinical characteristics, and microbial profile of Candida species isolated from diabetic patients to aid healthcare providers in improving patient management, analyze demographic and clinical correlations of candidiasis and identify common specimen sources and risk factors associated with infection severity.

Methods: A cross-sectional analysis was conducted on 35 diabetic patients with suspected fungal infections. Data included: Demographics: Age, sex. Clinical variables, Specimen type (BAL, sputum, pleural fluid), ward (ICU, nephrology, respiratory,), comorbidities (hypertension, cystic fibrosis), and symptoms (pulmonary, dizziness). Microbiological data: Candida species identification and yeast growth patterns (overgrowth, invasive, undergrowth). Statistical analysis used descriptive frequencies (percentages) for categorical variables.

Results: This study had 35 cases, including 24 men (68.6%) and 11 women (31.4%). Most of the patients were in their 20–30 years (28.6%, n=10), followed by those in their 60s (25.7%, n=9) and 50s (17.1%, n=6). Specimens: Bronchoalveolar lavage (BAL) was most common, 24 (68.6%), followed by sputum, 9 (25.7%), and others, 2 (2.58%). Ward distribution: About 34.3% of the mentioned specimens were collected from ICUs, 28.6% from nephrology, and 25.7% from pulmonology wards. Comorbidities: 14(40%) of the total patients had a history of diabetes mellitus (DM) and hypertension (HTN),10 (28.6%) had DM without HTN, 6 (17%) had DM and cystic fibrosis, and other predisposing factors for fungal infections. Symptoms:The patients were hospitalized for common pulmonary complaints (56%), dizziness (8.6%), and chest pain (5.7%). Yeast patterns: Our findings of direct microscopic investigations showed: Candida colonizing forms, 16(45.7%), and Candida invasive form, 12(34.3%). Candida species:The morphologic and molecular identifications resulted: Candida

Conclusion: These findings underscore the necessity for targeted antifungal stewardship in high-risk diabetic populations, particularly those in ICUs or with pulmonary involvement. Further studies should investigate antifungal resistance patterns within this cohort.

keywords: Diabetes mellitus, candidiasis, Candida species, fungal infections.

PM-11

Prevalence, Antifungal Susceptibility, and Biofilm-Forming Ability of Candida Species from Clinical Samples

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Background and aim: The present study aimed to investigate and identify Candida species in clinical samples of individuals referred to Imam Reza (AS) Hospital in Birjand and determine the antifungal susceptibility pattern and biofilm formation ability of the clinical Candida sp. Isolates.

Methods: This study was conducted on 100 Candida isolates from different clinical samples. Isolates were confirmed using phenotyping and molecular methods. Antifungal susceptibility of the isolates was determined using the M27-A3/S4 broth microdilution method, as outlined in the Clinical and Laboratory Standards Institute (CLSI) guidelines. Biofilm formation was measured by the colorimetric microtiter method.

Results: The most Candida species identified was Candida albicans (48%) and followed by Candida glabrata (34%), Candida dublensis (9%), Candida tropicalis (5%), Candida parapsilosis (1%), Candida krusei (1%), and two mixed colonies of Candida albicans and Candida glabrata were identified. Evaluation of the susceptibility to antifungal agents of isolates, the lowest sensitivity was to fluconazole (76%), and the highest sensitivity was to amphotericin B (100%). Comparison of drug resistance showed no significant difference between resistance and sensitivity to antifungal (P0.05). However, no significant difference in biofilm formation was observed between Candida isolates (p= 0.91).

Conclusion: The results of the present study showed that periodic and regional investigations of the incidence of Candida infections, along with monitoring the pattern of anti-fungal susceptibility of isolates identified from different sources of clinical samples, can aid in the treatment process, inform the choice of an appropriate therapeutic protocol, and prevent treatment failure.

keywords: Candidiasis, Antifungal, drug resistance, biofilm

PM-12

Chronic obstructive pulmonary disease, as a critical risk factor in cases of pulmonary candidiasis

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Background and aim: Candida yeasts are encountered in four body sites including skin, oral, vaginal and gastro-intestinal tracts. Also Candida is commonly colonized in upper and lower respiratory airways, associated to chronic obstructive pulmonary disease (COPD), malignancies and chronic pneumonia, HIV infection, and prolonged hospitalization. Our study aimed to detect and identify Candida species in clinical specimens of cases with COPD as the target patients.

Methods: The study subjects were Candida strains which were obtained from cases of COPD referred to the Center of Medical Mycology, UMS University, Urmia, Iran, for the pulmonary disorder complains. BAL and sputum samples were processed into microscopic investigations and molecular identifications with PCR-RFLP at the level of species.

Results: Totally, 510 cases of pulmonary disorders of COPD were entered in our study. Totally, 22.6% were women and 77.4% men, from all, 34.7% were in the age range of 20-30 as the most frequent age groups. Totally 43 (8.4%) were involved by pulmonary disorders including COPD, CF and a history of COVID-19. Among them, 8 (34.7%) suffered by COPD. Also, 53(85.5%) showed a pulmonary symptom and sign. Total of the involved cases, 9(39%) with dizziness, 6 (26%), had productive cough, and one (4%) suffered by chest pain. Our findings of microscopic direct examination showed yeast overgrowth in 13(56.5%) of cases followed by yeast invasive bodies in 6(26%) other cases with low numbers of yeast cells. The morphologic and molecular identifications showed C. albicans 15(24.2%), C. dubliniensis and C. tropicalis 9(14.2%) itch, C. glabrata 5(8.1), C. guiliermondi 2(3.2%) and other non albicans Candida species 3(4.8%).

Conclusion: As our findings of the present study, most of the pulmonary risk factor of the candida involvement was COPD followed by Cystic fibrosis. Also, the most of Candida species isolated from the studied cases , were C. albicans .

keywords: Candida, COPD, Pulmonary disease, molecular method

PM-13

Fluconazole resistance in oral Candida-biome among children referred to a pediatric Center

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Background and aim: Candida species are part of the normal flora of the oral cavity in children and can become invasive in immunocompromised cases, leading to oral candidiasis. This study aimed to identify the Candida species isolated from the oral cavities of children referred to Shafizadeh Amir-Kola Hospital in Babol, Iran, and to evaluate their antifungal susceptibility profiles with a focus on identifying resistant Candida.

Methods: This cross-sectional study enrolled a total of 150 paediatric patients by using sterile swabs. Candida species were identified using phenotypic (CHROMagar) and molecular (PCR-RFLP) methods. The antifungal susceptibility of the isolates to amphotericin B, fluconazole, and nystatin was evaluated in accordance with the CLSI-M27-A3 guidelines.

Results: Thirty-four samples of Candida were identified using morphological and molecular methods. PCR-RFLP results using the MspI restriction enzyme confirmed the following species: Candida albicans (25 isolates); Candida parapsilosis (four isolates); Candida glabrata; Candida tropicalis; Candida krusei; and Clavispora lusitaniae. Antifungal susceptibility testing based on geometric mean minimum inhibitory concentrations (MICs) identified amphotericin B (0.016 µg/mL) and nystatin (0.194 µg/mL) as the most potent agents. An MIC of 32 was observed for fluconazole in three isolates.

Conclusion: C. albicans remains the leading oral Candida-biome although new and less common species are also reported today. These results highlight the challenge of azole resistance in Candida species as normal oral flora, indicating the presence of fluconazole-resistant isolates in three isolates. Therefore, identifying different species and examining their drug sensitivity can play an important role in the prevention and treatment of possible oral candidiasis.

keywords: Candida; antifungal susceptibility testing; pediatric; oral candidiasis

PM-14

In vitro activity of cinnamaldehyde versus terbinafine against isolates of the Trichophyton mentagrophytes complex

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Background and aim: Superficial dermatophytosis affects an estimated 20–25% of the global population, and members of the Trichophyton mentagrophytes complex are among the most frequent causative agents. Terbinafine remains a first-line therapy, yet resistance is increasingly reported and prolonged systemic use may be limited by adverse events. Cinnamaldehyde, a major bioactive constituent of cinnamon, has broad antimicrobial properties. This study compared the in-vitro activity of cinnamaldehyde with terbinafine against isolates from the T. mentagrophytes complex.

Methods: Ten isolates from the T. mentagrophytes complex were obtained from the Pasteur Biobank, including four terbinafine-susceptible and six terbinafine-resistant isolates (resistance defined as MIC 0.25 µg/mL). Antifungal susceptibility testing was performed by CLSI M38-A2 broth microdilution in 96-well plates using RPMI 1640. Cinnamaldehyde was dissolved in DMSO and a solvent control was included. MIC endpoints were read at 80% growth inhibition after incubation at 25 °C for 5 days. MIC ranges, geometric means, and MIC_{50}/MIC_{90} values were Calculated.

Results: Terbinafine displayed strong in-vitro activity against the terbinafine-susceptible isolates, with MICs ranging from 0.01 to 0.06 µg/mL and an MIC_{50} of 0.02 µg/mL. In contrast, terbinafine MICs were substantially higher among resistant isolates (2–4 µg/mL, MIC_{50} 3 µg/mL), indicating a pronounced shift toward reduced susceptibility. For cinnamaldehyde, MIC values were less differentiated between the two groups. In susceptible isolates, cinnamaldehyde MICs ranged from 2 to 8 µg/mL (MIC_{50} 2 µg/mL), while in resistant isolates they ranged from 2 to 4 µg/mL (MIC_{50} 3 µg/mL). Overall, cinnamaldehyde maintained comparable inhibitory concentrations across terbinafine-susceptible and terbinafine-resistant isolates, whereas terbinafine showed a marked increase in MIC in the resistant group.

Conclusion: In this set of T. mentagrophytes complex isolates, terbinafine remained highly active only in the susceptible group and showed a clear loss of in-vitro potency among resistant isolates. By comparison, cinnamaldehyde demonstrated measurable activity across both groups, with MIC values that remained within a similar range in terbinafine-resistant isolates. These findings support cinnamaldehyde as a candidate for further investigation—particularly through formulation development (e.g., topical delivery) and subsequent in vivo/clinical evaluation—rather than positioning it as an immediate replacement for terbinafine

keywords: Trichophyton mentagrophytes complex; cinnamaldehyde; terbinafine; broth microdilution; MIC

PM-15

Docking- and Dynamics-Guided Design of a Novel Multi-Epitope Vaccine Against Invasive Aspergillosis Incorporating Exosomal Mp1 Protein and hBD-3

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Background and aim: Invasive Aspergillosis (IA), primarily caused by Aspergillus fumigatus, presents a significant mortality risk, particularly in immunocompromised patients. With the emerging threat of azole-resistant strains, there is an urgent need for novel preventive strategies. Fungal extracellular vesicles (EVs) carrying antigens like Mp1 are promising targets for vaccine development. This in silico study aimed to design a multi-epitope subunit vaccine based on the exosomal Mp1 protein, utilizing Human Beta-Defensin 3 (hBD-3) as an adjuvant to stimulate Toll-like Receptor 4 (TLR4) effectively.

Methods: In this study, the Mp1 protein sequence was retrieved from the UniProt database. cytotoxic T-lymphocyte (CTL) and helper T-lymphocyte (HTL) epitopes were predicted and screened for antigenicity, non-allergenicity, and non-toxicity using immunoinformatics algorithms (NetCTL, IEDB). The final vaccine construct was designed by linking selected epitopes with specific linkers (GPGPG, AAY, KK) and fusing hBD-3 to the N-terminus using an EAAAK linker. The tertiary structure was modeled via AlphaFold2, refined, and validated. Molecular docking and 10 ns molecular dynamics (MD) simulations were performed to assess the interaction with TLR4. Finally, an immune response was simulated using the C-ImmSim server.

Results: The designed chimeric vaccine (385 amino acids, ~42 kDa) demonstrated high stability, solubility, and antigenicity. Molecular docking revealed a strong and stable binding affinity between the vaccine construct, the TLR4 complex, MHC I, and MHC II. MD simulation confirmed the dynamic stability of the vaccine-receptor complex with low RMSD fluctuations. Immune simulation predicted a robust induction of both humoral and cellular immunity, characterized by high levels of IgG and IgM antibodies and significant secretion of Th1-polarized cytokines, including IFN-γ and IL-2.

Conclusion: The novel multi-epitope vaccine targeting exosomal Mp1 shows high potential for eliciting protective immunity against A. fumigatus. The incorporation of hBD-3 as a safe adjuvant can enhance efficacy by activating innate immune pathways without inducing harmful systemic inflammation. These findings provide a solid foundation for further experimental validation in animal models.

keywords: Invasive Aspergillosis; Aspergillus fumigatus; Vaccine; Exosomes; Molecular, Docking; Molecular, Dynamics

PM-16

Cladosporium tenuissimum-induced sinusitis in a woman with immune-deficiency disorder

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Background and aim: The prevalence of fungal rhinosinusitis (FRS) is increasing. fungal sinusitis is a widespread infection that affects both healthy and immunocompromised individuals. The most common causes of fungal sinusitis are Aspergillus and Zygomycetes. but they can also appear in other sinuses. Specifically, phaeohyphomycotic refers to unusual and opportunistic infections caused by skin fungi that are distinguished from other hyphomycetes in the tissue by melanincontaining cell walls. Cladosporium tenuissimum infection caused by chronic fungal sinusitis in a 65-year-old woman with rheumatoid arthriti. Cladosporium tenuissimum are somewhat differentiated using colony color and microscopic shapes, and the final differentiation is done by molecular tests

Methods: Risk factors; A 65-year-old woman was diagnosed with rheumatoid arthritis and was treated with sulfasalazine. She traveled to several countries, including the UK, America, Canada, and Mexico. Due to decay of the upper jaw teeth, the patient has also had one case of root canal treatment and several cases of implants.Symptoms: Nasal congestion, anosmia, headaches, sinus pain, colored discharge, runny nose and occasional fever.Diagnosis: CT scan detected masses in the sphenoid and frontal sinuses. In the laboratory, direct microscopic examination and cultured on Sabouraud dextrose agar medium and direct smear from culture and PCR confirmed Cladosporium tenuissimum infection. The colonies were olive-green to olive-brown with a velvety or powdery appearance. Slide culture observed hyphae, conidiophores, and ovoid conidia. The fungal DNA was extracted from culture media according to instruction of the DNA extraction kit (Yekta Tajhize). GenBank under the accession number ON965336.

Results: We report a rare case of , chronic rhinosinusitis (CRS) with fungus balls in the sphenoid sinus and adhesive mass in the frontal sinus with Cladosporium tenuissimum. Fungus balls are usually very difficult to treat and there is no other way than surgery and removal. For this reason, it is very necessary to carry out detailed radiological examinations and identify the fungal agent in the laboratory in the early stages and treat the infection in time

Conclusion: We describe rare cases of CRS with Cladosporium tenuissimum. It is possible that susceptible patients are affected by saprophytic and low-risk fungi such as these

keywords: Sinusitis Cladosporium Disorder Fungus ball

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-17

Antifungal Activity and Drug Susceptibility of Rosemary and Milk Thistle Extracts against Oral Candida Isolates from Patients with Alzheimer's Disease

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Background and aim: Oral Candida infections are common in hospitalized Alzheimer's patients due to immunological changes and reduced salivary flow. Resistance to conventional antifungals such as nystatin and fluconazole complicates treatment, emphasizing the need for alternatives. Rosemary (Rosmarinus officinalis) and milk thistle (Silybum marianum) have documented antifungal properties. This study aimed to evaluate the antifungal activity of their aqueous extracts against oral Candida isolates and compare efficacy with standard antifungal drugs, providing insight into potential complementary or alternative therapies for resistant oral candidiasis in this population.

Methods: Oral swabs were collected from hospitalized Alzheimer's patients, and Candida isolates were identified using standard microbiological techniques. Aqueous extracts of rosemary and milk thistle were prepared via maceration and filtration. Antifungal susceptibility to plant extracts and conventional drugs (nystatin, fluconazole) was tested using broth microdilution according to CLSI guidelines. Minimum inhibitory concentrations (MICs) were determined. Species identification was confirmed by morphological and biochemical assays. Data were analyzed to compare the antifungal efficacy of plant extracts with standard drugs and to assess species-specific susceptibility patterns, focusing on isolates resistant to conventional antifungals.

Results: Both rosemary and milk thistle extracts inhibited all tested Candida isolates, including strains resistant to nystatin and fluconazole. Candida albicans showed slightly higher susceptibility than non-albicans species. MICs for rosemary ranged from X–Y µg/mL and for milk thistle from A–B µg/mL. Overall, plant extracts demonstrated comparable or superior antifungal activity relative to conventional drugs in resistant isolates, suggesting potential as complementary therapies for oral candidiasis in hospitalized Alzheimer's patients.

Conclusion: Aqueous rosemary and milk thistle extracts effectively inhibited oral Candida isolates, including antifungal-resistant strains, and may serve as complementary or alternative therapies. Further studies are recommended to evaluate clinical efficacy, optimal dosing, and safety for routine use.

keywords: Candida, Rosemary, Milk thistle, Antifungal, Alzheimer's

PM-18

Rising drug-resistant Candida species causing recurrent vulvovaginal candidiasis in Urmia , Iran

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Background and aim: Vulvovaginal candidiasis (VVC) is a frequent infection due to Candida yeast overgrowth in vaginal tract. Candida albicans causes 80-95% of all VVC cases in the world. To investigate the drug resistance in Iranian women with VVC which treated long time with azoles, we studied susceptibility of Candida species isolated from VVC cases to clotrimazole and fluconazole and molecular identification of studied Candida yeasts in the level of species.

Methods: Our subjects were 20-45 years old women with symptomatic vaginitis were asked to take in part in the study. From all cases approached in the gynecology clinic, 192 women allowed vaginal swabs to be obtained. All specimens were cultured on sabouraud agar medium containing glucose (4%), peptone (1%), agar (1.5%). The fresh colonies (12-24 hours growth at 30°C) were used as DNA templates for the colony-PCR.

Results: From the yeast isolates, 76.3% (74 cases) were identified as C. albicans followed by C. glabrata and C. krusei 9 (9.3% each) and other non albicans Candida species 4 (4.1%). The total sensitivity to tested antifungal drugs include 45.4% of cases were resistant and 30.9% sensitive. From all C. albicans isolates, 37(52.1%), 27(38%) and 7(9.9%) were sensitive, resistant and intermediate to antifungal drug Fluconazole and 46(64.8%), 15(21.1%) and 10(14.1%) to clotrimazole respectively.

Conclusion: In vitro resistance remains rare women with routine vaginitis caused by C. albicans, although other non albicans Candida species are most frequent agents of azole resistant yeasts.

keywords: Azole resistant, Candida, Vulvuvaginal Infection

PM-19

PCR-RFLP based identification for the dermatophytes isolated from Iranian Northwestern cases of Skin and Nail infections

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Background and aim: The most common cutaneous fungal infections are caused by dermatophyte fungi including Microsporum Trichophyton, and Epidermophyton species. To get better perception of dermatophyte distribution in Northwest of Iran, we studied the identification of isolated dermatophytes from human specimens by using the fast and cheap molecular method, PCR based restriction fragment length polymorphism (PCR-RFLP).

Methods: The study samples were collected from clinically suspected cutaneous lesions. All the specimens were transported to Medical Mycology Center, UMS University of Medical Sciences. First of all, a conventional diagnosis was carried out which included microscopic examination and culture on sabouraud dextrose agar medium with antibiotics: chloramphenicol and cycloheximide. All the dermatophyte isolates were then identified at the level of species by the molecular method of PCR-RFLP

Results: From the tested 357 clinical specimens, 30 dermatophytic isolates were identified. Totally, 38% of all cases of Tinea were 1 to 12 years old and 54% were female. The percentage rate of dermatophyte species were Trichophyton mentagrophytes (36%), Microsporum canis (32%), Microsporum gypseum (16%), Trichophyton rubrum (4%), and Epidermophyton floccosum (12%).

Conclusion: By using of PCR-RFLP, a fast and reliable identification of these species is possible. This molecular method provided an opportunity for dermatophyte identification at the species level.

keywords: Dermatophyte, Molecular Epidemiology, RFLP

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-20

Study of the frequency of otomycosis in patients referred to the ENT clinic in Fasa

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Background and aim: Otomycosis is a superficial infection of the external ear with one or more fungal agents. This infection can occur acutely, sub-acutely or chronically and involve different parts of the external ear. Identifying the type of infection-causing species is one of the most important diagnostic steps in the treatment of infectious diseases. Therefore, this study was conducted with the aim of investigating the prevalence of otomycosis in Fasa and determining the genus and species of fungi isolated by laboratory methods.

Methods: In case of suspicion of disease based on signs and symptoms, sampling was done from 70 patients by an ENT doctor if the patients did not use any antifungal drugs or topical ointments and creams and did not contact the sampling site with water for 24 hours. Direct smear with KOH 10% and culture in Sabouraud dextrose agar were performed on the samples. According to the positive results, slide culture test was used to determine the genus and species.

Results: Among 70 patients with otomycosis, 65 patients had clinical symptoms of otomycosis, and the highest number was in the age group of 31 to 40 years. 41 patients had a previous history of hearing loss and 10 patients had a history of being in the swimming pool. The highest amount of samples observed was related to hyphae, followed by hyphae and bacteria. It showed 47% of cases related to bacterial and fungal similarity. Many of the identified fungi were from the group of mycelial fungi related to Aspergillus niger and Aspergillus flavus and from the group of yeast fungi, Candida paraplosis and then saprophytic molds. All participants in this study were taking Ciplex drops, betamethasone drops, and clotrimazole drops. Of the 70 participating patients, 37 were completely cured and 8 were not treated.

Conclusion: In summary, in this study, the most common causes and risk factors of otomycosis were in the age group of 31 to 40 years and in women. About half of the cases showed factors related to bacteria and fungi. Most of the identified fungi were from the group of mycelial fungi related to Aspergillus species.

keywords: Otomycosis, Aspergillus, KOH smear

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-21

Molecular and Cellular Mechanisms of Sperm Impairment in Men with Seminal Fungal Infections: A Systematic Review

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Background and aim: Male infertility is a multifactorial condition, and accumulating evidence suggests that microbial infections, including fungal pathogens, may adversely affect sperm quality and reproductive potential. Seminal fungal infections are often asymptomatic and underdiagnosed, yet their contribution to sperm dysfunction remains insufficiently characterized. This systematic review aims to summarize current evidence on fungal infections in semen and to elucidate the molecular and cellular mechanisms through which they impair sperm function.

Methods: A systematic literature search was conducted in PubMed, Scopus, Google Scholar, and Web of Science databases up to 2025, using keywords related to fungal infections and male reproductive health, including fungal infections, Candida, male infertility, sperm function, oxidative stress, and apoptosis. Studies evaluating fungal presence in human semen and their effects on sperm parameters were included. The review was performed in accordance with PRISMA guidelines.

Results: Studies have reported the prevalence of seminal fungal infections to range from 5% to 26%, with higher rates observed among infertile men and those with underlying conditions such as diabetes, immunodeficiency, obesity, or poor hygiene. Although various fungal species have been sporadically detected in the male genital tract, the majority of available clinical and mechanistic evidence relates to Candida species. Candida-associated sperm dysfunction involves multiple interrelated mechanisms, including fungal adhesion and agglutination, mitochondrial dysfunction with reduced ATP production, caspase-mediated apoptosis, oxidative stress–induced membrane and DNA damage, and local inflammatory responses. Chronic infections, particularly those associated with antifungal resistance, further exacerbate sperm impairment and are linked to reduced success rates in assisted reproductive technologies.

Conclusion: Seminal fungal infections represent an underrecognized factor in male infertility. Current evidence indicates that Candida species are the predominant fungal pathogens affecting sperm function, while data on other fungi remain limited. Routine screening and targeted management of seminal fungal infections may improve reproductive outcomes. Further studies are needed to clarify the role of non-Candida fungi and to explore novel therapeutic strategies.

keywords: Seminal fungal infection; Male infertility; Candida species; Sperm dysfunction; Oxidative

PM-22

A Rare Case of Chromoblastomycosis Caused by Alternaria infectoria with Concurrent Myiasis in a Kidney Transplant Recipient

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Background and aim: Chromoblastomycosis is a chronic subcutaneous mycosis that primarily involves the skin and underlying soft tissues. We report the case of a 46-year-old woman with a history of kidney transplantation who developed chromoblastomycosis while receiving long-term immunosuppressive therapy. She presented with dark-colored verrucous and ulcerative lesions on both legs. Microscopic examination of skin scrapings revealed characteristic muriform (Medlar) bodies, supporting the diagnosis. The etiologic agent was identified as Alternaria infectoria through two consecutive fungal tissue cultures and ITS region sequencing, representing an uncommon causative species for chromoblastomycosis. Combination therapy with voriconazole and terbinafine led to complete clinical resolution within five months.

Methods: The patient's medical history was notable for kidney transplantation, and she was receiving long-term immunosuppressive therapy. Direct microscopic examination of skin scrapings treated with 10% potassium hydroxide (KOH) demonstrated septate hyphae together with characteristic thick-walled muriform (Medlar) bodies, consistent with chromoblastomycosis. Tissue specimens were inoculated onto Sabouraud dextrose agar (SDA) supplemented with chloramphenicol and incubated at 30°C for 20 days. Grayish colonies became visible on the ninth day of incubation. Microscopic evaluation of the cultured isolate showed pigmented septate hyphae and chains of ovoid conidia with both transverse and longitudinal septa, suggesting an Alternaria species. Definitive species identification was achieved by sequencing the internal transcribed spacer (ITS) region of rDNA, which confirmed the isolate as Alternaria infectoria (GenBank accession no. OR685707).

Results: Antifungal susceptibility testing was conducted using the broth microdilution method according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. The patient was treated with oral voriconazole at 200 mg/day without therapeutic drug monitoring. Oral terbinafine was initiated at 250 mg/day and reduced to 125 mg/day after six weeks. Following 5 months of combination antifungal therapy, the lesions resolved completely, with both clinical recovery and negative follow-up fungal cultures confirming treatment success.

Conclusion: This case expands the spectrum of fungal pathogens implicated in chromoblastomycosis by identifying Alternaria infectoria as the causative agent. The favorable clinical outcome achieved with combined voriconazole and terbinafine therapy underscores the value of individualized antifungal treatment strategies for managing complex cases of chromoblastomycosis.

keywords: Chromoblastomycosis, Alternaria, Dematiaceous fungi

PM-23

Evaluation of cell surface hydrophobicity and biofilm formation in Candida albicans isolates from patients with substance use disorder in Ahvaz, Iran

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Background and aim: Candida albicans is an opportunistic pathogen whose virulence factors, such as biofilm formation and cell surface hydrophobicity (CSH), contribute to its pathogenicity and drug resistance. This study investigated the prevalence, drug resistance patterns, and these key virulence factors in C. albicans isolates from a high-risk population of individuals with substance use disorder.

Methods: Oral swabs were collected from 245 patients in addiction treatment centers in Ahvaz. Isolates were identified using culture, PCR, and DNA sequencing. Virulence factors were assessed by the Crystal violet assay for biofilm formation and the microbial adhesion to hydrocarbons test for CSH. Antifungal susceptibility testing against fluconazole, itraconazole, and caspofungin was performed.

Results: Of 245 patients, 165 (67.3%) were colonized, yielding 244 yeast isolates, with C. albicans (33.2%) being predominant. Among 92 C. albicans isolates tested, 47.9% were strong biofilm producers. A strong positive correlation was found between CSH and biofilm density (r=0.74, p0.001). Biofilm formation was significantly higher in isolates resistant to fluconazole, itraconazole, and caspofungin (p0.05). CSH was significantly associated only with resistance to caspofungin (p=0.02).

Conclusion: A high colonization rate and prevalence of strong biofilm-forming C. albicans isolates were found in this vulnerable population. The strong correlation between CSH and biofilm formation, and their significant association with antifungal resistance, highlight the critical role these intertwined virulence factors play in the pathogenicity and treatment challenges of candidiasis in patients with substance use disorder.

keywords: Candida albicans, Biofilm, Hydrophobicity, Drug Resistance, Substance Use Disorder

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PM-24

Presence of HSP90 Gene in Amphotericin B Resistant Aspergillus Species Isolated from Iranian Immunocompromised Patients

نیره قدس [1] © Ⓟ

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Background and aim: Aspergillosis is an opportunistic infection caused by Aspergillus spp in immunocompromised patients. The role of HSP90 in Aspergillus drug resistance is still unknown. The aim of this study was to evaluate the correlation between the presence of HSP90 gene and polyene resistance in Aspergillus spp using PCR.

Methods: In this study, 32 Aspergillus strains were used, which were isolated from patients susceptible to aspergillosis through Bronchoalveolar lavage (BAL) and identified by conventional methods. The isolates were cultured on Sabouraud dextrose agar (SDA). Susceptibility testing against amphotericin B was conducted according CLSI standards (M38-A). Also, the presence of HSP90 gene was evaluated using PCR.

Results: Of 32 Aspergillus strains used in this study, 16 (50%) isolates were identified as A. Flavus, 12 (37.5%) isolates as A. fumigatus, and 4 (12.5%) isolates as A. terreus. Among these species, 19 (59.37%) isolates were sensitive to amphotericin B whereas 13 (40.62%) were resistant. Moreover, there was a significant difference between the presence of HSP90 gene and resistance to amphotericin B in Aspergillus species.

Conclusion: The presence of HSP90 gene provides evidence that shows this gene may play important role in resistance to amphotericin B in Aspergillus isolates. Although numerous regulatory genes are involved in resistance mechanisms, they remain to be more clarified.

keywords: Aspergillus spp, Amphotericin B, HSP90 gene, PCR

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-25

Comparison of the production of enzymes involved in pathogenesis in Candida species isolated from patients with COVID-19 associated oral candidiasis hospitalized in Razi hospital, Rasht compared with healthy subjects

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Background and aim: Oral candidiasis is a frequent opportunistic infection among hospitalized patients with COVID-19, largely due to immune dysregulation, invasive interventions, and polypharmacy. Candida species are common members of the oral microbiota; however, under favorable conditions, they may express virulence factors that contribute to disease development. Enzymes such as secreted proteinases, esterases, and hemolysins play a critical role in tissue invasion, nutrient acquisition, and host damage. This study aimed to compare the production of key pathogenicity-related enzymes in Candida species isolated from hospitalized COVID-19 patients with oral candidiasis and from healthy individuals, in order to better understand their virulence potential.

Methods: This case–control study included 86 Candida isolates obtained from oral swab samples: 43 isolates from hospitalized COVID-19 patients with oral candidiasis and 43 isolates from healthy individuals representing normal oral Candida flora. Species identification was performed using standard phenotypic and microbiological methods. The enzymatic activity of three major virulence factors—secreted aspartyl proteinase, esterase, and hemolysin—was evaluated using specific culture-based assays, and activity indices were calculated accordingly. Statistical analysis was conducted using appropriate tests, with a significance level set at p 0.05 and a confidence interval of 95%.

Results: The results demonstrated that the enzymatic activities of esterase, proteinase, and hemolysin were significantly higher in Candida isolates obtained from hospitalized COVID-19 patients compared to those from healthy individuals (p 0.05). Among the studied species, Candida albicans exhibited higher esterase and hemolysin activity than non-albicans Candida species in both groups. Nevertheless, all Candida isolates showed measurable enzymatic activity, indicating inherent pathogenic potential. The highest overall enzyme production was observed in isolates from COVID-19–associated oral candidiasis, suggesting an enhanced virulence profile under disease-related host conditions.

Conclusion: The present study showed that the Candida species isolated from patients with COVID-19 associated oral candidiasis and healthy individuals have the potential to produce enzymes involved in pathogenesis, but the activity and pathogenicity of these enzymes in the species isolated from patients is much higher than that of healthy individuals. Therefore, it can be concluded that commensal strains are opportunistic and are able to cause disease in favorable conditions such as COVID-19.

keywords: Oral Candidiasis, COVID-19, Virulence Factors.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-26

Investigation of the antifungal effect of watery and alcoholic extract of Myrtus communis on the growth of Candida species: in vitro

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Background and aim: Denture stomatitis is a common inflammatory condition among denture wearers, with Candida species recognized as its primary etiological agents. Increasing antifungal resistance and the undesirable side effects associated with conventional antifungal drugs have encouraged the search for effective herbal alternatives. Myrtus communis is a medicinal plant known for its antimicrobial properties, yet its antifungal activity against oral Candida species remains underexplored. This study aimed to evaluate and compare the antifungal effects of aqueous and alcoholic extracts of Myrtus communis on Candida species isolated from patients with denture-related candidal stomatitis under laboratory conditions.

Methods: In this experimental in-vitro study, aqueous and alcoholic extracts of Myrtus communis leaves were prepared using the maceration method. Candida species isolated from patients with denture-related candidal stomatitis, including Candida albicans, Candida tropicalis, Candida parapsilosis, Candida glabrata, and Candida krusei, were evaluated. Antifungal activity was assessed by determining the minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC) using the microdilution method, in accordance with CLSI guidelines. All experiments were performed under controlled laboratory conditions.

Results: All Candida isolates demonstrated resistance to the aqueous extract of Myrtus communis. In contrast, the alcoholic extract exhibited significant antifungal activity against all tested species. Candida tropicalis showed the highest susceptibility, with MIC and MFC values of 16 µg/mL. For Candida albicans and Candida parapsilosis, MIC and MFC values were 32 µg/mL, while Candida glabrata required 64 µg/mL. The highest resistance was observed in Candida krusei, with MIC and MFC values reaching 256 µg/mL. These findings highlight species-dependent differences in antifungal susceptibility.

Conclusion: The results indicate that the alcoholic extract of Myrtus communis possesses considerable antifungal activity against Candida species associated with denture stomatitis, whereas the aqueous extract lacks effectiveness. The superior efficacy of the alcoholic extract may be attributed to improved extraction of bioactive compounds with antifungal properties. Given the increasing resistance to conventional antifungal agents and their adverse effects, Myrtus communis alcoholic extract may represent a promising natural alternative for managing denture-related candidal stomatitis. Further clinical studies are recommended to validate its therapeutic potential and safety in vivo.

keywords: Denture Stomatitis, Myrtus communis, Plant Extracts, Antifungal Agents

PM-27

Evaluation of the Antifungal Activity of Caprylic Acid Compared with Azoles Against Candida Species Isolated from Patients with Vulvovaginal Candidiasis

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Background and aim: Vulvovaginal candidiasis (VVC) is one of the most prevalent infections of the female genital tract, affecting a large proportion of women at least once during their lifetime. Candida albicans is the primary causative organism; however, an increasing prevalence of non-albicans species has been reported in recent years. This shift, along with the growing resistance to commonly used azole antifungal agents, has compromised the effectiveness of standard treatments. These challenges underscore the need for alternative or adjunctive therapeutic options. Caprylic acid, a naturally derived compound with documented antifungal activity, represents a potential alternative for improving the management of vulvovaginal candidiasis.

Methods: A cross-sectional study was conducted on 322 participants. Species identification was performed using phenotypic methods (CHROMagar Candida, CMA, and germ-tube test), and Multiplex PCR (YEAST PLEX) was applied for non-albicans isolates. Antifungal susceptibility testing was performed on 30 isolates using disk diffusion and broth microdilution for fluconazole (FLC), clotrimazole (CTZ), and caprylic acid (CAP). MIC_{50}, MIC_{90}, and geometric mean MIC values were calculated.

Results: Eighty individuals were diagnosed with VVC (24.84%). C. albicans accounted for 78.75% of isolates, while non-albicans species represented 21.25%. Pruritus (57.5%) and burning sensation (51.25%) were the most common symptoms and were significantly more frequent in culture-positive women. The highest prevalence occurred in the 25–34-year age group (43.75%). In disk diffusion testing, CAP showed stronger inhibitory activity than FLC and CTZ, producing larger inhibition zones. Based on broth microdilution, 65.6% of isolates were susceptible to FLC and 6.66% to CTZ. Additionally, 50% of isolates were susceptible to 5% CAP, and the remaining 50% to 10% CAP.

Conclusion: The antifungal activity of tested agents followed the order CAP FLC CTZ. CAP demonstrated notable inhibitory effects at 250–500 µg/mL. With further studies, caprylic acid may be considered a promising complementary option in antifungal therapy.

keywords: Vulvovaginal candidiasis (VVC), Candida albicans, Caprylic acid (CAP), Fluconazole (FLC),

PM-28

Identification and antifungal susceptibility patterns of onychomycosis caused by Aspergillus spp

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Background and aim: Onychomycosis affects nearly 300 million people worldwide annually, and between 2 and 22% of onychomycosis cases are caused by non-dermatophytic fungi (49). Onychomycosis is difficult to treat. The management of this chronic, slowly progressive disease is complicated by the long duration of treatment (often more than a year) and the high risk of recurrence (20-25%) (57).

Methods: In this study, isolates were collected from 25 patients with onychomycosis referred to the Pasteur Institute of Iran, Tehran, between 2012 to 2025. Samples were examined macroscopically, microscopically and molecularly using ITS gene sequencing. In vitro antifungal susceptibility testing to amphotericin B (AMB), itraconazole (ITC), voriconazole (VRC), caspofungin (CFG), and posaconazole (POS) was performed according to CLSI M38A2 guidelines.

Results: All cases were confirmed by clinical pictures, laboratory findings and isolation of etiological Aspergillus species belonging to five main species, namely Aspergillus flavus, Aspergillus niger, Aspergillus oryzae, Aspergillus numius and Aspergillus hortae. Antifungal resistance was observed in 5 out of 25 isolates (20%), all of which belonged to Aspergillus niger.

Conclusion: In this study, it was determined that antifungal resistance to the drugs used for treatment has increased and further research is needed to find alternative treatments because this disease is of great importance, especially in patients with underlying diseases and can be life-threatening for the patient.

keywords: Onychomycosis, Aspergillus, Antifungal Resistance, Azole

PM-29

Nosocomial bloodstream Infection by Rhodotorula species in pediatric patients with malignancy and Antifungal Susceptibility pattern

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Background and aim: Fungemia is a life-threatening infection in patients with malignancy, and early diagnosis and use of appropriate antifungal drugs are essential in this disorder. In this regard, Rhodotorula species., as the third most common yeast isolated from blood cultures, have received more attention today, and antifungal therapy plays an important role in this field. In this study, we aimed to investigate the prevalence of fungemia caused by Rhodotorula species and also antifungal susceptibility patterns in pediatric patients with malignancy.

Methods: Two hundred and five blood samples from patients with malignancy hospitalized in Baqaei Hospital of Ahvaz were cultured to diagnose Rhodotorula-induced fungemia. Rhodotorula species were identified by phenotypic and PCR methods. Antifungal susceptibility testing was performed using disk diffusion test according to the standard protocol CLSI M27M44S.

Results: In total, 4 of 205 patients (1.95%) were positive for the presence of R. glutinis, and no morbidity due to Rhodotorola fungemia were observed. Fluconazole, voriconazole and caspofungin resistance was observed in 4 R. glutinis. There was no known breakpoint for PCZ. Therefore, the inhibition zone diameter was recorded. R. glutinis showed high MICs for posaconazole (18-38).

Conclusion: In the present study, 4 cases of Rhodotorula fungemia were initially observed, and given that the patients recovered after catheter removal, we assumed that this was a fungal colonization. Seifi et al. reported a prevalence of Rhodotorula species in Ahvaz hospitals of 12%, with a predominance of R. glutinis (86%), which was expected to lead to a higher incidence of Rhodotorula fungemia. We speculated that although patients were infected with Rhodotorula species, R. glutinis had low pathogenicity in patients with malignancy or that early diagnosis prevented the development of true

keywords: Fungemia, Rhodotorula, malignancy

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July 20-23, 2026

PM-30

Epigenetic Alterations Induced by Aflatoxin B1 and Their Role in Hepatocellular Carcinogenesis

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Background and aim: Aflatoxin B1 (AFB1) is a highly potent mycotoxin produced mainly by Aspergillus flavus and Aspergillus parasiticus and is classified as a Group 1 human carcinogen. Chronic dietary exposure to AFB1 represents a major public health concern, particularly in regions with inadequate food safety control, and is strongly associated with hepatocellular carcinoma (HCC). Although AFB1-induced DNA adduct formation and mutagenesis have been extensively characterized, growing evidence indicates that epigenetic alterations play a central role in AFB1-driven hepatocarcinogenesis. This systematic review summarizes current evidence on epigenetic mechanisms induced by AFB1 and their contribution to HCC development.

Methods: This review was conducted in accordance with PRISMA guidelines. PubMed, Scopus, and Web of Science databases were searched up to the end of 2024 for human, animal, and in vitro studies reporting AFB1-associated epigenetic alterations, including DNA methylation, histone modifications, and non-coding RNA deregulation.

Results: Evidence indicates that AFB1 induces epigenetic dysregulation through three primary pathways: aberrant DNA methylation, altered histone modification patterns, and deregulation of non-coding RNAs. AFB1 forms mutagenic DNA adducts, particularly targeting the TP53 tumor suppressor gene and inducing characteristic G→T transversions that compromise genomic stability. These genetic events are accompanied by promoter hypermethylation of tumor suppressor genes, global DNA hypomethylation, and dysregulated microRNAs such as miR-122 and miR-34a. Notably, AFB1 carcinogenicity is enhanced by synergistic interactions with hepatitis viruses, highlighting a multifactorial mechanism of HCC initiation. Persistent epigenetic alterations have been observed long after exposure, suggesting durable epigenomic reprogramming.

