ICCMCR-C2

Proceeding of The Second International Conference of Iraqi Center for Cancer and Medical Genetics Research

29 & 30 October 2025
Baghdad - Iraq

DOI : 10.29409/cm28t103

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ICCMGRC2 Editorial: Today's Research, Tomorrow's Cure

Today's Research, Tomorrow's Cure, was the banner of the Second International Conference of Iraqi Center for Cancer and Medical Genetics (ICCMGRC2) which organized by the Iraqi Center for Cancer and Medical Genetic Research (ICCMGR), Mustansiriyah University, in collaboration with Dijlah University and Asian Pacific organization for cancer prevention (APOCP). The conference aims to promote the research culture, accelerate new discoveries in cancer research and medical genetics, and close the gap between the laboratory discoveries and clinical practice. This year the conference received 55 submissions from Iraq, Malaysia, India, and Iran; 47 were accepted (85% acceptance; 15% rejection) following rigorous peer review by more than 42 experts (2–3 reviewers per paper). Submissions spanned 24 universities and institutions, with active contributions from Iraq's Ministry of Health both public and private sectors. Papers were presented as oral presentations and posters that were classified into six categories summarized below.

1- Clinical Cancer Research

Clinical contributions reflected Iraq's steady move toward targeted, safer, and earlier cancer management. In the field of the targeted Radiotherapy, first Iraqi experience with Lutetium-177 Prostate-Specific Membrane Antigen (Lu-177 PSMA) therapy in metastatic prostate cancer demonstrated favorable safety and meaningful prostate-specific antigen responses, establishing a local model for precision radioligand therapy. While in the early Detection, the Iraq Healthy Lung Project, based on Low-Dose Computed Tomography (LD-CT), outlined a pathway for nationwide screening to improve lung-cancer survival through stage migration. For molecular pathology studies of Maternally Expressed Gene 3 (MEG3) and microRNA Let-7i-3p/5p dysregulation in acute lymphoblastic leukemia, Runt-related transcription factor 1 (RUNX1) variants in acute myeloid leukemia, and the detection of Epstein–Barr virus (EBV) DNA in breast tumors illustrated how molecular assays are being integrated into Iraqi clinical systems. Reduced-Toxicity Chemotherapy study in acute promyelocytic leukemia, comparison of All-Trans Retinoic Acid (ATRA) plus Arsenic Trioxide (ATO) versus ATRA plus conventional chemotherapy confirmed that the ATO-based regimen minimizes hematologic toxicity while maintaining remission rates. In conclusion, these papers collectively signify Iraq's progress toward evidence-driven, molecularly guided oncology.

2- Cancer and Medical Genetics

Genetics papers showed that mutation profiling has become a prognostic and therapeutic compass rather than a diagnostic luxury. In regard to chromosomal and Gene Variants, work on Philadelphia chromosome (BCR-ABL1) translocations in chronic myeloid leukemia, Epidermal Growth Factor Receptor (EGFR) mutations in non-small-cell lung cancer, and RUNX1 variants in myeloid leukemia refined local mutation frequencies and clinical correlations. Studies on the inherited and pediatric disorders on screening for Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) mutations expanded genetic testing capacity in pediatric settings. While DNA-Repair and stability studies of the RecQ like helicase (RECQL) gene in breast cancer and laser-microfluidic assessments of DNA damage provided inexpensive yet reliable diagnostic surrogates for resource-limited laboratories. In conclusion, these contributions support establishing an Iraqi Mutation Registry and harmonized molecular panels as the infrastructure for national precision medicine.

3- Nano and Molecular Cancer Therapeutics

This section explored novel, selective, and low-toxicity therapeutic strategies using nanotechnology, molecular targeting, and viral therapy. Investigations of Gold Nanoparticles (GNPs) in murine breast-cancer models revealed reduced tumor and organ damage, suggesting GNPs as safe radiosensitizers or drug carriers. Research on Thymol Nanocarriers showed efficient delivery into hepatocellular carcinoma cells, inducing apoptosis via increased BCL-2-associated X protein (BAX) and decreased B-cell lymphoma 2 (BCL2) expression. Inhibition of Monocarboxylate Transporter 1 (MCT1) reversed Epithelial-to-Mesenchymal Transition (EMT) markers, suppressing metastasis in lung models and indicating metabolism-based vulnerabilities. Studies from ICCMGR demonstrated that Newcastle Disease Virus (NDV) inhibits adhesion and spread of esophageal adenocarcinoma cells in three-dimensional (3D) culture, modulating Caspase-3, Cyclin-Dependent Kinase Inhibitor 1 (p21), and Ki-67 proliferation index. In conclusion, these investigations promote integrated molecular–nano–viral therapy aimed at higher precision and lower systemic toxicity.