Conclusion: AFB1-induced epigenetic alterations represent a critical molecular link between environmental mycotoxin exposure and hepatocellular carcinoma. Integrating fungal source control, molecular surveillance, and epigenetic biomarkers may substantially reduce the burden of AFB1-associated HCC.

keywords: Aflatoxin B1, Epigenetic dysregulation, Hepatocellular carcinoma, Aspergillus

PM-31

Cytokine Responses to Invasive Aspergillus fumigatus Infection in Tumor-Bearing Mice

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Background and aim: Invasive aspergillosis (IA) is a life-threatening fungal infection in immunocompromised hosts, including cancer patients. Tumor-associated immune dysregulation may alter cytokine responses to fungal pathogens, thereby influencing disease outcome. However, cytokine alterations induced by Aspergillus fumigatus infection in tumor-bearing hosts remain poorly characterized. The present study investigated cytokine response alterations in $CD4^+$ T cells following invasive Aspergillus fumigatus infection in a tumor-bearing mouse model.

Methods: Female BALB/c mice were divided into four groups: tumor-bearing mice with IA, tumor-bearing mice without infection, IA-only mice, and healthy controls. Invasive aspergillosis was induced by intravenous inoculation of A. fumigatus conidia. Splenocytes were isolated and cultured, and cytokine levels (IL-4, IFN-γ, IL-10, and TNF-α) in culture supernatants were quantified using ELISA. Statistical analysis was performed using one-way ANOVA.

Results: Tumor-bearing mice infected with A. fumigatus demonstrated significant alteration in cytokine production compared with healthy controls. IL-4 levels were significantly increased in the tumor + IA group ($P = 0.031$), indicating a shift toward a Th2-dominant immune response. IFN-γ production showed a non-significant decrease, suggesting impaired Th1-mediated antifungal immunity. IL-10 levels were significantly elevated in tumor-only and IA only groups compared with controls, while no significant increase was observed in the tumor plus IA group. TNF-α levels showed an increasing trend in infected groups, although differences were not statistically significant.

Conclusion: Invasive A. fumigatus infection in tumor-bearing mice is associated with marked cytokine imbalance characterized by enhanced IL-4 production and altered regulatory cytokine responses. This Th2-skewed cytokine profile may contribute to impaired antifungal immunity and increased susceptibility to invasive aspergillosis in cancer hosts. Understanding cytokine dysregulation in this study may aid in improving immunomodulatory strategies for high-risk patients.

keywords: Cytokines, Invasive aspergillosis, Tumor-bearing mice

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-32

Bilateral COVID-19-Associated Mucormycosis and Aspergillosis Co-infection with Cranial Nerve Palsy in a Young Diabetic Patient: A Case Report Emphasizing the Role of Aggressive Multimodal Therapy

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Background and aim: COVID-19-associated mucormycosis-aspergillosis co-infection is a severe, often fatal complication in diabetics. Rhino-orbital-cerebral disease with cranial nerve involvement has a poor prognosis and young patients with bilateral neurological impairment rarely survive. We present a surviving case of a young diabetic male with bilateral co-infection and facial nerve palsy to highlight pivotal management strategies.

Methods: A 29-year-old male with uncontrolled type 2 diabetes presented with a three-day history of rapidly progressive left-sided facial swelling, ptosis, and subsequent complete left-sided facial nerve (CN VII) palsy, resulting in complete left-sided facial paralysis. Symptoms emerged approximately one month after recovery from moderate COVID-19 pneumonia treated with remdesivir and dexamethasone. Nasal endoscopy revealed necrotic eschar. Urgent imaging (PNS CT and Brain MRI) confirmed extensive bilateral sinus involvement with orbital and intracranial extension. Direct microscopy of debrided tissue demonstrated both non-septate and septate hyphae. Mycological culture confirmed a mixed fungal infection, with molecular identification confirming Aspergillus flavus alongside Rhizopus arrhizus.

Results: The patient was managed with intravenous liposomal amphotericin B alongside three functional endoscopic sinus surgeries (FESS) and four intraocular amphotericin B injections. Despite aggressive therapy, right eye enucleation was required due to progressive orbital invasion. The total hospitalization was 63 days. At discharge, vision was preserved in the left eye, and only mild residual facial weakness was noted, with no documented evidence of active infection.

Conclusion: This case demonstrates that survival is achievable in severe bilateral mucormycosis-aspergillosis co-infection with cranial nerve involvement through aggressive multimodal therapy. Key interventions included early and aggressive use of systemic liposomal amphotericin B, which provides activity against both causative pathogens, alongside repeated surgical debridement. Crucially, the local administration of intraocular amphotericin B served as a pivotal adjunctive measure to control invasive disease. Young age and the absence of major comorbidities beyond diabetes may improve prognosis. A coordinated, multidisciplinary approach remains essential in managing these high-risk co-infections, even in resource-limited settings.

keywords: COVID-19-associated mucormycosis; Aspergillosis; Co-infection; Cranial nerve palsy.

PM-33

Emphysematous pyelonephritis in a diabetic patient

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Background and aim: Emphysematous pyelonephritis (EP) is an infection of the kidney tissue that is necrotizing and gas-producing and primarily affects individuals with diabetes mellitus. Fungal EP is a rare etiology that is typically caused by candida species. Limited data suggests that diabetes mellitus and female sex are prominent risk factors for fungal EP, like bacterial type.

Methods: We have presented a case of persistent fever, nausea, and flank pain with the diagnosis of EP.

Results: We have reported a 67-year-old female with a history of diabetes mellitus and prior urological procedures who developed emphysematous pyelonephritis due to Candida albicans. She was treated with systemic fluconazole and underwent other urological interventions as necessary. However, due to a persistent fever, amphotericin B was administered via nephrostomy for 3 days, after which her fever resolved. She ultimately recovered and was discharged in good condition.

Conclusion: This case highlights the critical need for innovative treatment strategies to address persistent infections, such as nephrostomy irrigation with antifungal agents. These interventions not only help target and reduce the fungal burden within the urinary tract but also enhance overall patient outcomes by reducing the risk of systemic spread. As the landscape of fungal infections continues to evolve, incorporating these advanced irrigation techniques into clinical practice could provide a vital tool in combating resistant infections, thereby improving management protocols for patients facing similar complications.

keywords: Emphysematous pyelonephritis, Candida, Diabetes mellitus, Candidiasis

PM-34

Evaluation of antifungal supplement properties of Fluconazole-loaded nanostructure lipid carriers on Candida species from vaginal discharge

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Background and aim: Candida is one of the most common fungal infections in humans, including vulvovaginal candidiasis. Antifungal drugs such as fluconazole are effectively used to treat candidiasis; however, drug resistance has been observed in many cases. Therefore, new treatment strategies are essential. Recently, nanoparticles such as nanostructured lipid carriers (NLCs) have been widely used in drug delivery. Fluconazole (FLZ) is a lipid-soluble antifungal agent utilized in treating candidiasis. The current study aimed to investigate the characteristics and antifungal activity of NLC-loaded FLZ.

Methods: Fluconazole-loaded lipid nanostructures were prepared using solvent evaporation and demonstrated suitable physicochemical properties. Fungal samples from women with vulvovaginal candidiasis were collected from the medical mycology laboratory and identified through microscopic examination with 10% KOH, followed by culture on Sabouraud dextrose agar containing chloramphenicol (SC). For identification, samples were further cultured on CHROMagar™. The effect of NLC-Fluconazole was evaluated using the standard CLSI M27-A2 protocol via the broth microdilution method on Candida species by determining the minimum inhibitory concentration (MIC) and comparing it to the MIC of Fluconazole. FLZ-resistant C. albicans strains were previously confirmed to have an MIC ≥ 8 µg/ml according to CLSI guidelines.

Results: The average zeta potential was measured at 25°C and a fixed angle of 90° using a zeta sizer device. Its value ranged from 0 to -50 mV, with an average of -26.6 mV. The average particle size of NLC-FLZ was 477.3 nm, and the polydispersity index (PDI) was 0.343. Among the 20 patient samples collected, 14 were identified as Candida albicans, 2 as Candida glabrata, 2 as Candida tropicalis, 1 as Candida krusei, and 1 as Candida parapsilosis. The minimum inhibitory concentration required to inhibit 90% of isolates (MIC90) for Fluconazole was 4 µg/mL for C. albicans, 32 µg/mL for C. glabrata, 4 µg/mL for C. tropicalis, 8 µg/mL for C. krusei, and 4 µg/mL for C. parapsilosis. In contrast, the MIC90 values for FLZ-NLC were significantly lower at 0.5, 0.25, 0.5, 0.25, and 0.5 µg/mL, respectively. (p0.05)

Conclusion: This study is part of an unpublished investigation. Specifically, the antifungal activity of NLC-Fluconazole was evaluated against Candida strains isolated from Woman with VVC in Ardabil. Based on the data obtained from this study, it is found that NLC-FLZ formulations with acceptable physicochemical properties are easily prepared and used. The resulting nanostructures, due to the small size of the drug particles, increase the stability and penetration of the drug, and due to the lipid properties, they increase the stability of the drug at the desired location. Based on the results

keywords: Candida, NLC, Microdilution broth, Fluconazole, Drug

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-35

Anti-fungal Activity of Terbinafine-Loaded Lipid Nanostructures on Dermatophyte Species Isolated from Animals

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Background and aim: A group of filamentous fungi known as dermatophytes are responsible for causing lesions on the skin, hair, and nails. These fungi are keratinophilic and induce lesions by secreting the enzyme keratinase, as well as through the host's immune response. The disease caused by these fungi, dermatophytosis, is zoonotic and can affect both humans and animals, causing lesions on the skin and hair. Drug resistance and the transmissibility of this disease have created complex treatment challenges for physicians. One proposed approach is the use of nanodrug carriers to improve drug delivery and treatment efficacy. The aim of this study is to

Methods: Terbinafine-loaded lipid nanostructures were prepared using solvent evaporation and exhibited suitable physicochemical properties. Fungal samples from animals with dermatophytosis were collected from slaughterhouses and identified through microscopic examination with 10% KOH, followed by culture on Sabouraud dextrose agar containing chloramphenicol and cycloheximide (SCC). The effect of NLC-terbinafine was determined using the standard CLSI M38-A2 protocol through the broth microdilution method on dermatophyte species by calculating the minimum inhibitory concentration (MIC) and comparing it to the MIC of terbinafine.

Results: Of the 30 samples collected, 21 were from sheep, 6 from goats, 2 from cattle, and 1 from a camel. Microsporum canis was isolated in 17 cases (56.66%), Trichophyton verrucosum in 6 cases (20%), Trichophyton mentagrophytes complex in 5 cases (16.66%), and 2 cases involved unidentified species. The MIC50 values of Terbinafine against M. canis, T. verrucosum, T. mentagrophytes, and unidentified dermatophytes were 0.5, 0.5, 0.125, and 0.125 µM, respectively. For NLC-Terbinafine, these values were 0.125, 0.0625, 0.125, and 0.0313 µM, respectively. Scanning electron microscopy (SEM) images at both higher and lower magnifications revealed that the nanoparticles were spherical, with particle sizes ranging from 58.8 to 96.3 nm.

Conclusion: This study is part of an unpublished investigation and represents the first published report on the effects of this formulation on isolated fungal species. Specifically, the antifungal activity of NLC-terbinafine was evaluated against dermatophyte strains isolated from animals with dermatophytosis lesions in Ardabil. Consistent with previous research, zoophilic dermatophyte species were prevalent in slaughtered domestic animals, with Microsporum canis being the most frequently isolated species. The observed reduction in minimum inhibitory concentration (MIC) for species treated with NLC-terbinafine may be attributed to the drug's enhanced binding to the dermatophyte cell

keywords: Dermatophyte, NLC, Microdilution broth, Terbinafine, Drug

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-36

Prevalence of Trichophyton Indotineae in Patients with Dermatophytosis at Razi Hospital, Tehran, Iran, in 2025

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Background and aim: Dermatophytes are among the most common etiologic agents of superficial fungal infections affecting the skin, hair, and nails. They can cause a wide spectrum of clinical manifestations, ranging from localized lesions to extensive and treatment refractory disease. In recent years, the emerging species Trichophyton indotineae has attracted increasing attention as an important cause of dermatophytosis, particularly in cases with poor response or resistance to conventional antifungal therapy. Accurate identification of this species and determination of its prevalence in referral centers are essential for appropriate therapeutic decision making and public health planning.

Methods: This descriptive cross sectional study was conducted over a four month period in 2025 at Razi Hospital, Tehran, on patients with clinically and microscopically confirmed dermatophytosis who had not recently used systemic or topical antifungal agents. Clinical specimens were cultured on Mycosel agar for fungal isolation. Dermatophyte isolates were identified using PCR with T. indotineae–specific primers, and selected isolates were further confirmed by ITS region amplification and sequencing.

Results: During the study period, a total of 83 skin scraping samples were collected from 83 patients with clinical manifestations suggestive of dermatophytosis. Among these, 39 samples (47%) showed fungal growth in culture and exhibited macroscopic and microscopic features consistent with dermatophytes. Based on molecular assays, 32 (82%) of the 39 isolates were confirmed as T. indotineae.Patients with T. indotineae dermatophytosis ranged in age from 17 to 56 years, with a mean age of 33.3 years. Both sexes were almost equally affected, with 17 males (53.1%) and 15 females (46.9%). Regarding the clinical forms of the disease, 23 patients exhibited dermatophyte involvement confined to a single body site , while 9 patients showed involvement of multiple body sites. Among these, the most common presentation was Tinea cruris, observed in 19 of 32 patients (59.37%), followed by Tinea corporis and Tinea cruris in 9 patients (28.13%) and Tinea corporis in 4 patients

Conclusion: The findings of this study indicate a shift in the leading cause of dermatophytosis toward T. indotineae, particularly in cases of tinea cruris. Precise identification of dermatophyte isolates is therefore crucial, especially in this clinical form, to guide effective treatment and inform public health strategies.

keywords: Dermatophyte, Trichophyton indotineae, Superficial fungal infection, Dermatophytosis, PCR

PM-37

A three years report of fungal infections in children referred to an Iranian Northwestern pediatric hospital, Focus on molecular identification

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Background and aim: There are a variable infections caused by fungi involve children 1- 10 years old. Except keratinophilic dermatophytes which cause ringworm and tinea in children by direct and indirect transmission of dermatophyte arthrospores, all opportunistic fungi including Candida, Aspergillus, Pneumocystis and Mucorals make diseases in children suffered by one or more risk factors of immunity system. Detection and identification of the fungal agents of infections before starting treatment, help health care services to prevent undesired events. The study aim was obtaining a comprehensive data of cases involved and the fungal agents' identification.

Methods: All cases of suspected to fungal infections in the University Pediatric Hospital during last three years (Sep 2022 to Oct 2025), entered our study. The clinical specimens were collected in hospital and transported to Medical Mycology Center, UMS University, Urmia, Iran. A demographic and history database was made for each case. The processing on specimens and microscopic investigation were carried out in Med. Mycology center. All isolated fungi from cases of microscopic detection were profiled into culture, morphologic and molecular identification.

Results: Totally 86 cases were included in the study. From all, 47(54.7%) were men and 39 (45.3%) women. The most common age range was 5 years for 52(60.5%) cases. The most number of collected clinical specimens were peritoneal fluid and wound discharge 15(17.4%) each followed by scalp scrape sample 14(16.3%). The clinical manifests of recorded were epidermal disorders: scaly patch 17(19.8%), alopecia 6(7%), bullae 2(2.3%) and other skin lesions 10(11.6%) and respiratory tract symptoms 3(3.5%), also 47(54.7%) of cases with not any symptoms were studied. For the primary diagnosis, microscopic investigation detected mainly, dermatophyte invasive bodies 20(23.3%), yeast overgrowth 9(10.5%), yeast low numbers 8(9.3%) and invasive yeast elements 3(3.5%). Fungal isolates from the cases samples which identified included: Trichophyton mentagrophytis 6(7%), Trichophyton verrucosum 4(4.7%), Candida albicans 4(4.7%), non albicans Candida 3(3.5%) and other non-identified Candida species 5(5.8%) and also 2(2.4%) cases of Aspergillus and one case of Rhizopus species.

Conclusion: Although a variety of fungal infections of children were diagnosed in the present study, some fungal genera including candida and dermatophytes were most identified.

keywords: Candida, Trichophyton, Children, identification

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-38

Evaluation of Antifungal Resistance Patterns in Candida parapsilosis Complex Isolates from Clinical Sources in Iran

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Background and aim: Candida parapsilosis complex is considered one of the most important non-albicans Candida species causing bloodstream and hospital-associated infections. The increasing frequency of antifungal resistance, particularly to azoles and echinocandins, has become a growing challenge in clinical management. Continuous surveillance and identification of resistant isolates are therefore crucial to guide effective antifungal therapy and infection control.

Methods: A total of 510 C. parapsilosis complex isolates were collected between May 2023 and December 2024 from clinical samples in multiple Iranian hospitals. Species identification was performed by PCR–RFLP and confirmed for selected isolates by sequencing. Antifungal susceptibility testing for major antifungal agents—including azoles, echinocandins, and amphotericin B—was carried out according to the CLSI M27-A4 microdilution method.

Results: The majority of isolates were obtained from clinical samples. Overall, a small proportion of isolates showed elevated MIC values to azoles or echinocandins. Notably, all resistant strains were recovered from clinical sources,. In vitro susceptibility results indicated that voriconazole and amphotericin B were the most effective agents against the tested isolates

Conclusion: The detection of azole- and echinocandin-resistant C. parapsilosis strains, even at low frequency, highlights the emerging threat of antifungal resistance in hospital settings. The absence of resistant isolates in environmental and hand samples may suggest that antifungal exposure and selection pressure in clinical environments play a key role in resistance development. This study provides an overview of antifungal resistance trends among Candida parapsilosis complex isolates in Iran.

keywords: Candida parapsilosis, antifungal resistance,Clinical Sources

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-39

Most common fungi causing Nail infections in cases of Northwestern Iranian Medical Centers

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Background and aim: The most common fungal nail infections are caused by dermatophyte fungi including Trichophyton, and Epidermophyton followed by Candida, Aspergillus and other saprophytic molds. Because of the multi-factorial and variable causing agents of nail infections, the antifungal therapies are variable. In this study, the predominant agents and most isolated fungi of nail infections were identified and reported.

Methods: The clinical specimens including nail scraped and extracted samples were collected from cases with hyperkeratotic, dark colored and distrophic nails and transported to Medical Mycology Center, UMS University. A primary direct microscopic investigation for invasive fungal element was performed. Culture and Molecular identification were carry out using the selective culture media and PCR-RFLP method.

Results: Total of the 134 clinical specimens, 72(53.7%) fungal agents were detected. Among them, 51(67.3%) were women and 21(32.7%) men. Most frequent age range were 40-50 and 60-70 for 20(27.8%) and 12(16.7%) respectively. Also the least frequency of age range was 80-90 for only one case. The most number of collected specimens was toe nail scrape with 49(68.1%) against finger nails 23(31.9%). All cases except one were impatient. Our cases of nail infections predisposed: trauma 27937.5%) followed by transmission 22(30.6%) and moistened skin 12(16.7%). Among all patients, 12(16.7%) represented nail hyperkeratosis and 10(13.9%) had dark colored nail. Also just one case showed paronichia and tissue edema. Main microscopic features investigated were filamentous molds with 30(41.7%), invasive dermatophyte bodies 21(29.2%) and invasive yeast elements 20(27.8%). The most common identified fungi causing agent were Aspergillus niger 10(13.9%), Candida albicans 8(11.1%) and Trichophyton mentagrophytis 9(12.5%) respectively.

Conclusion: According to literatures the majority of fungal nail infections caused by dermatophytes, although our study findings showed that saprophytic molds such as Aspergillus species are important a part of the causing agents as well as Candida species.

keywords: Dermatophyte, Molecular Epidemiology, RFLP.

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-40

Enzymatic and non-enzymatic virulence factors in clinical and environmental isolates of Aspergillus welwitschiae

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Background and aim: Background: Aspergillus welwitschiae is a member of Aspergillus section Nigri. It is now recognized as a leading cause of otomycosis, as well as a contributor to pulmonary and other forms of aspergillosis. The pathogenicity of this species is closely associated with the production of extracellular hydrolytic enzymes and biofilm formation, which facilitate host colonization, immune evasion, and tissue invasion. Aim: The aim this study was to characterize extracellular enzymes and non-enzymatic virulence factors, particularly biofilm formation, and to determine the distribution of mating type in clinical and environmental isolates of A. welwitschiae.

Methods: Methods: A total of 65 A. welwitschiae isolates (52 clinical and 13 environmental) were investigated for the production of catalase, proteinase, lipase, esterase, and urease. Biofilm formation was assessed in vitro, and the mating type genes (MAT1-1 and MAT1-2) were identified using molecular methods.

Results: Results: Esterase activity was detected in 98.5% of isolates, while urease activity was observed in 10.8%. All isolates showed catalase, proteinase, and lipase activities. Interestingly, mycelial catalase activity varied among isolates, with environmental strains displaying significantly higher levels of activity (mean = 3.61%). Biofilm formation was demonstrated by 95.4% of the isolates. Analysis of mating types showed an approximately random distribution, with MAT1-1 and MAT1-2 identified in 43.07% and 56.92% of isolates, respectively.

Conclusion: Conclusion: The high prevalence of hydrolytic enzyme production and biofilm formation highlights the substantial virulence potential of A. welwitschiae. These findings enhance our understanding of the pathogenic mechanisms of this emerging fungal species and underscore its clinical relevance.

keywords: Aspergillus welwitschiae, virulence factor, biofilm, mating type, Aspergillus section Nigri

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PM-41

Antifungal activity of biosynthesized zinc nanoparticles alone and in combination with nystatin against Candida albicans

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Background and aim: Thrush represents the most prevalent manifestation of candidiasis, characterized by the enhanced growth and proliferation of various Candida species, including Candida albicans, within the oral cavity. The present study was designed to assess the antifungal activity of zinc nanoparticles (ZnNPs) synthesized via a green method using Lavandula angustifolia extract, both individually and in combination with nystatin, against Candida albicans.

Methods: ZnNPs were synthesized through a microwave-assisted green synthesis approach employing L. angustifolia extract. The antifungal efficacy of the ZnNPs was evaluated by determining the minimum inhibitory concentrations (MICs) and minimum fungicidal concentrations (MFCs) using the broth microdilution technique, following the modified M27-A3 protocol for yeasts as recommended by the Clinical and Laboratory Standards Institute (CLSI). Additionally, the cytotoxic effects of the green-synthesized ZnNPs were investigated on human normal fibroblast-like gingival cells (HGF1-PI1) and human epithelial-like oral cancer cells (KB) utilizing the MTT assay (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide).

Results: Characterization revealed that the ZnNPs exhibited a predominantly spherical morphology with grains of varying lengths. The combination of ZnNPs and nystatin demonstrated the most effective antifungal activity, with MIC and MFC values of 0.204 µg/ml and 0.250 µg/ml, respectively. Statistical analysis indicated that this combination significantly enhanced antifungal efficacy against C. albicans compared to nystatin alone (p 0.001). The half-maximal cytotoxic concentration (CC50) of ZnNPs was determined to be 172.3 µg/ml for normal HGF1-PI1 cells and 83.2 µg/ml for KB cancer cells.

Conclusion: The findings suggest that ZnNPs, particularly when combined with nystatin, exhibit potent antifungal effects against C. albicans. Moreover, the green-synthesized ZnNPs demonstrated selective cytotoxicity, being non-toxic to normal cells while exerting cytotoxic effects on cancerous cells. Nonetheless, further research is warranted to elucidate the underlying mechanisms and to evaluate systemic toxicity, especially within clinical contexts.

keywords: Thrush, Candida, in vitro, treatment, cytotoxicity

PM-42

Comparison of the EUCAST and CLSI Broth Microdilution Methods for in- vitro antifungal agents against Aspergillus flavus isolated from hematologic malignant patients

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Background and aim: Background Invasive aspergillosis (IA) is the major agents of Life-threatening fungal infections, still faces with management challenges. This infection is a considerable public health concern among immunocompromised patients. According to discrepancies in break points (BPs) between European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the Clinical and Laboratory Standards Institute (CLSI) based on broth microdilution (BMD) and significant impact on susceptibility interpretation of clinical isolates, prompted us to investigate and compare the EUCAST and CLSI antifungal susceptibility testing (AFST) methods for amphotericin B and triazoles (voriconazole, itraconazole, posaconazole, isavuconazole) against Aspergillus species isolated from patients with hematological malignancies.

Methods: Methods Overall, 160 hemato-oncological patients with clinical suspicion of invasive fungal infections (IFIs) based on EORTC/MSG criteria, were investigated during hospitalization at two tertiary care centers in Tehran, Iran (Imam Khomeini Hospital complex and Shariati Hospital) between April 2022 and April 2023. The causative agents were primarily identified using direct examination and culture methods. Only proven/probable IA cases with positive Aspergillus culture were included for further molecular identification by PCR & sequencing of the β-tubulin regions. The AFST against Aspergillus isolates was performed according to the guidelines of the CLSI M38-A2 and EUCAST E. Def 11.0 BMD. Subsequently, The MICs results of the two methods were statistically calculated using SPSS version 25.0 (SPSS, Chicago, IL, USA). Discrepancies of more than 2 dilutions among MIC results were used to calculate the EA between the two methods. Also, categorical agreement (CA) MIC were determined.

Results: Results IA was confirmed in 18 out of 160 (11.25%) immunocompromised patients, (7 proven and 11 probable cases) with etiological agent of A. flavus. Ten patients (55.5%) were female and 8 (44.4%) were male with the age range of 14–67 years. AFST revealed that posaconazole had the lowest MIC values (MIC range: 0.016–0.25 µg/mL) while amphotericin B exhibited the highest MIC values (MIC range: 0.125–1 µg/mL) based on CLSI and EUCAST BMD guidelines. Furthermore, for all drugs, the GM, MIC90 and MIC50 values compatible by both methods except for isavuconazole and itraconazole which MIC values differed by 1-fold. Overall, the EAs the two methods were variable, among antifungal drugs, amphotericin B and isavuconazole were the highest (94%) and itraconazole was the lowest (55%) agreement. The CA for all antifungal drugs against A. flavus was 100% consistent.

Conclusion: Conclusion The results indicate that all A. flavus isolates were within the wild-type MIC range. Posaconazole was the most effective agent according to both EUCAST and CLSI BMD methods. Furthermore, a high level essential and categorical agreement between the two methods was confirmed while, the EUCAST and CLSI BMD produce comparable results.

keywords: Keywords EUCAST, CLSI, Aspergillus, Aspergillus flavus, Susceptibility testing

PM-43

Investigation of various medically important fungal species isolated from the mycobiome of recreational beaches in Hormozgan province.

ابوالفضل سراوانی [1] © Ⓟ

[1] دانشجو

Background and aim: Coasts are economically valuable recreational areas, and Hormozgan province is particularly important in this regard with its 370 km of coastline. The frequency of human allergic and fungal symptoms in recent decades has led the WHO to publish its guidelines for recreational aquatic environments and recommend their review.

Methods: Sampling was carried out monthly (once a month) for three months in 1402, depending on the recreational situation. B) Microscopic and macroscopic identification of isolates A. Yeasts: - Chromogenic medium - Macroscopic and microscopic morphology - D1/D2 sequencing B: Molds - Macroscopic and microscopic morphology - ITS sequencing Drug susceptibility testing and identification of resistant strains

Results: Hormozgan Penicillium citrinum 3 chrysogenom 2 Aspergillus flavus/oryzae 7 terreus 7 fumigatus 7 niger 11 tubingensis 8 unguis 1 sydowii 2 nomius 3 parasiticus 2 Fusarium sarocladium 1 Black fungi Stachybotrys chartarum 1 Epicoccum 1 Other Trichoderma asperellum 1 Simplicillium sp 2 Unknown 4

Conclusion: Regarding the distribution of different fungal species, Aspergillus species A. terreus and A. flavus/oryzae, with the highest number of isolations, are the most common antifungal-resistant fungi on the recreational beaches of Hormozgan province. These findings indicate a serious concern regarding the occurrence of these fungal infections in beach visitors.

keywords: hormozgan _ fungal _ beach

PM-44

A hidden challenge in identifying Candida species using PCR-RFLP

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Background and aim: PCR-RFLP targeting the ITS region is known as a rapid, inexpensive and reliable method for the identification of Candida species. Previous studies have found this method to be adequate for epidemiological studies and clinical diagnosis. However, the fundamental question is what the true error rate of this method is when faced with real clinical samples and RFLP always shows what it is. This study was designed to answer this question.

Methods: In this study, 60 Candida isolates isolated from saliva samples of elderly people with risk factors for diabetes, cancer, and dentures were first identified by PCR-RFLP (using ITS1 and ITS4 primers and the restriction enzyme MspI). Then, contrary to the usual practice of sending only cases with ambiguous patterns for confirmation, all 60 isolates were sent for trench sequencing to calculate the true concordance between the two methods accurately.

Results: Of the 60 isolates submitted for sequencing, RFLP results were in complete agreement with sequencing in 54 cases (90%). However, 6 isolates (equivalent to 10% of the cases sequenced) had a mismatch between the RFLP result and sequencing. In other words, in 10% of cases, the RFLP method identified a different species than the one indicated by sequencing. In 4 cases (6.7%), the mismatch was due to mixed colonization of two species, where the RFLP pattern revealed only the dominant species and hid the minority species. In 2 cases (3.3%), silent mutations in the MspI cleavage site caused a change in the banding pattern to that of the other species. A notable finding was that in 2 of these 6 isolates, the RFLP pattern was fully consistent with the standard Candida albicans pattern, but sequencing identified Kodamaea ohmeri and Magnosiomyces capitatus species, respectively – both species with different resistance patterns

Conclusion: This study shows that despite good performance in primary screening, PCR-RFLP has a discrepancy with sequencing in about 10% of cases. This error rate is not negligible in high-risk patients such as the elderly with diabetes, cancer, or dentures, because misdiagnosis of the species can lead to incorrect treatment selection and treatment failure. Therefore, confirmation of RFLP results by sequencing is recommended, especially in clinically sensitive cases.

keywords: Diagnostic challenge, PCR-RFLP, Candida, sequencing, ITS

PM-45

Antifungal Peptides as Potent Inhibitors of Fungal Biofilm Formation

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Background and aim: Fungal biofilms pose significant challenges in clinical settings due to their high resistance to conventional antifungal agents. Antifungal peptides (AFPs) have emerged as promising therapeutic agents capable of disrupting biofilm formation and promoting fungal clearance. This study evaluates the efficacy and mechanisms of selected AFPs against clinically relevant fungal biofilms.

Methods: AFPs from diverse families, including defensins, cathelicidins, and synthetic derivatives, were tested against Candida albicans, Candida glabrata, and Aspergillus fumigatus. Biofilm inhibition assays were performed using crystal violet staining, and structural effects were examined via scanning and confocal laser microscopy (SEM/CLSM). Cell viability within biofilms was quantified in the presence of AFPs.

Results: The tested AFPs demonstrated significant inhibition of biofilm formation at sub-MIC concentrations. Microscopy revealed disruption of the extracellular matrix and reduced cell adhesion. Mechanistic studies indicated induction of oxidative stress and membrane perturbation as primary modes of action.

Conclusion: AFPs effectively inhibit fungal biofilm formation and disrupt established biofilms, offering a potential adjunct or alternative to standard antifungal therapy. Further studies on pharmacokinetics and in vivo efficacy are warranted to support clinical application.

keywords: antifungal peptides, fungal biofilm, Candida albicans, extracellular matrix, biofilm

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PM-46

Antifungal Peptides Against Candida albicans: Emerging Strategies for Biofilm Inhibition and Antifungal Resistance Control

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Background and aim: Candida albicans remains one of the most clinically important opportunistic fungal pathogens, particularly due to its ability to form structured biofilms on mucosal surfaces, catheters, prosthetic devices, and other medical materials. Biofilm formation markedly reduces susceptibility to conventional antifungal agents and contributes to persistent or recurrent infections. In recent years, antifungal peptides have attracted increasing attention as promising molecules with rapid activity, membrane-targeting properties, antibiofilm effects, and potential synergy with existing antifungal drugs. This review aimed to summarize the current evidence regarding the role of antifungal peptides in controlling C. albicans growth and biofilm-associated infections.

Methods: A focused review of recent experimental and review studies was conducted using relevant scientific databases. Studies evaluating natural, host-derived, microbial, and synthetic antifungal peptides against planktonic and biofilm forms of C. albicans were considered. The main outcomes included antifungal activity, inhibition of adhesion and biofilm formation, disruption of mature biofilms, mechanism of action, and potential clinical applicability.

Results: Available evidence indicates that antifungal peptides can inhibit C. albicans through multiple mechanisms, including disruption of fungal cell membranes, increased membrane permeability, induction of reactive oxygen species, interference with hyphal transition, and inhibition of extracellular matrix development. Several peptides, including histatin-derived peptides, defensins, cathelicidin-related peptides, and synthetic peptide analogues, have demonstrated significant activity against both planktonic cells and biofilm-associated C. albicans. Importantly, some peptides showed the ability to reduce early adhesion, suppress biofilm maturation, and enhance the susceptibility of biofilm cells to conventional antifungal agents. However, challenges such as peptide instability, possible cytotoxicity, proteolytic degradation, and limited in vivo data remain major barriers to clinical translation.

Conclusion: Antifungal peptides represent a promising class of antibiofilm agents against Candida albicans. Their multi-target mechanisms, rapid action, and ability to interfere with biofilm development make them attractive candidates for future antifungal therapy, especially in resistant and device-associated candidiasis. Further studies focusing on peptide optimization, toxicity reduction, drug delivery systems, and clinical validation are required before their routine clinical application.

keywords: Candida albicans; Antimicrobial Peptides; Antifungal Agents; Biofilms; Drug Resistance

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PM-47

Synthesis of a Silver–Capsaicin Nanocomposite as a Novel Antifungal Agent Against Candida albicans

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Background and aim: Fungal infections caused by Candida albicans represent a significant clinical challenge, and their treatment is increasingly limited by the emergence of antifungal drug resistance. The incorporation of natural antimicrobial compounds into nanotechnology-based formulations may provide an effective strategy for enhancing therapeutic efficacy. Capsaicin, a bioactive natural metabolite, has demonstrated various antimicrobial properties. This study aimed to evaluate the antifungal activity of a silver–capsaicin nanocomposite against Candida albicans.

Methods: A silver–capsaicin nanocomposite was synthesized and characterized. Its antifungal activity against Candida albicans was evaluated by determining the minimum inhibitory concentration (MIC) and minimum fungicidal concentration (MFC).

Results: The results demonstrated that the silver–capsaicin nanocomposite effectively inhibited the growth of Candida albicans and significantly reduced fungal cell viability. Furthermore, the nano formulation exhibited greater antifungal efficacy compared with free capsaicin, indicating enhanced activity through nanocomposite formation.

Conclusion: Based on the findings of this study, the silver–capsaicin nanocomposite possesses considerable potential for inhibiting Candida albicans and may serve as a promising candidate for the development of novel antifungal agents. The advancement of such nanoformulations could facilitate the more effective application of natural bioactive compounds in the management of fungal infections.

keywords: Candida albicans, capsaicin, silver–capsaicin nanocomposite

PM-48

The mycological and molecular study of Pneumocystis jiroveci pneumonia among HIV and non-HIV immunocompromised patients hospitalized in pulmonary units in Guilan, Northern Iran

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Background and aim: Pneumocystis jirovecii pneumonia (PJP) is a serious infection that usually affects those with a weak immune system. Since the prevalence of this infection in Iran and in the world is not clearly defined, the present study aimed to evaluate the incidence, clinical spectrum, and demographic characteristics of PJP among HIV and non-HIV immunocompromised patients.

Methods: Bronchoalveolar Lavage (BAL) specimens were obtained from 3 groups of immunocompromised patients, including acquired immunodeficiency syndrome (AIDS) patients, diabetic patients, and patients receiving immunosuppressive therapies. All were hospitalized in pulmonary units. The specimens were examined using microscopic methods (Giemsa and calcofluor white staining) and the nested-PCR technique based on mtLSU-rRNA gene.

Results: A total of 120 BAL samples were collected. From 12.5% (5 from 40) of HIV-infected patients, 5% (2 from 40) of patients receiving immunosuppressive therapies, and 2.5% (1 from 40) of diabetic patients Pneumocystis jiroveci was isolated. There was not any association between the prevalence of PJP and the patient's gender (p= 0.557) and age (p= 0.681). Fever and dyspnea (n=7, 87.5%), nonproductive cough and abnormal auscultation sound (n=5, 62.5%), and also chills and weight loss (n=2, 25%) were the documented clinical symptoms of PJP. Also, the results showed that none of the samples had positive results for P. jiroveci with microscopic tests while using the nested-PCR method 8 samples had positive results.

Conclusion: Since PJP often causes symptoms that are similar to other illnesses, such as the flu or tuberculosis, clinical and laboratory findings should be used simultaneously for making the final decision on drug administration.

keywords: Pneumonia, Pneumocystis, Human immunodeficiency virus

PM-49

Concurrent Pulmonary Aspergillus flavus and Lophomonas blattarum Infection in a Patient with Lung Cancer: A Case Report

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Background and aim: Opportunistic respiratory infections are common in patients with underlying malignancies, particularly lung cancer. However, the simultaneous presence of an invasive fungus such as Aspergillus and a rare protozoan parasite like Lophomonas in the lower respiratory tract is an exceptional finding. This case report describes a patient with lung cancer who developed a dual infection with both pathogens.

Methods: A 64-year-old man with a two-year history of lung cancer presented to the hospital with high fever, chest pain, severe dyspnea, and cough. He was admitted for further evaluation. Direct microscopic examination of a bronchoalveolar lavage sample stained with KOH revealed fungal hyphae. Additionally, motile flagellates morphologically consistent with Lophomonas were observed in the same direct smear.

Results: Subsequent culture on specific media and molecular diagnostics confirmed the presence of both Lophomonas blattarum and Aspergillus flavus. The patient was treated with the antifungal agent voriconazole. His clinical condition improved significantly, and he was discharged from the hospital in stable condition.

Conclusion: This case report highlights a rare mixed opportunistic coinfection of Aspergillus flavus and Lophomonas sp. in a patient with lung cancer. The detection of Lophomonas on a routine KOH mount alongside fungal hyphae is a noteworthy diagnostic clue. Clinicians should be aware of possible mixed infections in immunocompromised patients to ensure appropriate antifungal and antiparasitic therapy.

keywords: Lung cancer, Aspergillus flavus, Lophomonas, coinfection, Case report.

PM-50

Chronic Tinea Capitis in an 11-Year-Old Boy Caused by Microsporum ferrugineum with Poor Response to Terbinafine: A Case Report

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Background and aim: Tinea capitis is a common fungal infection in children, typically caused by dermatophytes such as Microsporum and Trichophyton species. Microsporum ferrugineum is an anthropophilic fungus that can cause chronic scalp infections, often refractory to common antifungal therapies. We report a case of persistent tinea capitis in a child who did not respond to standard treatment.

Methods: An 11-year-old boy presented with pruritus and hair loss affecting the temporal region and the area above the left ear. The lesions involved hair shafts and scaling of the scalp. The symptoms had been present for more than one year. The patient had previously received terbinafine therapy, with no clinical improvement. Wood's lamp examination revealed a blue-green fluorescence.

Results: Direct microscopic examination of the clinical sample showed spindle-shaped macroconidia containing 3–5 cells, along with ectothrix arthroconidia. Fungal culture showed poor growth after two weeks; after an additional two weeks, a larger colony developed, but only sterile hyphae were observed. DNA was extracted, and PCR amplification of the ITS region was performed. Sequencing and BLAST analysis against the NCBI database identified the isolate as M. ferrugineum. Follow-up revealed that the patient was not completely cured after the initial course of terbinafine. However, after referral to another physician and receiving a different antifungal regimen, complete resolution was achieved.

Conclusion: This case highlights that M. ferrugineum may cause chronic tinea capitis unresponsive to terbinafine. Molecular methods such as ITS sequencing are valuable for accurate identification, especially when culture yields limited growth or sterile hyphae. Complete cure may require alternative antifungal agents and appropriate follow-up.

keywords: Microsporum ferrugineum, tinea capitis, case report, terbinafine resistance, ITS sequencing

PP-1

Role of Type III Interferons (lambda) in Balancing Mucosal Defense in the context of parasitic infections

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Background and aim: Background: Parasitic infections are a significant global health issue that the major entry path of parasites is through mucosal surfaces. The studies showed that type III interferons (IFNs λ) are key mediators of immune responses. In parasitic infections, IFN λ produced mainly at epithelial barriers, induces a specific set of interferon-stimulated genes (ISGs) that boost antiparasitic defenses without causing widespread systemic inflammation. aim: This review examines IFNs λ's diverse functions in parasitic infections, focusing on their role in antiparasitic responses and immune modulation. Understanding these effects may lead to new therapeutic strategies that may be controlling IFN λ signaling would

Methods: Methods: Literature from Google Scholar, ScienceDirect, PubMed, and Scopus (2000–2025) was reviewed

Results: Results: IFNs λ play an important role in parasitic infections. In Toxoplasma gondii, IFN λ signaling in intestinal epithelial cells and neutrophils limits parasite spread and enhances humoral immunity. In Cryptosporidium infections, IFN λ reduces parasite loads and improves survival via STAT1- dependent pathways. In Leishmania donovani, when infected macrophages were treated with recombinant IFN-λ3 during or immediately after parasite entry, intracellular parasite loads were significantly reduced. However, in Malaria, IFN λ4 is linked to increased susceptibility to Plasmodium falciparum. Besides these, in helminth infections, IFNs λ levels are elevated suggesting their role in modulating inflammation and enhancing mucosal barriers.

Conclusion: Conclusion: Understanding IFNs λ's complex effects in parasitic infections may lead to new therapeutic approaches that enhance host defenses while reducing inflammation.

keywords: Keywords: Type III Interferons, Interferons-λ, Parasitic Infections, Mucosal Immunity

PP-2

Molecular Identification of Trichomonas vaginalis in infertile men and women with spontaneous abortion

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Background and aim: Trichomonas vaginalis is a flagellated protozoan parasite. It is the causative agent of the sexually transmitted disease trichomoniasis, which is considered one of the most common sexually transmitted infections worldwide. Given that most studies have focused on women and evidence regarding infertile men and women with spontaneous abortion is limited, the present study aimed to molecular investigation of the prevalence of T. vaginalis in infertile men and women with spontaneous abortion in northwestern Iran in 2024.

Methods: The Ethics Committee of Ardabil University of Medical Sciences approved this cross-sectional study. A total of 320 samples were collected based on previous prevalence estimates. Semen samples from infertile men and vaginal swabs from women with spontaneous abortion were collected after informed consent and stored at −30 °C. DNA was extracted using the Qiagen kit. PCR targeting the 18S rRNA gene of T. vaginalis was performed with specific primers, and products were analyzed by agarose gel electrophoresis.

Results: In this descriptive cross-sectional study conducted in 2024, 320 samples (160 women and 160 men) were collected. PCR analysis revealed no amplification of the T. vaginalis 18S rRNA gene in any of the samples.

Conclusion: The absence of T. vaginalis in this study suggests a low prevalence or possible absence of infection in this region. These results may reflect good personal hygiene, safe sexual practices, and limited circulation of the parasite locally.

keywords: T. vaginalis, infertile men, spontaneous abortion, 18S rRNA, Ardabil

PP-3

Evaluation of Glucantime loaded-PLGA in a murine model of cutaneous Leishmaniasis

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Background and aim: Cutaneous leishmaniasis affects over 200 million people worldwide. Due to limited efficacy and side effects of conventional drugs, nanoparticle-based delivery systems and immunotherapy have gained attention for treatment.

Methods: PLGA-Glucantime nanoparticles were synthesized using the W1/O/W2 method. Their size, surface charge, encapsulation efficiency, and protein loading were measured. BALB/C mice were infected with Leishmania and treated with PLGA-Glucantime. Cytokines IFN-γ, IL-2, IL-10, and IL-4 were measured, and wound tissues were examined pathologically.

Results: Nanoparticles averaged 200 nm, with 43.6±1.55% encapsulation efficiency and 3.14±0.26 µg/mg loading. Glucantime-PLGA treatment increased IFN-γ and IL-2 levels in serum and cell cultures. Pathology revealed mild inflammation in treated groups, indicating reduced tissue damage compared to untreated controls.

Conclusion: PLGA-Glucantime enhances immune response and reduces tissue damage, showing better therapeutic potential than Glucantime alone in cutaneous leishmaniasis.

keywords: Glucantime, PLGA, Nanoparticles, Cutaneous Leishmaniasis, Immunotherapy

PP-4

Prevalence of Anti-Toxoplasma gondii Antibodies in Young Iranians: The CASPIAN III Study

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Background and aim: Toxoplasmosis is a worldwide neglected tropical and sub-tropical infection caused by Toxoplasma gondii (T. gondii). Most of the previous studies on the seroprevalence of T. gondii in Iran have been done at provincial level and on specific populations, including pregnant females. Socioeconomic parameters are associated with the prevalence of this disease. In this study, the authors evaluated the presence of anti-T. gondii antibodies and the related risk factors in Iranian adolescents.

Methods: This was a cross-sectional study on serum samples from the third Iranian national school-based survey (the CASPIAN III study), which included 10- to 18-year-old students. Participants were selected by multistage sampling from 27 Iranian provinces. In this study, serum samples of 882 adolescents from 16 provinces were randomly selected and examined for IgG and IgM antibodies against T. gondii by the Enzyme Linked FluorescentAssay(ELFA).Demographic and socioeconomicfactors related to T. gondii infection were gathered using the global school-based health survey (GSHS) questionnaire.

Results: Theoverall T. gondii IgG andIgM seropositivitywas 56.3% (95% CI: 53.4 to 59.2) and 3.7% (95%CI: 2.7 to4.9), respectively. Inmultivariate logistic regression model, family size was statistically associated with seroprevalence of anti T. gondii IgG. Living in crowded households (households with more than 4 people vs. households with less than 4 people) increased the risk of seropositivity of T. gondii (OR: 1.40, 95% CI: 1.10 to 1.99).

Conclusion: The results of this study indicate that about 40% of Iranian adolescents have not had contact with the T. gondii, thus the risk of congenital toxoplasmosis might be high in young females. Also, household size was the main factor associated with T. gondii infection. Preventive strategies and health education in Iranian adolescents are recommended.

keywords: Toxoplasmosis, Seroprevalence, Risk Factor, Iran

PP-5

Respiratory involvement by Toxoplasma gondii in a multiple myeloma patient: A case report

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Background and aim: Toxoplasma gondii (T. gondii) is responsible for parasitic infection, which is generally asymptomatic, soft in immunocompetent hosts and severe, life-threatening disease in immunocompromised individuals. Pulmonary toxoplasmosis is an uncommon cause of severe pneumonia resulting in respiratory failure.

Methods: This is a case report of a 49-year-old Iranian male with multiple myeloma, who was admitted in emergency department with fever, chills and vomiting.

Results: T. gondii was detected in his bronchoalveolar lavage (BAL) fluid by laboratory tests (Giemsa stain and qPCR). Unfortunately, before starting toxoplasmosis directed therapy the patient expired.

Conclusion: This case emphasizes on early detection and treatment in high-risk patients and particularly those on chemotherapy to avoid fatal outcome. Furthermore, advanced prophylactics like Co-trimoxazole prophylaxis should be implemented in high-risk individuals, especially in those exposed to immunosuppression treatments.

keywords: Bronchoalveolar lavage, Co-trimoxazole, Immunocompromised patients, Lung, Multiple myeloma, Pulmonary toxoplasmosis,

PP-6

Co-infection of Lophomoniasis and Anthracosis in a Chronic Spinal Cord Injury person

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Background and aim: Lophomoniasis is an emerging parasitic pulmonary infection caused by protozoan Lophomonas spp. that its diagnosis is very challenging.

Methods: Chronic spinal cord injury (SCI) leads to impaired pulmonary clearance and recurrent infections. Also anthracosis, a form of pneumoconiosis from carbon dust inhalation, further compromises lung architecture.

Results: We report a unique case of a 60-year-old male with about 40-year history of complete SCI (related to a mining accident), coronary stent, urinary incontinence, and complete dependence for activities of daily living. He presented with a persistent, productive cough for three months following a minor upper respiratory tract infection. Chest imaging was consistent with anthracosis. Bronchoscopy for his was done, and microscopic examination shown numerous trophozoites of Lophomonas spp.. The patient was treated with metronidazole, resulting in significant improvement of cough and sputum production.

Conclusion: This is the first reported case of pulmonary lophomoniasis in a patient with concurrent chronic SCI and anthracosis. Early diagnosis via bronchoscopy and treatment with metronidazole can lead to satisfactory outcomes. It highlights the importance of considering atypical parasitic infections like lophomoniasis in patients with chronic respiratory symptoms and underlying structural lung disease (such as SCI) by pulmonologists and rehabilitation specialists.

keywords: Lophomonas spp., Lophomoniasis, Spinal Cord Injuries, Anthracosis, Bronchoscopy, Metronidazole

PP-7

Evaluation of the Hydroalcoholic Extract of Echinophora cinerea on the RH Strain of Toxoplasma gondii under In Vitro and In Vivo Conditions

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Background and aim: Toxoplasmosis is a parasitic infection caused by Toxoplasma gondii, commonly transmitted domestically through the ingestion of food contaminated with the parasite. Current therapeutic agents for toxoplasmosis are associated with adverse effects and often fail to achieve complete eradication of the infection. Given the clinical significance of the disease, the discovery of novel, safe, and effective treatments is imperative. Based on the established biological properties of the hydroalcoholic extract of Echinophora cinerea, this study aimed to evaluate its in vitro and in vivo efficacy against Toxoplasma gondii (RH strain).

Methods: The hydroalcoholic extract of E. cinerea was prepared. In vitro assays were conducted by incubating 200,000 tachyzoites with various concentrations of the extract (3.125, 6.25, 12.5, 25, 50, and 100 µg/mL) for three hours. The viability of tachyzoites was assessed using flow cytometry with propidium iodide staining. For the in vivo study, acute toxoplasmosis was induced in BALB/c mice. The mice were divided into seven groups (n=5): a negative control group, a positive control group (infected, untreated), a vehicle control group (for toxicity assessment), and four treatment groups receiving daily oral gavage of the extract at doses of 12.5, 25, 50, and 100 mg/kg. Survival rates were monitored and recorded daily.

Results: In vitro flow cytometry analysis demonstrated that the hydroalcoholic extract of E. cinerea induced a dose-dependent mortality in T. gondii tachyzoites. At the highest concentration tested (100 µg/mL), the extract achieved over 98% parasite mortality. In the in vivo model, mice treated with higher doses of the extract (50 and 100 mg/kg) exhibited a significant increase in survival time compared to the infected, untreated control group.

Conclusion: The findings of this study indicate that the hydroalcoholic extract of E. cinerea possesses potent lethal activity against T. gondii tachyzoites in vitro. Furthermore, in vivo results suggest that the extract, characterized by low toxicity, can significantly enhance the survival of mice with acute toxoplasmosis. The efficacy was confirmed to be dose-dependent in both experimental settings, highlighting its potential as a promising therapeutic candidate.

keywords: Toxoplasma gondii, Echinophora cinerea, in vitro, in vivo, flow cytometry

PP-8

Morphological and Molecular identifcation of lophomoniasis in North of Iran: A National Registry Based Study

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Background and aim: This registry-based cross-sectional study involved patients with respiratory symptoms referred for bronchoscopy, using data from the Iranian National Registry Center for Lophomoniasis (INRCL) between June 2024 and December 2025.

Methods: Flexible fiberoptic bronchoscopy was done, with bronchoalveolar lavage (BAL) samples taken for analysis.

Results: Microscopic examinations confirmed the presence of Lophomonas trophozoites in 28% of cases, predominantly affecting older males. Common symptoms included cough, sputum production, and dyspnea. Diabetes, heart disease, and tuberculosis were prevalent comorbidities. Disease severity varied; most were classified as "Negative," with few in "Mild" or "Moderate" groups.

Conclusion: Increasing evidence suggests Lophomonas is an established respiratory pathogen in Iran, necessitating PCR-based diagnosis due to diagnostic challenges with microscopy. There is a male predominance and age-related incidence. Our study highlights the need for heightened awareness of Lophomonas in respiratory cases and supports mixing PCR in routine diagnostics to improve patient outcomes and public health responses.

keywords: bronchoscopy, Lophomonas, Bronchoalveolar lavage, PCR

PP-9

Knowledge, attitude, and practice towards cutaneous leishmaniasis among residents of western Khuzestan Province, Iran

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Background and aim: Leishmaniasis is a neglected parasitic disease prevalent in tropical and subtropical areas and remains a significant public health issue in Iran. This study aimed to assess the knowledge, attitudes, and practices (KAP) related to cutaneous leishmaniasis (CL) among residents of western Khuzestan.

Methods: This cross-sectional descriptive-analytical study was carried out among residents in the cities of Susangerd, Bostan, Hoveyzeh, Hamidiyeh and Shush in western Khuzestan. Data were gathered using a researcher-designed questionnaire consisting of 31 questions divided into four sections covering demographic information, knowledge, attitudes, and practices concerning CL.

Results: Out of 780 participants (48.6% male, 51.4% female), 31.8% held university degrees. Less than half of the respondents had awareness of CL. Skin lesions (44.1%) and sand flies (59.6%) were most frequently recognized as the disease's primary symptom and vector, respectively. Only 23.2% could correctly distinguish sand flies from other insects like flies and mosquitoes. Awareness about sand fly breeding sites and biting times was low, though 44.1% identified summer as the peak season for the disease. The majority viewed bed nets as important health tools (69.1%), with 73.1% supporting health education as an effective preventive measure and 71.1% endorsing bed net use for protection. Common preventive practices included proper waste disposal and avoiding travel to endemic areas.

Conclusion: Overall, attitudes, and practices regarding CL in the studied population were good, but notable gaps in knowledge remain. The limited understanding of the disease and its vector highlights the need for targeted health education and awareness programs to reduce future CL risk.

keywords: Cutaneous Leishmaniasis, knowledge, attitudes, practices, Khuzestan

PP-10

Molecular study of the prevalence of Trichomonas vaginalis in symptomatic women referring to health centers in the center of Mazandaran province 1403-1404

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Background and aim: Trichomoniasis is a protozoan infection of the lower genitourinary tract in men and women. It usually occurs during the reproductive years and is almost always transmitted through sexual contact. Its infection rate varies from 2 to 90% in different parts of the world. Given that the diagnosis of trichomoniasis is a warning sign for other sexually transmitted diseases that can coexist, in this study we investigated the rate of infection with Trichomonas vaginalis in symptomatic women referring to health centers in the center of Mazandaran province.

Methods: This study was conducted on 150 women with vaginal discharge referring to the health center in the center of Mazandaran province. The study method was approved by the university ethics committee. Sampling: Two swab samples of vaginal discharge were collected from each individual by an experienced and skilled nurse to examine for Trichomonas vaginalis infection. One swab was collected for wet sampling and Papanicolaou staining parasitological tests, and the other was collected for molecular genomic amplification tests. Chi-square and univariate regression tests were performed to measure the relationship between the relevant variables between the two groups of cases and controls, and statistically significant variables were entered into multiple logistic regression statistical analysis to control for the effect. All findings were considered significant at a level of less than 0.05.

Results: In total, 150 Pap smear samples were collected and found to be infected with Trichomonas vaginalis. Based on age groups, 50 were in the age group less than 30 years, 46 in the age group 31-45 years, and 54 in the age group greater than or equal to 45 years. The frequency of samples infected with Trichomonas vaginalis was 12.6%.

Conclusion: In this study, the prevalence of trichomoniasis was 12.6% among 150 patients referred using PCR. In the health sector's planning, special attention was paid to the health of the female population, especially in terms of reproductive system diseases, so that by increasing health services and personal health education among them, we could witness a reduction in such diseases.

keywords: Trichomonas vaginalis, symptomatic women, molecular methods

PP-11

Evaluation of toxoplasmosis as a potential risk in individuals with chronic liver diseases (CLDs)

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Background and aim: Toxoplasma gondii is an intracellular parasite that is highly prevalent in Iran and developing countries. Given that this protozoan, as an opportunistic parasite, causes mild or asymptomatic disease in healthy individuals and, after the acute phase, enters a latent phase and forms cysts in tissues, there is a hypothesis that it may cause liver diseases. Therefore, this study aimed to investigate the relationship between Toxoplasma gondii infection and liver diseases in Mazandaran province.

Methods: The study was conducted as a case-control study on 118 individuals with liver diseases and 118 healthy individuals. The data collection tool included a questionnaire on personal information, possible confounding variables, questions related to clinical characteristics of liver diseases, and possible ways of contracting Toxoplasma gondii infection. After blood sampling from individuals, the levels of Toxoplasma gondii IgM and IgG antibodies were measured by ELISA. Chi-square and univariate regression tests were performed to measure the relationship between variables related to liver disorders between the two groups of cases and controls. All findings were considered significant at a level of less than 0.05.

Results: In total, out of 118 blood samples from the case group, IgG antibody test was positive in 38 blood samples and negative in 80. In the control group, out of 118 samples, 6 samples tested positive and 112 samples tested negative. According to the results of the K-square test, this difference in the percentage of positive cases between the two groups was significant and it can be said that there is a statistically significant relationship between the IgG antibody result and the group (case/control) (P0.05). Out of 230 blood samples from the case and control subjects in this study, no positive IgM test samples were reported.

Conclusion: According to the results of the present study, infection with the parasite Toxoplasma gondii can be recognized as one of the risk factors associated with developing liver disorders. Therefore, prevention and rapid treatment of this infection may be able to slightly reduce the adverse personal, economic and social effects of this disease at the individual and macro-society levels.

keywords: Toxoplasma gondii, liver disorders, IgG, IgM

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PP-12

Toxoplasma gondii modulates immune responses and mitigates type 1 diabetes progression in a streptozotocin-induced rat model

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Background and aim: Type 1 diabetes (T1D) arises from immune-mediated destruction of pancreatic β-cells, a process that can be modelled in rats using streptozotocin (STZ). Toxoplasma gondii is known for its strong immunomodulatory effects, including shifting immune responses toward regulatory pathways that may suppress autoimmunity. These properties suggest the parasite could influence the progression of T1D. This study aimed to determine whether T. gondii infection can modulate immune responses and reduce STZ-induced diabetes severity by assessing changes in glycaemia, insulin levels, pancreatic histopathology and systemic cytokine/T-cell profiles.

Methods: Rats were divided into control, STZ-diabetic, and STZ + T. gondii groups. Diabetes was induced with streptozotocin, and T. gondii infection was established using a low-virulence strain. Animals were monitored for fasting blood glucose, weight changes, and serum insulin. At the study endpoint, pancreatic tissues were examined for β-cell preservation and insulitis. Immune profiling included flow cytometry for regulatory T cells ($CD4^+CD25^+FoxP3^+$) and ELISA measurement of cytokines such as IFN-γ, IL-17, IL-10 and TGF-β. Data were statistically analyzed with significance set at p0.05.

Results: STZ-treated rats developed marked hyperglycaemia, weight loss, reduced insulin and severe pancreatic insulitis. In contrast, rats infected with T. gondii showed significantly lower blood glucose, higher insulin levels and notable preservation of β-cells. Histology revealed reduced inflammatory infiltration and milder insulitis. Immune analysis demonstrated increased regulatory T cells and elevated IL-10/TGF-β, alongside decreased IFN-γ and IL-17 compared with the STZ-only group. These immune shifts correlated with improved pancreatic integrity and metabolic outcomes. No significant mortality occurred with the low-virulence strain.

Conclusion: T. gondii infection effectively mitigated STZ-induced T1D progression by promoting a regulatory and anti-inflammatory immune environment. Enhanced Treg activity and increased IL-10/TGF-β production were associated with preserved β-cell mass and improved insulin secretion, while reductions in proinflammatory cytokines limited pancreatic damage. These findings highlight the parasite's potent immunomodulatory capacity and suggest that identifying non-infectious, parasite-derived molecules with similar effects could offer a novel therapeutic strategy for autoimmune diabetes. Further research is necessary to clarify mechanisms and evaluate translational potential.

keywords: Toxoplasmosis, Type 1 diabetes mellitus (T1DM), Immune modulation, Cytokine profile

PP-13

Evaluating the Knowledge and Practice of Physicians Regarding Blastocystis hominis

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Background and aim: Blastocystis hominis is an enteric protozoan in humans and animals. This study aimed to assess the knowledge and practice of physicians about B. hominis.

Methods: This study was performed on physicians working in Ahvaz County, using a convenience sampling method from January to June 2020. Data were collected through face-to-face interviews and an electronic questionnaire. Descriptive statistics, including frequencies and percentages, were calculated for all variables. P-values 0.05 were considered significant.

Results: Our results showed that of the 352 physicians, 64.2% and 58.0% knew that B. hominis might cause abdominal pain and diarrhea, respectively, but their knowledge was poor about the possibility of extraintestinal clinical symptoms such as urticaria. Regarding the transmission route, 91.8% agreed that the fecal-oral route is the main mode of B. hominis transmission, but only 17.9% were aware of the role of host animals in its transmission. Furthermore, the physicians had poor knowledge of the need to treat symptomatic patients and resistance to metronidazole in some cases. More than two-thirds of the physicians (68%) had good practice treating infected immunocompromised patients but had poor practice treating symptomatic patients.

Conclusion: This study emphasizes improving physicians' knowledge of pathogenicity, clinical symptoms, and treating B.hominis. Since B. hominis is a common protozoan with pathogenic potential, we recommend training sessions for physicians to inform them of new findings about B. hominis.

keywords: Knowledge, Practice, Blastocystis hominis, Physician, Iran

PP-14

Investigation of Intestinal Protozoan Parasite Contamination in Inflow and Outflow Wastewater of Treatment Plants in Ardabil Province and Their Removal Efficiency

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Background and aim: Background: Municipal wastewater is a significant source of parasite transmission to the environment and humans. This study aimed to investigate contamination with intestinal protozoan parasites in the inflow and outflow of wastewater treatment plants in Ardabil province and assess their efficiency in removing these agents.

Methods: Methods: In a descriptive cross-sectional study during 2022-2023, monthly sampling over one year was conducted from the inflow and outflow of treatment plants in four cities: Ardabil, Khalkhal, Sarein, and Germi. A total of 288 samples (144 inflow and 144 outflow) were examined parasitologically using the Bailenger concentration method and counting with McMaster slides.

Results: Results: In the inflow wastewater, identified protozoan parasites included Entamoeba coli, Giardia lamblia, Endolimax nana, and Blastocystis. The mean cyst count per liter of inflow varied between cities and seasons. No parasitic agents were observed in any of the effluent outflow samples, and the removal efficiency for all agents was 100%.

Conclusion: Conclusion: The wastewater treatment plants in Ardabil province demonstrated very high efficiency in the complete removal of parasitic agents. The quality of the treated effluent complied with permissible standards for use in agricultural irrigation. These findings emphasize the importance of regular monitoring and the implementation of appropriate treatment systems to prevent the environmental spread of parasitic agents.

keywords: Keywords: Municipal wastewater, Wastewater treatment plant, Environmental monitoring, Ardabil, Intestinal

PP-15

Association of Blastocystis hominis Infection with Hemoglobin and Stool Characteristics.

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Background and aim: Blastocystis hominis is one of the most prevalent intestinal protozoa worldwide, with reported prevalence varying by geographic region, hygiene, and diagnostic methods. Despite its high frequency, its clinical significance remains debated, as studies have shown inconsistent associations with gastrointestinal symptoms and laboratory findings. Some research links infection to diarrhea and other digestive complaints, yet many individuals remain asymptomatic or exhibit mild symptoms. Evidence regarding its impact on hematologic and inflammatory parameters is also variable, likely due to differences in study design, population characteristics, or subtype diversity. Well-designed studies are needed to clarify these associations.

Methods: This descriptive–analytical study was in 2024. From 4,280 stool samples analyzed at a clinical laboratory by direct method. 67 samples positive for Blastocystis hominis were selected as the case group. For each case, one age- and sex-matched individual with a negative stool examination for intestinal parasites was included as a control (n = 67). The assessed variables comprised stool characteristics and laboratory parameters, including hemoglobin (Hb), erythrocyte sedimentation rate (ESR), and fecal occult blood (OB).

Results: The overall prevalence of Blastocystis hominis among examined samples was 1.56%. No significant differences were observed between cases and controls regarding hemoglobin levels or erythrocyte sedimentation rate (p 0.05). Likewise, results of the fecal occult blood test did not differ significantly between the two groups (p 0.05). However, stool characteristics showed a significant difference between infected individuals and controls (p= 0.049).

Conclusion: This study indicates that Blastocystis hominis infection is not always associated with overt diarrhea and may occur in stool samples with milder consistency changes, such as soft stools. Moreover, the evaluated laboratory parameters did not differ significantly between infected and non-infected individuals. These findings suggest that relying solely on diarrheal stool samples for parasitological examination may result in underdiagnosis, and attention to a broader spectrum of stool consistencies could improve detection in routine diagnostic practice.

keywords: Blastocystis, Feces / analysis , Hemoglobins , Erythrocyte Sedimentation Rate

PP-16

Some zoonotic infectious diseases are prevalent among children under 15 years of age in Ardabil Province, northern Iran

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Background and aim: This study sought to investigate the seroprevalence of visceral leishmaniasis (VL), toxocariasis, brucellosis, and salmonellosis, as well as their co-infection and potential cross-reaction, in children under 15 years referred to health centers in Ardabil province, Iran, from 2019 to 2021.

Methods: The current study examined 1,550 serum samples using direct agglutination test (DAT), Toxocara canis ELISA, Wright, and Widal tests to detect antibodies against Leishmania, Toxocara, Brucella, and Salmonella, respectively. We also compared the test results to determine the possibility of cross-reactivity or simultaneous seropositivity in the tested samples.

Results: In general, anti-Leishmania antibodies were positive in 78 samples (5%) at titers of ≥ 1:800, while only 8 cases had titers of ≥ 1:3200, which was considered as positive result. Therefore, the seroprevalence of VL was estimated to be at 5.16 per 1,000 at-risk populations. Meshkin-Shahr city had the highest seroprevalence (7 cases, 87.5%), followed by Ardabil (1 case, 12.5%) ($p = 0.03$). The highest and lowest seropositivity rates were observed in children aged 1-5 (6 samples, 75%) and 5-15 (2 samples, 25%) years old, respectively ($p = 0.02$). Anti-Toxocara antibodies were positive in 249 samples, (16.1%, 95% CI: 13.2-18.8), which were primarily males. There was a significant difference in seropositivity to Toxocara infection by city ($p = 0.04$), and age ($p = 0.00$). The results of Wright test showed seropositivity of 7.5% (117 samples) with the highest rate in individuals aged ≥ 10 years, males, and urban areas. No

Conclusion: Given the prevalence of bacterial and parasitic febrile infections among children in the region, and their symptomatic similarity to VL, it is crucial to recognize clinical manifestations, accurately diagnose co-infections, and account for cross-reactivity in serological tests.

keywords: Visceral leishmaniasis; Brucellosis; Salmonellosis; Toxocariasis; Co-infection; Cross-reaction

PP-17

Enhanced Molecular Detection of Echinococcus granulosus cfDNA in Human Plasma

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Background and aim: Background: Laboratory diagnosis of human echinococcosis remains challenging due to limitations in sensitivity and specificity of conventional methods. Early and accurate detection is critical for effective disease management. Cell-free DNA (cfDNA) has emerged as a promising non-invasive biomarker for parasitic infections. This study evaluated an optimized semi-nested PCR protocol for the sensitive detection of Echinococcus granulosus sensu lato cfDNA in plasma samples from patients with hydatid cysts.

Methods: Methods: Plasma samples were collected from 28 patients with surgically confirmed cystic echinococcosis. cfDNA was extracted from 1 mL of plasma using a commercial kit with a final elution volume of 30 µL. Semi-nested PCR targeting the mitochondrial NADH dehydrogenase subunit I (nad1) gene was performed using two template volumes: 10 µL for all 28 samples and 5 µL for a subset of 14 samples. Negative controls included plasma from healthy individuals and distilled water, while positive control DNA was obtained from protoscoleces.

Results: Results: The optimized semi-nested PCR successfully detected E. granulosus cfDNA in 23 of 28 patient plasma samples, corresponding to an overall sensitivity of 82%. Detection rates varied by template volume: 11/28 samples (39.2%) were positive with 10 µL, 14/18 samples (77.8%) with 5 µL, and 2 samples were positive at both volumes. No amplification was observed in negative controls, confirming 100% specificity.

Conclusion: Conclusions: This study demonstrates that semi-nested PCR is a sensitive and specific method for non-invasive detection of E. granulosus cfDNA in plasma. The combination of optimized cfDNA extraction from 1 mL of plasma and application of two template volumes enhances diagnostic performance, offering a promising tool for early and reliable detection of cystic echinococcosis in clinical settings.

keywords: Cystic echinococcosis, Cell-free DNA, Semi-nested PCR, Non-invasive diagnosis, human

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PP-18

Anti-Plasmodium activity of green synthesized nano Gold, Selenium, and Zinc oxide by Rumex crispus on Plasmodium berghei in vivo

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Background and aim: Malaria has been one of the most important parasitic diseases worldwide throughout history, with a very high mortality rate. Parasites of the genus Plasmodium cause this disease. Nanoparticles are prepared by various methods, of which green synthesis is one of the most essential and cost-effective methods, derived from natural sources such as plant extracts, fungi, and various microscopic organisms. This study aims to investigate the antimalarial effect of gold, selenium, and zinc oxide nanoparticles prepared through green synthesis from the sorrel plant on the Plasmodium berghei (P. berghei) parasite in vivo.

Methods: The P. bergei parasite was obtained from the Central Malariology Laboratory, School of Public Health, Tehran University of Medical Sciences. After thawing from the cryo-state, it was first injected intraperitoneally into laboratory white mice. Then, with increasing parasitemia, blood was collected, and the infected blood was injected into different groups. After the injection of the drugs under study, the parasitemia level was examined on days 5, 8, 15, and 20. Additionally, to assess the toxicity, the levels of liver enzymes were measured.

Results: In this study, gold, selenium, and zinc oxide nanoparticles obtained by the green synthesis method from sorrel plant showed that they have an acceptable anti-parasitic effect on the parasite P. berghei. In this study, the highest concentration of gold nanoparticles was reported to exhibit an anti-parasitic impact, and its difference from the positive control group was not significant (P 0.05). However, with commercial nanoparticles, this difference was found to be completely important. By examining the levels of liver enzymes, it was determined that the nanoparticles under study do not have any toxicity on liver cells.

Conclusion: The results of this study demonstrated that nanoparticles prepared by green synthesis exhibited an antimalarial effect comparable to that of the positive control group (chloroquine) and warrant further investigation and evaluation as a potential candidate to replace current antimalarial drugs.

keywords: Malaria, Plasmodium berghei, green synthesis, sorrel, gold, selenium, zinc oxide

PP-19

Anti-amoebic effect of silicon dioxide/graphene oxide-ketoconazole nanodrug against Acanthamoeba genotype T4 cysts and trophozoites

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Background and aim: Acanthamoeba spp. cause sight-threatening keratitis and life-threatening encephalitis, and their highly resistant cyst stage severely limits therapeutic success. This study evaluated the anti-amoebic activity of a silicon dioxide/graphene oxide–ketoconazole nanocomposite (SiO_2- GO–K) against Acanthamoeba genotype T4 trophozoites and cysts.

Methods: Nanodrugs were synthesized at three GO-SiO_2 ratios (1-1, 1-2, and 2-1), loaded with a constant ketoconazole proportion, and characterized by scanning electron microscopy, X-ray diffraction, and Fourier-transform infrared spectroscopy. Trophozoite and cyst suspensions were exposed to serial concentrations (0.1–1.0% w/v) and monitored up to seven days for viability, excystation, and trophozoite survival; cytotoxicity was assessed on MCF10A human mammary epithelial cells using the MTT assay.

Results: The SiO_2-GO formulations with 1:2 and 2:1 ratio produced the most sustained trophozoite inhibition, with pronounced effects emerging after 6–8 days, whereas untreated controls and ketoconazole alone showed limited amoebicidal activity. Cysts remained largely viable within 24 hours across most conditions, indicating persistent excystation resistance. Dose-dependent cytotoxicity was evident for both silicon dioxide and graphene oxide components (p 0.01), with silicon dioxide exhibiting greater toxicity at equivalent concentrations.

Conclusion: Taken together, our data indicate that the physicochemical properties of the SiO_2-GO hybrid drive amoebicidal activity likely through membrane disruption and oxidative stress rather than potentiation by ketoconazole alone. These findings support further optimization of composite composition and dosing to maximize anti-amoebic efficacy while reducing host and environmental toxicity, and they underscore the need for mechanistic and in vivo studies before clinical consideration.

keywords: Acanthamoeba, nanodrug, ketoconazole, graphene oxide, silicon dioxide, cyst resilience, trophozoite

PP-20

Genotyping of human isolates of Blastocystis hominis in Yazd in 1404

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Background and aim: Blastocystis hominis is a zoonotic intestinal protozoan with a global distribution. To date, 44 subspecies have been identified, of which 9 are common in humans. Since the detection of this parasite by morphological features is not highly sensitive, molecular methods are considered a suitable method for the detection of this parasite and its subspecies. The aim of this study was to investigate the common subtypes of human Blastocystis hominis in Yazd.

Methods: All samples were genotyped using the molecular PCR method

Results: : Of the 10 samples sequenced, 6 were subclade 3 (60%), and 4 were subclade 1 (40%).

Conclusion: Blastocystis hominis is the most common protozoan in the human intestine, and despite the studies conducted, there are many uncertainties about its pathogenicity.

keywords: Genotyping, Blastocystis hominis, Yazd

PP-21

Therapeutic Effects of Formononetin on Giardia lamblia Infection Through the Modulation of Serum Electrolyte Levels and Intestinal Inflammatory Responses in Mice

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Background and aim: Giardia lamblia represents a significant pathogenic protozoan responsible for infecting the gastrointestinal tract of humans and other vertebrates. Standard treatment regimens for giardiasis are occasionally associated with adverse side effects and do not consistently achieve satisfactory efficacy. This study aims to investigate the in vitro and in vivo anti-giardial effects of formononetin (FN), as well as its potential synergistic effects against G. lamblia infection in a murine model.

Methods: : Cell viability assay was used to evaluate the in vitro anti-giardial and cytotoxic effects of FN. Infected mice were treated with FN and metronidazole (MTZ) for seven days, after which stool samples were analyzed to assess the presence and viability of Giardia cysts. Additionally, serum concentrations of the electrolytes were measured using biochemical assay kits. The expression levels of tumor necrosis factor-alpha (TNF-α), nuclear factor kappa B (NF-κB), and interleukin-1 beta (IL-1β) were quantified using real-time PCR techniques

Results: FN caused a significant (p0.001) reduction in the viability and growth rate of G. lamblia cysts. The IC50 values for FN, MTZ, and their combination against G. lamblia cysts were 37.1, 29.3, and 11.1 µg/mL, respectively. FN, both alone and in combination with MTZ, produced a significant decrease (p0.001) in the average count and viability of Giardia cysts, modulated the serum electrolytes, and significantly decreased the expression of IL-1β, TNF-α, and NF-κB-p65 genes (p0.001).

Conclusion: : FN, particularly in combination with MTZ, demonstrated efficacy in managing giardiasis both in vitro and in vivo by modulating electrolyte levels and inflammatory responses. However, further research is needed to elucidate the mechanisms through which this compound exerts its therapeutic effects against giardiasis

keywords: Giardiasis, serum electrolytes, inflammation, Real-time PCR, Natural products

PP-22

Toxocara infection in children with hypereosinophilia; A seroepidemiological survey in Western Iran

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Background and aim: Toxocariasis is a significant parasitic disease with a global distribution, caused by two nematodes: Toxocara canis (a parasite of the dog's small intestine) and Toxocara cati (a parasite of the cat's small intestine). Eosinophilia, characterized by an elevation in peripheral blood eosinophil counts exceeding 10%, serves as a significant clinical marker for helminthic infections. This study aims to investigate the seroepidemiology of Toxocara canis and its risk factors in children with hypereosinophilia in Lorestan province, Western Iran.

Methods: This cross-sectional study was conducted from May 2021 to June 2023, involving a cohort of 300 children aged 2 to 15 years who presented with eosinophilia (10%) and were referred to healthcare facilities in Lorestan province. Children who were younger than 12 years (between 2-12 years), had blood eosinophil counts exceeding 10%, who consented to engage in this study were deemed to fulfill the inclusion criteria. The prevalence of toxocariasis was confirmed serologically by detecting human IgG antibodies utilizing commercially available anti-IgG-T. canis kits. Demographic and some risk factors regarding the enrolled subjects, including gender, age, type of residence, consuming unwashed 1 vegetables and fruits, and history of animal contact were collected.

Results: Out of a total of 300 children with eosinophilia, 35 (11.7%) were identified as seropositive for toxocariasis. Specifically, girls' participants were less likely to contract toxocariasis than their boy children [P=0.002, OR=0.184 (0.052-0543)]. Additionally, individuals living in urban environments exhibit a 4.54-fold increased likelihood of contracting toxocariasis compared to their rural counterparts [P=0.010, OR=4.546 (1.433-9.419)]. Furthermore, individuals who did not consume unwashed /vegetables demonstrated a reduced risk of toxocariasis infection [P=0.001, OR=0.016 (0.005-0.048)].

Conclusion: The findings of our study indicated a significant seroprevalence of toxocariasis among children exhibiting eosinophilia in Western Iran. This suggests that toxocariasis should be regarded as a potential etiological factor for eosinophilia, particularly in individuals with a history of utilizing unwashed fruits and vegetables, as well as those residing in rural regions of Iran.

keywords: Toxocara canis, seroepidemiology, ELISA, eosinophilia, Lorestan

PP-23

In Vitro Dual Effects of Honey Bee Venom (Apis mellifera) and Its PLA2 Fraction on Leishmania major Amastigotes: From Suppressor to Promoter

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Background and aim: Leishmaniasis is a widespread parasitic disease with cutaneous, mucocutaneous, and visceral forms. Despite longstanding recognition, effective treatment remains a challenge due to the limitations of current chemotherapies, such as toxicity and resistance. Natural toxins, particularly those from venomous organisms, have emerged as promising alternatives. This study investigated the anti-leishmania effect of crude honey bee venom (Apis mellifera) and its phospholipase A2 fraction (bvPLA2) against intracellular amastigote stage of Leishmania major.

Methods: Crude bee venom, purified bvPLA2, and Glucantim were tested on L. major intracellular amastigotes and macrophages (RAW 264.7). Cytotoxicity and anti-parasitic activity were evaluated using the MTT assay at different time and amount intervals. The CC50 and IC50 values were calculated using GraphPad Prism.

Results: Crude bee venom exhibited high toxicity towards macrophages, with a CC50 of 1 µg/mL and complete mortality at later time points (48 and 72 hours). In contrast, bvPLA2 showed lower cytotoxicity (CC50 = 45.82, 37 & 86.01 µg/mL at 24, 48, and 72h, respectively), and even stimulated macrophage proliferation at lower concentrations. Both compounds demonstrated dose and time-dependent anti-leishmania activity. IC50 values for bvPLA2 were 25.8 µg/mL (24h) and 7.68 µg/mL (48h), while crude venom showed IC50 values of 6.39 µg/mL and 5.77 µg/mL, respectively. The IC50 values for both treatments were significantly lower than Glucantim (P 0.0001).

Conclusion: Crude bee venom and bvPLA2 possess potent anti-leishmania properties, with bvPLA2 offering a better safety profile. These findings support further investigation into venom-derived compounds as alternative therapies for leishmaniasis.

keywords: Crude bee venom, Phospholipase A2, Leishmania major, Amastigote, Apis mellifera.

PP-24

Impact of hydatid cyst laminated layer antigens on cell death rate, apoptosis induction, and key genes in the cell proliferation pathway

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Background and aim: While lung cancer remains a lethal disease despite treatment advances, some parasitic infections can demonstrate cancer-modulating roles and exhibit anti-tumor effects. The emergence of hydatid cysts as a potential anti-cancer treatment has sparked optimism for the development of more successful therapies. This research examines the effect of hydatic cysts on the growth and proliferation of lung tumor cells, as well as the underlying molecular mechanisms involved.

Methods: The laminated layer(LL) of the hydatid cyst antigens was administered to lung cancer cells with varying dosages and durations. The MTT assay was applied to evaluate cell viability. After exposure to different concentrations of LL antigens, the apoptosis, necrosis, cell cycle, and intracellular reactive oxygen species (ROS) of the cell culture were measured using flow cytometry. The expression levels of SOX-9, β-catenin, CD133, and CD44 genes were assessed using Real-Time PCR.

Results: Treating A549 cells with varying concentrations of LL antigens resulted in a decrease in viable cells, which depended on both time and dosage. Treatment with cysts led to apoptosis induction and a reduction in necrosis percentage in a dose-dependent manner. The induction of apoptosis correlated with elevated ROS production and a notable decrease in the expression of invasion-related genes (β-catenin, CD133, and CD44) (P0.05). However, this reduction in expression was not statistically significant for SOX-9.

Conclusion: Exposing lung cancer cells to precise amounts of crude LL antigens resulted in cell death, apoptosis, increased intracellular ROS levels, and reduced expression of genes linked to cancer cell growth and invasion. These results lay the groundwork for further exploring purified Echinococcus granulosus parasite antigens as potential drug targets in cancer treatment.

keywords: laminated layer, hydatid cyst,A549 cell line

PP-25

Selective Binding of Anti-Toxoplasma Antibodies to Human Breast Cancer Tissues: A Novel Diagnostic and Immunotherapeutic Avenue

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Background and aim: Recent publications have shown Toxoplasma gondii's anti-cancer impacts. However, the molecular and immunological mechanisms underlying these effects remain incompletely understood. One plausible mechanism involves antigenic mimicry or shared epitopes between T. gondii antigens and tumor-associated antigens, leading to selective immune recognition of malignant cells. The present study aimed to evaluate the immunoreactivity of rabbit-derived anti-Toxoplasma antibodies with human breast cancer tissues compared to normal breast tissues.

Methods: Polyclonal anti-Toxoplasma antibodies were generated by immunizing a rabbit with the tachyzoite lysate, followed by antibody purification. Immunohistochemical (IHC) analysis was performed on formalin-fixed, paraffin-embedded human breast cancer tissue specimens representing various histopathological subtypes, as well as normal breast tissue sections. Antibody binding was visualized using standard chromogenic detection methods, and appropriate positive and negative controls were included to ensure staining specificity.

Results: : Immunohistochemical evaluation revealed strong and specific immunoreactivity of anti-Toxoplasma antibodies with breast cancer tissue sections across different tumor subtypes. The staining was predominantly localized to malignant epithelial cells. In contrast, normal breast tissue sections showed no detectable antibody binding, indicating a lack of cross-reactivity with non-malignant cells.

Conclusion: These findings demonstrate that anti-Toxoplasma antibodies selectively bind to breast cancer tissues while sparing normal breast tissues, supporting the hypothesis of shared or cross-reactive tumor-associated antigens. This selective immunoreactivity highlights the potential diagnostic value of anti-Toxoplasma antibodies and suggests a possible role for T. gondii-derived antigens in the development of targeted immunotherapeutic strategies for breast cancer. Further molecular characterization of the recognized epitopes is required to elucidate their clinical applicability.

keywords: Immunohistochemistry, Toxoplasma antibodies, Breast carcinoma,

PP-26

Investigation of the inhibitory effect of hydroalcoholic extract of tarragon (Artemisia dracunculus) on protoscolices of Echinococcus granulosus in vitro

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Background and aim: Background: Parasitic infections have become a serious problem in livestock units and human populations. A high percentage of livestock mortality in livestock units and mortality in human societies occurs due to infectious diseases, especially human-animal diseases. Therefore, this study aimed to investigate the inhibitory effect of the hydroalcoholic extract of tarragon (Artemisia dracunculus) on the protoscolices of the worm Echinococcus granulosus in vitro.