4- Artificial Intelligence and Bioinformatics in Cancer Research

Digital innovation emerged as a transformative tool linking data science to oncology. In machine-learning diagnostics, algorithms analyzing Circular RNA (circRNA) expression achieved > 93 % accuracy for non-invasive breast-cancer detection using blood samples. In drug-response prediction; analysis of single-cell RNA Sequencing (scRNA-seq) datasets

reached about 98 % accuracy in predicting sensitivity to cis-diamminedichloroplatinum (Cisplatin), showcasing artificial intelligence in personalized therapy design. While in computational biomarkers study, Pan-cancer bioinformatics identified DEXH-Box Helicase 58 (DHX58) as a candidate biomarker for disease course and drug responsiveness. Regarding the molecular docking and imaging, AI-assisted docking and radiomic pipelines accelerated identification of anticancer compounds and objective grading of tumor histology. In conclusion, Iraqi researchers can develop explainable AI models to enable earlier diagnosis and optimized treatment planning.

5- Clinical and Cancer Immunity

Immunology studies clarified how the tumor–immune microenvironment determines outcome. In study about immune evasion mechanisms, accumulation of Tumor-Associated Macrophages (TAMs) with high expression of Programmed Death-Ligand 1 (PD-L1) and Interleukin-10 (IL-10), coupled with low Human Leukocyte Antigen-DR (HLA-DR), was associated with immune suppression and enhanced tumor growth. In another study, elevated Programmed Cell Death Protein 1 (PD-1), PD-L1, and Interleukin-6 (IL-6) levels in acute myeloid leukemia confirmed their role in immune escape and disease persistence. Further work, associations between Tumor Necrosis Factor-alpha (TNF-α), IL-6, C-Reactive Protein (CRP), and tumor markers such as Carcinoembryonic Antigen (CEA) and Carbohydrate Antigen 199- (CA199-) emphasized chronic inflammation as a driver of malignancy. In conclusion, the collective evidence advocates for standardized immune profiling and the formation of multidisciplinary immunotherapy clinics to translate immune biology into durable clinical responses.

6- In-Vitro Experimental Cancer Research

Preclinical investigations used cultured cells to validate therapeutic hypotheses and assess safety. Drug Cytotoxicity and Synergy study findings indicated that Metformin could impact normal testicular cells under prolonged exposure, while combining Paclitaxel with p-Synephrine produced synergistic effects against glioma cells. Another study about natural products; extracts and essential oils from Iraqi medicinal plants such as Salvia palaestina showed selective killing of cancer cells with limited toxicity to normal cells. Another study about the adoption of 3D spheroid cultures enhanced predictive accuracy for drug-response testing. In conclusion, the trend emphasizes reproducible, affordable laboratory models as the backbone of translational cancer research in Iraq.

Conference recommendations

Three strategic essentials arose from ICCMGRC2 discussions; 1- Standardize Precision Pathways; Establish a unified Iraqi Mutation Registry, incorporate validated molecular and immunologic panels into routine diagnostics, and ensure equitable access to precision testing nationwide. 2- Importance of novel biological therapeutics; Advance Newcastle Disease Virus and nanoparticle delivery into regulated pre-clinical and early-phase studies, while exploring metabolism-immune-targeted drug combinations guided by robust biomarkers and AI-based prediction tools. 3- Build Data, Skills, and Trials; Create a national de-identified cancer data platform, train a new generation of bioinformaticians and molecular pathologists, and encourage starting the path of clinical research.

Conclusion

The ICCMGRC2 Conference showed a dynamic transition of Iraqi oncology from descriptive observation to integrated precision practice. Through group work, shared data infrastructure, and translational research, the discoveries presented here can close the gap between today's research and tomorrow's cure, translating laboratory research in to clinical applications for better future for Iraq and the region.

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Scientific Committee Chair for Second Conference of Iraqi Center for Cancer and Medical Genetic Research.