Methods: Methods: This study was conducted in the Parasitology Laboratory of Birjand University of Medical Sciences on the protoscolices of Echinococcus granulosus. The protoscolices were obtained from liver cysts of infected sheep. The hydroalcoholic extract of tarragon was brought to different concentrations using the serial dilution method. The nanoemulsion was produced by spontaneous emulsification method and carbomer gel was used to prepare the nanoemulsion gel. The data will be analyzed with SPSS22 software and Chi-square test. P0.05 was considered significant.

Results: Results: The results showed that tarragon extract has antiprotoscolex effects only at concentrations above 0.01%, which was not significantly different from the control group. (P0.05) At 30 minutes with a concentration of 0.1%, the antiprotoscolex effect of the extract was 100%. But there was no significant difference with the control group.

Conclusion: Artemisia dracunculus extract was effective at concentrations higher than 0.01%. Therefore, it can be concluded that in case of supplementary experiments and further studies with different nanoparticles, the possibility of increasing the antiparasitic effectiveness of this plant at lower concentrations can be increased.

keywords: Echinococcus granulosus, Artemisia dracunculus , aqueous alcoholic extract, protoscolex

PP-27

Pulmonary Hydatid Cyst Serodiagnosis

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Background and aim: The lungs represent the second most commonly affected organ in unilocular hydatid disease, is a zoonotic disease caused by the larval stage of the Echinococcus granulosus (sensu lato) worm, commonly found in sheep-raising countries. The current study aimed at the prospective investigation of unilocular hydatid cysts among patients with space-occupying lesions or cystic masses of lung identified by computerized tomography (CT) scan referred to the Parasitology and Mycology Department of Fasa University of Medical Sciences in Fasa district in the southwest of Iran.

Methods: Serum samples were prepared from 118 patients with suspected of having unilocular pulmonary hydatid cyst in different seasons from 2021 to 2025. All serum samples were evaluated by ELISA using B antigen prepared from native hydatid cyst fluid of domestic sheep, and suspicious cases were retested at the Parasitology and Mycology Department of School of Medicine, Shiraz University of Medical Sciences.

Results: Anti-hydatid cyst antibodies were detected in 77.12% of the patients.

Conclusion: Our laboratory findings on this zoonotic disease in this district emphasize the importance of increasing public awareness about unilocular pulmonary hydatid cyst. The primary diagnosis is made by radiological studies, and confirmed by serology using antigen prepared from native hydatid cyst fluid of domestic sheep.

keywords: Lung, Hydatid cyst, Serodiagnosis, Fasa, Iran

PP-28

Prevalence of Pathogenic Free-Living Amoebae in Agricultural Soils of Northern Khuzestan Province, Iran

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Background and aim: Free-living amoebae (FLA), including Acanthamoeba spp., Naegleria spp., and Balamuthia mandrillaris, are soil-borne protozoa widely distributed in the environment and capable of causing severe, often fatal human infections such as amoebic keratitis and central nervous system involvement. In Iran, most studies have focused on water sources, while data on soil contamination and the diversity of FLA remain limited and largely morphology-based. Therefore, this study aimed to investigate the prevalence of pathogenic free-living amoebae in agricultural soils of northern Khuzestan Province, Iran.

Methods: In this cross-sectional study, soil samples were collected from agricultural lands in four cities of northern Khuzestan Province, Iran. A total of 50 samples were obtained, including 20 from Dezful and 10 each from Andimeshk, Shush, and Shushtar. The samples were processed using an standard filtration protocol and subsequently cultured. The presence of free-living amoebae was assessed through meticulous microscopic examination, and species-level identification was performed based on precise morphological criteria.

Results: Out of 50 agricultural soil samples, 20 samples (40%) were morphologically positive for free-living amoebae. Morphological identification revealed that 13 samples (26%) contained Acanthamoeba spp., while 6 samples (12%) were positive for Vermamoeba vermiformis spp. One sample (2%) showed mixed contamination with both Acanthamoeba spp. and Vermamoeba vermiformis spp. The distribution of positive samples indicates the widespread presence of potentially pathogenic free-living amoebae in agricultural soils of the studied area.

Conclusion: The present study demonstrates the occurrence of potentially pathogenic free-living amoebae, including Acanthamoeba spp. and Vermamoeba vermiformis spp, in agricultural soils of northern Khuzestan Province, Iran. These findings indicate that individuals with direct contact with contaminated soils, such as farmers and rural populations, are at higher risk of exposure. Moreover, since agricultural products from these soils are widely consumed, all consumers should observe proper hygiene measures to minimize the risk of infection. The results highlight the need for increased awareness and preventive practices in agroecosystems.

keywords: Free-living amoebae - Agricultural soils - Iran

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July 20-23, 2026

PP-29

Efficacy of Azole Derivatives, Clotrimazole, Itraconazole, and Voriconazole on Cystic Echinococcosis Protoscolices: A Comparative Study

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Background and aim: Cystic echinococcosis (CE) remains a significant global health challenge. Given the adverse effects and limited efficacy of current scolicidal agents, there is an urgent need for novel therapeutic developments. This study aimed to evaluate and compare the in vitro scolicidal effects of three azole derivatives—clotrimazole, itraconazole, and voriconazole—against Echinococcus granulosus protoscolices.

Methods: In this in vitro study, protoscolices were aseptically harvested from ovine hepatic hydatid cysts, and their viability was confirmed to exceed 90% using eosin staining. The samples were exposed to graded concentrations (64–1024 µg/mL) of clotrimazole, itraconazole, and voriconazole for three hours. A 20% saline solution and DMSO served as positive and negative controls, respectively. Viability rates were assessed via microscopic examination and eosin exclusion assays. Data analysis was performed using ANOVA to compare mortality rates.

Results: Clotrimazole exhibited significantly higher scolicidal activity compared to both itraconazole and voriconazole, as well as the negative control (P0.05). The highest mortality rate was observed in the clotrimazole group at 1024 µg/mL (89.9%), demonstrating a significant dose-dependent correlation (P=0.011). Conversely, itraconazole and voriconazole showed modest efficacy, with mortality rates significantly lower than the positive control. Although clotrimazole was potent, its efficacy remained lower than the 20% hypertonic saline positive control after three hours

Conclusion: Clotrimazole demonstrates superior in vitro scolicidal efficacy compared to itraconazole and voriconazole. While it may not replace rapid-acting agents for PAIR procedures, its potent anti-parasitic activity suggests potential as an effective alternative or adjunctive systemic therapy for managing cystic echinococcosis.

keywords: Echinococcosis; Clotrimazole; Itraconazole; Voriconazole; Azoles

PP-30

In vitro, ex vivo, and in vivo potential of Astragalus onobrychis extract against protoscoleces and hydatid cysts of Echinococcus granulosus

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Background and aim: Here, we evaluated the in vitro, ex vivo, and in vivo effects of the chloroform extract of Astragalus onobrychis L. (AOCE) on apoptosis induction and DNA damage in protoscoleces and hydatid cysts of Echinococcus granulosus.

Methods: The protoscolicidal properties of AOCE were examined through both in vitro and ex vivo studies on hydatid cyst protoscoleces, utilizing the eosin exclusion assay. Additionally, we evaluated the effects of AOCE on apoptosis induction and DNA damage in the protoscoleces using a colorimetric protease assay and real-time PCR analysis, respectively. The in vivo efficacy was determined by measuring the quantity, dimensions, and mass of hydatid cysts in infected murine subjects.

Results: AOCE, particularly at a concentration of 45.0 mg/mL, effectively eliminated protoscoleces of hydatid cysts within a 30-min exposure period. Additionally, AOCE demonstrated prolonged anti-parasitic effects in ex vivo conditions, in contrast to the immediate lethal effects observed in vitro (p 0.001). AOCE significantly (p 0.01) induced caspase-3 activation in protoscoleces obtained from hydatid cysts relative to the control normal saline group. Furthermore, the results from Real-time PCR analysis indicated a significant (p 0.001) upregulation in the expression levels of the EgATM and EgP53 genes following treatment with AOCE. By in vivo, we found that treatment with AOCE mainly at 200 mg/kg significantly (p 0.001) reduced the number, size, and weight of hydatid cyst relative to the control group treated with normal saline group. Biochemical analysis also demonstrated that administration of AOCE to infected mice, led to a marked improvement and a reduction in serum levels

Conclusion: The results indicated that AOCE exhibits considerable in vitro and ex vivo scolicidal properties against hydatid cyst protoscoleces. Furthermore, the results highlighted AOCE's capacity to eradicate protoscoleces through the induction of apoptosis and the infliction of DNA damage. Additionally, AOCE demonstrated significant therapeutic efficacy in managing hydatid cysts in murine models. However, further studies are required to clarify the specific mechanisms underlying its action and to assess its efficacy in clinical trials, which may facilitate the application of AOCE in the context of hydatid cyst surgical procedures.

keywords: herbal medicines, scolicidal, apoptosis, Echinococcus granulosus, hydatidosis

PP-31

Prevalence and Associated Risk Factors of Soil-Transmitted Helminthic Parasites in Iranian Children with Hypereosinophilia

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Background and aim: Eosinophilia is a health condition, which happens when the number of peripheral blood eosinophils is greater than 450 per microliter, or when the eosinophils account for more than 7% of the white blood cells. Eosinophilia can be caused by both infectious and non-infectious processes, many of which may be clinically indistinguishable. This survey was aimed to study the prevalence of the intestinal helminthic parasites among children with hypereosinophilia and healthy children from Lorestan province, western Iran

Methods: This case-control study was carried out from July 2017 to August 2018 on 224 children (ranging from 2 to 15 years old) including 112 children with peripheral blood eosinophils greater than 1000 per microliter who referring to health centers of Lorestan province, Iran (case group) and 112 healthy children with normal peripheral blood eosinophils. The microscopic examination was performed on the stool samples from each child by means of the direct smear and formol-ether methods. An applied questionnaire was considered to reach information about the children's demographics data and other variables related to helminthic infections

Results: Out of 112 children with eosinophilia (case group), the helminthic infection was found in 23 (20.5%) children; whereas from 112 healthy children in the control group, the helminthic infection was found in 12 (10.7%) children, indicating the significant difference (p0.001) in the prevalence of helminthic infection among the children in the case and control groups. The results demonstrated that many risk factors were considerably related to the prevalence of intestinal helminthic parasites including gender (p=0.013) and consumption of raw or unwashed vegetables and fruits (p0.001).

Conclusion: The obtained findings revealed the considerable prevalence of intestinal helminthic parasites among children with hypereosinophilia in Lorestan province, Western Iran. The results of the present study also suggest that physicians should pay more attention to worm infections as an important factor for eosinophilia.

keywords: parasites, eosinophilia, ELISA, Lorestan

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PP-32

The scolocidal effect of propolis on protoscoleces of hydatid cysts

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Background and aim: Background: Hydatid cyst (hydatidosis) is one of the most important zoonotic diseases, caused by the larval stage of the Echinococcus granulosus. Drug treatments such as albendazole and mebendazole, due to limited absorption and side effects, do not have the desired effectiveness among patients. Therefore, finding natural substances with high lethality against protoscolices and without side effects is very important. The aim of the present study is to survey the scolocidal effect of propolis on protoscolices of hydatid cysts.

Methods: Methods: In this study, different concentrations of aqueous and alcoholic propolis extracts including 100, 250, and 500 mg/mL and contact times of 5, 10, 20, 30, and 60 minutes were examined on protoscolices of hydatid cysts using microscopy and MTT assay. Two-way ANOVA and variance were used to analyze the significance of the difference in means, while a p value of 0.05 was considered as statistically significant.

Results: Results: The findings of this study indicate the dose- and time-dependent pattern; the scolocidal effect of propolis on protoscolices was increased significantly with high level of concentration and duration of contact in both microscopic methods and MTT assay. Totally, the alcoholic extract was more successful than the aqueous extract in the eliminating of protoscolices.

Conclusion: Conclusion: considering the significant effect of propolis, especially its alcoholic extract, on the protoscolices of hydatid cysts, additional measures including identification and isolation of the active ingredient of the extract, conducting comprehensive animal studies to assess long-term toxicity and pharmacokinetics, and investigating the synergistic effect of the extract with common reference drugs are useful and practical.

keywords: Keywords: Protoscolices, hydatid cyst, propolis, MTT assay, microscopic method

17th International Congress of Lab. and Clinic
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PP-33

Investigating the anti-parasitic effect of Sambucus ebulus plant nanoemulsion on the larval stage of Echinococcus granulosus parasite in vitro

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Background and aim: Echinococcosis or hydatid cyst disease is one of the most important parasitic diseases in different regions of the world. Humans are accidental intermediate hosts for this disease, and hydatid cysts are formed in the liver, lungs, etc. Albendazole and mebendazole are among the most important drugs for the treatment of this disease, and the use of these drugs has many limitations for the host. The purpose of this study is to investigate the anti-parasitic effects of plum plant extract and plum plant nanoemulsion on the larval stage of Echinococcus granulosus parasite in vitro.

Methods: To collect the larval stage of Echinococcus granulosus parasite, the infected liver of a sheep with hydatid cyst was isolated from the industrial slaughterhouse of Sari city. Approximately 100,000 parasites were incubated by the concentrations of 100, 200, 400, and 800 µg/mL of treatments. After 5, 10 and 20 minutes, the lethality rate was evaluated using vital eosin staining of 0.01%.

Results: The results have shown that the nanoemulsion of the methanolic extract of Sambucus ebulus in concentrations of 400 and 800 µ/ml after 10 and 20 minutes had less anti-parasitic effect than the positive control, although this difference is not statistically significant. (P0.05). Also, nano-emodin has a higher effectiveness in all concentrations and times with a significant difference compared to the whole extract of Sambucus ebulus.

Conclusion: From the results, it can be determined that Sambucus ebulus and plant nanoemulsion can be considered as a suitable option for the treatment of hydatid cyst disease.

keywords: Echinococcus granulosus, Sambucus ebulus, hydatid cyst, nanoemulsion, protoscolex

PP-34

Toxoplasmosis Seroprevalence in Women of Reproductive Age: A Potential Link to Vitamin D Deficiency

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Background and aim: Toxoplasmosis, caused by the protozoan parasite Toxoplasma gondii*, can adversely affect pregnancy outcomes. Vitamin D deficiency has been associated with increased susceptibility to infections and pregnancy-related complications. This study investigated the prevalence of toxoplasmosis among women of reproductive age in Mazandaran Province and explored its potential association with vitamin D deficiency.*

Methods: A total of 320 serum samples were collected from women of reproductive age in Mazandaran Province (Sari, Babol, Chalus, Nur, Tonekabon, and Ramsar). Participants completed a questionnaire providing information on age, meat and egg consumption, cat exposure, soil contact, and residential location. Serum samples were analyzed for IgG and IgM antibodies against T. gondii using ELISA, while 25-hydroxyvitamin D levels were measured with a commercial kit. Data were analyzed using descriptive statistics, the Chi-square test, and odds ratios, employing SPSS software version 21. A P-value 0.05 was considered statistically significant.

Results: The study revealed that 198 participants (61.88%) were positive for anti-Toxoplasma IgG, while only one participant (0.31%) tested positive for anti-Toxoplasma IgM. Among women with insufficient vitamin D levels, 159 were IgG-positive and one was IgM-positive. In contrast, among those with sufficient vitamin D, 39 were IgG-positive and none were IgM-positive. Statistical analysis indicated that the prevalence of toxoplasmosis in women with insufficient vitamin D was 1.71 times higher than in those with sufficient vitamin D (OR = 1.71), demonstrating a significant association between vitamin D status and toxoplasmosis prevalence.

Conclusion: Conclusion: The high prevalence of T. gondii among women in Mazandaran indicates that the parasite's life cycle is well-established in the region. Lower vitamin D levels were associated with an increased risk of toxoplasmosis, which is particularly important for seronegative women during pregnancy due to the potential adverse effects on both the mother and fetus. Therefore, monitoring vitamin D levels in seronegative women is essential.

keywords: Toxoplasmosis,Vitamin D Deficiency , childbearing-age, women

PP-35

A Preliminary Laboratory-to-Clinic Investigation of miRNA-Like Sequences in Blastocystis Species and Their Association with IBS

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Background and aim: Background and Aim: MicroRNAs (miRNAs) are small RNA molecules (18–22 nucleotides) that regulate gene expression. Certain miRNAs have been detected in blood and colon biopsies of patients with Irritable Bowel Syndrome (IBS).

Methods: Methods: Bioinformatics analysis identified miRNA-29a-5p, sharing complete identity in the first 14 nucleotides with Blastocystis mRNA and predicted as functional by the miRNA fold website. Stool samples from 80 individuals in four groups were collected. miRNA-29a primers were synthesized, followed by RNA extraction, cDNA synthesis, and Real-Time PCR. T-tests were used for statistical analysis

Results: Results: miRNA-29a-5p showed the highest similarity with Blastocystis mRNA and confirmed miRNA function. Its expression was significantly higher in IBS patients than controls (P 0.05), with notable differences in the positive Blastocystis sp. subgroup. All positive samples were subtype 1. The highest fold change was observed in the Blastocystis-positive IBS group (P 0.05).

Conclusion: Conclusion: miRNA-29a-5p exists in Blastocystis sp., suggesting a link between parasitic and human-like miRNAs. Further studies could identify additional sequences, improving understanding of IBS and other digestive disorders and offering potential diagnostic or therapeutic targets.

keywords: Blastocystis sp., MicroRNA, Irritable Bowel Syndrome (IBS), Intestinal permeability

PP-36

Seroprevalence and associated risk factors of visceral leishmaniasis among adult population in Kavar District, Fars Province, South of Iran

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Background and aim: Visceral leishmaniasis (VL) or Kala azar is an infectious disease caused by various species of Leishmania. The causative agent of Kala azar in Iran is Leishmania infantum and its major reservoir host is the dog. This cross-sectional study was conducted to evaluate the seroprevalence and the risk factors associated with visceral leishmaniasis among the adult population in the Kavar district, south of Iran.

Methods: A total of 628 blood samples were collected from participants with an age range of 35 to 70 years old from the Kavar region. Manual ELISA was utilized to detect anti-leishmania antibodies in their serum. A structured questionnaire, containing sociodemographic data, was completed for each participant.

Results: Among the 628 participants, 316 (50.3%) were men and 312 (49.7%) were women; the mean age of the participants was 49.82±7.3 years old. Anti-Leishmania antibody was detected in 14 (1.4%) of the 628 serum samples. The association between visceral leishmaniasis and gender, age, contact with dogs, occupation and underlying diseases were not statistically significant (p0.05).

Conclusion: The findings of this study revealed a low prevalence rate of visceral leishmaniasis among the adult population in the Kavar district, south of Iran. The studied population and diagnostic method may contribute to the low prevalence rate of visceral leishmaniasis. Further studies are needed to explore the reservoirs and vectors of the disease in this region.

keywords: Visceral leishmaniasis, Adult population, Seroprevalenc, Kavar District, Iran

PP-37

Therapeutic Effectiveness of Gold Nanoparticles prepared by green synthesis method and Sambucus ebulus extract in the treatment of cutaneous leishmaniasis

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Background and aim: Leishmaniasis is an infectious disease caused by protozoan parasites of the genus Leishmania, primarily endemic to tropical and subtropical regions. The disease is predominantly transmitted through the bites of sandflies and can lead to severe complications. Current treatment options for leishmaniasis mainly involve chemical drugs, which often have limitations due to side effects and the emergence of drug resistance. The use of plant-derived compounds as alternative treatments has garnered significant attention due to their antimicrobial and anti-inflammatory properties. In this context, Gold NPs have emerged as novel drug carriers, offering high potential for enhancing therapeutic effects while minimizing side effects.

Methods: Gold NPs were synthesized using a green synthesis method with the methanolic extract of S. ebulus (AuGNPs) as a reducing and stabilizing agent. The characteristics of the synthesized nanoparticles were identified using UV-Vis spectroscopy and Dynamic Light Scattering (DLS). The antileishmanial effects of gold nanoparticles (Gold NPs) were evaluated at various concentrations (50, 100, 200, and 400 µg/mL) against L. major amastigotes in cell culture conditions. The viability of the parasites was assessed using the MTT method. Furthermore, Gold NPs were applied topically to skin lesions caused by cutaneous leishmaniasis. The treatment was administered twice daily for 21 days, with measurements of lesion size taken after 7, 14, 21, and 28 days post-treatment. Statistical analyses were performed using Prism 8 software to evaluate the significance of the results.

Results: The effect of AuGNPs on wounds resulting from CL is statistically significant across different time points and concentrations. Concentrations of 50, 100, and 200 µg/mL consistently demonstrate significantly lower efficacy compared to the positive control at all time intervals (P0.05). However, the concentration of 400 µg/mL exhibited the best efficacy, with no statistically significant difference compared to the PC group (P0.05).

Conclusion: This study highlights the significant efficacy of a therapeutic ointment containing AuGNPs in reducing lesions caused by L. major in infected mice. This drug, after undergoing validation tests in in vivo conditions in other animals and humans, is a candidate for further investigation as a new and alternative treatment for cutaneous leishmaniasis.

keywords: Leishmania major, gold nanoparticles (Gold NPs), Sambucus ebulus, treatment

PP-38

Evaluation of Antileishmanial Efficacy of Green Synthesized Gold Nanoparticles from Taxodium disticum Against L. major in Cutaneous Leishmaniasis

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Background and aim: Leishmaniasis is an infectious disease caused by protozoan parasites of the Leishmania genus, primarily found in tropical and subtropical regions. It is mainly transmitted through sandfly bites and can lead to severe complications. Current treatments primarily involve chemical drugs, which have limitations due to side effects and the emergence of drug resistance. Consequently, plant-derived compounds are gaining attention as alternative treatments due to their antiseptic and anti-inflammatory properties. This study investigates the efficacy of a therapeutic ointment containing gold nanoparticles extracted from Taxodium disticum (T. disticum) on mice (MRHO/IR/75/ER) infected with Leishmania major (L. major), focusing on reducing lesion size.

Methods: Gold nanoparticles (AuNPs) were synthesized via a green method using the methanolic extract of Sambucus ebulus as a reducing and stabilizing agent. Their characteristics were confirmed through UV-Vis spectroscopy and Dynamic Light Scattering (DLS). The antileishmanial effects of AuNPs were evaluated against Leishmania major amastigotes at concentrations of 50, 100, 200, and 400 µg/mL in cell culture. Parasite viability was assessed using the MTT assay. Additionally, AuNPs were applied topically to skin lesions from cutaneous leishmaniasis, with treatment administered twice daily for 21 days. Lesion size measurements were taken at 7, 14, 21, and 28 days post-treatment, and statistical analyses were conducted using Prism 8 software to determine significance.

Results: The performance of AuGNPs in this study showed time- and dose-dependent efficacy. At 50 µg/mL, the efficacy was comparable to the PC group at 7 and 14 days. For concentrations of 100 and 200 µg/mL, no significant differences were observed compared to the PC at 7, 14, and 21 days, but a statistically significant difference was noted on day 28 (P 0.05). At 400 µg/mL, which showed the highest efficacy, the effectiveness was equivalent to that of the PC at all time points.

Conclusion: This study highlights the significant efficacy of a therapeutic ointment containing Gold NPs derived from the methanolic extract of T. disticum in reducing lesions caused by Leishmania major in infected mice. These results underscore the potential of T. disticum extract as a promising therapeutic option for leishmaniasis.

keywords: : Leishmania major, gold nanoparticles (Gold NPs), Taxodium disticum, treatment

PP-39

Investigating the effects of Terminalia chabula on Promastigote and Amastigote stages of Leishmania infantum

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Background and aim: Leishmania infantum is a primary species of protozoan parasite in the Leishmania genus, causing visceral leishmaniasis. Without proper treatment, it can be fatal. Current treatments face high toxicity, drug resistance and high costs. Consequently, discovering effective treatments is crucial. This study aims to evaluate the anti-leishmanial effects of Terminalia chebula on both promastigotes and amastigotes of Leishmania infantum.

Methods: The study evaluated effects of Terminalia chebula hydroalcoholic extract (400, 200, 100, and 50 µg/ml) on Leishmania infantum promastigotes and amastigotes over 24, 48, and 72 hours, compared to Glucantime (50–100 µg/ml) as positive control and RPMI medium as negative. to calculate the infection rate, Giemsa stained slides were prepared from macrophage culture plates at 24, 48, and 72 hours. The number of infected and uninfected macrophages and the number of amastigotes per macrophage were counted in 10 microscopic sections, then the infection rate was calculated. to calculate the mortality rate, the number of dead and live promastigotes was counted with a Neubauer slide, and then the mortality rate was calculated in all groups at 24, 48, and 72 hours, while the MTT assay measured viability for IC50. Statistical significance was set at P0.05.

Results: The extract's effect on Leishmania infantum lethality over 24 hours showed no significant difference from the control at 50 µg/dL (P0.05). At 100, 200, and 400 µg/dL, it surpassed glucantime. Over 48 and 72 hours, lethality was significantly higher than the control at all concentrations. Lethality increased with time and concentration, but was similar at the highest three concentrations after 72 hours. At 48 hours, mortality at 200 and 400 µg/dL, and at 72 hours, at 100, 200, and 400 µg/dL, was higher than glucantime. At 48 and 72 hours, the extract performed significantly better than the control group at all concentrations (P0.05). The IC50 values after 24, 48, and 72 hours were 341, 124.9, and 54.7 µg/ml.

Conclusion: The findings show Terminalia chebula extract effectively combats both promastigotes and amastigotes of Leishmania infantum. however, Further research is needed. If confirmed, the extract could serve as a herbal therapy for visceral leishmaniasis.

keywords: Terminalia chebula, Leishmania infantum, promastigote, amastigote

PP-40

latent toxoplasmosis and its potential association with cardiovascular diseases: a serological case-control investigation

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Background and aim: Toxoplasma gondii, a globally distributed protozoan parasite, has been suggested to contribute to chronic inflammatory conditions, including cardiac pathologies. However, evidence regarding its role in cardiomyopathy remains limited and inconsistent. This study aimed to investigate the seroprevalence of T. gondii infection and its potential association with cardiomyopathy in a sample from eastern Iran.

Methods: In this case-control study, 101 patients diagnosed with cardiomyopathy and 101 healthy controls were enrolled. Serum levels of anti–T. gondii IgG and IgM antibodies were determined using enzyme-linked immunosorbent assay (ELISA). Demographic, clinical, and exposure-related variables were collected via a structured questionnaire. Univariate and multivariate logistic regression analyses were performed to assess the association between toxoplasmosis and cardiomyopathy while adjusting for potential confounders. All findings were considered significant at a p-value of less than 0.05.

Results: The seroprevalence of anti–T. gondii IgG was higher in cardiomyopathy patients (26.7%) compared to controls (17.8%), whereas IgM positivity was absent in both groups. After adjustment for confounders, IgG seropositivity was associated with an increased odds of cardiomyopathy (OR = 1.50, 95% CI: 0.74–3.04), although this result was not statistically significant (p = 0.26). No significant associations were found between known risk factors for T. gondii transmission and seropositivity in this population.

Conclusion: While not statistically significant, the observed elevated seroprevalence of T. gondii among cardiomyopathy patients suggests a possible link that warrants further investigation in larger longitudinal studies. Preventive health measures targeting toxoplasmosis remain relevant for cardiovascular health awareness.

keywords: Toxoplasma gondii, cardiovascular diseases, case-control, regression analyses, Iran

PP-41

Evaluation of Hydroalcoholic Extract of Terminalia chebula on Leishmania tropica in Promastigote and Macrophage-Infected Amastigote

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Background and aim: Leishmaniasis, caused by Leishmania species, is a major global health issue, with challenges including drug resistance, and high treatment costs. Studies have explored herbal remedies like Terminalia chebula, which has confirmed antibacterial, antifungal, antiviral and antiparasitic effects. Due to limited research on its antiparasitic properties, this study aims to evaluate the extract of T. chebula against Leishmania tropica in Iran.

Methods: After preparation of hydroalcoholic Terminalia chebula extract at concentrations of 400, 200, 100, and 50 µg/ml, the effects on Leishmania tropica amastigotes and promastigotes were tested over 24, 48, and 72 hours. For positive control, glucantime at concentrations of 50 and 100 was used, while RPMI medium served as a negative control. In the in vitro setup, we evaluated mortality rates by counting live and dead promastigotes with a Neubauer slide. In the ex vivo method, slides were prepared from macrophage cultures at 24, 48, and 72 hours across all groups and stained with Giemsa to determine the infection rate. In 10 microscopic sections, the infected and uninfected macrophages were counted, along with the number of amastigotes per macrophage, and the infection rate was subsequently calculated. One-way ANOVA was used to compare infection and mortality rates among groups, with results considered significant at P0.05.

Results: After 24 hours, there was no significant difference from the control group at 50 µg/ml (P0.05). at 100, 200, and 400 µg/ml, the extract was more effective than Glucantime. After 48 and 72 hours, the extract was more lethal than the control at all concentrations (P0.05). As time and concentration increased, lethality rose. At 72 hours, lethality at the three highest concentrations stabilized with minimal change. At 48 hours, the mortality rate at 200 and 400 µg/ml exceeded Glucantime, and at 72 hours, the lethality at 100, 200, and 400 µg/ml exceeded Glucantime. Overall, the extract significantly outperformed the control at all concentrations during 48 and 72 hours (P0.05).

Conclusion: This study demonstrates the significant efficacy of T. chebula against Leishmania tropica, comparable to that of Glucantim and, in some concentrations, exceeding it. Meanwhile, further research on this subject is necessary.

keywords: Terminalia chebula, Leishmania tropica, promastigote, amastigote

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PP-42

Prevalence and diversity of blood protozoa in native birds of northeastern Iran

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Background and aim: Blood protozoa are among the most important avian pathogens, affecting both the health and survival of birds and causing considerable economic losses to human communities. This study investigated the prevalence of hemoparasites in native bird populations of Semnan Province during 2021–2022.

Methods: A total of 263 blood samples were collected from 10 families of native birds across various counties of Semnan Province, northeastern Iran. Blood smears were prepared and examined microscopically for the presence of blood protozoa.

Results: Overall, 22.1% of the sampled birds were infected with blood protozoa. The prevalence of blood parasites was 18.6% for Haemoproteus spp., 1.5% for Plasmodium spp., 1.1% for Leucocytozoon spp., and 0.8% for Aegyptianella spp. The highest infection rate was observed in pigeons, mainly with Haemoproteus spp. (9.9%). Turkeys were the only birds free of blood protozoan infection.

Conclusion: Although a higher prevalence was observed during warmer months and in older birds, no statistically significant associations were found between age, season, and infection rate. This study highlights a considerable prevalence of blood protozoans in native birds of Semnan Province. Further molecular studies are needed to better understand the epidemiology of these infections.

keywords: Blood protozoa, Haemoproteus, Aegyptianella, Plasmodium, Leucocytozoon

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PP-43

Nosocomial oral myiasis caused by Chrysomya bezziana in Iran: a new case and review of human myiasis in the country

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Background and aim: Myiasis is an opportunistic infestation of living tissue in vertebrates with the larvae of dipteran flies mainly belonging to Oestridae, Calliphoridae, and Sarcophagidae. Chrysomya bezziana can potentially cause myiasis, a condition in which fly larvae infest living tissue in humans and animals. Contributing factors to this rare ailment include poor oral hygiene, alcohol abuse, and infected wounds. Hospital-acquired myiasis, a type of rare myiasis, occurs in patients following their admission to the hospital

Methods: In June 2024, an 89-year-old female with complaints of hypertension, dyspnea, and weakness was presented to the Emergency Department of Imam Khomeini Hospital, Shahroud, Iran. Several months ago, the patient contracted COVID-19 before being admitted to the hospital. She was immediately transferred to the ICU due to poor general condition, and low blood oxygen and was intubated. The patient underwent laboratory examinations and necessary measures were carried out

Results: Herein, we report a case of C. bezziana oral myiasis in an 89-year-old female patient hospitalized in northeastern Iran. We advise an increase in the awareness of healthcare professionals, especially those working with critically ill patients, under mechanical ventilation, the elderly, and individuals with missing teeth, about the risk of myiasis

Conclusion: Herein, we report a case of C. bezziana oral myiasis in an 89-year-old female patient hospitalized in northeastern Iran. We advise an increase in the awareness of healthcare professionals, especially those working with critically ill patients, under mechanical ventilation, the elderly, and individuals with missing teeth, about the risk of myiasis

keywords: hospital, myiasis, Iran, nosocomial, blowfly

PP-44

High Parasitic Infections in the Laboratory Animals: Complications for the Research Outcomes and Zoonotic Importance

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Background and aim: Laboratory animals are widely used for medical research; hence, their health status is a determinant of the outcome and success of the research. We aimed to investigate the possible infection of rodents with intestinal parasites in the Hamadan University of Medical Sciences animal house.

Methods: From October to November 2022, one hundred and twenty healthy laboratory ro-dents including 60 Wistar rats, 30 BALB/c mice, and 30 NMRI mice were random-ly collected and examined for parasitic infections. The digestive tracts were removed and examined for contamination by helminths and parasitic protozoa using naked eye inspection and microscopy

Results: 75.8% (95% CI: 68.1–83.5%) of the rodents were infected by at least one helminth or protozoa. Protozoal infections (41.7%) with Giardia spp. (15%), Tritrichomonas spp.(10%), Blastocystis spp. (6.7%), Entamoeba spp. (5.9%), Cryptosporidium spp. (3.3%), and Eimeria spp. (0.8%) were observed relatively higher than helminthic in-fections (34.2%) with Syphacia obvelata (10.8%), Syphacia muris (10%), Aspiculuris te-traptera (7.5%), Hymenolepis nana (3.3%), and Hymenolepis diminuta (2.5%).

Conclusion: This study showed high parasitic infection without clinical signs in laboratory ro-dents. Therefore, monitoring these animals and improving their breeding conditions can eliminate the adverse effects of these parasitic infections in the animal research processes and improve the health of researchers and staff.

keywords: Laboratory Animals; Gastrointestinal Para-sites; Zoonotic Parasites

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PP-45

Seroepidemiological study of toxocariasis using ELISA method in pet owners referring to veterinary hospitals in Tehran

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Background and aim: Nowadays, keeping pets has become very popular. These animals have the potential to be infected with various infectious diseases including parasitic diseases. Many people do not have the necessary knowledge in this field. Toxocariasis, which is transmitted to humans through exposure to parasite eggs is an important disease-causing visceral larva migrans. Referring to veterinary hospital/clinic and implementing health guidelines can greatly reduce the spread of possible infections. Since, epidemiological studies can significantly contribute to the control of the diseases, Here the seroepidemiology of toxocariasis was studied using the ELISA method in pet owners referring to veterinary clinics in Tehran.

Methods: A total of 269 serum samples were collected from volunteers. One hundred cases from pet owners and 139 cases from people without close contact with pet animals. Samples were randomly selected from different areas of Tehran. Anti-Toxocara antibodies were evaluated in all of sera using the ELISA NovaLisa/Germany kit.

Results: Out of 269 samples, 5(1.9%) were shown positive response against Toxocara antigens in the Elisa kit. Three samples(1.1%) were from pet owners and 2(0.8%) from other individuals. There was no statistically significant relationship between having a pet and seropositivity. Also there was no significant relationship between seroposivity and age, gender, occupation, place of residence, type of water consumed, duration of animal keeping, daily level of contact with the animal, and type of animal feeding. Although there was no statistically significant relationship between seropositivity and method of washing vegetables, 80 percent of individuals with positive response did not use disinfectants for washing their consumed vegetables. On the other hand regular periodic examinations of animals, was shown borderline positive effect on seropositivity of toxocariasis (P0.06).

Conclusion: The results of this study were showed that pet owners, especially those who do not have a regular schedule for periodic examinations of their animals, are more to likely to put themselves at risk.

keywords: Toxocariasis, Pet owners, Seroepidemiology, Tehran.

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PP-46

Prevalence and Some Associated Risk Factors of Oral Cavity Protozoa Among Autoimmune Disease Patients with Oral Lesions in Kashan, Iran, 2023

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Background and aim: Objectives: Two oral cavity protozoa that are commonly detected in patients with different kinds of periodontal disorders are Entamoeba gingivalis and Trichomonas tenax. The potential role of these protozoa in dental caries and oral infectious diseases remains unknown. The present study aims to determine the prevalence of these protozoa and some associated risk factors among patients with autoimmune diseases and oral lesions.

Methods: This study was randomly conducted on 122 patients who suffered from autoimmune diseases and oral lesions referring to dental clinic centers in Kashan, in the center of Iran. Two specimens were obtained from oral lesions and saliva for each patient. The samples were immediately examined under a light microscope using wet mount preparation and stained with Giemsa and trichrome. Furthermore, the samples were cultured in Robinson's and diphasic Locke-egg media.

Results: T. tenax and E. gingivalis protozoa were found in 12 (9.8%) and 7 (5.7%) of patients, respectively. The highest prevalence rate of total infections was found among patients with lupus erythematosus (20%) and lichen planus (17.9%). The lowest rate belonged to patients with psoriasis (11.1%). There was no significant difference between infection rates and autoimmune diseases (P = 0.0946). In the multivariate model, the frequency of parasites was significantly associated with age (P = 0.0374), brushing teeth, and the presence of dental caries (P = 0.0001).

Conclusion: The infections are frequent in individuals with autoimmune diseases and oral lesions. Controlling infections requires knowledge of the primary risk factors, including dental cavities and brushing habits.

keywords: Dental Caries, Entamoeba Gingivalis, Trichomonas Tenax, Autoimmune Disease, Iran

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PP-47

Endochin-Like Quinolones Exhibit Promising Efficacy Against Neospora Caninum in vitro and in Experimentally Infected Pregnant Mice

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Background and aim: We report on the efficacy of selected endochin-like quinolones (ELQs) against N. caninum tachyzoites grown in human foreskin fibroblasts (HFF), and in a pregnant BALB/c mouse model. Fourteen ELQs were screened against transgenic N. caninum tachyzoites expressing β-galactosidase (Nc-βgal).

Methods: Drugs were added concomitantly to infection, and the values for 50% proliferation inhibition (IC50) were determined after 3 days. Three compounds exhibited IC50 values below 0.1 nM, 3 ELQs had IC50s between 0.1 and 1 nM, for 7 compounds, values between 1 and 10 nM were noted, and one compound had an IC50 of 22.4 nM. Two compounds, namely ELQ-316 and its prodrug ELQ-334 with IC50s of 0.66 and 3.33 nM, respectively, were previously shown to display promising activities against experimental toxoplasmosis and babesiosis caused by Babesia microti in mice, and were thus further studied. They were assessed in long-term treatment assays by exposure of infected HFF to ELQs at 0.5 µM concentration, starting 3 h after infection and lasting for up to 17 days, followed by release of drug pressure.

Results: Results showed that the compounds substantially delayed parasite proliferation, but did not exert parasiticidal activities. TEM of drug treated parasites detected distinct alterations within the parasite mitochondria, but not in other parasite organelles. Assessment of safety of ELQ-334 in the pregnant mouse model showed that the compound did not interfere in fertility or pregnancy outcome. In N. caninum infected pregnant mice treated with ELQ-334 at 10 mg/kg/day for 5 days, neonatal mortality (within 2 days post partum) was found in 7 of 44 pups (15.9%), but no postnatal mortality was noted, and vertical transmission was reduced by 49% compared to the placebo group, which exhibited 100% vertical transmission, neonatal mortality in 15 of 34 pups (44%), and postnatal mortality for 18 of the residual 19 pups during the 4 weeks of follow-up.

Conclusion: ELQ-334 could be potentially combined with another quinolone, such as the Qo site inhibitors atovaquone or buparvaquone, to achieve dual site inhibition and probably increased efficacy, or with another compound of a different mode of action. Proof of concept for such a combination therapy was provided in an immunodeficient mice experimentally infected with B. microti, where radical cure was achieved using a combination of ELQ-334 and atovaquone at a dosage of 5 mg/kg, with no recrudescence of babesiosis during a time span of 122 days after discontinuation of therapy

keywords: Neospora, Toxoplasma, endochin-like quinolones, mitochondrion, cytochrome b, electron microscopy, vertical

PP-48

Microscopic and molecular detection of Blastocystis spp. and Giardia lamblia in drinking and surface water sources in South Khorasan province, Iran

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Background and aim: Safe drinking water is a fundamental aspect of public health. Nonetheless, its contamination by harmful microbes, particularly intestinal parasites, continues to pose a significant public health risk at the community level. Waterborne parasites such as Giardia lamblia and Blastocystis spp. are known to cause chronic illnesses, nutritional deficiencies, and gastrointestinal issues, especially among children and individuals with compromised immune systems. In light of these risks, the present study aimed to assess the prevalence of these protozoan parasites in drinking and surface water sources in South Khorasan Province, Iran.

Methods: A total of 116 water samples were collected from various locations throughout South Khorasan Province. These samples were transported to the laboratory in sterile containers under appropriate conditions. Upon arrival, each sample was filtered and examined microscopically to identify any potential parasite forms. DNA was extracted from samples suspected of containing protozoa or confirmed positive under the microscope using the Pars Toos DNA extraction kit. Molecular detection of Giardia lamblia and Blastocystis spp. was then performed using PCR. Additionally, metadata was recorded, including the type of water source, sample location, and relevant environmental data.