New Hope for Cancer Patients in Iraq: The Rise of Lu-177 PSMA Therapy

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Abstract

Background: Recent advances in precision medicine have transformed cancer management through theranostics—the integration of diagnostic and therapeutic modalities on the same molecular target. While Iraq has long utilized theranostic methods for thyroid cancer, the introduction of Lutetium-177 Prostate-Specific Membrane Antigen Radioligand Therapy (Lu-177 PSMA RLT) represents a major leap forward. On January 4, 2023, Warith International Cancer Institute (WICI) in Karbala launched Iraq's first Lu-177 PSMA therapy program, offering new hope to patients with advanced prostate cancer.
Methodology: According to the Iraqi Cancer Registry 2022, prostate cancer is the third most common malignancy among men, with 1,387 new cases reported. From August 2021 to October 2025, 89 male patients were diagnosed with prostate cancer at WICI; 101 were referred for Lu-177 PSMA evaluation, and 81 met eligibility criteria based on PSMA PET/CT findings and clinical assessment. Patients receiving fewer than two cycles were excluded from the analysis.
Results: From January 2023 to September 2025, the Nuclear Medicine Department at Warith International Cancer Institute treated approximately 81 male patients with more than 270 cycles of Lu177 PSMA-617 (ready to use). Despite the brief period since the program's inception, this initiative reflects a significant achievement and commitment to advancing cancer treatment in Iraq. Over half of the patients demonstrated an initial partial response to treatment, as evidenced by a significant decline in prostate-specific antigen (PSA) levels and partial response observed through Gates-68 PSMA positron emission tomography/computed tomography (PET/CT) imaging. Only minority of these patients experienced lowgrade side effects and self-limiting toxicities
Conclusion: This pioneering Iraqi experience demonstrates the feasibility, safety, and effectiveness of Lu-177 PSMA therapy. The successful implementation of this treatment at Warith International Cancer Institute marks a new era in precision oncology and stands as a beacon of hope for cancer patients in Iraq.

Keywords
Theranostics, Iraq, Warith, Lu-177 PSMA Radioligand Therapy, Prostate Cancer

Iraq Healthy Lung Project (IHLP): Towards Implementation of Lung Cancer Screening in Iraq

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Abstract

Background: Lung cancer remains one of the leading causes of cancer mortality in Iraq, largely due to late-stage diagnosis and the absence of organized screening. The Iraq Healthy Lung Project (IHLP), launched in May 2024, is the first structured national initiative to introduce targeted low-dose computed tomography (LDCT) screening for early detection of lung cancer among high-risk individuals.
Methods: The IHLP adapts the NHS Targeted Lung Health Check protocol to the Iraqi context and integrates risk prediction models, spirometry, imaging, and smoking cessation within a standardized pathway. The program operates in a phased, multi-centre framework across Karbala and Basra provinces. Eligible participants are aged 50–79 years with a smoking history of ≥20 pack-years or a calculated risk score of ≥1.5% using the Liverpool Lung Project (LLPv3) model; former smokers qualify if they quit within the past 15 years. Recruitment is conducted via hospital call centres and community outreach led by the Warith Foundation for Public Health. Nodule management follows BTS 2015 and Lung-RADS guidelines, and biological samples are collected for biobanking and future research.
Results: Between May 2024 and June 2025, 566 individuals were screened, and 164 (29%) met the criteria for LDCT. Among LDCT participants, 44% had no nodules, 26% had nodules <5 mm, 13% had indeterminate nodules, and 17% were excluded for clinical or technical reasons.
Conclusion: The IHLP has demonstrated operational feasibility, established a governance framework, and built research capacity for lung cancer screening in a fragile healthcare setting. Despite infrastructural and financial challenges, the program provides a foundation for national expansion and development of Iraq-specific risk prediction models.

Keywords
Lung Cancer Screening, Low-Dose Computed Tomography (LDCT), Iraq Healthy Lung Project (IHLP), Risk Prediction Models, Public Health Initiative.

Clinicopathological Study of Craniofacial Tumors

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Abstract

Background: A wide range of benign and malignant lesions that impact the mouth cavity and face and have different clinical manifestations and histological presentations are included in oral and maxillofacial lesions and malignancies. Because of their unique location, these tumors interfere with speaking and swallowing, which can lead to tooth movement, bone growth, and the destruction of nearby craniofacial components.
Aims of the study: The purpose of this study is to undertake a clinicopathological evaluation of craniofacial tumor care among Iraqi patients.
Materials and Methods: A total of 586 patients, including (≈42%) males and (≈58%) females, joined in the study and attended the Ramadi Teaching Hospital (Anbar), Zuhur Private Hospital (Baghdad), Razi Private Hospital (Baghdad), and Rashid Private Hospital (Anbar) for diagnosis and treatment. Full patient demographics were recorded, along with a clinical examination to assess the location, color, size, and consistency of the lesions, as well as lymph node examinations, radiographic, CT, U/S, and MRI examinations, and the necessary laboratory tests. The surgical treatment involved both local and general anesthesia.
Results: Of all samples collected, 28% of the patients were between the ages of 31 and 40, 60% of the samples were presented as a mass, 42% underwent surgical excision, 22% underwent laser surgery, 5% had squamous cell carcinoma, 10% had pyogenic granuloma, 12% had radicular cysts, and 5% had ameloblastoma, the most common odontogenic tumor.
Conclusion: The results of this study offer important insights into the frequency of cancers and diseases of the mouth and maxillofacial region in Iraq. Due to aesthetic defects and functional damage, several cystic and neoplastic pathoses are specific to the maxillofacial region. These variations in prevalence and pattern have been found to be caused by occupational, social, and environmental factors.