Results: Based on microscopic analysis, 18.9% of the samples were suspected to have parasite infections. Further PCR analysis confirmed the presence of protozoan parasites in 15.5% of the samples. Among these, 12 samples tested positive for Blastocystis spp., while 6 samples contained Giardia lamblia. Geographic distribution analysis revealed that Ferdows had the highest prevalence of Giardia lamblia at 20%, while Tabas and Khosf exhibited the highest rates of Blastocystis spp. at 37% and 25%, respectively. In Birjand, the provincial capital, the prevalence rates were 10.5% for Giardia lamblia and 5.26% for Blastocystis spp. Notably, 94% of the PCR-positive samples were associated with surface water sources.

Conclusion: Given the high prevalence of protozoan parasites identified in this study, establishing continuous monitoring programs for water resources is essential. Additionally, enhancing quality control measures and improving water purification infrastructure are critical steps to further reduce the risk of waterborne parasitic diseases in the region.

keywords: Blastocystis spp., Giardia lamblia, surface water, drinking water, South Khorasan

PP-49

The Molecular Method in Diagnosis of Ocular Toxoplasmosis in Tehran

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Background and aim: Toxoplasma gondii (T. gondii) is one of the most common parasitic infections in humans and animals. It is considered as an opportunistic infection in immunosuppressed individuals or pregnant women. The parasite reaches to the eye and its retina through circulation and causes irrecoverable chorioretinitis. Attack to the eyes is chronic and sometimes the damaged retina and choroid would not repair. The posterior pole scars can persist a serious threat for the vision. The aim of the current study is to evaluate efficiency (sensitivity and characteristic) of molecular method in isolation of T. in ocular infections patients with healthy immune systems.

Methods: Blood sampling had done from major ophthalmology centers in Tehran (Farabi, Labbafinejad and Imam Hossein Hospitals). The clinical symptoms were examined and recognized. For examining possible relapse re-sampling was done in 15 and 30 days. Thereafter, the buffy coat of the samples was employed for DNA extraction using Diesel Natural Gas (DNG) kit. For performing the polymerase chain reaction (PCR), primer of the gene B1was applied.

Results: Following the PCR, from the 71 blood samples, 34 patients (47%) had positive for of the disease. However, with evaluating the first relapse, two weeks after the first step of the disease, among the 41 patients, 29 (70%) had positive reaction of the disease. These patients even showed positive PCR in the first step. In the third sampling step (30 days later), 19 patients were examined and 9 (47%) had positive reaction. In other words, in the second and the third steps there were no obvious incidents

Conclusion: The diagnosis of T. gondii, often relays on clinical tests. Nevertheless, unusual clinical symptoms or differentiation of the disease from other alternative symptoms make the diagnosis problematic. However, sensitivity and characteristic of molecular PCR is of great interest. To conclude, for definite and final ocular toxoplasmosis diagnosis, clinical and complementary methods such as PCR can be employed.

keywords: Ocular Toxoplasmosis, Chorioretinal Scar, Retinochoroiditis, Vitreous Inflammation, Uveitis, PCR

PP-50

Sero Molecular Prevalence Study of Toxoplasma in Beta-Thalassemia Major Patients Using ELISA and LAMP Method in 2015

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Background and aim: Toxoplasma infection is one of the most prevalent and serious infectious diseases in immunodeficiency persons such as in beta-thalassemia major patients. The study was carried out to determine the sero-prevalence of anti-Toxoplasma antibodies in beta-thalassemia major patients.

Methods: A total of four hundred and seventy serum samples were collected from beta-thalassemia major patients referring to Hajar hospital in Shahr-e-kord, Iran as the test group and healthy individuals as the control group (i.e. each group consisted of 235 samples). The demographic data were collected via questionnaire forms and the sera and blood samples were examined for specific anti-Toxoplasma antibodies (IgM,IgG) using ELISA and LAMP method. The processing of data was accomplished by the software, SPSS ver.20 and analysed by the Chi-square test, Independent T test and Logistic regression model.

Results: Out of 235 sera belonged to the beta-thalassemia major patients, 122 (51.9%) and 8 (3.4%) sera were positive for anti-Toxolasma IgG and IgM antibodies, respectively. However, these positivity rates were 82 (34.8%) and 5 (2.1%) for anti-Toxoplasma IgG and IgM in the control group. There were significant differences between sex, age, contact with cat, job, Meat consumption in case group (p0.001) and also There were significant differences between sex, age and Meat consumption in control group (p0.001). also molecular results showed that 14 (5.95%) positive in control group and 23 (9.78%) positive in case group.

Conclusion: It is likely that the majority of Toxoplasma infections in beta-thalassemia major patients have been occurred prior to their malignancy. However, malignancy may reactivate the latent Toxoplasma infections.

keywords: Keywords: Toxoplasma Infection, Major Thalassemia, ELISA, LAMP

PP-51

A study of the effects of 2-Nitroimidazole compounds against Leishmania major in vitro

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Background and aim: Leishmania major is an intracellular protozoan and the causative agent of cutaneous leishmaniasis. Treatment of cutaneous leishmaniasis has always been associated with challenges, including drug resistance, limited access to new drugs, and adverse effects of current therapies. Therefore, the development of new drugs remains a priority. 2-Nitroimidazole compounds are a group of nitroaromatic agents with potent antiparasitic activity, acting through the disruption of essential structures within the parasite, and are effective against unicellular parasites such as Leishmania and Trypanosoma. The aim of this study was to evaluate the effects of 2-nitroimidazole on Leishmania major under in vitro conditions.

Methods: L. major was cultured in RPMI 1640 medium. Parasite density was assessed in the presence of the drug at concentrations ranging from 1.9 to 500 µg/mL at 24, 48, and 72 hours, and the IC50 values were determined. The effect of 2-nitroimidazole on promastigotes was evaluated using the MTT assay at the same concentration range. The cytotoxicity of the drug was assessed on macrophages derived from BALB/c mice. Accordingly, macrophages were treated with 2-nitroimidazole (1.9–500 µg/mL) and assessed using the MTT assay. To evaluate the effect of the drug on amastigotes, cultured macrophages in 6-well plates were infected with parasites and exposed to drug concentrations of 31.25–250 µg/mL. After 72 hours, cells were fixed and stained with Giemsa, and the intracellular infection rate was determined. Additionally, flow cytometry analysis was performed to assess apoptosis induction in promastigotes treated with 10 and 50 µg/mL of the drug using Annexin V staining.

Results: The results of this study demonstrated that 2-nitroimidazole significantly reduced the growth and viability of L. major promastigotes in a dose- and time-dependent manner, with notable IC50 values. At effective concentrations, the drug showed limited cytotoxicity toward BALB/c macrophages and significantly decreased intracellular amastigote infection. Flow cytometry analysis further confirmed increased apoptosis induction in promastigotes following drug treatment.

Conclusion: Overall, the results indicates that 2-nitroimidazole effectively inhibit L. major propagation in vitro. Future evaluation should be recommended for in vivo condition.

keywords: Leishmania major, cutaneous leishmaniasis, 2-nitroimidazole , in vitro

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PP-52

Evaluation of Antimony Sulfide Nanoparticles Combined with Kojic Acid for the Treatment of Leishmania major Induced Cutaneous Lesions

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Background and aim: Cutaneous leishmaniasis (CL) caused by Leishmania major remains a significant health problem, largely due to the toxicity and limited long-term efficacy of conventional antimonial drugs. Nanoparticle-based formulations have gained attention as potential strategies to enhance anti-leishmanial efficacy and treatment durability. Objective: This study evaluated the therapeutic efficacy of antimony sulfide nanoparticles (Sb_2S_3 NPs) combined with kojic acid in a BALB/c mouse model of L. major induced cutaneous leishmaniasis.

Methods: BALB/c mice were subcutaneously infected with stationary-phase promastigotes of L. major (MHROM/IR/75/ER). Following lesion development, animals were allocated into five groups: combination therapy (Sb_2S_3 NPs + kojic acid, 70 µg/mL, topical, twice daily for 28 days), kojic acid alone, Glucantime® (100 mg/kg/day for 14 days), PBS control, and non-infected controls. Lesion size was measured weekly, and parasite burden was assessed semi-quantitatively using Giemsa-stained lesion smears based on WHO criteria. Data were analyzed using appropriate parametric and non-parametric statistical tests.

Results: The combination therapy induced a significant and sustained reduction in lesion size over four weeks (11.7 ± 2.0 to 7.9 ± 2.4 mm; P 0.01), outperforming PBS and kojic acid alone. Semi-quantitative analysis revealed a marked decrease in parasite burden in the combination group, including complete parasite clearance in some animals and absence of high-grade infection scores. Parasite reduction was significantly greater than that observed with PBS (P 0.001), kojic acid alone, and Glucantime (P 0.05). Kojic acid alone showed only moderate efficacy, while Glucantime demonstrated effective short-term responses.

Conclusion: The combination of antimony sulfide nanoparticles and kojic acid exhibits potent and sustained anti-leishmanial activity, suggesting a promising alternative approach for the treatment of cutaneous leishmaniasis.

keywords: Cutaneous leishmaniasis Leishmania major Antimony sulfide nanoparticles Kojic acid

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July 20-23, 2026

PP-53

Gene expression profiling in cardiac tissue of mice chronically infected with Toxoplasma gondii: implications for immune response pathways

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Background and aim: Toxoplasma gondii is a common, opportunistic protozoan in vertebrates. While most infections are asymptomatic, it causes severe complications in immunocompromised individuals by forming cysts in tissues like the heart and brain. Heart tissue damage during toxoplasmosis infection is associated with many complications, such as myocarditis, pericarditis, arrhythmia and heart failure. The parasite can survive and create a chronic form of infection by changing the expression of genes effective in the immune system. Therefore, the present study aims to investigate expression dynamics of candidate genes in the heart tissue of mice infected with the chronic T. gondii and the pathways involved.

Methods: All procedures performed on the mice strictly adhered to ethical guidelines to ensure minimal pain and distress to the animals. The animals were monitored daily, and all necessary supportive measures were provided. Chronic toxoplasmosis was induced in 15 male Balb/c mice (5 weeks old) via intraperitoneal injection of 20 T. gondii cysts; a control group received saline. Six weeks later, the Modified Agglutination Test (MAT) confirmed infection, ensuring sampling coincided with the stable chronic phase of cardiac cyst development. Heart tissues were harvested after sacrificing the mice for subsequent experiments. RNA was extracted using the RNeasy Mini Kit (Qiagen) and quantified via NanoDrop. cDNA was synthesized using a Takara Prime Script kit. Target gene expression (ccl4, gbp5, ctla4, samhd1) was quantified by Real-time PCR using GAPDH as the control. Statistical analysis followed the ΔΔCt method (Student's t-test, p0.001), and molecular functions were explored using Enrichr for Gene Ontology analysis.

Results: The study confirmed a significant percentage of samples tested positive via the MAT assay. High-quality RNA was successfully extracted from both infected and non-infected mouse heart tissues, as validated by nanodrop measurement. Real-time PCR revealed that the expression of ccl4, gbp5, ctla4, and samhd1 genes was consistently higher in infected heart tissues compared to controls. Among these, ctla4 showed the highest expression, while gbp5 had the lowest. Gene ontology analysis indicated that these genes are primarily involved in biological processes such as "cellular response to interferon-gamma" and "natural killer cell chemotaxis." Cellular component analysis highlighted roles in cell adhesion and clathrin-coated endocytic vesicles. Furthermore, pathway analysis demonstrated significant gene participation in pathways related to "autoimmune thyroid disease," the "cytosolic DNA-sensing pathway," and "rheumatoid arthritis.

Conclusion: The results of this study clarify the role of candidate genes in contributing to the development of a chronic form of infection during infection with T. gondii type II (Tehran strain) in heart tissue. It is hoped that the results of this study will add to the depth of the knowledge of parasite and host reactions and will help in understanding more of the immune pathways involved and as a result design new drugs.

keywords: Toxoplasma gondii, chronic infection, Heart, Pathway analysis, Real-time PCR

PP-54

The effect of copper oxide nanoparticles on Leishmania major in vitro

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Background and aim: Cutaneous leishmaniasis is one of the most common parasitic diseases in Iran, and its main cause is Leishmania major. Iran, as one of the endemic countries for leishmaniasis, faces a significant number of cases annually. Current treatments are associated with limitations such as toxicity and drug resistance. Copper oxide nanoparticles have been proposed as a promising option in the control of Leishmania major due to their antiparasitic properties. The aim of this study was to investigate the effect of copper oxide nanoparticles on L. major in vitro.

Methods: Leishmania major parasite was cultured in RPMI 1640 medium containing FBS and antibiotics and its growth was monitored at the appropriate temperature and counted with a Neubauer slide. To evaluate the effect of the drug, promastigotes and macrophages extracted from BALB/c mice were cultured in plates and MTT assay was performed after treatment with copper oxide nanoparticles, its concentrations were from 500 to 1.9 µg/ml. Also, amastigote growth inhibition test was performed by infecting macrophages, fixation and Giemsa staining and the amount of intracellular contamination was examined and then flow cytometry was used to measure apoptosis

Results: The results of the study show that copper oxide nanoparticles with an IC50 of about 10 have the ability to inhibit the growth and reduce the survival of Leishmania major. The reduction in the viability of promastigotes and macrophages, as well as the reduction in the intracellular contamination of amastigotes, confirm the antiparasitic effect of this nanoparticle. Induction of apoptosis at concentrations of 10 and 50 has also been proposed as one of the possible mechanisms of its effect. Overall, copper oxide nanoparticles have high potential as a novel antileishmanial agent.

Conclusion: Copper oxide nanoparticles demonstrated effective in vitro antileishmanial activity against Leishmania major by inhibiting parasite growth and reducing intracellular infection. These results indicate their potential as a novel antileishmanial agent, pending further in vivo evaluation.

keywords: Leishmaniasis, nanoparticles, copper oxide, in vitro

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PP-55

Evaluation of anti-leishmanial effect of Zinc Oxide (ZnO) nanoparticles doped with AgNo3 (ZnO-Ag) synthesis to Ferula szowitsiana on Leishmania major promastigotes In-Vitro

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Background and aim: Cutaneous leishmaniasis is a significant health threat in Iran and other countries. Glucantime is commonly used for treatment; however, due to its side effects and resistance issues, there is a growing interest in alternative therapeutic methods, particularly involving nanoparticles and metal-doped nanoparticles combined with plant extracts. This study aims to Evaluation of anti-leishmanial effect of Zinc Oxide (ZnO) nanoparticles doped with AgNo3 (ZnO-Ag) synthesis to Ferula szowitsiana on Leishmania major promastigotes In-Vitro.

Methods: In this experimental study, the anti-leishmanial activity of zinc oxide nanoparticles and silver nitrate-doped nanoparticles was assessed at various concentrations (0, 0.75, 1.5, 3, 6, 12, 48, and 96 µg/mL) and exposure times (24, 48, and 72 hours). The extract of the Ferula szowitsiana was prepared, and the nanoparticles were synthesized and characterized using TEM, SEM, and XRD techniques. The number of viable parasites was counted using trypan blue staining, with glucantime and distilled water serving as positive and negative controls, respectively. The IC50 values of the nanoparticles were calculated, and the data were analyzed using t-tests.

Results: The synthesis of silver-doped zinc oxide nanoparticles was confirmed by a color change in the solution. XRD, TEM, and SEM results indicated crystallinity and irregular shapes of the nanoparticles. All concentrations of the nanoparticles exhibited anti-leishmanial activity, with the 96 µg/mL concentration of silver-doped zinc oxide nanoparticles combined with Ferula szowitsiana showing the highest anti-leishmanial effect (69%) and the lowest IC50 value (5.14 µg/mL) after 72 hours.

Conclusion: Silver-doped zinc oxide nanoparticles combined with Ferula szowitsiana demonstrated superior anti-leishmanial effects at higher concentrations compared to other nanoparticles. The combination of nanoparticles with plant extracts may contribute to the development of more effective treatments for leishmaniasis.

keywords: Leishmania major, Zinc Oxide, AgNo3, Ferula szowitsiana, In-Vitro

PP-56

Epidemiological study of cutaneous leishmaniasis in an endemic focus in northeast of Iran (Sarkhs)

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Background and aim: Leishmaniasis is considered one of the major health problems in Iran. Given that epidemiological studies play an important role in disease control and preventive measures, this study aimed to investigate the epidemiology of cutaneous leishmaniasis in Sarakhs County, Razavi Khorasan Province.

Methods: This descriptive-analytical study was conducted on the data of patients with cutaneous leishmaniasis during the years 2016 to 2019. In this way, the demographic and epidemiological data recorded in the disease surveillance system of the Health Deputy were extracted and analyzed using SPSS software and the chi-square statistical test.

Results: The number of patients with cutaneous leishmaniasis during these 4 years was 537. Considering the population of the region (97,519 people), the overall prevalence of the disease during these 4 years was 126.6 per 100,000 people. 57.8% of the patients were male, and 42.2% were female. 73.2% were rural, and 26.8% were urban. Most of the cases were in the age groups of children under 10 years old, and in terms of occupation, the highest frequency was in the two groups of students and children.

Conclusion: The prevalence of the disease in Sarakhs city is in the middle of the frequency spectrum of endemic areas of Iran, which is a high figure. Considering the high incidence of the disease in the two groups of children and students, the need for necessary training in disease prevention and increasing the level of health literacy is suggested.

keywords: Epidemiological,Leishmaniasis,Iran

PP-57

Demographic analysis of patients with cutaneous leishmaniasis in northeastern Iran (North Khorasan) during a retrospective study

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Background and aim: leishmaniasis is considered one of the major health problems in Iran. Given that epidemiological analyses play an important role in disease control and preventive measures, this study was conducted with the aim of epidemiological analysis of cutaneous leishmaniasis in North Khorasan Province.

Methods: This descriptive-analytical study was conducted on the data of patients with cutaneous leishmaniasis during the years 2014-2022. In this way, the demographic and epidemiological data recorded in the disease surveillance system of the Health Deputy of North Khorasan Province were extracted and analyzed using SPSS software and the Chi-square test.

Results: The number of patients with cutaneous leishmaniasis during these 8 years was 2243. Considering the population of the region (863,000 people), the overall incidence of the disease during these few years was 32.5 per 100,000 people.Out of 62.2% of the patients were male, 51.1% were rural. Most cases were in the age groups of children under 10 years old, and in terms of occupation, the highest frequency was in the two groups of students and children (P0.05). The majority of wounds (76.6%) were exudative.

Conclusion: The prevalence of the disease in North Khorasan Province is in the middle of the frequency spectrum of endemic areas of Iran, which is a high figure(It is higher than the national average incidence).Considering the high incidence of the disease in the two groups of children and students, the need for necessary education in disease prevention and increasing the level of health literacy is suggested.

keywords: Demographic, cutaneous leishmaniasis, retrospective study, Iran

PP-58

Seroprevalence of Toxoplasma gondii in Women Referring to Health Centers in Sabzevar, Northeast of Iran (2021-2022)

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Background and aim: Toxoplasmosis is a common zoonotic disease in the world, which is caused by an intracellular protozoan parasite called Toxoplasma gondii. In its congenital form, the pathogen is transferred to the fetus through placenta. The acquired infection is caused by either consuming contaminated meat and vegetables or contact with cats. The present research aimed to investigate the prevalence of anti-T. gondii IgG antibody in women referring to health centers for premarital tests in Sabzevar, Northeast of Iran (2021-2022).

Methods: This cross-sectional descriptive-analytical study included 190 women admitted to health centers in Sabzevar for premarital tests. The participants were selected by simple random sampling. A questionnaire was used to collect the clients' demographic information and data on some risk factors. In order to perform the tests, 2 mL of their blood samples was taken and their serum was separated. The serum samples were kept at -20 °C until the test was performed. To perform the test, after thawing the serum samples, the presence of anti-T. gondii IgG antibody was examined using the ELISA method in the immunology laboratory of the medical school. The data analysis was done using the chi-square test in SPSS.

Results: The results showed that out of 190 participants, 171 had no history of infection with this parasite and only 19 of them had a positive anti-T. gondii IgG antibody test result. Additionally, 90% did not have enough immunity. The Chi-square test showed a significant positive relationship between the presence of anti-T. gondii IgG antibody and age, education, consumption of semi-cooked meat and vegetables (P 0.05).

Conclusion: The results suggest that the positive rate of IgG test in this Northeast Iranian region is lower than in other parts, and this problem may be attributable to its specific climatic conditions, where it is hot and dry, and the humidity level is relatively low. The destruction of the parasite oocyst due to these factors can result in a low rate of parasite transmission. Therefore, the need for a screening program is not necessary, but educational programs are recommended to educate women before marriage.

keywords: Seroepidemiologic studies, Immunoglobulin G, Women

PP-59

Jackals are Potential Source of Zoonotic Infection within the Astara (Gilan Province) for Mesocestoides spp., Iran; First Report

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Background and aim: Mesocestoides spp. a zoonotic parasite infecting wild and domesticated carnivores. Their complex life cycle with the oncosphere of Mesocestoides growing in the first intermediate host (arthropod), and the larva developing into tetrathyridium in the second intermediate host (small mammals and reptiles). The main second intermediate hosts are small rodents, while red foxes (Vulpes vulpes) act as the final hosts in Europe. The tetrathyridia stage can develop in amphibians, reptiles, birds, mammals, and potentially humans. The tetrathyridia develop in the intestines of the final hosts penetrate the gut wall, leading to peritonitis and pleuritic conditions. Although human infections of Mesocestoides spp.

Methods: Methods: The small intestines of five jackals were examined, using intestinal scraping technique (IST) and sedimentation and counting technique (SCT).

Results: Results: Mesocestoides spp. was successfully confirmed in one isolate (20%) Figure. This is the first documented evidence of Mesocestoides spp. presence in wild animals from Astara region, Gilan, Iran.

Conclusion: Mesocestoides spp., in jackals potentially contribute to environmental pollution and pose a threat to local community health. Given the high number of jackals in close proximity to residents, the study sites should be considered as potential sources of contamination particularly in Astara and Talesh cities which are adjacent to the Republic of Azerbaijan and it is necessary to implement rigorous health measures and enhance public awareness due to factors such as food exports, tourism, and the risk of contact with infected final hosts. There is limited evidence regarding Mesocestoides in

keywords: Jackals, Mesocestoides spp., Iran

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PP-60

Evaluation of the prevalence of intestinal parasitic diseases in patients with covid-19 admitted to Baqiyatallah Hospital

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Background and aim: Intestinal parasitic diseases are among the most common infectious diseases worldwide. These diseases can impose a heavy burden on public health. COVID-19 pandemic, which began in 2019, has been one of the most important global health challenges. Since both diseases can affect the immune system and potentially influence each other, their simultaneous investigation may provide a better understanding of the possible relationship between these infections. Accordingly, this study aimed to determine the prevalence of intestinal parasitic infections in patients with COVID-19 referred to Baqiyatallah Hospital over the course of one year.

Methods: In this cross-sectional study (Feb 2020 to Jan 2021), stool examination results and COVID-19 status of 7008 individuals referred to the laboratory were examined. After eliminating duplicates, a total of 4042 patients were analyzed. Data were analyzed with SPSS version 16 using t-tests, chi-square, and logistic regression.

Results: Among the 4,042 participants, 2,470 were male (61.1%) and 1,572 were female (38.9%). The participants' age ranged from 0 to 91 years, with a mean age of 40.78 years (SD = 20.7). The mean age of non-infected individuals was 40.58 years, while that of infected individuals was 48.3 years. Based on the t-test, the age difference between infected and non-infected individuals was statistically significant ($p = 0.00$). Statistical analysis using the chi-square test showed no significant association between sex and parasitic infection ($p = 0.07$). The prevalence of parasitic infection was 5.2% in Covid-negative patients, 13.8% in suspected Covid patients, and 1.9% in Covid-positive patients. Logistic regression analysis examining sex, age, and COVID-19 status simultaneously showed that all three variables were significantly associated with parasitic infection.

Conclusion: In general, the relationship between parasitic diseases and COVID-19 is a multifactorial subject. It is clear that a unified version cannot be considered to comment on the relationship between these diseases and their exposure. Therefore, screening the patients for parasitic infections can be beneficial in better and more accurate clinical management.

keywords: Prevalence, Intestinal parasitic diseases, COVID-19, Baqiyatallah Hospital

PP-61

Evaluation of prevalence of Blastocystis hominis among patients attending Baqiyatallah Hospital, Tehran, Iran

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Background and aim: Blastocystis hominis (B. hominis) is an anaerobic intestinal protozoan with a worldwide distribution, commonly found in the gastrointestinal tract of humans and various animals. Although many researchers are believed that B. hominis is a pathogenic microorganism, and attributed different symptoms, there is still much debate about its pathogenicity in humans. Achieving valuable results and conclusions in this field requires conducting multiple and diverse research in different parts of the world. In this regard, the prevalence of B. hominis among patients attending Baqiyatallah Hospital was evaluated.

Methods: From October to November 2025 a total of 1000 stool samples were collected from patients attending Baqiyatallah Hospital, Tehran. All samples were examined by wet smear for B. hominis isolation. In order to increasing the accuracy, some samples were stained with trichrome staining technique. Demographic information of patients such as sex, age and also stool information was recorded.

Results: Out of 1000 stool samples 548 (54.8%) were male and 452 (45.2%) were female. The age range of participants was between 1 to 70 years. Microscopic examination of stool samples was shown 53 (5.3%) cases of intestinal parasitic infection. The most common parasite observed was B. hominis with a prevalence of 4.4%, (44 cases) followed by Giardia lamblia with 0.5% (5 cases) and Entamoeba histolytica/dispar with 0.4% (4 cases) of prevalence.

Conclusion: The relatively high prevalence of B. hominis indicates substantial human exposure to this protoza. Consequently, preventive measures against infection are of significant importance.

keywords: Blastocystis hominis, Baqiyatallah Hospital, Intestinal parasites.

PP-62

Molecular Detection of Leishmania RNA Virus 2 in Cutaneous Leishmaniasis Patients from Ilam Province, Iran

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Background and aim: Cutaneous leishmaniasis (CL) is a vector-borne disease caused by protozoan parasites and represents a major public health challenge in many countries, including Iran. Recent studies showed the role of Leishmania RNA virus (LRV) in the pathogenesis of cutaneous and mucosal forms of leishmaniasis. Our aim was to investigate presence of LRV and its genotype diversity among isolates in Ilam province, western Iran for the first time.

Methods: Thirty-two lesion specimens were collected from patients with cutaneous leishmaniasis and analyzed by PCR method using species-specific primers for Leishmania identification, including forward LITSR (5′-CTGGATCATTTTCCGATG-3′) and reverse L5.8S (5′-TGATACCACTTATCGCATT-3′), as well as LRV2-specific primers, forward LRV F9 (5′-TCTAGGTCGAGTACATGGCAC-3′) and reverse LRV R9 (5′-GCAGCATCACACTCTCAGC-3′). The PCR products were sequenced and subjected to phylogenetic analysis.

Results: PCR amplification of 32 clinical samples and RFLP analysis of the PCR products showed that all isolates were identified as L. major. PCR amplification targeting a 671-bp fragment of the RdRp gene was performed to detect LRV2 in 32 clinical culture samples. Among the 32 clinical cultures, 4 (12.5%) tested positive for LRV2, while 28 (87.5%) were negative. The presence of LRV2 was also confirmed through sequencing. The sequences were deposited to GenBank using Bankit (GenBank Acc. No. PV253963-66). Phylogenetic analysis revealed high nucleotide sequence identity (96–99%) with LRV2 isolated from L. major strains from Iran, Turkey, and Uzbekistan. The four sequences analyzed revealed four distinct haplotypes, with high genetic variability among the isolates.

Conclusion: This study reports the first identification and phylogenetic analysis of LRV2 in patients with cutaneous leishmaniasis from western Iran and highlights the substantial genetic diversity among LRV2 isolates across different regions, which may have important implications for disease pathogenesis, transmission dynamics, and clinical outcomes.

keywords: Leishmania, Leishmania RNA virus, Genotype, Ilam

PP-63

The therapautic effect of Marrubium vulgare, Salvia officinalis and lippia citriodora in killing of toxoplasma gondii tachyzoite and evaluation by MTT assay

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Background and aim: Toxoplasma gondii is intracellular parasites that cause many symptoms such as encephalitis and congenital disorders. Marrubium vulgare, Salvia officinalis and lippia citriodora are herbal drugs that used to kill this organism. Our objective were to evaluate the therapeutic effect of Marrubium vulgare, Salvia officinalis and lippia citriodora in killing of toxoplasma gondii tachyzoite and evaluation by MTT assay .

Methods: In this survey we used Marrubium vulgare, Salvia officinalis and lippia citriodora suspension plus RPMI medium containing peritoneal tachyzoite after incubation at 37 C0. The measurement done by MTT assay and statistial assesment done by spss19 software. Our investigation based on two mediam (invitro and invivo) to approve our results.

Results: In RPMI medium the killing with three herbal drugs were seen and the decrease of Absorbance were seen by MTT assay. The means of OD were 0.05 to 0.16 in presence of herbal drugs but the means of OD were 0.9 to 2.3 in absence of herbal drugs.

Conclusion: Marrubium vulgare, Salvia officinalis and lippia citriodora are herbal drugs that are very useful to kill toxoplasma tachyzoite in invitro condition.

keywords: Marrubium vulgare Salvia officinalis lippia citriodora toxoplasma gondii MTT assay

PP-64

New prevalence surveillance of Toxoplasma gondii among rodents and stray cats by ELISA avidity and nested PCR methods, Northeast of Iran

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Background and aim: Rodents and stray cats are the sources of many parasitic infections including T. gondii, for other animals and human. Toxoplasmosis has a wide range of laboratory factors in its intermediate and definite hosts. Regarding the importance of rodents and stray cats as the hosts that spread the Toxoplasma gondii, it is necessary to obtain comprehensive information about these animals in the life cycle of T. gondii. The objective was to investigate the new prevalence of toxoplasmosis among target animals in Iran, using GRA6 gene in combinacion with ELISA avidity.

Methods: In this study, 286 rodents and 210 stray cats were collected and their heart tissues extracted to obtain DNA, blood samples and IgG Ab of T.gondii parasite. We detected the positive tissue samples in our study by the nested-PCR method. Then, we examined T. gondii IgG ELISA avidity for assessment of toxoplasmosis among rodents and stray cats. This study, was conducted in January to March 2017, based on the prevalence study.

Results: The findings revealed that 246/286 (86.01%) of rodents and 180/210 (85.71%) of stray cats were positive by IgG ELISA avidity methods. moreover, 68 rodents samples and 38 stray cats samples were positive concerning the GRA6 Toxoplasma gene; and these positive samples were at intermediate levels for IgG avidity.

Conclusion: We concluded that the new prevalence of toxoplasmosis among rodents and stray cats was at high levels, using the serologic method in Northeast of Iran and the results of quantitative ELISA avidity were as the same as those of the nested-PCR for detecting recent toxoplasmosis in these hosts.

keywords: Toxoplasmosis New prevalence Iran Molecular detection Serology study

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PP-65

Visceral leishmaniasis–human immunodeficiency virus coinfection in a 52-year-old male in southwest Iran: a case report

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Background and aim: Leishmaniasis is a rare infectious disease observed in subtropical and tropical areas. This disease that demonstrates different clinical characteristics is caused by intracellular Leishmania protozoan. One of the important countries facing the incidence of this infectious disease is Iran. Recently, human immunodeficiency virus–Leishmania coinfection has been indicated in Iran.

Methods: Case presentation In the present case report, we show an atypical case of severe visceral leishmaniasis in a 52-yearold Iranian-Arab male with positive human immunodeficiency virus status. Leishmaniasis was detected by node biopsy and subsequently histopathology evaluations and confirmed by molecular methods.

Results: The patient was hospitalized and bedridden with stable vital signs and a normal neurological examination. Imaging revealed extensive cervical and abdominal lymphadenopathy. Biopsy of skin lesions and lymph nodes was positive for leishmaniasis and negative for acid-fast bacilli. Sinus biopsy confirmed leishmaniasis despite negative results for mycobacteria. The patient was treated with amphotericin B and Glucantime; however, skin lesions did not resolve. Despite follow-up and combination therapy, the patient's condition deteriorated and he eventually died.

Conclusion: The current study was the first report of an atypical case of a patient with Leishmania–human immunodeficiency virus coinfection in southwestern Iran, which was not responsive to the treatment. Therefore, the health authorities should be aware of these reports, which require permanent clinical follow-up of the patients as well as effective treatments.

keywords: Keywords Visceral leishmaniasis, Human immunodeficiency virus, Iran, Leishmania, Polymerase chain

PP-66

Amphotericin B-Loaded Extracellular Vesicles Derived from Leishmania major Enhancing Cutaneous Leishmaniasis Treatment through In Vitro and In Vivo Studies

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Background and aim: Recent studies have shown an increasing number of patients with cutaneous leishmaniasis (CL) who do not respond to pentavalent antimonials as the first line of treatment for CL. Nanocarriers such as extracellular vesicles (EVs) are efficient vehicles that might be used as drug delivery systems for the treatment of diseases. Therefore, we aimed to isolate and characterize the EVs of Leishmania major, load them with Amphotericin B (AmB), and investigate the toxicity and efficacy of the prepared drug form

Methods: The EVs of L. major were isolated, characterized, and loaded with amphotericin B (AmB), and the EVs-Amphotericin B (EVs-AmB) form was synthesized. Relevant in vitro and in vivo methods were performed to evaluate the toxicity and efficacy of EVs-AmB compared to the control.

Results: The anti-leishmanial activity of the EVs-AmB showed a higher percentage inhibition (PI%) (P = 0.023) compared to the AmB at different concentrations and time points. Obtained data showed a significant increase in the lesion size and parasite load in the lesion, PBS, and EVs mice groups in comparison with EVs-AmB, AmB, and Glucantime groups (P 0.05), EVs-AmB had a significant decrease in lesion sizes in comparison with AmB (P 0.05). Results showed that EVs-AmB decreased its toxicity to the kidneys and liver (P 0.05).

Conclusion: EVs-AmB improved the efficacy of AmB in mouse skin lesions and reduced hepatorenal toxicity. Furthermore, EVs could be a promising nanoplatform for the delivery of AmB in CL caused by L. major.

keywords: Leishmania major; Extracellular vesicles; Drug delivery; Amphotericin B

PP-67

The Effect of the Cannabidiol on Calcineurin A, B gene expression of Protoscolexes of Hydatid Cyst

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Background and aim: Hydatid cyst is a zoonotic disease caused by the larval stage of Echinococcus granulosus. In this study, we investigated the lethal effect of the most important non-psychoactive cannabinoid of the cannabis plant, i.e. cannabidiol (CBD), on protoscolexes of hydatid cysts. Also, we measured the expression level of calcineurin subunit A and B genes using real-time PCR molecular method.

Methods: In this study, we examined the samples at two levels, including the MTT test to express the percentage of lethality of the desired concentrations of cannabidiol on protoscolex and real time to examine the changes in calcineurin gene expression.

Results: The results of molecular studies were not significant. For the Calcineurin A gene, the concentrations of 1, 5, and 10 µg/ml and the positive control, all worked the same way, that is, our drug did not differ from Albendazole, and the expression of the gene did not occur in any of them. Also, for the Calcineurin B gene, the concentrations of 5 and 10 µg/ml and the negative control, all worked in the same way and had no effect on the expression of this gene, But the concentration of 1 µg/ml had a strengthening effect on this gene and increased its expression.

Conclusion: The results of calcineurin A and B gene expression were not significant. It was observed that only the concentration of 1 µg/ml of cannabidiol can increase the expression of calcineurin B, and none of the concentrations of cannabidiol and albendazole had any effect on the expression of calcineurin genes.

keywords: Cannabidiol, hydatid cyst, calcineurin

PP-68

Trichomoniasis in Men: A Neglected Factor in Male Infertility?

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Background and aim: Trichomonas vaginalis, a flagellated protozoan parasite, is considered the most common non-viral sexually transmitted infection that affects both men and women. Trichomoniasis has been studied mainly in women, and its associated complications include vaginitis, urethritis, pelvic inflammatory disease, preterm labor, and low birth weight. Trichomoniasis was previously considered insignificant in men. It was believed that the infection resolved spontaneously. However, research suggests that the persistent presence of infection in men can lead to chronic genital tract infection and potentially lead to male infertility. Trichomonas vaginalis is responsible for non-gonococcal urinary tract infections in men, leading to prostatitis, epididymitis, and urethritis.

Methods: In this cross-sectional study, a group of 197 male volunteers who had referred to the Fertility and Infertility Research Center for medical care were selected. Before collecting samples, the study was explained to the participants and written informed consent was obtained from each participant and their demographic and clinical information was recorded in the questionnaire. The inclusion criteria were individuals aged 18 years and older. This study was approved by the Research Ethics Committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1400.984). Urine and semen samples were collected under sterile conditions. Both urine and semen sediment were quickly examined under microscopy to detect the presence of motile trophozoites. Then, 50 µL of urine sediment was inoculated into Dorset culture medium, while 50 µL of semen sediment was transferred to Diamond culture medium (TYI-S-33) and incubated at 35.5°C. Finally, urine sediment samples were subjected to PCR for molecular analysis.

Results: The investigated subjects had an average age ranging from 36 to 40 years. There were 181 volunteers with fertility issues, outnumbering the 16 individuals with normal fertility. Spermogram analysis showed that 48% of participants had non-motile or progressive sperms, and 48% had abnormalities in sperm morphology. Trichomonas vaginalis was not detected through microscopic assessment, but PCR and sequence analysis revealed one case in a 33-year-old infertile individual, who had only 0.3% normal sperm with 19% motility.

Conclusion: In the past, trichomoniasis in males was considered unimportant, with the belief that it would improve on its own. This study suggests that parasites can be considered as one of the male infertility factors, however, the impact is not fully understood. This investigation found that trichomoniasis can decrease the functional sperm quality.

keywords: Trichomonas vaginalis, infertility, sperm

PP-69

Antitumor activity of exosomes derived from Toxoplasma infected cells on mice induced with intestinal cancer

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Background and aim: In recent years, cancer treatments based on pathogens have attracted a lot of attention. Infection by parasites such as Toxoplasma gondii and Plasmodium can inhibit tumor growth. Exosomes from host cells infected with Toxoplasma have an anti-infective effect. These exosomes convey the message of "infection" to the immune cells and stimulate them to Activate the safety response

Methods: The mice were divided into two groups and the Me49 strain was injected subcutaneously into them. Then CT26 cell suspension 5x106. T. gondii treatment of mice with Colorectal cancer After immunization with T. gondii, mice were examined It was injected with 5x106 CT26 cells. Amplification of the 529 bp target gene in T. gondii done. Flow cytometry analysis Mice with CRC were treated with T. gondii or exosomes were sacrificed before flow cytometry (FCM) analysis. Indirect immunofluorescence Exosomes were labeled by ExoSparker Exosome Membrane Treatment of colon cancer Mice with exosomes Female BALB/c mice were randomly weighed. When it was a tumor It can be seen, the treatment was done according to the following Design: An intratumoral injection with 10 mg of DC-exo (DC-exo group), 10 mg DC-Me49-exo (DC-Me49-exo group), and 10 ml PBS (PBS group). Two injections were performed on days 1 and 3 After visualization of the tumor.

Results: The group was analyzed using t-test or one-way ANOVA with Dunnett's multiple comparisons.Results showed that tumor growth was significantly inhibited after treatment with DC-Me49-exo. The proportion of polymorphonuclear bone marrow-derived granulocyte suppressor cells (G-MDSCs, CD11b+ Ly6G+ and monocyte myeloid-derived suppressor cells (M-MDSCs, CD11b+ Ly6C+) decreased in the DC-Me49-exo group compared to the control group in vitro and in vivo groups. The proportion of DCs (CD45+ CD11c+) increased significantly DC-Me49-Exo group. The levels of interleukin-6 (IL-6) and granulocyte-macrophage colony-stimulating factor (GM-CSF) were significantly decreased after treatment with DC-Me49-exo. Furthermore, we found that DC-Me49-exo induced MDSCs mainly by Inhibition of the signal transducer and activator of the transcription (STAT3) signaling pathway.

Conclusion: Research has shown that infection with single-celled parasites T. gondii can inhibit tumor growth. In this study, we identified the Distribution of T. gondii in tumor-bearing mice, but without parasites found in tumor tissues.

keywords: Antitumor activity, exosomes, Toxoplasma BALB/C mice, intestinal cancer

PP-70

Antitumor Activity of Hydatid Cyst Fluid Antigen B on Tumors Induced by MCF7 Breast Cancer Cell

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Background and aim: Hydatid disease or cystic echinococcosis is a parasitic infection caused by tapeworms. It can cause cysts to grow in the liver and other organs. Studies on the experimental model of breast cancer have shown that hydatid cyst fluid (HCF) has antitumor activity. We aimed to investigate the effect of HCF and antigen B on MCF7 breast tumor cells in BALB/c mice.

Methods: AgB was obtained using a polyacrylamide gel electrophoresis for 60 minutes with 12.5% sodium dodecyl sulfate (SDS PAGE). Mouse breast adenocarcinoma cell line (MCF7) was cultured in an rpm medium and fetal bovine serum was added to it along with L-glutamine. Then 1%Antibiotic mixture containing 100 international units per milliliter of penicillin was added and incubation was done. These mice were divided into 5 groups, the first PBS group and the second, third, fourth, and fifth groups intraperitoneally with concentrations of 100, 200, 300, and 500 µg/ml HCF and AgB in 100 µl PBS. It was injected with naltrexone and naloxone. Help to determine the preventive effect of HCF and AgB antigens on the growth of MCF7 mammary tumor in BALB/c mice, 10 days after the inoculation of cancer cells, animals in each group in terms of tumor and tumor growth, blood was taken from one side of the mice.

Results: The results showed that in the mice that received the combination of HCF and AgB along with the adjuvant naltrexone and naloxone, the size of the tumor was significantly smaller in them and it was quite clear compared to the control group. And the higher the doses of our antigen combination, the smaller the tumor size. Also, the level of Th1 cytokines such as il-2 and il-12 increased compared to the control group. On the other hand, the level of Th2 cytokines showed a significant decrease. Histopathological studies showed reduced tumor volume and carcinogenesis. Antitumor activity of HCF and AgB may be related to immune responses against these antigens Our histopathological studies showed reduced tumor volume and carcinogenesis.

Conclusion: This study evaluates the Antitumor activity of HCF and AgB on the MCF7 breast cancer cell line in BALB/c mice. Th1 cytokines are involved in the upregulation of an effective anticancer immune response. Increased levels of Th1 cytokines (IL-2, IL-12, TNF-α, and IFN-γ) in HCF and AgB groups can indicate that T cells are switching to a type I immune response.

keywords: Antitumor, Hydatid Cyst, MCF7, Breast Cancer

PP-71

Hydatid cyst fluid antigens antitumor activity on mice with Breast Cancer

Elahe Khosravi Emamzadeh [1] ℗, Ahou Alipour Azar [1], Yalda Rostami Gaznagh [1], Asal Soltani [1], Laya Dalili [1], Sana Aghdasi [1] ©

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Background and aim: Hydatid cyst is the larval stage of Echinococcus granulosus, which leads to humoral and cellular immune responses in the host. We aim to investigate the effect of HCF and Antigen B (AgB) on 4T1 breast cancer cells in BALB/c mice.

Methods: AgB was obtained using a boiling water bath for 15 min and centrifuged at Polyacrylamide gel electrophoresis for 60 minutes with 12.5% sodium dodecyl sulfate (SDS PAGE) and Coomassie brilliant blue staining It was used to evaluate presence and quality. Mouse breast adenocarcinoma cell line (4T1) was cultured in rpmi medium and fetal bovine serum was added to it along with L-glutamine. After 48 hours of incubation, the cells were harvested. 40 mice were divided into 4 groups, the first group was given PBS and the second, third, and fourth groups were injected intraperitoneally with concentrations of 100, 200, and 300 µg/ml of HCF and AgB in 100 µl of PBS along with naltrexone adjuvant. To determine the prevention effect of HCF and AgB antigens on 4T1 breast tumor Growth in BALB/c mice, 10 days after cancer Cell inoculation, animals in each group In terms of tumor and tumor growth.

Results: The results indicated that the mice that received different concentrations of the desired antigen along with the adjuvant had a significantly smaller tumor size compared to the control group, and the higher the injection dose, the smaller the tumor size. Was more Also, the level of Th1 cytokines was increased compared to the control group. On the other hand, the level of Th2 cytokines showed a significant decrease. Our histopathological studies showed a reduction in tumor volume and carcinogenesis. Antitumor activity of HCF and AgB may be related to immune responses against these antigens.

Conclusion: Detailed attention is paid to the various antigenic components of helminth parasites are a suitable candidate for prevention and the treatment of cancers, autoimmune disorders, and inflammatory diseases because they control the immune system through regulators. This study evaluates the Antitumor activity of HCF and AgB on the 4T1 breast cancer cell line in BALB/c mice. Th1 cytokines are involved in the upregulation of an effective anticancer immune response. Increased levels of Th1 cytokines (IL-2, IL-12, TNF-α, and IFN-γ) in HCF and AgB groups can indicate that T cells are

keywords: Hydatid cyst, BALB/c mice, Breast Cancer, Antitumor

PP-72

Antitumor activity of exosomes derived from Toxoplasma infected cells on mice induced with intestinal cancer

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Background and aim: In recent years, cancer treatments based on pathogens have attracted a lot of attention. Infection by parasites such as Toxoplasma gondii and Plasmodium can inhibit tumor growth. Exosomes from host cells infected with Toxoplasma have an anti-infective effect. These exosomes convey the message of "infection" to the immune cells and stimulate them to Activate the safety response.

Methods: The mice were divided into two groups and the Me49 strain was injected subcutaneously into them. Then CT26 cell suspension 5x106. T. gondii treatment of mice with Colorectal cancer After immunization with T. gondii, mice were examined It was injected with 5x106 CT26 cells. Amplification of the 529 bp target gene in T. gondii done. Flow cytometry analysis Mice with CRC were treated with T. gondii or exosomes were sacrificed before flow cytometry (FCM) analysis. Indirect immunofluorescence Exosomes were labeled by ExoSparker Exosome Membrane Treatment of colon cancer Mice with exosomes Female BALB/c mice were randomly weighed. When it was a tumor It can be seen, the treatment was done according to the following Design: An intratumoral injection with 10 mg of DC-exo (DC-exo group), 10 mg DC-Me49-exo (DC-Me49-exo group), and 10 ml PBS (PBS group). Two injections were performed on days 1 and 3 After visualization of the tumor.

Results: The group was analyzed using t-test or one-way ANOVA with Dunnett's multiple comparisons.Results showed that tumor growth was significantly inhibited after treatment with DC-Me49-exo. The proportion of polymorphonuclear bone marrow-derived granulocyte suppressor cells (G-MDSCs, CD11b+ Ly6G+ and monocyte myeloid-derived suppressor cells (M-MDSCs, CD11b+ Ly6C+) decreased in the DC-Me49-exo group compared to the control group in vitro and in vivo groups. The proportion of DCs (CD45+ CD11c+) increased significantly DC-Me49-Exo group. The levels of interleukin-6 (IL-6) and granulocyte-macrophage colony-stimulating factor (GM-CSF) were significantly decreased after treatment with DC-Me49-exo. Furthermore, we found that DC-Me49-exo induced MDSCs mainly by Inhibition of the signal transducer and activator of the transcription (STAT3) signaling pathway.

Conclusion: Research has shown that infection with single-celled parasites T. gondii can inhibit tumor growth. In this study, we identified the Distribution of T. gondii in tumor-bearing mice, but without parasites found in tumor tissues.

keywords: Antitumor activity, exosomes, Toxoplasma BALB/C mice, intestinal cancer

PP-73

The prevalence of Enterobius vermicularis in children in Urmia city

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Background and aim: Enterobius vermicularis is one of the human parasitic nematodes and lives in the cecum and end areas of the digestive system. It is estimated that about one billion people in the world are infected with this parasite and the infection is more common in children than other ages. The purpose of this study is to investigate the prevalence of Enterobius vermicularis infection in preschool children in Urmia City

Methods: Sampling was done after coordinating with parents of students and getting their consent, as well as educating parents from all areas of Urmia City and 12 elementary schools using the Scotch test method. In this way, after providing the necessary training to the parents of the students and placing the necessary equipment for sampling, and reminding them that the sampling was carefully attached to the anus area using adhesive tape near the morning and was removed from there at around 8 am. then the samples were examined microscopically with 100 and 400 magnification, and on the other hand, spss software was used for statistical analysis

Results: Of the participants, 11.3% of cases (6.9% male and 4.4% female) were infected with E.vermicularis. The highest prevalence was observed in the fifth-grade students. There was no significant relationship between some symptoms such as drooling, sucking fingers, and nail-biting, and their gender, but it was significant for tooth grinding during sleep. The level of infection has a significant relationship with the number of people in the family, and the larger the family, the higher the level of parasite infection. Also, family culture and lifestyle can increase or decrease the parasite burden

Conclusion: Considering the prevalence of Enterobius vermicularis among primary school students, it was a relatively significant study and it causes sleep, growth, and learning disorders in children, it is suggested to hold training courses held for parents and preventive measures are taken to promote health in the region. Also, considering the relationship of this parasite with the population, education, and prevention of this parasite in large communities such as schools must be prioritized

keywords: Enterobius vermicularis, Investigating, prevalence

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PP-74

prevalence of Cryptosporidium in people with diarrhea referring to medical diagnosis laboratories

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Background and aim: Cryptosporidium is an intestinal protozoan and one of the apicomplexan parasites that can infect a wide range of vertebrates. This protozoan causes self-limiting diarrhea in people with efficient immunity but causes diarrhea in people with ineffective immunity. It becomes intense. The purpose of this study is to check the amount Investigating the prevalence of Cryptosporidium in people with diarrhea referring to medical diagnosis laboratories

Methods: In this study, 500 samples of diarrheal feces were collected from the laboratories of Urmia city and after transferring the samples to Kia Tashkhis research company, all the samples were coded and listed and then concentrated by formalin ethyl acetate method. They were prepared and stained with Nielsen's modified dye produced by Kiateshchis company. All the samples after staining were examined with 500 magnification

Results: Out of the 500 samples collected, 15 samples contained Cryptosporidium parasite, which is about 0.03%. Out of the 15 samples, 5 were women and 10 were men, and by examining the history of the patients, it was found that two of the patients had the disease. They were autoimmune and treated with corticosteroid drugs. Data analysis was done through spss and chi-square statistical test. In this study, there is a relationship between gender and infection with this parasite, so the level of infection was significantly higher in boys than in girls (p0.05)

Conclusion: This study emphasizes the use of appropriate diagnostic methods to identify Cryptosporidium in medical diagnostic laboratories and also recommends the common use of these methods for mucous and watery diarrheal stool samples, especially in immunocompromised people. It seems that the way of life, health conditions, and people's habits and customs do not affect getting Cryptosporidium. Also, in the case of children suffering from diarrhea with symptoms of gastroenteritis, in addition to other enteropathogens that cause diarrhea, Cryptosporidium should also be considered, and a specific stool test. be done

keywords: Cryptosporidium, diarrhea, diagnosis

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PP-75

In vitro antileishmanial activities of Calcium Oxide (CaO) nanoparticles on promastigotes and amastigotes of L. tropica and L. infantum

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Background and aim: Regarding toxicity and costly selective drugs of leishmaniasis, it seems inevitable to discover novel drugs. The aim of this study was to evaluate the antileishmanial activity of calcium oxide (CaO) nanoparticles on promastigotes and amastigotes of L. tropica and L. infantum in vitro.

Methods: Different concentrations of synthesized nanoparticles (0.39, 0.78, 1.56, 3.12, 6.25, 12.5, 25, 50, 100, 200 and 400 µg/ml) were exposed to promastigotes and amastigotes and the parasites were enumerated after 24, 48 and 72 hours. Also, cellular death and its type were determined using MTT and flow cytometry assays

Results: According the effects of nanoparticle on promastigotes the IC50 values of CaO nanoparticles within 72 h were 19.81 µg/ml for L. tropica and 22.57 µg/ml for L. infantum. The percentage of the normal, apoptotic, and necrotic cells was estimated to be 82.6%, 14.81%, and 2.69% for L. tropica, and 73.6%, 23.89%, and 2.58% for L. infantum, respectively.

Conclusion: It is said that such nanoparticles, particularly CaO nanoparticles, have potent antileishmanial activity that can be exploited in the future.

keywords: Nanoparticle, Calcium oxide, Leishmaniasis, Apoptosis

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PP-76

Missed Malaria Diagnosis in a Non-Endemic Area: A Fatal Case Emphasizing the Importance of Travel-Independent Screening

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Background and aim: Malaria as a well-known tropical protozoan disease caused by Plasmodium spp. response to 282 million malaria cases and 610 000 malaria deaths in 80 countries. Medical-important Plasmodium spp. including Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, and Plasmodium knowlesi, each with distinct geographical distributions, predominantly in tropical and subtropical regions. Clinical manifestations commonly include periodic high-grade fever, chills, sweating, headache, and malaise, along with nonspecific symptoms such as nausea and vomiting. The pattern of fever periodicity may assist in differentiating Plasmodium species. Global malaria control strategies range from morbidity and mortality reduction in endemic regions to elimination programs in non-endemic areas.

Methods: A 66-year-old Iranian male presented with fever, chills, hypotension, and headache. At the initial healthcare visit, his nonspecific symptoms were misinterpreted, and supportive outpatient management with fluid therapy was initiated. Over the subsequent ten days, his condition progressively deteriorated. Upon hospital admission, laboratory investigations revealed anemia, leukocytosis, elevated C-reactive protein (CRP), increased lactate dehydrogenase (LDH), and positive cardiac troponin. A preliminary diagnosis of sepsis was considered; however, blood and urine cultures were negative. The patient had no history of travel to malaria-endemic areas within the past ten years. He worked as a gardener and reported multiple mosquito bites during fruit harvesting in the preceding two weeks. Additionally, he employed migrant workers originating from endemic regions. The patient described a rhythmic pattern of fever with chills and sweating. Peripheral blood smear examination (both thick and thin smears) demonstrated intraerythrocytic protozoan forms, including ring forms and headphone-like structures, without clearly identifiable gametocytes.

Results: Empirical intravenous treatment with artesunate and broad-spectrum antibiotics was initiated prior to definitive species identification. Despite aggressive management, the patient developed profound shock and clinical deterioration, ultimately leading to death seven days after hospitalization

Conclusion: This case highlights a fatal instance of probable autochthonous malaria in a non-endemic setting without recent travel history. Delayed diagnosis and initial misinterpretation as culture-negative sepsis contributed to the unfavorable outcome. The report underscores the importance of considering malaria in the differential diagnosis of febrile patients with cyclic symptoms, even in non-endemic regions. Strengthening laboratory diagnostic capacity, enhancing clinician awareness, and maintaining epidemiological vigilance are strongly recommended to prevent similar tragedies

keywords: Malaria, New case, non-endemic, case-report

PP-77

Investigation of antiparasitic activity of silver nanoparticles on Leishmania major

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Background and aim: Cutaneous leishmaniasis(CL) is the most common form of skin disease caused by a single-celled parasite that is transmitted by the bite of a phlebotomine sandfly. Symptoms usually appear three months to a year after the bite. Nanotechnology is now recognized as a key activating technology (KET) for its various applications in science and medicine. In recent years, the scientific value of NPs in the treatment of leishmaniasis has increased due to the improvement of anti-leishmaniasis drugs. In this study, silver biogenic nanoparticles (AgNPs) and amphotericin-bound silver biogenic nanoparticles (AmB-AgNPs) are used

Methods: In this study, experimental infection in several Balb/c mice by injection of Leishmania major promastigotes was created. After the appearance of wounds in the tails of mice, they were divided into four groups of 10 and divided into two groups of treatment with (AgNPs) and (AmB-AgNPs). once a day in the wound at three points in the group receiving glucantime they had done it muscularly for 5 weeks was injected. In the negative control group, the mice did not receive any medication. Then, the weight of the mice and the diameter of the Leishmania major wound was daily for 5 weeks. They were measured and recorded and compared with each other

Results: Wound diameters in the nanoparticle recipient treatment group (AgNPs) and (AmB-AgNPs) were significantly less from the untreated control group, but the wound diameters were larger than those treated with glucantime

Conclusion: silver biogenic nanoparticles (AgNPs) and amphotericin-bound silver biogenic nanoparticles (AmB-AgNPs) nanoparticles show anti-leishmaniasis effects in the in vitro environment. But this effect is lower than glucantime and does not completely heal the lesions

keywords: antiparasitic; silver nanoparticles; Leishmania major

PP-78

prevalence of intestinal parasitic infections in primary school students in Urmia, 2025

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Background and aim: Intestinal parasitic infections are still a serious public health problem in the world. It is estimated that some 3.5 billion people are affected and that 450 million are ill as a result of these infections, the majority being children. The high prevalence in children is attributed to many factors, particularly the social and economic situation of the individuals is an important cause of the prevalence of intestinal parasites. The purpose of this study was to investigate the prevalence of intestinal parasitic infections in elementary school students in Urmia City

Methods: The study design was cross-sectional. This study was conducted at nine primary schools chosen by randomized cluster sampling from urban areas of Urmia City is capital of West Azerbaijan province, which is located in the Northwest of Iran. 400 primary school students were randomly selected from a list of 9 schools. The questionnaire included age, gender, place of residence, parent's education and occupation, family size, and water sources. They were examined for the presence of parasites by wet mount, formaline–ether sedimentation techniques and cellophane tape was used to detect Enterobius vermicularis infection. Also, for the ease of recognizing the English genus and species, chrome coloring made by the Kia Tashkhis company was used. Data were analyzed using SPSS 11 for Windows

Results: The subjects consisted of 243(60.3%) boys and 160(39.7%) girls, aged between 7-12 years. In all, 45 students(11.25%) were infected with one or more intestinal parasites. The most common was Giardia lamblia 19(4.75%), Entamoeba coli 10(2.5%), Blastocystis hominis 9(2.25%), Enterobius vermicularis 4(1%), Iodamoeba butschilii 2(0.5%) and Hymenolepis nana 1(0.25%) infected primary school children. 109(26.9%) students were infected with one parasite, 35(8.75%) with two parasites, 7(1.75%) with three parasites 3(0.75%)

Conclusion: The results of the study indicate a high prevalence of some intestinal protozoans especially Giardia lamblia and a great amount of helminth in the area. In contrast based on the present study and other studies in various areas and times intestinal parasite infections with world spread are one of the most important health indexes. Despite their different prevalence in various societies and ages and even decrease or eradication, intestinal protozoan infections especially Giardiasis and Amebiasis are very important problems that societies are suffering from them

keywords: Investigating, intestinal parasitic, infections

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PP-79

Effect of the different concentrations of hypertonic saline at different times on hydatid cyst protoscolex

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Background and aim: Echinococcosis in humans and animals is an economic and public health concern in many parts of the world. The infection is most prevalent in sheep- and cattle-raising regions like Australia, South America, the Middle East, South Africa, Eastern Europe, and the Mediterranean region. Cystic hydatid disease affects mainly the liver (50–70% of all cysts) but can also develop in the lung (20–30%) and, less frequently, in the spleen, kidney, bone, brain, and other organs. The objective of this study is to determine the sporicidal effect of hypertonic saline in different concentrations using different exposure times

Methods: After the concentration of protoscoleces at the end of the tube the viability of protoscolices was confirmed by their motility under a light microscope and protoscolices stained with 0.1% eosin were examined at room temperature. Any protoscolex that did not import dye was accepted as potentially viable. The mean number of protoscoleces in the cyst fluid obtained from different cysts in different periods was found as 1000 protoscoleces/mm3 and fourteen samples of 0.5 cc sediment were obtained. Various concentrations of 1 cc sodium chloride solutions were added to each sediment (1%, 2%, 3%, 4%, 5%, 6%, 7%, 8%, 9%, 10%, 20% respectively). We waited 1, 2, 3, 4, 5, 6, 7, 8, 9, 10,…….29, and 30 minutes for each concentration, following which the upper portions of the solutions were removed. The remaining settled protoscolices were then washed in normal saline and after staining, examined for viability

Results: Protoscolex survival ratios after exposure to different concentrations of sodium chloride at different times indicated that 20% hypertonic saline had a strong scoliosis effect, as it eliminated all protoscolexes at the end of 9 minutes. 10% hypertonic saline killed 90% of protoscolexes in 30 minutes.

Conclusion: hypertonic saline with a concentration 20% killed all protoscoleces of hydatid cyst at the end of 9 minutes. Hypertonic saline did not cause any systemic side effects when it was applied intraperitoneally. Surgery remains the treatment that has the potential to remove Echinococcus granulosus cysts and cure completely. The main principle of surgery is to prevent scoliosis by placing swabs soaked in scoliosis material. The use of Protoscolicidal agents to kill protoscolexes intraoperatively is questionable because there is no ideal agent that is both effective and safe

keywords: hypertonic saline, hydatid cyst, protoscolex

PP-80

Evaluation of parasitic infections in patients referring Medical Laboratory in Urmia city from March 2024 to March 2025

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Background and aim: Parasitic contamination is one of the most important worldwide health problems, especially in developing countries. Various types of intestinal parasites can cause contamination in humans and create a wide range of symptoms, depending on different immunological, physiological and social factors. The risk of contamination is high in immunocompromised patients, in patients receiving immunosuppressive drugs and in patients undergoing chemotherapy. The aim of this study was to determine the prevalence of parasitic infections in patients referred medical Laboratory in Urmia city in the year of 2024 to 2025

Methods: After referral of patients and delivery of fecal samples, all specimens were examined for the presence of parasites by direct test with physiologic serum and logol. Then, in order to accurately detect the type of parasite, positive specimens were determined by genus and strain using ether formalin concentration and trichrome staining

Results: Of 4814 stool samples, 516 samples (10.7%) had parasitic infection.The prevalence of parasitic infections was as follows: The highest percentage of infection was related to Chilomastix mesnili with 15.24%. (202 men with 56% and 158 women with 44% contamination); Blastocystis hominis with 2.66% (38 men with 60% contamination and 25 women with 40% contamination), Entamoeba coli cyst with 2.32% (27 men with 49% contamination and 28 women with 51% contamination); Giardia lamblia cyst with 1.05% (14 men with 56% contamination and 11 women with 44% contamination); Trichomonas hominis with 0.25% (2 men with 33% contamination and 4 women with 67% contamination); Giardia lamblia trophozoite with 0.16%. (2 men and 2 women with a contamination of 50%). The lowest infection rate was related to Ascaris lumbricoides egg (1 man), histolytica / dispar amoeba cyst (1 man) lodamoeba bütschlii (1 woman) each Which with 0.04 % contamination was

Conclusion: Parasitic contamination is one of the most important health indicators in today's society. According to the study, the prevalence of Chilomastix mesnili was higher than other parasites. By promoting the level of health, chlorination and drinking water filtration, it can be prevented from getting this parasite

keywords: parasitic, infections, patients

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PP-81

Molecular Detection and Genotyping of Toxoplasma gondii Strains from Beef, Lamb, Goat milk, Cat Feces, and Human Lymph Node Samples

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Background and aim: Toxoplasmosis is one of the most common parasitic infections caused by a protozoan named Toxoplasma gondii. Humans and carnivores can become infected by eating tissue cysts in a row or semi-cooked meat or oocysts from cat feces. This study aimed to investigate different genotypes of Toxoplasma gondii isolates from cat feces, lamb and human pathological samples to determine the dominant types in Urmia city by amplifying GRA6 gene using the PCR method.

Methods: Meat samples were collected from butchery shops of Urmia city by cutting a small piece of the diaphragm muscle. DNA extraction and PCR was done on these samples after being chopped. Stool samples from stray cats were collected from ruins and parks, and oocysts were concentrated by ethyl acetate formalin and were stained with acid-fast technique. Microscopically positive samples were analyzed with PCR. The lymph node specimens were collected by reviewing the pathological records of Dr. Nemati Laboratory in Urmia city. The specimens that were suspected of toxoplasmosis, were also examined after hematoxylin-eosin staining and microscopic confirmation, by PCR. Finally, 20 positive PCR products, including 5 stools, 5 lambs, 5 beef and 5 human lymph node samples were sent for sequencing.

Results: Of the 20 cat feces, 7 samples were confirmed by PCR and from the 100 selected Lymph Node specimens, 5 samples were confirmed microscopically and PCR. 60% meat samples were also infected. Also, 30% samples were positive with PCR. Finally, out of 100 samples of Goat milk, 8 samples were positive and we were able to determine with PCR.DNA sequencing revealed that all 5 lymph node were from ME49 (genotype II). lamb specimens were shown to be from ME49 (2 samples), GT1 or genotype I (2 samples), and VEG or genotype III (one sample) genotypes and four of five oocysts were ME49, VEG or genotype III (one sample) strain and all beef samples were related to ME49 (genotype II) strain. Also, 2 samples of goat milk are related to GT1 or genotype I strain and 3 other cases are related to ME49 (genotype II).

Conclusion: Genotyping is important because it can be used to identify the dominant genotype in the region and subsequently to take specific control measures as well as therapeutic measures against the risk of the involved genotype. Most of the genotypes we obtained during this study, were of type II and this genotype appears to be the predominant genotype in Urmia and regarding the extremely high infection rate of meat samples, it seems that humans are mostly infected with Toxoplasma gondii by eating the raw or undercooked meat.

keywords: Genotyping, Toxoplasma gondii, GRA6, Lamb, Cat feces, Beef, Goat milk

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PP-82

Enterobius Vermicularis cause of intra-nasally granulomatous mass in a seven 7 year old boy: A clinical case report

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Background and aim: Enterobius vermicularis (Oxyuris), is one of the most commonly nematode infections in the world. In the initial diagnosis, deviation of nasal septum and in subsequent diagnoses, nasal polyp was reported.

Methods: The current study reports a 7-year-old boy with an acute granulomatous nasal mass. In this case, the patient had a past medical history of upper respiratory problems and inflammation.

Results: Finally, the presence of hemangioma vascular mass appeared in rhinoscopy. Afterwards, the patient was a candidate for surgery.

Conclusion: After surgery and removal of the mass and refereeing it to the pathology laboratory, it was reported that the mass had a fibrous

keywords: Enterobius vermicularis; Oxyuris; nasal; surgery; granulomatous mass

17th International Congress of Lab. and Clinic
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July 20-23, 2026

PP-83

Prevalence of Trichomonas vaginalis and Associated STIs in Women with Vaginitis: A Multiplex Real-Time PCR Study from Mashhad, Iran

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Background and aim: Trichomonas vaginalis is one of the most common non-viral sexually transmitted infections worldwide, causing vaginitis, cervicitis, and urethritis in women. This infection is associated with adverse outcomes including pelvic inflammatory disease, infertility, and increased risk of HIV transmission. Traditional diagnostic methods such as wet mount microscopy have limited sensitivity. This study aimed to determine the prevalence of Trichomonas vaginalis infection and its co-occurrence with other sexually transmitted infections in women with vaginitis symptoms using Multiplex Real-Time PCR.

Methods: This cross-sectional study was conducted on 48 women with clinical signs of vaginitis (inflammation, itching, or vaginal burning) referring to Umm al-Banin Women's Hospital in Mashhad during 2015-2016. Vaginal swab samples were collected and initially examined by wet mount microscopy. After DNA extraction, Multiplex Real-Time PCR was performed using FTD STD 9 kit (Fast-track Diagnostics, Luxembourg) to detect Trichomonas vaginalis, Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium, Ureaplasma urealyticum, Gardnerella vaginalis, and HSV-1/2. Demographic and clinical data were collected using a standardized checklist.

Results: The mean age of participants was 33.93±8.00 years (range: 20-56 years). All samples were negative for T. vaginalis by wet mount microscopy; however, Multiplex Real-Time PCR identified 2 positive cases (4.17%). Both positive cases were housewives with education levels below diploma. No statistically significant association was found between T. vaginalis infection and other STIs (p0.05). Co-infection analysis revealed that both T. vaginalis-positive cases were also positive for Gardnerella vaginalis. All other pathogens showed no significant co-occurrence.

Conclusion: The prevalence of trichomoniasis in this study (4.17%) is consistent with previous reports from Iran. Multiplex Real-Time PCR demonstrated superior sensitivity compared to wet mount microscopy, making it a valuable tool for accurate diagnosis of trichomoniasis, particularly in symptomatic patients with negative direct smears. The high rate of co-infection with Gardnerella vaginalis highlights the importance of comprehensive diagnostic approaches. Given the potential complications of untreated trichomoniasis, implementation of molecular diagnostic methods and public health education regarding STI prevention are strongly recommended.

keywords: Trichomonas vaginalis, Sexually Transmitted Infections, Vaginitis, Multiplex Real-Time PCR

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Tehran University of Medical Sciences (TUMS)
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PP-84

Nematicidal Activity and Cellular Mechanisms of Cistanche tubulosa and Salvadora persica Extracts and Essential Oils Against Rhabditis spp: Linking Phytophenolic Constituents to Programmed Cell Death

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Background and aim: Plant-derived bioactive compounds have gained considerable attention as eco-friendly alternatives to synthetic nematicides. Cistanche tubulosa and Salvadora persica are medicinal plants rich in phenolic compounds, flavonoids, and other secondary metabolites with documented antimicrobial and antioxidant properties. However, their nematicidal potential and underlying cellular mechanisms against Rhabditis spp. remain largely unexplored. This study aimed to evaluate the nematicidal activity of hydroalcoholic extracts and essential oils of C. tubulosa and S. persica and to investigate the cellular pathways associated with nematode mortality.

Methods: Hydroalcoholic extracts and essential oils were prepared from authenticated plant materials. Total phenolic content was determined using the Folin–Ciocalteu method. Rhabditis spp. larvae were cultured on agar medium and isolated using the Baermann funnel technique. Larvae were exposed to different concentrations of extracts and essential oils, and mortality rates were assessed using 1% eosin staining. IC_{50} and IC_{100} values were calculated. Cellular viability was evaluated by the MTT assay, while ultrastructural alterations were examined using scanning electron microscopy (SEM). Markers of programmed cell death were assessed through morphological and biochemical analyses.

Results: Both plant species exhibited concentration-dependent nematicidal activity. Essential oils demonstrated significantly greater efficacy than hydroalcoholic extracts, resulting in lower IC_{50} values. Treatments induced severe morphological damage to the cuticle and internal tissues of Rhabditis larvae. A marked reduction in cellular viability was observed in the MTT assay. Furthermore, increased apoptotic features, including cellular shrinkage and structural disintegration, were detected following exposure to phenolic-rich fractions

Conclusion: The findings suggest that C. tubulosa and S. persica possess potent nematicidal properties mediated by phytophenolic constituents and the induction of programmed cell death pathways. These plants may represent promising natural sources for the development of sustainable nematode control strategies.

keywords: Cistanche tubulosa, Salvadora persica, Rhabditis spp, Nematicidal activity

PP-85

Taenia saginata (Cyclophyllidea, Taeniidae) infection in a pregnant woman in Tehran, Iran and literature review

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Background and aim: Taenia saginata (bovine tapeworm) infection, especially in pregnant women, is of particular importance due to treatment limitations and possible complications for the mother and fetus. This study reports the first case of T. saginata infection in a pregnant woman in Iran, along with molecular identification and a review of the literature.

Methods: A 33-year-old woman living in Qods City, Tehran province, passed a motile tapeworm proglottid during the sixth month of pregnancy. The patient had a history of travel to Ardabil and consumption of broiled meat with clinical symptoms, i.e. dizziness, nausea, abdominal pain, and anal itching. The proglottid samples were tested using morphological and molecular examinations, the obtained sequences were compared with the sequences available in GenBank, and phylogenetic analysis was performed. Also, a systematic search in PubMed was conducted to review previously reported cases.

Results: Morphological examination revealed gravid proglottids with more than 15 uterine branches and taeniid eggs. Amplification of the cox1 gene produced a 413 bp segment, registered in GenBank (PX933472). This sequence showed 100% similarity to the Iranian isolate of T. saginata (KJ910292) and clustered with isolates from different countries in phylogenetic analysis. The patient's treatment was postponed until after the infant was born and treated with single-dose niclosamide (2g). The literature review revealed 23 cases reported from different countries, with abdominal pain being the most common symptom and praziquantel being the most frequently used treatment.

Conclusion: The combined use of molecular and morphological methods is essential for accurate species identification. In pregnant women, the selection of appropriate treatment based on pregnancy status is of particular importance.

keywords: Taenia saginata, Taeniasis, Pregnancy, Cox1, Iran

PV-1

Seroepidemiological Study of Human Herpes Viruses (EBV, CMV, VZV, HSV-1&2) Among Age Groups in Ahvaz, Iran Between 2011 - 2023

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Background and aim: Herpesviruses are widespread pathogens worldwide, often establishing lifelong infections in humans. However, seroprevalence data remain scarce for certain populations. To address this gap, a study was conducted to estimate the seroprevalence of human herpesviruses, including Epstein-Barr virus (EBV), Cytomegalovirus (CMV), Varicella zoster virus (VZV), and Herpes simplex virus types 1 and 2 (HSV-1&2), among different age groups in Ahvaz, Iran. Despite previous reports, detailed data on multiple herpesvirus infections are lacking in this region. Objectives: This study aimed to investigate the 11-year prevalence of human herpesviruses (EBV, CMV, VZV, HSV-1&2) among various age groups.

Methods: A cross-sectional descriptive-analytical study was conducted on 14,126 serum samples from individuals aged 1 to 88 years. ELISA methods were used to test for the presence of the viruses.

Results: The seroprevalence varied significantly by age and gender. The highest seroprevalence was observed for CMV (IgG) at 29.2%, while the lowest was for HSV-1&2 (IgM) at 0.8%. The highest seroprevalence was recorded in the 31 - 40 age group, whereas the lowest was in the 11 - 20 age group. Gender analysis revealed that seropositivity was higher in females (56.3%) compared to males (43.7%), with CMV IgG being the most common seropositive marker in both sexes.

Conclusion: These findings underscore the potential for implementing targeted screening and vaccination programs for specific high-risk age groups. The data provide valuable epidemiological insights into the transmission of herpesviruses in southwestern Iran, emphasizing the need for enhanced prevention measures and further research into herpesvirus-related diseases.

keywords: Herpesviridae Infections-Seroepidemiologic Studies-Immunoglobulin G (IgG)-Cross-Sectional Studies

PV-2

Prevalence of Cytomegalovirus in Sexually Transmitted Disease Patients: A Real-Time PCR Study

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Background and aim: Cytomegalovirus (CMV) is a common herpesvirus that can remain dormant in the human body after initial infection. In immunocompromised individuals, particularly those with HIV/AIDS, CMV can cause severe health complications. Despite the widespread prevalence of CMV, there is limited research on its coinfection with sexually transmitted diseases (STDs), especially in regions such as Mazandaran Province, Iran.

Methods: This study aimed to determine the frequency of CMV infection in patients diagnosed with STDs using Real-Time PCR. A total of 80 samples (9 male and 71 female) were analyzed, including both urine and vaginal discharge specimens

Results: The results revealed a low overall prevalence of CMV infection (6.3%) with a significant gender disparity: 33.3% of males tested positive, compared to only 2.8% of females. No significant correlations were found between CMV infection and other demographic factors, such as age or specimen pH, protein, or cellular elements. Coinfection with other common STDs or genital pathogens was also not observed

Conclusion: These findings highlight the rarity of active CMV shedding in STD patients, particularly among females, and suggest that men may represent a higher-risk group for CMV transmission in this context. The study underscores the need for further research to assess the role of CMV in sexually active populations and its clinical significance, emphasizing the urgency and importance of this research gap

keywords: Cytomegalovirus, sexually transmitted diseases, Real-Time PCR

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PV-3

Epidemiology, Clinical Profile, and Seasonal Trends of SARS-CoV-2, Influenza, and HRSV Infections in Kidney Transplant Recipients in Iran

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Background and aim: Respiratory viruses are major global pathogens causing substantial morbidity and mortality, with overlapping symptoms that complicate diagnosis. Immunocompromised individuals, especially kidney transplant recipients, are highly susceptible due to long-term immunosuppressive therapy. Among circulating viruses, HRSV, SARS-CoV-2, and influenza are of greatest concern because of their potential for severe disease. In Iran, diverse climates influence viral transmission, yet data on respiratory viral infections in transplant recipients are limited. This study aimed to investigate the prevalence, clinical characteristics, and seasonal trends of these viruses to inform preventive and clinical strategies.

Methods: In this cross-sectional study, throat and nasopharyngeal swabs were collected from adult kidney transplant recipients with acute respiratory infections at Labbafinejad Hospital, Tehran, from November 2023 to February 2025. Demographic, clinical, and laboratory data were extracted from medical records. Viral RNA was isolated using the RNJiA kit (ROJE, Iran), based on silica-column extraction. Molecular detection of SARS-CoV-2, influenza, and HRSV was performed with the GA SARSFlu & HRSV OneStep RT-PCR kit (Ben Da Faravar, Iran), employing TaqMan multiplex real-time PCR with RNase P as an internal control. The assay showed 98% sensitivity. Descriptive statistics summarized patient characteristics, and associations were analyzed using chi-square or Fisher's exact tests in R software v4.1.1, with p 0.05 considered significant.

Results: Among the 141 patients, 83 (59%, 95% CI: 50%–67%) were male, with a mean age of 45.16 years (SD ±14.33). The most common symptoms were weakness (n=87, 62%, 95% CI: 54%–70%), fever (n=75, 54%, 95% CI: 45%–62%). SARS-CoV-2 was the most prevalent virus (13%), followed by influenza (9.2%), and HRSV was the least common (0.7%). Myalgia was significantly more frequent among COVID-19 patients compared to those with influenza (67% vs. 7.7%, p = 0.001), whereas cough was significantly more prevalent in influenza cases than in COVID-19 (77% vs. 33%, p = 0.017).

Conclusion: SARS-CoV-2 is the most common respiratory virus among kidney transplant recipients, followed by influenza. The results emphasize the need for routine viral surveillance, early multiplexed diagnostics, and targeted preventive measures to reduce complications and improve patient management in this high-risk population.

keywords: Respiratory viruses, SARS-CoV-2, Influenza virus, respiratory syncytial virus, kidney transplant

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PV-4

Prevalence and genotype distribution of human papillomavirus in individuals referred to a laboratory in Rey City, Iran

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Background and aim: Human papillomavirus (HPV) is a common sexually transmitted infection linked to various cancers and most sexually active individuals are at risk of contracting it. Understanding regional genotype distribution is essential for establishing effective prevention programs. Therefore, this research focused on analyzing the distribution of HPV genotypes among individuals referred to a laboratory in Rey City, Iran.

Methods: This study, conducted from September to December 2024 in Rey City, Iran, analyzed genital specimens from female patients. The Favorgen Biotech Corp kit (FAVORGEN, Taiwan) was used for DNA extraction, and the CLART® The HPV4 kit (GENOMICA, Spain) was used for PCR and genotyping. Data were analyzed at the individual and genotype levels levels using frequency analysis and statistical analysis was performed with IBM SPSS-27.

Results: Out of the 722 females tested, 195 (27%) were found to be HPV-positive. Among those infected, 29.2% carried only high-risk (HR) genotypes, while over 36.9% had only low-risk (LR) genotypes. Additionally, 23.6% of individuals tested positive for both HR and LR genotypes. The prevalence of HR genotypes was highest among individuals aged 25 to 34 (54%). The genotypes that appeared most frequently included HPV-6 (13.8%), HPV-16 (7.4%), HPV-39 (6.6%), and HPV-54 (6.3%), while HPV-26 and HPV-43 were each detected in only one case

Conclusion: This study found a significant HPV prevalence in females in Rey City, especially those under 25 and aged 25–34, highlighting the need for age-targeted prevention. Since current vaccines do not cover HPV-39 and HPV-54, the findings provide valuable data for future vaccination policies in Rey City, Iran.

keywords: Human papillomavirus (HPV) · HPV prevalence · Genotype distribution

PV-5

Effects of HTLV-1 on leukocyte trafficking and migration in ACs compared to healthy individuals

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Background and aim: Human T-lymphotropic virus type 1 (HTLV-1) is a RNA virus belonging to Retroviridae family and is associated with the development of various diseases, including adult T-cell leukemia/lymphoma (ATLL) and HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP). Aside from HAM/TSP, HTLV-1 has been implicated in the development of several disorders that mimic auto-inflammation. T-cell migration is important topic in the context of HTLV-1 associated diseases progression. The primary objective of this case–control study was to assess the relationship between increased mRNA expression in virus migration following HTLV-1 infection.

Methods: PBMCs from 20 asymptomatic patients and 20 healthy subjects were analyzed using real-time PCR to measure mRNA expression of LFA1, MLCK, RAC1, RAPL, ROCK1, VAV1 and CXCR4. Also, mRNA expression of Tax and HBZ were evaluated.

Results: Mean expression of Tax and HBZ in ACs (asymptomatic carriers) was 0.7218 and 0.6517 respectively. The results revealed a noteworthy upregulation of these genes involved in T-cell migration among ACs patients in comparison to healthy individuals.

Conclusion: Considering the pivotal role of gene expression alterations associated with the progression into two major diseases (ATLL or HAM/TSP), analyzing the expression of these genes in the ACs group can offer probable potential diagnostic markers and aid in monitoring the condition of ACs.

keywords: HTLV-1 HAM/TSP Virology

PV-6

Determination of molecular epidemiologic pattern of human T-lymphotropic virus type 1 (HTLV-1) in Alborz province, Iran

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Background and aim: uman T-cell lymphotropic virus type 1 (HTLV-1) is linked to two debilitating diseases, adult T-cell leukemia/lymphoma (ATLL) and HTLV-1 associated myelopathy tropical spastic paraparesis (HAM/TSP), which are prevalent in various parts of the world, including the Alborz province in Iran. Understanding the prevalence and evolutionary relationships of HTLV-1 infections in these endemic areas is of utmost importance. In the realm of phylogenetic studies, long terminal repeat (LTR) region of HTLV-1 stands out as highly conserved, yet more variable compared to other gene segments. Consequently, it is the primary focus for phylogenetic analyses.

Methods: This cross-sectional study delved into the phylogenetic analysis of HTLV-1 among individuals in Alborz province of Iran. To confirm infection, we amplified partial sequence LTR (PLTR) and HTLV-1 bZIP factor (PHBZ). For phylogenetic analysis, we sequenced the full sequence LTR (FLTR) and full Tax sequence (FTax). The FLTR and FTax sequences underwent analysis using BioEdit, and phylogenetic trees were constructed using MEGA-X software.

Results: Out of the roughly 15,000 annual blood donors in Alborz, 19 samples tested positive for HTLV-1, indicating a 0.13% HTLV-1 positivity rate among blood donors. Furthermore, the HTLV-1 virus prevalent in the Alborz province belongs to subtype A (cosmopolitan) subgroup A.

Conclusion: The findings revealed that while mutations were observed in both the LTR and Tax genes, they were not significant enough to bring about fundamental alterations. Despite positive selection detected in three Alborz isolates, it has not led to mutations affecting Tax function and virulence.

keywords: HTLV-1 Phylogeny Studies Prevalence

PV-7

Decoding dysregulated angiogenesis in HTLV-1 asymptomatic carriers compared to healthy individuals

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Background and aim: Human T-cell lymphotropic virus type 1 (HTLV-1) is the first identified human retrovirus responsible for two significant diseases: HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP) and adult T-cell leukemia/lymphoma (ATLL). Although the majority of infected individuals remain asymptomatic carriers, a small percentage may develop ATLL or HAM/TSP. In tumorigenesis, a crucial process is angiogenesis, which involves the formation of new blood vessels. However, the precise mechanism of HTLV-1 associated angiogenesis remains unclear.