Keywords
Craniofacial tumors, Clinicopathological study, Oral and maxillofacial lesions, Prevalence in Iraq, Squamous cell carcinoma

Occurance of hepatitis B infection in pediatric patient with cancer at Alhadbaa Hospital in Mosul/ Iraq.

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Abstract

Pediatric cancer patients face an increased susceptibility to hepatitis B virus (HBV) infection owing to immunosuppression resulting from the disease and its treatment, the frequent requirement for blood transfusions, and invasive procedures. This study sought to ascertain the prevalence of HBV infection within this community, identify correlated risk variables, and assess the preventive efficacy of HBV vaccine.

A cohort research was performed in the oncology unit of Alhadbaa Teaching Hospital in Mosul from December 2023 to March 2024. The study comprised 153 children (under 15 years) with cancer who were initially negative for HBV at diagnosis. Demographic data, cancer type, vaccination status (both routine and post-diagnosis), blood transfusion history, and HBV serology were collected and examined during follow-up.

Results: Over a follow-up duration of 3 months to 10 years, 12 patients (7.8%) seroconverted to HBV-positive, and 2 patients (1.3%) acquired hepatitis C virus (HCV), culminating in a total incidence of hepatotropic viruses of 9.1%. Statistical analysis indicated a greater prevalence of HBV infection in children who underwent several blood transfusions (≥3 units) and in those who were either unvaccinated or inadequately vaccinated against HBV. The infection rate was decreased relative to prior trials conducted in other countries.

This study highlights a considerable risk of nosocomial HBV transmission in pediatric oncology settings. The results strongly support the stringent enforcement of universal blood product screening, meticulous aseptic procedures, and the assurance of comprehensive HBV immunization regimens during early infancy and, importantly, at the point of cancer diagnosis for unvaccinated children.

Keywords
Pediatric cancer, Hepatitis B virus, HBV vaccination, Blood transfusion, Nosocomial transmission.

The Non-coding Code: Silent Regulators of MEG3 and Let-7i 3p/5p in the Progression of Acute Lymphoblastic Leukemia

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Abstract

Objective: Acute lymphoblastic leukemia (ALL) is one of common malignancy worldwide. The long non-coding RNA MEG3 functions as a tumor suppressor in various cancers, potentially influencing gene expression through transcriptional, translational, and epigenetic mechanisms. Let-7i plays a role in leukemia progression. This study aimed to evaluate MEG3 gene expression in adult ALL patients and investigate its possible regulatory interaction with Let-7i-3p and Let-7i-5p.
Methods: A total of 83 blood samples (from newly diagnosed ALL patients (n=53) and healthy controls (n=30) were collected. Hematological parameters were measured using a CBC analyzer. RNA was extracted and reverse transcribed into cDNA. Quantitative real-time PCR with gene-specific primers was used to assess MEG3 and Let-7i-3p/5p expression levels.
Results: ALL patients and healthy controls were matched for age (29.09.9± vs. 28.67.7± years, p=0.862) and sex (p=0.299). Hematological analysis revealed significant cytopenias in patients, including reduced Hb (8.601.75± vs. 14.722.51± g/dL; p<0.001), WBCs (4.912.84± vs. 7.969^10×1.57±/L; p<0.001), and PLT (156.96 ± 35.64 vs. 269.939^10×55.35±/L; p<0.001). Gene expression analysis revealed that MEG3 was significantly downregulated in ALL patients (fold change 0.5350.273±; p=0.001), whereas Let-7i-3p/5p were upregulated (fold changes 1.875 ± 0.732 and 1.857 ± 0.891, respectively; p < 0.01 for both), indicating a distinct dysregulation pattern associated with adult ALL.
Conclusion: This study demonstrates that adult ALL patients exhibit the classical hematological abnormalities of anemia, leukopenia, and thrombocytopenia. Molecular analysis revealed a significant downregulation of lncRNA MEG3, alongside upregulation of Let-7i-3p/5p, suggesting their potential involvement in leukemogenesis. These findings highlight the diagnostic and possibly prognostic relevance of MEG3 and Let-7i in adult ALL and provide a foundation for further research into their mechanistic roles and therapeutic targeting.