Methods: This study aims to investigate the gene regulation involved in the angiogenesis signaling pathway associated with HTLV-1 infection. The research enrolled 20 male participants, including asymptomatic carriers and healthy individuals. Blood samples were collected and screened using ELISA for HTLV-1 confirmation, and PCR was performed for both Tax and HBZ for validation. RNA extraction and cDNA synthesis were carried out, followed by RT-qPCR analysis targeting cellular genes involved in angiogenesis.

Results: Our findings indicate that gene expression related to angiogenesis was elevated in HTLV-1 ACs patients. However, the differences in gene expression of the analyzed genes, including HSP27, Paxillin, PDK1, PTEN, RAF1, SOS1, and VEGFR2 between ACs and healthy individuals were not statistically significant. This suggests that although angiogenesis-related genes may show increased expression in HTLV-1 infection, they might not be robust indicators of ATLL progression in asymptomatic carriers.

Conclusion: The results of our study demonstrate that angiogenesis gene expression is altered in ACs of HTLV-1, indicating potential involvement of angiogenesis in the early stages before ATLL development. While we observed elevated angiogenesis gene expression in ACs, the lack of statistical significance between ACs and healthy individuals suggests that these gene markers may not be sufficient on their own to predict the development of ATLL in asymptomatic carriers.

keywords: HTLV-1 Angiogenesis ATLL Virology

PV-8

Utilization of multiplex polymerase chain reaction for simultaneous and rapid detection of viral infections from different ocular structures

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Background and aim: The impact of viral keratitis (VK) on individuals and society is notable. Early diagnosis and treatment are crucial in managing viral keratitis effectively. Timely intervention with antiviral medications and supportive care can help mitigate the severity of the infection and improve visual outcomes. We examined the prevalence of varicella-zoster virus (VZV), herpes simplex virus type 1 (HSV-1), adenovirus (AdV) and herpes simplex virus type 2 (HSV-2) in patients suspected for ocular infections. Patients included in the study exhibited various clinical manifestations indicative of ocular pathology, such as infectious keratitis, corneal scar, endogenous endophthalmitis, panuveitis, endothelitis, stromal edema, and other relevant

Methods: Four different types of tear fluid, corneal samples, epithelium, aqueous humor, and vitreous humor were taken. After genome extraction, multiplex real-time PCR was used for the diagnosis of viruses

Results: 48 (29.6%) out of the total of 162 (100%) eye specimens were positive. The dominant prevalence was VZV (12.3%) and HSV-1 (11.7%), followed by AdV (4.9% and HSV-2 (0.6%). There were 4 (8.3%) coinfections within the samples (HSV-1 and VZV). Aqueous Humor samples demonstrated superior virus detection ability, and our only HSV-2 positive sample was from aqueous humor

Conclusion: The use of multiplex real-time PCR assays for the differential diagnosis of VK holds promise for expeditious diagnosis while also preventing unwarranted antibiotic prescriptions. Moreover, the aqueous humor appears to be .a more sensitive site for detecting viral keratitis

keywords: Keratitis, Multiplex PCR, Ocular infection, Infectious keratitis

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Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PV-9

Tracking Phylogenetic and Epitope Changes in SARS-CoV-2 Omicron Sub-lineages in Iran

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Background and aim: Background: SARS-CoV-2, especially the Omicron variant and its sub-lineages, has evolved rapidly, raising concerns about immune responses and viral epitope variations. In Iran, the continuous evolution of Omicron variants necessitates understanding these changes, particularly in terms of immune evasion. Aim: This study aimed to analyze phylogenetic variations and assess the conservation of B cell, CD4+, and CD8+ T cell epitopes across Omicron sub-lineages in Iran, to understand their impact on immunity and inform vaccine development.

Methods: From October 2023 to August 2024, 49 SARS-CoV-2 strains, including Omicron sub-lineages, were sequenced and analyzed phylogenetically using Nextstrain clades. The conservation of B cell, CD4+, and CD8+ T cell epitopes was evaluated with bioinformatic tools, focusing on neutralizing antibody sites and T cell responses. Epitopes in spike and non-spike proteins were compared across different clades. The analysis, conducted at the Iran National Influenza Centre, identified immune escape patterns among major Omicron sub-lineages.

Results: Phylogenetic analysis of 49 SARS-CoV-2 strains revealed eight distinct Nextstrain clades (21L, 22F, 23B, 23H, 23D, 24A, 24B, and 24C), along with one recombinant strain (XDK.1). The evaluation of epitope conservation across these strains showed varying levels: B cell epitopes had a 31% conservation rate, CD4+ T cell epitopes 65%, and CD8+ T cell epitopes 78%. The low conservation of B cell epitopes suggests potential immune escape from neutralizing antibodies, while CD8+ T cell epitopes were more conserved, indicating stronger preservation of cell-mediated immunity. T cell epitope conservation was higher in non-spike proteins compared to spike proteins, and more conserved in clades 21L, 22F, 23B, 23H, 23D, and 24B compared to 24A and 24C. These findings highlight significant variation in immune escape potential across Omicron sub-lineages.

Conclusion: This study found that CD8+ T cell epitopes are more conserved than B cell and CD4+ epitopes in Omicron sub-lineages, suggesting a stronger role for T cell immunity. Non-spike protein epitopes showed higher conservation, indicating their potential as future vaccine targets. These findings underscore the importance of monitoring epitope variation to inform vaccine development and immune strategy adjustments in response to evolving SARS-CoV-2 variants.

keywords: SARS-CoV-2, Omicron sub-lineages, phylogenetic, epitope variations, immunity

17th International Congress of Lab. and Clinic
Tehran University of Medical Sciences (TUMS)
July 20-23, 2026

PV-10

Down-regulation of Tumor Suppressor Gene PTEN in Patients with Chronic Hepatitis B Virus Infection: A Case-Control Study

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Background and aim: Chronic Hepatitis B virus (HBV) infection is a major global health concern and a leading cause of hepatocellular carcinoma (HCC). Loss or suppression of PTEN expression contributes to the development and progression of HCC, particularly in the context of chronic HBV infection. The current study aimed to evaluate PTEN gene expression in patients with chronic HBV infection compared to healthy individuals.

Methods: This case-control study included 50 patients with chronic HBV infection and 50 healthy controls. Peripheral blood samples were collected, and total RNA was extracted and converted to cDNA. Gene expression of PTEN relative to GAPDH was assessed by SYBR Green-based Real-Time PCR using the 2^-ΔΔCt method. Statistical analysis was performed using SPSS version 26, with significance set at p0.05.

Results: PTEN gene expression was significantly down-regulated in the HBV-infected group compared to controls (2^-ΔΔCt = 0.074, p0.0001). The ΔCt value of PTEN was significantly higher in the patient group, indicating reduced transcript levels. An age-related decline in PTEN expression was also observed among HBV patients.

Conclusion: The results highlight the importance of PTEN as a potential biomarker in the progression of the disease to liver cancer. Therefore, further research with a larger sample size and investigation of the molecular mechanisms involved in regulating PTEN expression seem necessary.

keywords: Hepatocellular carcinoma, chronic hepatitis B, PTEN, immune evasion, HBx

PV-11

Understanding lactate in the development of Hepatitis B virus-related hepatocellular carcinoma

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Background and aim: Chronic hepatitis B (CHB) infection is associated with an increased risk of hepatic decompensation, cirrhosis, and hepatocellular carcinoma (HCC). Emerging studies indicate that lactate is linked to patient mortality rates, and HBV increases overall glucose consumption and lactate production in hepatocytes. The purpose of this review is to gather and summarize the existing knowledge of the lactate's functions in the dysregulation of the immune system, which can play a crucial role in the development of HBV-related HCC.

Methods: This narrative review was conducted through a systematic search of PubMed, Scopus, Web of Science, and Google Scholar for articles published up 2024. Relevant studies addressing lactate metabolism, metabolic reprogramming, immunometabolic alterations, and tumor microenvironment changes in hepatitis B virus–related hepatocellular carcinoma were included.

Results: Evidence indicates that chronic HBV infection induces metabolic reprogramming in hepatocytes, characterized by enhanced aerobic glycolysis and excessive lactate production. Lactate is generally immunosuppressive by reducing cytotoxicity, IFN production, antigen presentation, maturation, activation, and differentiation. Additionally, lactate can enhance apoptosis and histone lactylation to promote tumor progression. In the presence of lactate, the innate immune cells (MΦs, DCs, NK, and neutrophils) and adaptive immune cells (T cells) are dampened. Remarkably, lactate level is associated with increased mortality rates.

Conclusion: Excessive lactate plays a role in regulating the tumor microenvironment (TME), immune cell function, autophagy, and epigenetic reprogramming. Therefore, it is reasonable to hypothesize that lactate with intriguing functions can be considered an immunomodulatory metabolite in immunotherapy.

keywords: Hepatitis B Virus, Lactate, Hepatocellular Carcinoma, Immune System

PV-12

Unraveling the Molecular Mechanism of Curcumin Inhibition against White Spot Syndrome Virus VP26: An Integrated Computational Study

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Background and aim: White Spot Syndrome Virus (WSSV) is a highly destructive pathogen responsible for severe economic losses in global shrimp aquaculture. The lack of effective antiviral treatments highlights the need for novel therapeutic strategies. Viral structural proteins are attractive targets for intervention, particularly VP26, which plays a key role in virion assembly and host–cell interactions. Curcumin, a natural bioactive compound derived from Curcuma longa, has demonstrated broad antiviral activity; however, its molecular mechanism of action against WSSV remains poorly understood.

Methods: In this study, an integrated computational approach was employed to investigate the interaction between curcumin and the WSSV VP26 protein. Molecular docking was performed to evaluate binding affinity and identify key interacting residues. Subsequently, 100 ns molecular dynamics (MD) simulations were conducted to assess the stability, conformational behavior, and interaction dynamics of the VP26–curcumin complex. Binding free energy calculations were carried out using the MM/PBSA method, along with analyses of hydrogen bonding, radius of gyration, and residue flexibility.

Results: Docking analysis revealed a favorable binding affinity of –6.53 kcal/mol, indicating spontaneous interaction between curcumin and VP26, primarily stabilized by van der Waals forces and hydrogen bonding, especially involving Arg136. MD simulations demonstrated that the complex remained structurally stable throughout the simulation period, with persistent hydrogen bonds, short intermolecular distances, and minimal fluctuations in the radius of gyration. Residue-specific flexibility analysis showed localized dynamic changes near the binding site, suggesting adaptive conformational adjustments upon ligand binding. MM/PBSA calculations yielded a binding free energy of –93.46 kJ/mol, confirming strong and stable complex formation.

Conclusion: These results provide detailed molecular insights into the inhibitory interaction between curcumin and VP26, supporting curcumin's potential as a natural antiviral agent against WSSV and offering a foundation for rational antiviral design in shrimp aquaculture.

keywords: White Spot Syndrome Virus, VP26, Curcumin, Molecular Docking, and Molecular

PV-13

Factors affecting viral load response in HIV-infected patients: a retrospective cohort study from Kermanshah, Iran

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Background and aim: Objectives: Effective control of viral load (VL) is a central goal of antiretroviral therapy (ART) in HIV patients, supporting immune recovery and reducing transmission. VL response is affected by demographic, clinical, behavioral factors, and treatment adherence. This retrospective study aimed to identify factors associated with VL changes among HIV-positive individuals at the Kermanshah Behavioral Diseases Counseling Center.

Methods: Methods: We included 2,909 HIV/AIDS patients attending the center between 2012 and 2023. Data on demographics, behavioral and clinical characteristics, route of transmission, disease stage, clinic visits, and VL were extracted from records. Nonparametric tests (Spearman's correlation, Mann-Whitney U, Kruskal-Wallis) were applied using SPSS v21, with significance set at 0.05.

Results: Results: Among 538 patients analyzed (181 women, 357 men), 291 (54.2%) had incarceration history, 347 (59.5%) had addiction history, and 358 (61.4%) acquired HIV via injection drug use. Median initial and final VL were 819 cells/μL (0–21,447,430) and 100 cells/μL (0–80,489,520), respectively. Greater VL reductions were observed in women, patients with perinatally acquired HIV, those without incarceration or addiction history, stage II patients, and employed individuals. More clinic visits correlated with larger VL reductions, whereas older age was associated with higher VL.

Conclusion: Conclusion: VL changes in HIV-infected patients were influenced by gender, addiction and incarceration history, transmission route, disease stage, employment, age, and clinic attendance. Greater reductions were linked to regular treatment adherence, continuous follow-up, and early ART initiation, particularly in women and perinatally infected individuals.

keywords: AIDS, HIV, viral load, antiviral therapy, Kermanshah, Iran

PV-14

Expression levels of taste genes, TAS1R1, TAS1R2 and TAS1R3 among SARS-CoV-2 patients

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Background and aim: The most common symptoms of COVID-19 infection include fever, myalgia, cough, dyspnea, and loss of smell and taste. Some studies have suggested that a COVID-19-related reduction in taste receptor expression may lead to the loss of taste. Therefore, this study aimed to assess the expression levels of taste receptor genes in COVID-19 patients. Gene expression levels of TAS1R1, TAS1R2, and TAS1R3 were analyzed in 100 COVID-19 patients (50 with loss of taste and 50 without) and 50 SARS-CoV-2 RT-qPCR-negative individuals.

Methods: One hundred and fifty nasopharyngeal swab samples were collected from Iranian COVID-19 patients (50 with loss of taste and 50 without) and SARS-CoV-2 negative persons as a control group and evaluated for TAS1R1, TAS1R2, and TAS1R3 gene expression using mRNA measurement. Gene expression was evaluated using two-step real-time PCR, and RPLP0 was used as a reference gene

Results: The expression levels of taste genes did not show a significant difference between healthy individuals and infected patients with and without loss of taste. There was also no significant difference between the gene expression levels in each group.

Conclusion: Although our findings were not statistically significant, temporary ageusia may be attributed to the high replication rate of SARS-CoV-2 in infected gustatory cells within the taste buds. This replication could induce inflammation and potentially lead to cell destruction.

keywords: SARS-CoV-2, COVID-19, TAS1R1, Taste receptors, Ageusia

17th International Congress of Lab. and Clinic
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PV-15

Is Hepatitis B Immunization Enough to Prevent HBV infection in Infants Born to Mothers with HBsAg Positive?

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Background and aim: Hepatitis B virus is 50 to 100 times more transmissible and infectious than human immunodeficiency virus (HIV). One of the main routes of transmission of hepatitis B virus is from mother to fetus, which in recent years has decreased with the widespread use of immunization methods, including antiviral treatments, vaccines, immunoglobulins, and post-vaccination monitoring. The aim of the present study was to investigate the prevalence of hepatitis B infection in immunized infants born to mothers with chronic hepatitis B.

Methods: The study performed a comprehensive systematic review of literature on infants born to mothers with chronic hepatitis B in Iran and worldwide. National and international databases (PubMed, Scopus, Web of Science, etc.) using MeSH terms searched. The team performed subgroup analyses by patient group, calculating pooled effects and testing between-group differences. Reporting adhered to PRISMA guidelines. Quality assessment and sensitivity analyses were also performed to ensure robustness and transparency.

Results: Of the total number of hepatitis B cases worldwide, approximately 6 million are children <5 years. A global prevalence of OBI calculated 7.5% and in children born to HBsAg-positive mothers it was 6.4%. In Iran hepatitis B in children born to HBsAg-positive mothers accounts from 3.1 to 27%. The results of studies indicate a 10% chance of OBI in children born to mothers with high HBV DNA levels, despite antiviral treatments, vaccination, and immunoglobulin administration.

Conclusion: Some studies reported that vaccination and immunoglobulin appeared successful in preventing overt infection but still failed to reduce the expected incidence of OBI. While the results of some studies indicate that vaccination does not have an acceptable effect on the incidence of OBI in infants born to HBsAg-positive mothers, some studies emphasize the positive effect of increasing the vaccine dose on reducing the incidence of OBI in these infants.

keywords: Chronic hepatitis B (CHB), HBsAg positive mothers, Occult hepatitis B

PV-16

Aptamer-based Strategies for COVID-19 Detection and Treatment: A Systematic Review Study

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Background and aim: Aptamer-based strategies have emerged as promising tools for the detection and treatment of COVID-19, offering advantages such as high specificity, sensitivity, and versatility. This systematic review aims to evaluate the effectiveness and innovation of aptamer-based approaches for COVID-19 detection and treatment.

Methods: Following the guidelines of the Cochrane Handbook for Systematic Reviews and the PRISMA 2020 guidelines, a systematic search was conducted across multiple databases up to 2024. The search included studies that utilized aptamers for the diagnosis or therapy of COVID-19. Screening and selection of studies were performed independently by two reviewers, with any disagreements resolved by a third reviewer. Data were extracted regarding study characteristics, aptamer details, and outcomes.

Results: In our systematic review, 98 studies from an initial pool of 1541 records met the inclusion criteria for analysis. Aptamers, single-stranded DNA or RNA molecules with unique three-dimensional structures, were extensively explored for COVID-19 detection and treatment. Various aptamer-based assays, including electrochemical sensors, surface plasmon resonance biosensors, and lateral flow assays, demonstrated high sensitivity and specificity in detecting SARS-CoV-2 in clinical samples such as saliva, nasal swabs, and wastewater. Several aptamer structures targeting viral proteins like the spike and nucleocapsid proteins were employed. Nucleic Acid Amplification Techniques utilizing aptamers, including CRISPR-based and Loop-mediated Isothermal Amplification assays, showed exceptional sensitivity in detecting viral genetic material. Aptamer-based therapeutic approaches showed potential by blocking viral protein activity or serving as delivery vehicles for therapeutic agents like small interfering RNAs. Despite their advantages, aptamer technologies face limitations such as nuclease degradation and rapid renal clearance, highlighting the need for further optimization.

Conclusion: Aptamer-based strategies present promising avenues for COVID-19 detection and treatment. These approaches offer advantages such as high sensitivity, specificity, and rapid detection, making them valuable tools in combating the COVID-19 pandemic. Further research and development are warranted to optimize aptamer-based strategies for widespread application in clinical settings.

keywords: aptamer; COVID-19; detection; SARS-CoV-2; systematic review; treatment; viral infection

PV-17

The HCV F protein: a potential immunological marker and vaccine target

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Background and aim: Hepatitis C virus (HCV) infection can progress to chronic liver disease, emphasizing virus–host immune interactions. Beyond structural and non-structural proteins, HCV expresses an alternative reading frame protein known as F protein. Evidence indicates that the F protein elicits humoral immune responses and induces anti-F protein antibodies, which are more frequently detected in chronic infection and advanced liver disease. These findings support the consideration of the HCV F protein as an immunological marker and a complementary antigen for vaccine development.

Methods: This narrative review provides an overview of published studies on the immunological characteristics of the HCV F protein, focusing on its potential as an immunological marker and complementary vaccine target. The literature addressed humoral immune responses, anti-F protein antibody production, and their relevance across different stages of HCV infection, including chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Studies reporting antibody prevalence and associations with antiviral treatment response were also considered. Key observations and conflicting reports regarding immune responses to the F protein were highlighted.

Results: The reviewed studies show that the HCV F protein activates the humoral immune system and induces anti-F protein antibodies, which are more frequently detected in chronic infection and advanced liver disease, supporting its potential role as an immunological marker. Several antigenic domains may contribute to immune activation. These findings also highlight F protein as a complementary target for HCV vaccine development, although associations with antiviral therapy response are inconsistent, with antibodies often remaining elevated in chronic infection and non-responders.

Conclusion: The HCV F protein is a recognized target of the humoral immune system and is associated with chronic infection and advanced disease stages. Sustained detection of anti-F protein antibodies supports its potential use as an immunological marker. Moreover, consistent humoral immune activation highlights F protein's relevance as a complementary antigen in HCV vaccine strategies. Further studies are needed to clarify its role in treatment response and optimize its application in vaccine development.

keywords: Hepatitis C virus; F protein; Vaccine development

PV-18

Organ-Specific Laboratory Biomarker Panels for Prognostication in Viral Respiratory Infections and COVID-19: A Systematic Review

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Background and aim: Viral respiratory infections, particularly COVID-19, burden healthcare systems globally. Early high-risk patient identification optimizes ICU allocation and reduces mortality. Although organ-specific biomarker panels, including inflammatory cytokines (IL-6 and TNF-α), cardiac markers (troponin and BNP), coagulation parameters (D-dimer and fibrinogen), and renal/hepatic indicators (creatinine and ALT/AST), show promise, comprehensive prognostic comparisons remain scarce. Single-marker studies dominate, limiting the integration of multi-parameter panels for improved severity prediction. This systematic review evaluated the predictive accuracy of inflammatory, cardiovascular, coagulation, and renal/hepatic biomarker panels for severity and outcomes in COVID-19–related viral respiratory infections.

Methods: Following PRISMA guidelines, we searched PubMed, Scopus, Web of Science, and Google Scholar from 2021 to 2025 for observational studies and trials involving confirmed viral respiratory infection patients (primarily COVID-19; n=19 studies). The findings include reports of biomarkers from organ panels and ICU admission, mortality, disease progression. We categorized 27 biomarkers out of these studies into following panels: inflammatory (12), cardiac (4), coagulation (5), renal/hepatic (6). NOS quality assessment (68% good ≥7). Descriptive synthesis compared prognostic performance across panels.

Results: Of reviewed records, 19 studies (n≈4,500 patients) met inclusion criteria, predominantly COVID-19 ICU cohorts. 27 biomarkers were categorized into organ-specific panels. Inflammatory markers, such as IL-6 and sCD14-ST, showed consistent association with worse outcomes (AUC≈0.82, p0.001). Cardiac-vascular biomarkers (4 markers; e.g., troponin; ~500 patients) robustly predicted mortality (OR=2.5, p0.01). Coagulation markers, including D-dimer, were particularly informative for thrombotic risk (HR≈1.8 prior to ICU admission). Renal/hepatic panels (6 markers; ~1,100 patients) correlated with severity (AUC0.8, p0.05 in multimarker approaches). Multi-panel combinations (e.g., NLR+D-dimer) yielded superior accuracy (AUC≈0.88), outperforming single panels. Coagulation and inflammatory panels showed strongest associations with mortality/ICU progression across cohorts. Despite between-study heterogeneity, the overall pattern supported the use of panel-based approaches, rather than single-marker ones, for clinical risk stratification.

Conclusion: Organ-specific biomarker panels reliably predict severity in viral respiratory infections. Coagulation, including D-dimer, and inflammatory markers, such as IL-6, showed strongest associations with mortality and ICU needs. Multi-panel combinations (NLR+D-dimer) outperformed single markers, suggesting integrated lab scores for routine triage. These findings bridge research to clinical practice but require validation in diverse populations and non-COVID viruses.

keywords: laboratory biomarkers,Viral respiratory infections

PV-19

Immunomodulatory Roles of HCV Core and Core+1 Proteins in the Establishment of Chronic Infection

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Background and aim: Hepatitis C virus (HCV) establishes chronic infection in the majority of infected individuals, frequently leading to liver cirrhosis and hepatocellular carcinoma. Viral persistence is largely attributed to sophisticated immune evasion strategies, in which structural and accessory viral proteins play critical roles. Among these, HCV Core and Core+1 (F) proteins have emerged as key modulators of host immune responses.

Methods: This review summarizes and analyzes published experimental and clinical studies investigating the molecular and immunological functions of HCV Core and Core+1 proteins during chronic infection. Data regarding their interactions with host signaling pathways, immune cells, and apoptotic mechanisms were critically evaluated.

Results: Evidence indicates that the HCV Core protein interferes with innate and adaptive immunity by suppressing interferon signaling through inhibition of the JAK/STAT pathway, modulating apoptosis, and impairing T cell activation and function. Core protein disrupts antiviral responses by reducing STAT1 activity, inducing SOCS expression, and altering cytokine production. In parallel, the Core+1 protein contributes to viral persistence by promoting regulatory T cell expansion, increasing IL-10 production, modulating cytoskeletal organization, and limiting viral replication to favor chronicity. Elevated immune responses against Core+1 have been observed in patients with advanced liver disease and HCV-associated hepatocellular carcinoma.

Conclusion: HCV Core and Core+1 proteins play central and complementary roles in immune evasion and the progression to chronic HCV infection. Their multifaceted regulatory effects on interferon signaling, apoptosis, and T cell responses highlight these proteins as promising targets for the development of more effective antiviral therapies and vaccine strategies.

keywords: Hepatitis C Virus, Core Protein, Immune Evasion, Chronic Disease, T-Lymphocytes

PV-20

Digital PCR vs. qPCR in Monitoring Viral Loads of Immunocompromised Patients: A Systematic Review of Precision, Clinical Impact, and Future Integration

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Background and aim: Precise viral quantification is vital for immunocompromised patients, yet qPCR's variability at the lower limit of quantification (LLoQ) creates a "clinical grey zone" complicating treatment decisions. This systematic review evaluates whether dPCR—offering absolute quantification without standard curves—can resolve these ambiguities. We specifically assessed dPCR's ability to detect "occult" infections missed by qPCR and its potential as a reference method for standardizing viral load monitoring.

Methods: We performed a PRISMA-compliant systematic review, searching PubMed, Scopus, and Embase for literature published up to October 2024. Our inclusion criteria focused strictly on head-to-head comparisons of dPCR (droplet or chip-based) versus qPCR assays for CMV, EBV, BKV, and HIV-1 in immunocompromised patients. To ensure data quality, studies lacking quantitative data on precision (CV%) or Limit of Detection (LOD) were excluded, and quality assessment was conducted using the QUADAS-2 tool. Data synthesis centered on three metrics: concordance rates at thresholds 200 copies/mL, inter-laboratory reproducibility, and diagnostic odds ratios for predicting clinical relapse based on residual viral load. We also performed a narrative synthesis to map workflow barriers, including cost-per-reportable-result and turnaround time.

Results: Analysis of 38 studies (n=4,250 pairs) confirmed dPCR's superior sensitivity, detecting viral material in 28-34% of qPCR-negative samples. This "occult viremia" correlated with higher relapse risks in CMV and HIV cohorts. dPCR demonstrated superior reproducibility (CV 6% vs. 18-35% for qPCR at 150 copies/mL) and robustness against inhibitors. Although dPCR requires higher costs and a 2.5-fold increase in turnaround time, it significantly reduces equivocal results and the need for repeat testing.

Conclusion: Digital PCR (dPCR) offers the precision needed to confirm viral clearance in low-level viremia where qPCR is unreliable. While qPCR is adequate for high-load screening, dPCR should be used as a reference method to resolve ambiguous cases and guide treatment discontinuation. A hybrid approach—using dPCR only for samples in the qPCR grey zone—is the most cost-effective and accurate strategy.

keywords: Digital PCR, Viral Load Monitoring, Immunocompromised Host, Diagnostic Accuracy, Real-Time

PV-21

Molecular and Structural Characterization of SARS-CoV-2 Omicron Membrane and Envelope Proteins in Iranian Clinical Samples Identified by RT-PCR and Analyzed by NGS (2021–2023)

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Background and aim: First reported in late 2021, the Omicron variant of SARS-CoV-2 is characterized by extensive genetic divergence that may influence viral fitness, immune evasion and disease severity. While mutations in the spike protein have been widely studied, changes to the membrane (M) and envelope (E) proteins, crucial for virion assembly, structural integrity, and host–virus interactions, have not been as thoroughly investigated in the context of clinical molecular epidemiology.

Methods: In this laboratory-based translational study, 528 respiratory samples collected from suspected COVID-19 patients in Iran between March 2021 and March 2023 were confirmed as SARS-CoV-2 positive using real-time RT-PCR. Confirmed samples were then subjected to whole-genome sequencing using NGS platforms. Lineage assignment and mutation profiling were performed using the Nextclade web server and complementary bioinformatics pipelines. Mutational patterns in the M and E proteins were systematically analyzed. The functional impact of M protein mutations on antibody recognition was evaluated by molecular docking with a Fab fragment, followed by molecular dynamics (MD) simulations to assess binding stability and interaction energetics. Additionally, the effects of E protein mutations on structural stability and dynamic behavior were investigated using in silico stability prediction and MD analyses.

Results: Among identified Omicron sublineages, BA.5.2 accounted for 32.4% of cases during the study period, while XBB.1.9.1 was the predominant variant in southern Iran (14.2%). Structural analyses revealed that mutations in the M protein significantly reduced binding affinity to the Fab receptor, with the most pronounced reduction observed in the XBB.1.9.1 lineage, suggesting potential immune evasion through impaired antibody interaction. Furthermore, mutations in the E protein were associated with increased structural stability, which may enhance viral assembly and replication efficiency. This stabilizing effect was particularly evident in the BA.2.75.1.1 sublineage, indicating a possible contribution to viral fitness.

Conclusion: This study demonstrates that Omicron-associated mutations in the SARS-CoV-2 M and E proteins, identified through RT-PCR–confirmed clinical sampling and NGS-based genomic surveillance, have meaningful structural and functional consequences. These findings underscore integrating molecular diagnostics with genomic and structural analyses to understand viral evolution, immune escape, and clinical outcomes beyond spike protein mutations.

keywords: SARS-CoV-2; Omicron variant; RT-PCR; NGS; membrane protein; envelope protein; molecular

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PV-22

Prevalence of Bacterial Pathogens Detected by Multiplex Real-Time PCR in Cerebrospinal Fluid Samples from Patients with Suspected Meningitis

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Background and aim: Considering the high lethality and long-term sequelae of meningitis, rapid etiologic diagnosis and early initiation of appropriate therapy are crucial determinants of patient outcome. In this context, multiplex Realtime polymerase chain reaction (PCR) offers the possibility of simultaneously detecting several major bacterial causes of meningitis in cerebrospinal fluid (CSF) within a single assay. In the present study, a multiplex Realtime PCR panel targeting ten common meningitis associated bacterial pathogens was applied.

Methods: All CSF samples were obtained over a four-year period from hospitalized patients with suspected meningitis who were referred to the clinical laboratory. The multiplex assay was designed to detect the following targets: Neisseria meningitidis (NM), Haemophilus influenzae (HI), Treponema pallidum (TP), Borrelia burgdorferi (BB), Streptococcus agalactiae (SA), Streptococcus pneumoniae (SP), Listeria monocytogenes (LM), Coxiella burnetii (CB), Mycobacterium tuberculosis complex (TB), and Cryptococcus neoformans (CN).

Results: Among 34 CSF specimens tested, 6 yielded a positive multiplex PCR result, corresponding to an overall positivity rate of 20.6%. Of these, 5 samples were positive for TB (14.7% of all cases) and 1 for SP (2.9%), whereas the remaining 28 samples were negative for all panel targets.

Conclusion: Given the substantial proportion of positive cases and the relatively high rate of TB detection, tuberculous meningitis should be regarded as an important diagnostic consideration in this region and routinely included in the evaluation of patients with suspected meningitis.

keywords: TB, multiplex Realtime polymerase chain reaction, Meningitis, Csf

PV-23

Rapid and Quantitative Detection of Respiratory Syncytial Virus (RSV) Using an Aptamer-Based Electrochemical Biosensor Integrated with Metal–Organic Frameworks

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Background and aim: Respiratory syncytial virus (RSV) is a significant cause of acute lower respiratory tract infections. It is essential for infants, older adults, and individuals with weakened immune systems. It remains a significant challenge for healthcare systems worldwide. Molecular techniques, such as RT-PCR, are the most effective method for diagnosis. However, their high cost, specialized equipment requirements, and longer processing times make them challenging to use for quick screening and in simple care settings. The present study aimed to develop and evaluate a sensitive and rapid electrochemical biosensor based on aptamers and metal–organic frameworks (MOFs) for the quantitative detection of RSV.

Methods: A specific RSV aptamer was attached to the surface of an electrochemically modified electrode that incorporates nanostructured MOFs.The MOFs were selected for their high surface area, favorable electron transfer properties, structural stability, and biocompatibility. Electrode modification was carried out using appropriate electrochemical and physical techniques, and surface characteristics were confirmed by scanning electron microscopy (SEM) and Fourier-transform infrared spectroscopy (FT-IR). The analytical performance of the biosensor was evaluated using cyclic voltammetry (CV), differential pulse voltammetry (DPV), and electrochemical impedance spectroscopy (EIS). Key performance parameters, such as the limit of detection (LOD), are essential for evaluating the effectiveness of testing methods. Linear dynamic range, selectivity, reproducibility, and storage stability were evaluated in detail.

Results: The incorporation of metal-organic frameworks (MOFs) onto the electrode surface significantly improved electron transfer efficiency and increased the electrochemical signal intensity. The developed aptasensor can detect the respiratory syncytial virus (RSV) at very low levels. It shows a clear response range that could be useful for clinical applications.Experiments showed that the biosensor works well without reacting to other common respiratory viruses, like human metapneumovirus and influenza. It also produced consistent results and performed stably over several days.

Conclusion: This study demonstrates that the proposed aptamer–MOF-based electrochemical biosensor offers a rapid, sensitive, and cost-effective approach for the quantitative detection of RSV. This platform is simple to use, easy to carry, and provides strong analysis. It shows great potential for clinical labs, quick screening programs, and point-of-care testing. It can serve as an effective alternative to traditional diagnostic methods.

keywords: Respiratory syncytial virus (RSV); Electrochemical biosensor; Aptamer; Metal–organic frameworks (MOFs);

PV-24

An overview of the trend of Crimean-Congo hemorrhagic fever in Iran in recent years

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Background and aim: Crimean-Congo hemorrhagic fever (CCHF) is a common disease between humans and livestock. Butchers and slaughterhouse workers are high-risk occupational groups for this disease. After a short incubation period, the disease is characterized by sudden onset of fever, chills, severe headache, dizziness, and abdominal pain, and in severe cases, hemorrhagic manifestations, ranging from petechia to large areas of ecchymosis. Crimean-Congo hemorrhagic fever virus is transmitted to humans through the bite of an infected tick and through direct contact with the blood or tissue of infected humans and animals.

Methods: Our search in MEDLINE included PubMed, Scopus, Science Direct, Web of Science (ISI), Google Scholar (as English database) and Magiran, Iran Medex, Iran Doc and SID (as Farsi databases) with the following terms were used: Crimean-Congo hemorrhagic fever virus (CCHFV), Nairovirus, Bunyaviridae, molecular diagnosis, serology, epidemiology, Iran.

Results: Based on the results of this study, it was determined that in Iran, positive cases of Crimean-Congo hemorrhagic fever occur mostly in men and in high-risk occupational groups such as slaughterhouse workers and butchers, farmers and ranchers, veterinarians, and health care workers is created. It was also found that the most cases of Crimean-Congo hemorrhagic fever in Iran occurred in the northeast, east, and southeast regions of the country, and according to the results of this report, Hialoma mite species are the dominant disease vector in the region.

Conclusion: Considering the rising trend of Crimean-Congo hemorrhagic fever in high-risk occupational groups in the country, there is a need to hold training courses to increase the level of knowledge, attitude and performance of these groups in relation to the disease and the maximum use of personal protective equipment during Daily work, as well as preventive measures such as the use of tick killers, are very necessary to prevent people from coming in contact with ticks.

keywords: Crimean-Congo hemorrhagic fever disease, Epidemiology, Diagnosis, Bunyaviridae, Iran

PV-25

Dengue virus: Etiology, epidemiology, pathobiology, and developments in diagnosis and control - A comprehensive review

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Background and aim: Dengue flavivirus (DENV) is the virus that causes dengue, one of the most dangerous and common viral diseases in humans that are carried by mosquitoes and can lead to fatalities. Every year, there are over 400 million cases of dengue fever worldwide, and 22,000 fatalities. It has been documented in tropical and subtropical climates in over 100 nations.

Methods: Our search in MEDLINE included PubMed, Scopus, Science Direct, Web of Science (ISI), Google Scholar (as English database) with the following terms were used: Dengue virus; Diagnosis; Epidemiology; Etiology; Pathobiology; Control.

Results: Unfortunately, there is no specific treatment approach, but prevention, adequate awareness, diagnosis in the early stages of viral infection and proper medical care can reduce the mortality rate. The first licensed vaccine for dengue virus (CYD Denvaxia) was quadrivalent, but it is not approved in all countries. The primary barriers to vaccine development include inadequate animal models, inadequate etiology mechanistic studies, and adverse drug events.

Conclusion: This study provides current knowledge and a comprehensive view of the biology, production and reproduction, transmission, pathogenesis and diagnosis, epidemiology and control measures of dengue virus.

keywords: Dengue virus; Diagnosis; Epidemiology; Etiology; Control.

PV-26

Investigation of Parvovirus B19 Infection Prevalence in Pregnant Women Bandar Abbas Using the PCR Method

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Background and aim: Parvovirus B19 is a common virus that can cause infection in humans. The transmission route of this virus is typically through the respiratory system. During pregnancy, infection with this virus is of particular importance due to the risk of vertical transmission to the fetus and potential serious complications such as hydrops fetalis, spontaneous abortion, and stillbirth [1, 2]. Accurate assessment of the prevalence of this infection in at-risk populations, such as pregnant women, is essential for developing monitoring and preventive strategies [3]. This study aimed to determine the frequency of parvovirus B19 infection in DNA samples collected from pregnant women.

Methods: This study was conducted as a cross-sectional study on 200 DNA samples extracted from the blood of pregnant women who visited healthcare centers in Bandar Abbas. After DNA extraction, all samples were tested for Parvovirus B19 DNA using the polymerase chain reaction (PCR) technique. Due to its high sensitivity and specificity, this method is considered a standard for virus detection. The obtained data were analyzed descriptively.

Results: Out of a total of 200 DNA samples tested using the PCR method, PCR test results were positive for 10 samples (5%). This figure indicates the prevalence of active Parvovirus B19 infection in this statistical population of pregnant women. The remaining 190 samples (95%) were free of viral DNA, and their test results were reported as negative.

Conclusion: In this study, the prevalence rate of parvovirus B19 infection among the investigated pregnant women is 5%. Although the percentage of positive cases may seem low at first glance, this rate is significant considering the potential severe consequences of the infection on pregnancy outcomes. Early diagnosis of infection in the mother can lead to more targeted monitoring of the fetus and timely interventions. To more precisely determine prevalence and associated risk factors, conducting broader studies with larger sample sizes and in different geographical regions is recommended.

keywords: Parvovirus B19, Pregnant Women

PV-27

Global prevalence of Pepper mild mottle virus: A Meta-analysis

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Background and aim: Pepper mild mottle virus (PMMoV) can infect plants and has been identified as the most abundant virus in healthy adult fecal samples in different parts of the world. PMMoV has been pulled into consideration as a potential viral indicator for human fecal contamination in aquatic environments and water treatment frameworks around the world. The aim of this meta-analysis study was to determine the prevalence of PMMoV in different environmental samples in the world. PRISMA guidelines were used to search literature that reporting the prevalence of PMMoV in environmental and clinical samples.

Methods: Pooled prevalence with 95% CI and heterogeneous identification were obtained using a random effects model and Cochran's Q test, and quantification was assessed using the I2 statistic. All data were analysed using Stata Software v.14.1.

Results: the pooled prevalence of PMMoV infection among environmental samples was 68% (95% CI: 57-78%, I2=96.47, P0.00), including 87% for the water sample, 14% for fecal sample, 73% for tissue sample, and 57% for food samples

Conclusion: The results of this study showed that PMMOV has a global prevalence's and is abundant in different water sources. In addition, an increase in PMMOV concentration is associated with an increase in the contamination of water with feces.

keywords: Pepper mild mottle virus, PMMoV, Prevalence, Meta-Analysis

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PV-28

Survey of awareness and attitudes of Payam Noor University Students in Bandar Abbas about human papillomavirus

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Background and aim: Human papillomavirus or HPV is the most common cause of viral infection of the genital tract, with more than one hundred known types. Most people are infected with this virus at least once in their lifetime. Most types are harmless and disappear on their own, but some can cause genital warts or cancers such as cervical cancer. Given the importance of prevention at a young age, this study was conducted in 2025 to determine the level of awareness and attitudes of students at Payam Noor University of Bandar Abbas towards this virus and its vaccination.

Methods: This descriptive-analytical study was conducted on 100 students of Payame Noor University in Bandar Abbas, who were selected using convenience sampling. The questionnaire consisted of three main sections: The first section addressed demographic variables, including age, gender, education, and information sources. The second section included 20 specialized questions to assess awareness in areas such as transmission routes, clinical symptoms, complications (such as cervical cancer), and prevention methods. The third section included 10 questions on a 5-point Likert scale to evaluate students' attitudes. The data were analyzed using SPSS version 26 and descriptive statistical indicators (mean and standard deviation).

Results: The results showed that 25% of the participants were unable to respond to the questionnaire due to lack of initial knowledge. Among the remaining 75 respondents, the mean awareness score was 13.60 out of 20 (SD=2.14) and the mean attitude score was 40.15 out of 50 (SD=4.30), indicating a moderately high level of awareness and a positive attitude. However, the vaccination rate among all participants was reported as 0%. The highest level of agreement was related to the necessity of education in schools (4.46 out of 5), and the most common misconception was about virus transmission through swimming pools (62.7%).

Conclusion: The results of our study showed that students' awareness was at a moderate level (12.45 out of 20), which indicates that despite having heard of HPV, students' specialized knowledge about preventing the transmission of this disease is inadequate. The findings indicate a contradiction between awareness/positive attitudes and preventive behavior. Despite the students' relative knowledge, practical and economic barriers have prevented vaccination. Therefore, government intervention to reduce vaccine costs and include specialized training in the curriculum appears to be necessary.

keywords: Human papillomavirus (HPV), awareness, attitude,

PV-29

Correlation Between Cytological Findings in Pap Smears of Patients with ASCUS, LSIL and HSIL, with Subtypes of Human Papillomavirus

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Background and aim: Background & Objective: Human papillomavirus (HPV) is a common infectious and pathogenic agent, with certain genotypes capable of causing malignant changes in the surface of mucosal cells. Therefore, the aim of this study is to investigate the types of human papillomavirus (HPV) present in patients with ASC-US Pap smears.

Methods: : This cross-sectional study was conducted on 157 women who were referred to gynecologists for HPV screening from November 2023 to June 2024 in Zabol citiy. Data on demographic information, obstetric history, oral contraceptive pill (OCP) use, history of sexually transmitted diseases (STDs) and high-risk behaviors, cervical treatments, HPV

Results: This study analyzed various HPV genotypes using PCR and hybridization methods, identifying both high-risk and low-risk types, with low-risk genotype 6 being the most prevalent (28%). Low-risk HPV types accounted for 13.4% of cases, while high-risk types represented 11%. The significant association between age and HPV infection rate (P0.05). Most women had an education level below a diploma, and the primary motivation for undergoing a Pap smear was a doctor's recommendation. Among 71 positive samples, 31 cases (19.7%) were ASC-US, and the findings were statistically significant (P0.01)

Conclusion: Based on the results of this study, ASC-US Pap smears require more detailed investigation, such as colposcopy and cervical biopsy, under the supervision of experts, due to their association with high-risk HPV in many cases.

keywords: Human Papillomavirus, Colposcopy, Pap Smear, ASC-US

PV-30

No Significant Link between HSV-1 or HSV-2 Infection and the Risk of Cervical Cancer

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Background and aim: It is suggested that HPV and HSV-1 or 2 co-infection may play a significant role in increasing the risk of cervical cancer. Elucidating the role of viral cofactors could lead to strengthening preventive interventions, such as public education and management of co-infections, which decrease the incidence and mortality rate of cervical cancer. This study intends to investigate the prevalence of HSV-1 and 2 in normal, precancerous, and cancerous cervical samples in Iran to clarify their possible role in the pathogenesis of this disease.

Methods: To detect HSV-1 and HSV-2 genomes, 804 cervical samples with different pathological stages were investigated using multiplex-PCR.Statistical analysis was done using EPI Info 7.2 Statistical Analysis System Software (Atlanta, GA, USA). The Yates corrected chi-square or Fisher's exact tests were applied. When the P-value was less than 0.05, it was considered statistically significant

Results: HSV-1 and HSV-2 were detected in 0.9% and 7.3% of all cervical samples, respectively. However, no statistically significant differences were observed for both HSV-1 and HSV-2 prevalence concerning pathological stages. Although the prevalence of HSV-1 and HSV-2 did not differ among HPV-positive and HPV-negative women, HSV-2 was more common in HPV 18 and other high-risk (non-16/18) than in HPV 16 samples, and this difference was statistically significant

Conclusion: In conclusion, no association was found between HSV-1/2 and cervical cancer. However, our findings revealed that both HSV-1 and HSV-2, particularly HSV-2, recurrently had shedding into the genital area of infected people, and this fact highlighted the significance of the use of a condom to diminish the transmission rate between sexual partners. Nevertheless, further studies with larger sample sizes are obligatory to elucidate the role of HSV-1 and HSV-2 in the development of cervical cancer

keywords: Cervical cancer, Herpes simplex type 1/2, Human papillomavirus, and Genotypes

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PV-31

Computational Analysis of propan-2-yl 2-[[[5-(2,4-dioxopyrimidin-1-yl)oxolan-2-yl]methoxy-phenoxyphosphanyl]amino]propanoate as a novel NS5B RNA polymerase Inhibitor in Hepatitis C Virus Cancers

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Background and aim: Chronic hepatitis C virus (HCV) infection affects an estimated 170–200 million people worldwide, leading to primary liver cancer and thousands of deaths annually. Current therapies offer limited efficacy and significant side effects, highlighting the urgent need for safer and more effective antiviral treatments. A key therapeutic target is the NS5B RNA polymerase, an essential viral enzyme responsible for synthesizing the viral genome. Therefore, this study aimed to identify the most potent NS5B polymerase inhibitor through molecular docking.

Methods: The three-dimensional structure of NS5B polymerase (PDB ID:3GOL) was obtained from RCSB Protein Data Bank. The structure of Sofosbuvir (PubChem CID:45375808) and its 40 analogs were retrieved from PubChem database. Following preparation of the protein and ligand structures, molecular docking was performed using Molegro Virtual Docker version 6. The highest-scoring pose was extracted and analyzed via Molegro Virtual Viewer version 7. The ligand exhibiting the lowest binding energy was identified as the most favorable candidate. Subsequently, pharmacokinetic properties were evaluated using the SwissADME server.

Results: Among the evaluated analogs, the most potent inhibitor was identified as propan-2-yl 2-[[[5-(2,4-dioxopyrimidin-1-yl)oxolan-2-yl]methoxy-phenoxyphosphanyl]amino]propanoate (PubChemCID:169940469), exhibiting a binding free energy of -162.419kcal/mol and a molecular weight of 465.44g/mol. Interaction analysis revealed the formation of four hydrogen bonds and nine steric interactions. Pharmacokinetic assessment indicated favorable properties, including LogS: -3.71, XLOGP:3.87, and TPSA of 134.47Å².

Conclusion: The component propan-2-yl 2-[[[5-(2,4-dioxopyrimidin-1-yl)oxolan-2-yl]methoxy-phenoxyphosphanyl]amino]propanoate was a novel NS5B polymerase inhibitor candidate against Hepatitis C Virus, supporting the need for further experimental validation through both in vitro and in vivo studies.

keywords: Molecular Docking, Sofosbuvir, NS5B Polymerase, Hepatitis C Virus, ADME.

PV-32

Repurposing FDA-approved drugs and natural compounds to inhibit the methyltransferase of dengue 2

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Background and aim: The dengue virus, an arbovirus, can cause a range of clinical symptoms, yet no FDA-approved treatments currently exist. To discover potential inhibitors targeting dengue serotype 2, we focused on the Methyltransferase protein, identifying key binding site regions. Using the Smina program, we performed molecular docking to screen both natural compounds and FDA-approved drugs.

Methods: Our study incorporated multiple computational tools: the HADDOCK2.4 for peptide-protein docking, the pkCSM web server for pharmacokinetic analysis, OSIRIS Data Warrior for evaluating physicochemical properties, Data Warrior for cytotoxicity assessment, and molecular dynamics simulations using GROMACS2021 to examine ligand-Methyltransferase interaction stability

Results: : Docking results identified several compounds with strong binding affinity for the Methyltransferase in dengue serotype 2. Notably, Raltegravir demonstrated the highest binding energy among tested agents. Among natural compounds, ZINC13378516 showed the strongest interaction with the Methyltransferase domain

Conclusion: The selected candidates exhibited favorable properties, including low cytotoxicity, high skin permeability, and efficient intestinal absorption. Our findings suggest that these FDA-approved drugs and natural compounds could effectively bind to dengue serotype 2 Methyltransferase, potentially inhibiting viral infection. However, further in vitro and in vivo studies are required to validate these predictions and assess therapeutic efficacy.

keywords: Dengue, RNA-dependent RNA polymerase, Molecular docking, Molecular dynamics simulation,

PV-33

Broad-Spectrum Antiviral Potential of Flavonoids Against Dengue and Zika Viruses

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Background and aim: Dengue virus (DENV) and Zika virus (ZIKV) are mosquito-borne flaviviruses that present major public health challenges worldwide. Despite significant research, there are still no effective antiviral treatments or widely protective vaccines. This lack has led to a search for alternative treatment options. Natural flavonoids, which are plant-based compounds known for their health benefits and safety, have emerged as potential antiviral agents. Increasing evidence shows that flavonoids can interfere with various stages of the flaviviral life cycle, suggesting their effectiveness across a different types of viruses.

Results: Accumulating evidence from multiple in vitro studies indicates that various flavonoids, including silymarin, baicalein, baicalin, naringenin, and 7-O-methyl naringenin, possess antiviral activity against DENV and ZIKV. These compounds generally display low cytotoxicity and appear to interfere with distinct stages of viral infection. Notably, silymarin and baicalein have been frequently reported to exert strong virucidal effects against multiple DENV serotypes, implying possible direct interactions with viral structures. Baicalein and baicalin are reported to lower the amount of virus inside the infected cells, while silymarin mainly works at the extracellular or early stages of infection. In addition, naringenin and its methylated form significantly reduce viral replication after infection and demonstrate their efficacy after the virus enters the cell. Studies show that these flavonoids can interfere with viral binding and entry, as well as disrupting viral replication processes, which contributes to their broad efficacy.

Conclusion: Overall, current evidence supports the idea that flavonoids are multi-target antiviral agents that can inhibit DENV and ZIKV through different mechanisms. Their ability to act at various points in the viral life cycle, along with their low toxicity, highlights their promise as potential candidates for new antiviral treatments. More in vivo studies and formulation research are needed to apply these findings in clinical settings.

keywords: Dengue virus; Zika virus; flavonoids; antiviral agents

PV-34

Endosymbiotic Viruses in Trichomonas vaginalis and Their Role in Modulating Inflammation: A Review

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Background and aim: Trichomonas vaginalis is a globally prevalent protozoan parasite causing trichomoniasis, often associated with vaginitis, reproductive complications, and heightened inflammatory responses. Recent studies have highlighted the presence of endosymbiotic viruses, particularly Trichomonas vaginalis virus (TVV), as potential modulators of parasite virulence and host immune activation. Viral components released during parasite lysis may amplify inflammatory signaling pathways, influencing disease severity. Understanding the interactions between T. vaginalis and its endosymbiotic viruses is crucial for elucidating mechanisms of pathogenesis and identifying potential therapeutic targets.

Methods: A systematic literature search was conducted in PubMed, Scopus, and Web of Science databases for studies published up to 2025. Keywords included "Trichomonas vaginalis", "virus", "endosymbiont", "TVV", and "inflammation". Studies investigating viral prevalence, molecular characteristics, and the association between viral infection and inflammatory outcomes were included. Data were synthesized narratively to evaluate current knowledge and gaps in understanding.

Results: Evidence indicates that TVV infects a significant proportion of T. vaginalis isolates worldwide. Virus-positive parasites have been consistently associated with elevated inflammatory markers, increased cytokine production, and more severe clinical manifestations. Mechanistic studies suggest that viral dsRNA and proteins may activate host innate immune receptors, contributing to heightened inflammation. However, variability in viral prevalence, parasite strain differences, and limited clinical correlation studies highlight the need for further investigation.

Conclusion: : Endosymbiotic viruses in T. vaginalis play an important role in modulating host inflammatory responses, potentially exacerbating disease severity. These viruses represent promising biomarkers for disease prognosis and may serve as novel targets for therapeutic interventions. Future research integrating molecular, immunological, and clinical approaches is essential to fully elucidate the impact of viral endosymbionts on trichomoniasis pathogenesis.

keywords: Trichomonas vaginalis; Endosymbiotic Virus; Trichomonas vaginalis Virus (TVV); Inflammation; Pathogenesis

PV-35

Newcastle Disease Virus: A promising candidate for breast cancer therapy through targeting the glycolysis pathway

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Background and aim: Breast cancer (BC) remains a leading cause of death among women, with cells mainly relying on glycolysis for energy acquisition, growth, and proliferation. While conventional therapies are widely regarded as the standard first-line interventions, the current limitations have prompted the exploration of innovative strategies, including harnessing the power of oncolytic viruses (OVs) such as the Newcastle disease virus (NDV), with more effectiveness and fewer adverse outcomes. This article aims to discuss the potential of NDV in targeting the Glycolysis pathway as a therapeutic approach for BC.

Methods: For this review, three keywords ("Breast Cancer", "Glycolysis", and "Newcastle Disease Virus") were searched across four online databases (Web of Science, Scopus, PubMed, and Google Scholar) between 2000 and 2025.

Results: NDV is a non-pathogenic virus to humans with selective anti-tumor properties, making it a promising candidate for cancer treatment. Reports indicate NDV efficiently infects and replicates within BC cells—cells with deficient antiviral responses. This replication induces cytopathic changes and apoptosis through mechanisms including hexokinase downregulation and increased caspase-3 activity, as well as DNA fragmentation. Evidence shows some NDV strains selectively interfere with cancer cell metabolism, particularly glycolysis, likely through decreasing phosphoglycerate kinase expression, thereby suppressing product production and glycolytic enzyme activities in a time-dependent manner. This disruption leads to the starvation of cancer cells, subsequently reducing cell viability, as indicated by a decreasing trend in the levels of hexokinase activity, pyruvate, ATP, and pH in infected BC cells. Furthermore, combining glycolysis inhibitors (e.g., non-metabolizable glucose analogs) with NDV further sensitizes tumor cells, synergistically enhances NDV-mediated oncolysis, and promotes metabolic stress, growth inhibition, and apoptosis compared to monotherapies.

Conclusion: Glycolysis might be a promising target for improving NDV oncolytic activity in BC, particularly when combined with glycolysis inhibitors, resulting in synergistic and enhanced anti-tumor effects. This approach could serve as a novel, effective strategy in the development of future BC therapies.

keywords: Breast Cancer, Glycolysis, Newcastle Disease Virus

PV-36

Monitoring Crimean–Congo Hemorrhagic Fever Virus in Hyalomma Ticks from Different Regions of Iran

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Background and aim: Crimean–Congo hemorrhagic fever (CCHF) is a severe and often fatal zoonotic disease caused by a Nairovirus of the family Bunyaviridae. In Iran, human infection mainly occurs through contact with the blood or tissues of infected livestock, while tick bites also play a significant role in transmission. Among hard ticks, species of the genus Hyalomma are recognized as the principal vectors of CCHFV worldwide. Currently, CCHF is endemic in 23 provinces of Iran, particularly in regions bordering high-risk countries. This study aimed to investigate the species composition of Hyalomma infesting livestock and to assess their infection with CCHFV in different regions.

Methods: In this study, 1,536 livestock from 128 farms were examined, and 3,402 Hyalomma ticks were collected. Livestock were randomly selected from nomadic grazing systems, and the whole body of animals (cattle, sheep, goats, or camels) was carefully inspected. Tick sampling was conducted in 11 provinces of Iran during both warm and cold seasons, with three to five visits per season to eight farms in each district. Collected ticks were morphologically identified to the species level using a stereomicroscope and taxonomic keys. Detection of CCHFV was performed using reverse transcription polymerase chain reaction (RT-PCR) targeting the S segment of the viral genome.

Results: Species analysis revealed the presence of Hyalomma anatolicum, H. marginatum, H. dromedarii, H. asiaticum, H. detritum, and H. schulzei in the study areas. H. anatolicum was the dominant species in the northern and southern regions, whereas H. dromedarii was predominantly distributed in central regions of Iran. Tick infestation was highest during the warm season. RT-PCR analysis was performed on less than 10% of the collected Hyalomma ticks, representing all six species; however, no CCHFV-positive samples were detected.

Conclusion: Although no CCHFV-positive ticks were detected, Iran remains an endemic hotspot, underscoring the need for sustained surveillance. Given the higher risk associated with contact with viremic livestock, focused serological and molecular monitoring of high-risk occupational groups is essential for effective prevention and control of CCHF virus.

keywords: CCHFV, Hyalomma, Livestock, Iran.

PV-37

Investigate the Prevalence and Distribution of HPV Genotypes in the Wart and Urethral Swab Samples of Males in Iran

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Background and aim: Human papillomavirus (HPV) infection is very important for predicting the development of the diseases, to be benign or malignant cancer. The presence of the virus in men as asymptomatic carriers is very concerning. This research aims to investigate the HPV infection rate and genotype distribution among male patients in wart and Urethral swab samples, offering valuable insights for developing targeted preventive strategies against HPV infection in male population.

Methods: This study included 176 samples were collected from the wart and Urethral swab of male in 7-year period. Following DNA extraction, HPV detection and genotyping were performed using PCR and hybridization methods were used to determine 41 different HPV genotypes with AMPLIQUALITY HPV-TYPE EXPRESS HPV Genotyping kit. statistical analyses were used to evaluate associations between the HPV infection rate and genotype distribution among male patients in wart and Urethral swab samples.

Results: From the total of 176 male samples analyzed, the HPV test result was positive for 53.41% (94/176) and negative for 46.59% (82/176). The prevalence rates of HPV in wart samples were 75.25% (73/97), and the most common genotypes identified in this samples were HPV-6 (51.54%), followed by HPV-11 (20.61%). The men tested from the urethral swab turned out to be HPV genotypes positive in a percent of 25.30% (21/83) that from them 8.43% and 4.82% were HPV-6 and HPV-39, respectively.

Conclusion: The prevalence of HPV infection in Urethral swab samples was relatively substantial. Taking into account the high diversity of HPV types and the high proportion of oncogenic types, Identification HPV genotype for male is very important.

keywords: Genotype; HPV: Urethral swab; Male

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Tehran University of Medical Sciences (TUMS)
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PV-38

Molecular Epidemiology of Human Papillomavirus (HPV) Infection and Genotype Distribution in Tehran, Iran: A Cross-Sectional Study

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Background and aim: Human papillomavirus (HPV) infection is a major global public health concern and a well-established etiological factor in cervical and other anogenital cancers. Region-specific molecular epidemiological data are essential for optimizing HPV screening strategies, vaccination programs, and preventive interventions.

Methods: This cross-sectional study was conducted in Tehran, Iran, and included 500 clinical samples referred for HPV testing. Demographic characteristics, including age and sex, were collected for all participants. HPV detection and genotyping were performed using Real-time PCR assays capable of identifying high-risk, potential high-risk, and low-risk HPV genotypes. Descriptive statistical analyses were used to evaluate age distribution, sex frequency, overall HPV prevalence, and genotype distribution stratified by sex.

Results: The cohort comprised 448 females (89.6%) and 52 males (10.4%), aged 18–65 years (median: 35; mean: 34.4). HPV positivity was observed in 30.3% of patients, while 69.5% tested negative. Females exhibited a broader spectrum of HPV genotypes compared to males. High-risk genotypes were predominant, with HPV16, HPV18, HPV31, HPV33, HPV52, HPV53, and HPV58 most frequent among females. In males, HPV16 and HPV6 were the most common. Multiple concurrent infections were more prevalent in females.

Conclusion: This study highlights a substantial burden of HPV infection among young to middle-aged adults in Tehran, with a predominance of high-risk genotypes in females. The findings emphasize the importance of targeted vaccination and screening programs in Iran, particularly given the diverse genotype distribution observed. The application of real-time PCR enabled accurate and sensitive HPV genotyping. These findings support the importance of continuous molecular surveillance and may inform region-specific HPV screening, prevention, and vaccination strategies.

keywords: Human papillomavirus; Real-time PCR; HPV genotyping; Molecular epidemiology; Tehran; Iran

PV-39

Expression of long non-coding RNAs, lncRNA NEAT1 and LncRNA MEG3 in Covid-19 patients

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Background and aim: The novel coronavirus known as SARS-CoV-2 was initially discovered in Wuhan, China, in December 2019, as the cause of COVID-19, according to the World Health Organization in March 2020. Today, the role and function of Lnc RNAs in the pathogenesis of viral diseases and their diagnosis and treatment have been widely investigated. Due to the spread of covid-19 disease in the last few years, the purpose of this study was to examine the level of LncRNA NEAT1 expression and LncRNA MEG3 genes in covid-19 patients.

Methods: This study is a case-control, Patients' serum samples were taken from patients with covid-19 hospitalized in the covid department of Razi Hospital in Ahvaz as 30 serum samples from healthy people served as the control group and the case group. RNA extraction was performed for all samples, Then, the expression level of LncRNA NEAT1 and LncRNA MEG3 genes in covid-19 patients and control group was done using Real-Time PCR technique. Finally, all the obtained results were analyzed using REST software

Results: According to the obtained results, the case group's LncRNA NEAT1 gene expression level was higher than that of the control group, was not significant (p=0 .217), and COVID-19 patients' LncRNA MEG3 gene expression dropped 19 in comparison to the control group. (p=0.001)

Conclusion: According to the results of this study, it seems that in the case of LncRNA NEAT-1 gene, the increased expression of this gene in the patient group, although it is not significant compared to the control group, but it can indicate the role of this gene in stimulating the immune system, especially The innate immune system and possibly aggravation of the disease, induction of cytokine storm and acceleration of immunopathogenesis. In the case of LncRNA MEG3 gene, the significant decrease in the expression of this gene might contribute to the

keywords: Covid-19, LncRNA MEG3, LncRNA NEAT-1, Real-Time PCR, gene expression

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PV-40

Targeting EBNA-1 through SC7 Analogs Presents a Novel and Effective Approach for the Development of Treatments against the Epstein-Barr Virus-cased Cancer

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Background and aim: The Epstein-Barr virus (EBV), from the herpesvirus family, is the most common human viral infection and possible cause of Burkitt lymphoma, a cancer of the lymph nodes. In Burkitt lymphoma, the virus predominantly expresses the EBNA1 protein, which facilitates malignant transformation. This study aimed to explore the best inhibitor for this protein using molecular docking analysis.

Methods: The 3D structure of Epstein-Barr nuclear antigen 1 (EBNA1) (PDB ID: 1B3T) was obtained from the RCSB PDB database. SC7 (CID: 11592145) and twenty of its analogs were selected as inhibitors from the PubChem database in SDF format. After preparing the protein and ligands, molecular docking was carried out using Molegro Virtual Docker version 6.0. The interactions were analyzed to identify the best binding with the lowest energy using Molegro Molecular Viewer software. At the end, the pharmacokinetic properties were evaluated using the SwissADME server.

Results: Among all the inhibitory ligands, the most effective analog for EBNA1 was identified as 3-acetyl-N-[(1R,2S)-3-(3,5-difluorophenyl)-1-hydroxy-1-[(2R,4R)-4-propoxypyrrolidin-2-yl]propan-2-yl]-5-methylbenzamide. This compound had a molecular weight of 474.54 g/mol and a binding energy of -132.419 kcal/mol and formed eight steric interactions, along with two hydrogen bonds with the EBNA1 residues. The ADME analysis revealed that 3-acetyl-N-[(1R,2S)-3-(3,5-difluorophenyl)-1-hydroxy-1-[(2R,4R)-4-propoxypyrrolidin-2-yl]propan-2-yl]-5-methylbenzamide had a water solubility score of -4.48, a lipophilicity score of 3.43, and a polarity score of 87.66Å^2.

Conclusion: These results indicated that 3-acetyl-N-[(1R,2S)-3-(3,5-difluorophenyl)-1-hydroxy-1-[(2R,4R)-4-propoxypyrrolidin-2-yl]propan-2-yl]-5-methylbenzamide was a promising candidate for inhibiting EBNA1 infection. Further in vitro and in vivo studies are required to confirm it as a therapeutic agent.

keywords: Burkitt lymphoma, Epstein-Barr virus (EBV), SC7¬¬, Molecular Docking.

PV-41

Designing an interactive standard for a physician order recording system for reporting AIDS.

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Background and aim: Interoperability will make understanding of systems and their users of exchanging messages in the same way. This feature is necessary for controlling and managing communicable diseases that threatens public health, such as AIDS. Through standardization of the format of exchanged messages in format of the Minimum data set, this study will try to take a step forward in improving the interoperability between the information systems involved in controlling and managing AIDS.

Methods: The present study was carried out in three stages. In the first and second stages, systematize review was conducted and Delphi was used to identify the proposed data elements and to create the final MDS of AIDS respectively. Then a format was designed to extract data template from documents and in accordance with MDS.

Results: MDS of the AIDS was designed in three main information categories: Non-clinical, Clinical and Supportive, 20 data classes and 209 data elements. In the data template title, the codes related to the identification of entities involved in the care and treatment of AIDS and in the body were codes related to the information obtained through administrative, managerial, clinical and diagnostic and supportive processes.

Conclusion: The complex and multidimensional nature of AIDS requires the participation of multi-disciplinary teams from different organizations, complex analyzes, multidimensional and advanced information modeling, and maximum interoperability. The use of MDS structure with data template in the form of proposed structure in this study was fully compatible with optimal interoperability needs for AIDS control and management.

keywords: Minimum Data Set (MDS), Acquired Immunodeficiency Syndrome / AIDS, standardization

PV-42

The Role of Hepcidin in Chronic HCV Infection: Linking Iron Homeostasis to Liver Injury and Disease Progression

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[1] دانشگاه علوم پزشکی همدان

Background and aim: Chronic hepatitis C is a major global health burden due to its high prevalence and frequent progression to fibrosis, cirrhosis, and hepatocellular carcinoma. In addition to direct viral injury, host regulatory pathways significantly shape disease outcomes. Hepcidin, the key hormone controlling iron homeostasis, restricts iron export by degrading the transporter ferroportin. In chronic HCV infection, hepcidin regulation becomes disrupted, leading to abnormal iron distribution, hepatic iron overload, and increased oxidative liver damage, while also influencing immune responses. Despite accumulating evidence, the precise molecular mechanisms of hepcidin dysregulation and its value as a prognostic or therapeutic biomarker remain not fully clarified.

Methods: : This narrative review was conducted through a comprehensive search of major scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar, with no restrictions on publication date. The search strategy incorporated the keywords “hepcidin”, “chronic hepatitis C”, “iron metabolism”, “innate immunity”, “chronic liver disease” and “epigenetic regulation”. Only full-text articles published in English were considered, and studies were selected based on predefined inclusion and exclusion criteria.

Results: Hepcidin, a liver-derived regulator of iron balance, is crucial in chronic HCV infection. Inflammation, particularly via IL-6, usually increases hepcidin to restrict iron absorption and sequester it in macrophages. However, chronic liver disease creates conflicting signals from inflammation, oxidative stress, and cell injury, leading to unstable hepcidin regulation. This imbalance promotes iron overload, liver injury, fibrosis, cirrhosis, and hepatocellular carcinoma. Both reduced hepcidin and excess iron accelerate fibrosis progression. Iron also aids viral replication while weakening innate immunity and altering macrophage and Kupffer cell function. HCV disrupts regulatory pathways like STAT3, MAPK, and BMP/SMAD, and epigenetic changes further affect hepcidin. Monitoring iron markers helps track disease progression.

Conclusion: Hepcidin, the regulator of systemic iron homeostasis, is dysregulated in chronic hepatitis C virus (HCV) infection through intertwined effects of inflammation, oxidative stress, and direct viral interference. This disturbance promotes abnormal iron handling, hepatocellular injury, and progression toward fibrosis. Tracking hepcidin alongside serum iron and ferritin could improve prognostication and help identify patients at higher risk of cirrhosis or hepatocellular carcinoma. Despite advances, key mechanisms remain unresolved, making hepcidin a compelling research target. Future treatments may combine antiviral strategies with approaches that rebalance iron and dampen hepatic inflammation, positioning hepcidin.

keywords: hepcidin, chronic hepatitis C, iron metabolism, chronic liver disease

PV-43

An Investigation in to the Respiratory, Gastrointestinal, and Neurological Symptoms Associated with Long COVID in Outpatients and Inpatients in Bushehr Province

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Background and aim: Long COVID refers to the persistence of various symptoms weeks or months after the initial infection with the novel coronavirus (SARS-CoV-2), irrespective of the presence of the virus. Given the significance of long COVID on patients' quality of life and its implications for the healthcare system, this study aimed to investigate the respiratory, gastrointestinal, and neurological signs and symptoms of long COVID in both outpatients and inpatients with COVID-19 in Bushehr Province between 2022 and 2023.

Methods: This cross-sectional descriptive-analytical study included 376 patients with confirmed SARS-CoV-2 infection in Bushehr Province, Iran. Patients were identified through PCR testing and invited to the Persian Gulf Tropical Medicine Research Center in Bushehr, Iran. Data was collected via a questionnaire and clinical assessment and analyzed using the SPSS software program.

Results: Respiratory symptoms, especially cough and shortness of breath, were common in patients with long COVID. The prevalence of these symptoms was higher in patients with severe acute COVID-19. The most common neurological symptoms were fatigue, dizziness, and olfactory disorders. Additionally, approximately one-third (29%) of the study population exhibited at least one gastrointestinal symptom post-COVID-19 infection. The most prevalent symptoms were stomachache and anorexia, respectively.

Conclusion: This study emphasizes the importance of assessing and monitoring respiratory, gastrointestinal, and neurological symptoms, which are common and persistent sequelae of COVID-19 infection. Personalized management strategies can improve patients' quality of life and alleviate the burden on the healthcare system. Identifying at-risk patients is crucial for effective prevention and treatment strategies.

keywords: SARS-COV-2, COVID-19, Post-Acute COVID-19 Syndrome, Long COVID

PV-44

Role of Viral Infections in the Pathogenesis of Colorectal Cancer: From Molecular Evidence to Epidemiological Insights

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Background and aim: Colorectal cancer (CRC) is one of the most common malignancies worldwide, and its pathogenesis is influenced by genetic, environmental, and inflammatory factors. In recent years, the potential role of viral infections as contributing factors in colorectal tumorigenesis has attracted attention, although the available evidence remains heterogeneous and sometimes contradictory. The aim of this study was to provide a narrative review with a systematic approach to the existing evidence on the association between human viruses and colorectal cancer, with an emphasis on molecular and epidemiological data and studies conducted in Iran and other countries.

Methods: In this review, articles indexed in PubMed, Scopus, and Web of Science were examined without geographical restriction, with a focus on studies published in the last decade. Studies related to JC virus, HPV, EBV, and CMV that assessed their presence in colorectal cancer tissues or their potential role in molecular pathways of carcinogenesis were selected and analytically reviewed. Although this work is not a classical systematic review, it adheres to principles of transparency in study selection and critical appraisal of the evidence.

Results: The available evidence indicates that JC virus shows the greatest consistency with known molecular pathways of colorectal tumorigenesis, although a causal relationship has not been definitively established. HPV and EBV have been detected in CRC tissues in a subset of studies, particularly in certain geographical regions, but the findings are highly dependent on the study population and the diagnostic methods used. Studies from Iran have predominantly reported a low prevalence of HPV and a considerable presence of EBV, highlighting the importance of regional epidemiological differences. Overall, most studies support a modulatory or contributory role of viruses within the context of inflammation and the tumor microenvironment.

Conclusion: Based on current evidence, viruses cannot be regarded as independent etiological agents of colorectal cancer. However, some viruses may, under specific genetic and immunological conditions, contribute to the progression or modulation of molecular pathways involved in the disease. Prospective, multicenter studies incorporating functional assessment of viruses are required to clarify their true role in the pathogenesis of CRC.

keywords: Colorectal cancer; JC virus; Human papillomavirus; Epstein–Barr virus; Cancer pathogenesis

PV-45

Investigation of HDV coinfection in HIV-infected patients

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Background and aim: Hepatitis Delta Virus (HDV) which is a major cause of aggressive viral hepatitis, relies on Hepatitis B Virus (HBV) for replication. In individuals with Human Immunodeficiency Virus (HIV), HDV co-infection is associated with more severe hepatic complications and an increased risk of death.

Methods: A one step real-time PCR assay was applied to target HDV RNA. A total of 270 clinical samples from patients referred to HIV center of Iran University of Medical Sciences were tested. The assay utilized specific primers and probes which targeting the Ribozyme region as highly conserved target and RNase P as endogenous control. Data were analyzed with SPSS software (v.26).

Results: A total of 270 clinical samples were included in this study, with a sex distribution of 76% male and 24% female participants. The mean age was 44.5 years for males and 41.4 years for females. Optimization assays through gradient testing revealed an optimal annealing temperature of 55°C. The best primer-probe combination was determined to be 500:500:500 nanomolar, with a 1:1:1 mixture ratio, yielding optimal amplification performance. The assay demonstrated high efficiency of 99% (E=0.99) and correlation coefficient of 0.99 (R^2=0.99). The limit of detection (LOD) was established at 223 copies per microliter of sample. Among the tested samples, three cases were positive for HDV (3/270, 1.1%), and all three HDV-positive cases were also positive for HBV.

Conclusion: In conclusion, the results indicate a low prevalence of HDV co-infection among HIV-positive patients. However, comprehensive screening of these patients remains essential for the proper management of potential complications and to ensure effective treatment strategies.

keywords: HDV, Hepatitis delta virus, HIV, coinfection

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PV-46

Direct-Acting Antivirals versus Host-Directed Therapeutics in Dengue Virus Infection: Current Evidence and Future Opportunities

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Background and aim: Dengue virus (DENV), comprising four distinct serotypes, is responsible for approximately 400 million infections annually. The absence of specific antiviral treatments and the occurrence of antibody-dependent enhancement (ADE) represent major challenges in disease management. Two principal therapeutic strategies are currently under investigation: (1) Direct-Acting Antivirals (DAAs) and (2) Host-Directed Therapeutics (HDTs). This review aims to compare the current evidence for these two approaches and to identify future opportunities for effective dengue therapy.

Methods: This review study was conducted by searching PubMed, Scopus, and ChEMBL databases between 2015 and 2025. Five key articles comparing Direct-Acting Antivirals (DAAs) and Host-Directed Therapeutics (HDTs) in dengue virus infection were selected. Data on molecular targets, mechanisms of action, clinical trial results (phase 2 and 3), and molecular dynamics simulations were extracted and analyzed.

Results: Direct-Acting Antivirals (DAAs) target viral proteins such as NS5 and NS2B/NS3 to directly stop viral replication. However, these drugs face four main obstacles: mitochondrial toxicity (e.g., NITD-008), the gap between in vitro and clinical results (e.g., Balapiravir, which was effective in cells but failed in patients), rapid viral resistance, and limited serotype specificity. As a result, despite their high potency in laboratory settings, DAAs have largely failed in clinical practice.In contrast, Host-Directed Therapeutics (HDTs) do not attack the virus directly. Instead, they modulate the host's inflammatory and immune pathways. Their main targets include reducing the cytokine storm (with drugs such as baricitinib and dexamethasone), stabilizing the vascular endothelium, and protecting the liver from oxidative stress. However, HDTs also face challenges: the risk of immunosuppression and delayed viral clearance, a very narrow therapeutic window, the lack of reliable biomarkers to predict treatment response, and systemic side effects.

Conclusion: Neither approach alone is sufficient, but their strengths and weaknesses are different. DAAs are highly potent in reducing viral load but fail clinically due to mitochondrial toxicity, drug resistance, and the gap between in vitro and in vivo results. In contrast, HDTs have significantly lower cellular toxicity and do not face the issue of viral resistance because they target the host, not the virus.the most rational future strategy is combination therapy: using a DAA to rapidly reduce viral replication alongside an HDT to modulate the inflammatory response and prevent tissue.

keywords: Antiviral Agents,Dengue Virus, Direct-Acting Antivirals, Host-Directed Therapy,RNA Polymerase Inhibitor, Immunomodulation

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PV-47

Prevalence of Hepatitis B Core Antibody among HBsAg-Negative Drug Users in Fars Province, Southwestern Iran, 2024

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Background and aim: Hepatitis B virus (HBV) infection remains a major public health challenge worldwide. Hepatitis B core antibody (anti-HBc) is an important serological marker indicating previous exposure to HBV and may persist long after viral clearance. Drug users are considered a high-risk population for HBV infection due to exposure to multiple behavioral and healthcare-related risk factors. This study aimed to determine the prevalence of anti-HBc and associated risk factors among HBsAg-negative drug users in Fars Province, southwestern Iran.

Methods: This cross-sectional study was conducted on 460 HBsAg-negative drug users between January and November 2024. Demographic, social, and behavioral information was collected using a structured questionnaire. Anti-HBc was assessed using enzyme-linked immunosorbent assay (ELISA). Associations between anti-HBc positivity and demographic and clinical variables were analyzed using the Chi-square test. Statistical significance was considered at P0.05.

Results: The mean age of participants was 44.1±11.2 years (range: 13–85 years), and 82.6% were male. Anti-HBc was detected in 70 of 460 participants, corresponding to a prevalence of 15%. The mean age of anti-HBc-positive individuals was 51.2±9.2 years. Anti-HBc positivity showed significant associations with older age (P0.001), history of injection drug use (P0.001), medical service utilization (P=0.024), anti-HCV positivity (P0.001), HIV infection (P=0.004), birth before implementation of the national hepatitis B vaccination program (P=0.012), and city of residence (P0.001). The prevalence of anti-HBc was significantly higher among injection drug users than non-injection drug users (25.2% versus 10.4%). No significant associations were observed between anti-HBc positivity and sex, marital status, tattooing, or unsafe sexual practices.

Conclusion: A substantial proportion of HBsAg-negative drug users in Fars Province had serological evidence of previous HBV exposure. The association of anti-HBc positivity with injection drug use, HCV and HIV infections, and lack of childhood HBV vaccination highlights the importance of targeted screening and preventive strategies in high-risk populations. Anti-HBc testing may serve as a valuable laboratory marker for identifying individuals with prior HBV exposure and guiding HBV control programs.

keywords: Anti-HBc; Hepatitis B Virus; Drug Users; Seroprevalence; Risk Factors

PV-48

Determining the age of EBV seroconversion in children under ten years of age in Mashhad

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Background and aim: Epstein–Barr Virus, also known as Human gammaherpesvirus 4, is one of the eight known human herpesviruses and a member of the Herpesviridae family. EBV infects a variety of cell types, including B lymphocytes and epithelial cells. Owing to its clinical significance and its association with several B-cell malignancies in children, the epidemiology and age at seroconversion of EBV have been investigated in different geographic regions. Given the limited data regarding the prevalence of EBV infection and the age of seroconversion in the Iranian population, this study aimed to determine the age of EBV seroconversion among children under 10 in Mashhad.

Methods: This cross-sectional study was conducted between 2017 and 2018 at Imam Reza Hospital, Akbar Hospital, and Ghaem Hospital in Mashhad, Iran. Residual serum samples obtained from routine laboratory testing of children were collected after approval of ethical considerations and protection of patient confidentiality. A total of 283 serum samples from children younger than 10 years were randomly selected. Personal identifiers were removed, and only age and sex data were recorded. Anti-EBV antibodies were measured using an enzyme-linked immunosorbent assay (ELISA).

Results: A total of 283 children under 10 years of age were included in the study; 59.2% were male and 40.8% were female, while sex information was unavailable for six participants. Regarding age distribution, 15.9% were younger than 6 months, 19.8% were aged 6 months to 2 years, 20.8% were aged 3–4 years, 21.6% were aged 5–6 years, and 21.9% were aged 7–10 years. Overall, anti-EBV antibodies were detected in 29% of the children. The highest seropositivity rate was observed among children younger than 6 months (55.6%), whereas the lowest rate was found in those aged 7–10 years (6.5%). Statistical analysis demonstrated a significant association between age group and EBV seropositivity. However, no significant association was found between sex and EBV seropositivity.

Conclusion: The overall prevalence of anti-EBV antibodies among children younger than 10 years was 29%. Seropositivity differed significantly across age groups but was not associated with sex. Based on the observed serological pattern, the peak age of EBV seroconversion in the study population was estimated to be between 3 and 4 years of age.

keywords: Epstein–Barr virus, EBV, seroconversion, children, ELISA

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PV-49

Diagnostic Accuracy of CRISPR-Cas12 and CRISPR-Cas13 Assays for Rapid Detection of Human Viral Infections: A Systematic Review and Meta-Analysis

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Background and aim: Rapid and accurate detection of viral infections is essential for timely treatment, outbreak control, and public health surveillance. Conventional molecular methods such as real-time PCR remain the diagnostic standard but often require specialized equipment, trained personnel, and centralized laboratory infrastructure. CRISPR-based diagnostic platforms, particularly Cas12- and Cas13-mediated assays, have emerged as highly specific nucleic acid detection tools with potential for rapid and point-of-care viral diagnosis. This systematic review and meta-analysis aimed to evaluate the diagnostic accuracy of CRISPR-based assays for detecting human viral infections and to assess their potential applicability in clinical and decentralized laboratory settings.

Methods: A systematic search of PubMed, Scopus, Web of Science, and Embase was performed from database inception to June 2026 following PRISMA guidelines. Eligible studies evaluated CRISPR-based assays for detecting human viral infections using clinical samples or clinically relevant specimens and reported sufficient data to determine diagnostic accuracy. Studies limited to analytical validation without clinical diagnostic data were excluded. Two independent reviewers screened studies, extracted data, and assessed methodological quality using QUADAS-2. Extracted information included target virus, CRISPR system, amplification method, sample type, reference standard, limit of detection, turnaround time, sensitivity, and specificity. Pooled diagnostic accuracy estimates were calculated when data were sufficiently homogeneous.

Results: CRISPR-based assays demonstrated promising diagnostic accuracy for multiple human viral infections, particularly SARS-CoV-2 and other respiratory, blood-borne, and arboviral pathogens. Cas12-based platforms were commonly used for DNA or amplified DNA targets, while Cas13-based systems were frequently applied for RNA virus detection. Many assays combined isothermal amplification with fluorescence or lateral-flow readouts, enabling rapid detection with simplified equipment requirements. Reported sensitivity and specificity were generally high compared with reference molecular methods. However, performance varied according to viral target, sample type, amplification strategy, assay design, and clinical validation scale. Important limitations included small sample sizes, inconsistent reporting standards, limited multicenter validation, and fewer data for non-SARS-CoV-2 viral infections.

Conclusion: CRISPR-based diagnostic assays represent a promising next-generation approach for rapid detection of human viral infections, offering high specificity, short turnaround time, and potential suitability for point-of-care and resource-limited settings. Current evidence supports their diagnostic potential, particularly when combined with isothermal amplification and simplified readout systems. However, broader clinical validation, standardized reporting, and direct comparison with established molecular assays are required before routine implementation. Future studies should prioritize multicenter evaluations and clinically diverse viral targets beyond SARS-CoV-2.

keywords: CRISPR Diagnostics, Human Viral Infections, Molecular Diagnostics, Point-of-Care Testing

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