Keywords
MEG3, Let-7i-3p, Let-7i-5p, Acute lymphoblastic leukemia (ALL), RT-PCR

Evaluation of RUNX1 genetic variations in Sample of Iraqi Acute myeloid Leukemia Patients

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Abstract

The RUNX1 gene is essential for hematopoiesis and is implicated in several hematological disorders, including acute myeloid leukemia. This study aims to examine the relationship between single nucleotide polymorphisms in the exon regions (4 and 7) of the runt homology domain for Runx1 and the risk of AML in Iraqi population. A total of 180 subjects were enrolled, with 120 AML patients and 60 healthy controls. Two novel variants were identified: at position 34886892 (genotypes TT, TA, AA) and at position 34834421 (genotypes CC, CT, TT). The A allele and TA genotype at the first variant were associated with increased susceptibility, whereas the T allele showed a protective effect. At the second variant, CT and TT genotypes were more frequent in AML patients, suggesting a role in disease predisposition. Additionally, rs1569084132 indicated that the GT genotype and T allele conferred risk, while the G allele was protective. In contrast, rs2146408980 showed no association with AML, and rs1203996669 deviated from Hardy–Weinberg equilibrium, limiting its interpretability. Collectively, these findings highlight that specific RUNX1 variants may act as either risk-promoting or protective factors, supporting their potential utility as biomarkers for AML susceptibility and prognosis in the Iraqi population.

Keywords
Hardy-Weinberg equilibrium, genetic susceptibility, polymorphism, AML

A sensitive lipid profile Biosensor towards point-of-care of cancer disease

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Abstract

Breast cancer is the most common malignancy among women worldwide and the leading cancer in Iraq, where it accounts for nearly one-third of all female cancers. Early detection and the identification of simple, reliable biomarkers remain critical for improving prognosis and guiding treatment decisions. Alterations in lipid metabolism have been increasingly recognized as contributors to tumor initiation and progression.
Objectives and Aims: This study aimed to investigate the relationship between serum lipid profile changes and breast cancer risk among Iraqi women, with the goal of evaluating their potential as predictive and monitoring biomarkers for point-of-care applications.
Methods: A total of 69 untreated breast cancer patients and 40 age-matched healthy women were enrolled between June and December 2024. Serum levels of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) were measured using a fully automated chemistry analyzer. Independent t-tests were used to compare groups, and results were further stratified by age, menopausal status, and body mass index (BMI).
Results: Breast cancer patients showed significantly higher TC, LDL, and TG levels, while HDL levels were markedly lower compared to controls ($p<0.05$). When analyzed by age groups, the differences remained significant, with patients over 40 years displaying the most pronounced lipid abnormalities. Stratification by menopausal status revealed consistent alterations in both pre- and postmenopausal women. Moreover, overweight and obese patients exhibited the most unfavorable lipid profiles, underscoring the role of obesity as an additional risk factor.
Conclusion: The findings demonstrate that dysregulated lipid metabolism is strongly associated with breast cancer risk and progression. Elevated TC, LDL, and TG, alongside reduced HDL, may serve as valuable biomarkers for disease prediction and monitoring. Incorporating lipid profile analysis into routine screening could enhance early detection strategies and support the development of point-of-care biosensors tailored to cancer diagnostics.

Keywords
Breast cancer, Lipid profile, Total cholesterol, Triglycerides, HDL, LDL

Looking For Epstein - Barr virus in Breast Tumors of Iraqi patients

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Abstract

The presence of Epstein-Barr virus (EBV) as a cause of some cancers was recognized over fifty years ago; however, its association with breast cancer remains controversial. Many researchers have used various methods to investigate the link between EBV and breast tumors. Some agree, while others disagree, so the topic continues to be debated. In this study, we employed a specific molecular technique to detect EBV DNA in freshly frozen breast tumor tissues of different grades from Iraqi women.

Tumors were collected from Iraqi women undergoing breast cancer surgery at Al-Yarmouk Teaching Hospital in Baghdad between 2015 and 2019. To reduce the risk of DNA contamination, an automated nucleic acid extraction system with a specialized kit for total nucleic acid extraction from human tissues was used to purify DNA from both normal and tumor breast tissues. Quantitative real-time PCR (qRT-PCR) was performed to detect EBV presence both qualitatively and quantitatively using a specific diagnostic kit. This kit included probes and primers designed to detect all EBV subtypes, along with internal, negative, and positive controls, as well as serial dilutions of DNA for generating a standard curve. A total of 85 frozen breast tumor samples were collected from patients immediately after diagnosis. For comparison, paired normal tissue samples were taken from the margins of each tumor, and all were confirmed normal through histopathological examination. Among all samples tested, EBV DNA was found only in three tumor tissues and was not present in their paired normal controls. These results do not definitively establish EBV as a probable cause of breast cancer.

Keywords
Epstein-Barr Virus (EBV), Breast Cancer, Real-time PCR (qRT-PCR), EBV DNA, Iraqi Women.

ODAM: A Novel Tumor Suppressor Silenced in Breast Cancer

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Abstract

Background: The Odontogenic, Ameloblast-Associated gene (ODAM) is a matricellular protein implicated in cell adhesion and odontogenesis. Emerging evidence suggests a role in tumor biology, with its expression observed in various epithelial malignancies, including breast cancer (BC). This study investigates the expression, clinical significance, and functional role of ODAM in BC, with a focus on its relationship with the AKT signaling pathway.
Methods: ODAM expression was quantified via quantitative real-time PCR (qRT-PCR) in breast tissues from malignant, benign, and control groups (35 samples for each group), normalized to the housekeeping gene GAPDH. Patient classification and dataset generation were based on oncologist evaluations and confirmed mammography findings. Serum AKT concentration was measured by ELISA test. Survival analysis was performed using a large public breast cancer dataset.
Results: ODAM expression was significantly downregulated in malignant breast tissues compared to benign and control groups, with a 66.6-fold reduction in ODAM expression in BC patients ($p<0.01$). This loss of ODAM was inversely correlated with serum AKT levels, which were significantly elevated in malignant patients (3.173 ng/ml) versus controls (1.510 ng/ml; $p<0.01$). ODAM overexpression in aggressive BC cells suppressed tumorigenic properties by inhibiting growth, migration, and invasion while promoting cell adhesion and apoptosis. Mechanistically, ODAM was found to inhibit PI3K/AKT signaling and upregulate the tumor suppressor phosphatase and tensin PTEN. Critically, Kaplan-Meier survival analysis revealed that high ODAM expression is a favorable prognostic biomarker, associated with significantly improved overall survival in BC patients (HR = 0.89, 95% CI = 0.80–0.98, p = 0.022).
Conclusion: ODAM acts as a novel tumor-suppressive gene in breast cancer, whose downregulation is associated with disease progression and poor prognosis. Its anti-neoplastic effects are mediated, at least in part, through the inhibition of the AKT signaling pathway. These findings suggest that ODAM may serve as a valuable prognostic biomarker and potential therapeutic target in breast cancer.

Keywords
AKT; Breast Cancer; Kaplan-Meier; ODAM.

Safety and Tolerability of ATRA/ATO Compared with ATRA-Based Chemotherapy in APL

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Abstract

Background: chemotherapy free induction in the management of acute promyelocytic leukemia provides the potential benefits of lowering myelosuppression and the consequent infections and bleeding, as well as lowering the early risk of hemorrhagic episodes.
Objective: primary end point to compare incidence and severity of hematologic and nonhematologic toxicity incidence during induction period for PML between the two treatment arms (ATRA and arsenic trioxide versus ATRA and chemotherapy). Secondary end points included rate of hematologic complete remission (HCR) after induction
Patients and methods: This study was a hospital-based prospective, randomized, single-center, open-label descriptive observational cohort study done in Hematology Center at Baghdad Teaching Hospital affiliated to Baghdad Medical City during the period from 1st April 2022 to the 1st of January 2023.study. All patients with APL who were 14 years or older and did not have visceral contraindications to arsenic therapy or other treatment were eligible for the study. Patients were randomly randomized to receive either ATRA + arsenic trioxide or ATRA + chemotherapy According PML risk.
Results: 38 patients fulfil the inclusion and exclusion criteria's and had been involved in the study. Their mean age was 38.2 years. More than half (52.6%) were male, and the male to female ratio was 1.1:1 as presented All the patients were with negative past medical history. Over than half of the participants presented with low or intermediate-risk APL (65.8 %) while the rest (34.8%) presented with high-risk APL. Minor impact of both regimen on the mean changes of hemoglobin concentration, WBC count, platelet count serum electrolytes, has been increased constantly in each group. Slight derangement in liver enzymes, PTT, PT, INR and QT interval in ATO group. More blood transfusion was required in the chemotherapy group. Both combination results in comparable incidence of edema, fever, phlebitis, hypertension, weight gain, nausea, vomiting, GIT hemorrhage, dry mouth, mucositis, infection, upper respiratory tract complaint, vaginal bleeding, arthralgia, myalgia, alopecia, headache, conjunctivitis, intracranial hemorrhage, ATRA syndrome, pseudocerebri, and supraventricular tachycardia.
Conclusion: In addition to the therapeutic benefits, this study found that the ATO group outperformed the non-ATO group in terms of considerably lowering hematological side-effect profiles also In terms of ATO›s common nonhematological toxicity.

Keywords
Acute Promyelocytic Leukemia (APL), All-trans Retinoic Acid (ATRA), Arsenic Trioxide (ATO), Chemotherapy-free Induction, Hematologic Toxicity, Complete Remission (CR)

Quantitative Assessment of Gastric Cancer Malignancy Using Digital Histopathological Texture Analysis: A Novel Approach for Objective Tumor Grading

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Abstract

Background: Gastric cancer remains a significant global health challenge, with traditional histopathological assessment being subjective and prone to inter-observer variability. This study investigates the application of quantitative texture parameters derived from digital histopathological images for objective malignancy assessment in gastric cancer.
Methods: Forty-three histological specimens of gastric adenocarcinoma with varying degrees of differentiation were analyzed using digital image processing techniques. Texture parameters were extracted using MaZda software, including first-order statistics, gray-level co-occurrence matrix (GLCM), gray-level run-length matrix (GLRLM), and autoregressive model parameters. Statistical analysis was performed to identify parameters correlating with malignancy progression.
Results: GLRLM parameters, particularly Long Run Emphasis (LngREmph), demonstrated the strongest correlation with tumor progression, decreasing from 1.7250.202± in normal tissue to 1.3400.072± in poorly differentiated adenocarcinoma. Autoregressive model parameter Sigma showed direct proportionality with malignancy degree. First-order statistics showed no significant correlation with malignancy progression.
Conclusions: Texture analysis, specifically GLRLM and autoregressive parameters, provides objective, quantitative measures for gastric cancer malignancy assessment, supporting the development of automated diagnostic systems and improving diagnostic accuracy in histopathological evaluation.

Keywords
Gastric cancer, texture analysis, digital pathology, GLRLM, histopathology, malignancy assessment, quantitative analysis

Evaluation the role of breast cancer stem cells on the recurrence of the disease in a sample of Iraqi women patients with breast carcinoma

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Abstract

Breast cancer is heterogeneous disease with various tumors composed of various manifestation starting from etiology, physiology and treatment of the disease. with different biological aspects. mainly carcinomas and the sarcomas. Cancer stem cells (CSCs) are a group of cells population of which possess some of stem cells characteristics features like stemness, or the ability of self renewal with higher degree of metastasis as compared to the non caner stem cells, one of the most recently clinical evidence is the relation between the breast cancer stem cells and the relapsing of the disease due to their developing ability of the resistance of chemotherapy with different cellular mechanisms and the persistence of a few population would be the source of the disease recurrence via directing the tumor microenvironment. in this study two different parameters had been used for identifying the breast cancer stem cells Epithelial cell adhesion molecule (EpCAM), that also known as epithelial-specific antigen (ESA) or CD 326, which is a trans membrane glycoprotein to be a cell-cell adhesion molecule. as well as to CD24 which is a tiny mucin-like glycosyl phosphatidylinositol both parameters being mesured via immunohistochemical technique, tissue samples were elucidate for patients form the Medical City Hospital in Baghdad and grouped as (Group A: Include 30 Iraqi women patients with breast carcinoma under treatment), (Group B: Include 30 Iraqi women patients with breast carcinoma undergo the recurrence of the disease after complete healing process,) and Group C: Include 30 tissue samples from the surrounding normal tissue after surgery procedures as a control group showing the normal texture of the breast tissue. The results of the immunohistochemical expression of EP-Cam protein and CD24 were showed a higher expression in Group A and Group B as compared to group C (45.77 % and 67%) respectively for the cancer stem cells within the tumor mass percentage of immunohistochemical expression upon cell scoring data of CD24 and EPCAM positive cells for the groups A and B (66,55)% as compared to group C (22.4%), (data are mean±SD) at (P≤ 0.05). as a conclusion both CD24 and EP-CAM markers can targeted as cancer stem cells Biomarkers which could help in the targeting therapy for theses› cells which have the main role in resistance of chemotherapy and recurrence of the disease.

Keywords
Breast Cancer Stem Cells (BCSCs), EpCAM, CD24, Chemotherapy Resistance, Disease Recurrence.

Effected of Programmed cell death-1/programmed cell death ligand-1 with Toxoplasmosis in Iraqi thalassemic Patients

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Abstract

Toxoplasma gondii is an intracellular protozoan parasite that can infect almost all warm-blooded hosts and is distributed globally. Thalassemia, a hereditary form of anemia, is frequently linked to immune system disturbances, which may increase vulnerability to persistent infections.

Objective: The present study investigated the seroprevalence of anti-Toxoplasma IgG and IgM antibodies and evaluated the involvement of soluble programmed death-1 (sPD-1) and its ligand (sPD-L1) in Iraqi patients with thalassemia suffering from chronic toxoplasmosis.

Methods: A total of 165 thalassemia patients and 80 healthy controls, aged 2–45 years (mean 15.387 ± 0.627), were recruited from Al-Karama Teaching Hospital, Baghdad, Iraq, between March and June 2022. Serological tests were performed to detect anti-Toxoplasma antibodies, and serum levels of sPD-1 and sPD-L1 were measured.

Results: Seropositivity for anti-Toxoplasma IgG antibodies was detected in 36.36% (60165/) of thalassemia patients compared to 31.25% (2580/) of healthy controls. Thalassemic patients with toxoplasmosis showed significantly higher IgG titers (41.475 ± 9.193 UI/ml) than seropositive controls (35.59 ± 8.336 UI/ml). Mean serum PD-1 levels were markedly elevated in thalassemia patients with (524.986 ± 136.845 pg/ml) and without toxoplasmosis (583.187 ± 111.592 pg/ml) compared with controls (399.62 ± 120.97 pg/ml). Similarly, sPD-L1 levels were significantly higher in thalassemic patients with toxoplasmosis (565.078 ± 119.312 pg/ml) and without toxoplasmosis (555.361 ± 92.410 pg/ml) than in healthy controls (0.266 ± 0.053 pg/ml).

Conclusion: Iraqi thalassemia patients exhibit a high seroprevalence of chronic toxoplasmosis, with significantly increased levels of sPD-1 and sPD-L1. These findings suggest a potential role of PD-1/PD-L1 signaling in immune regulation and disease progression in thalassemia patients with chronic T. gondii infection.

Keywords
Toxoplasma gondii, Thalassemia, Seroprevalence, sPD-1, sPD-L1

Evaluation of Antioxidant Levels and Interferon Gamma in Female Breast Cancer Patients Receiving Hormonal Therapy

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Abstract

This study aimed to evaluate the relationship between some antioxidants (albumin and glutathione) and the cytokine interferon gamma (IFN-γ) in female breast cancer patients receiving hormonal therapy. Previous research has suggested that hormonal therapy, particularly tamoxifen, may influence oxidative stress and immune cytokine regulation, but the exact effects remain unclear.

Blood samples were collected from 44 female breast cancer patients (aged 35–68 years) receiving hormonal therapy, and from 44 healthy females (aged 31–69 years) as a control group. Serum levels of albumin, glutathione, and IFN-γ were measured.

The results showed a slight but statistically significant increase in IFN-γ levels in hormonally treated patients compared to controls. The mean ± SD values were 1.52 ± 0.10 and 1.61 ± 0.21 for stage I and II patients, respectively, versus 0.80 ± 0.12 for both stages in the control group ($P < 0.05$). Although statistically significant, the absolute increase was modest, indicating a limited biological effect.

In contrast, albumin and glutathione levels were significantly decreased in both patient groups compared to controls (albumin: 3.1 ± 0.59 and 2.29 ± 0.44 vs. 5.2 ± 0.16 g/dL; glutathione: 5.1 ± 0.91 and 4.52 ± 0.79 vs. 17.5 ± 2.8 µmol/L; $P<0.05$).

These findings suggest that hormonal therapy may slightly activate immune cytokine responses while reducing antioxidant capacity.

In conclusion, a moderate relationship was observed between IFN-γ and antioxidant markers in hormonally treated breast cancer females, indicating that hormonal therapy may modulate both immune and oxidative processes.

Keywords
Albumin, Glutathione, Interferon Gamma (IFN-γ), Breast Cancer, Hormonal Therapy

Clinical Significance of Serum miR-222-3p Expression in Breast Cancer Patients Diagnostic and Prognostic Insights

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Abstract

Breast cancer (BC) remains a leading cause of malignancy-related deaths in women, emphasizing the need for low-cost, fast, sensitive and non-invasive biomarkers. Non-coding RNAs have emerged as a major focus of cancer research due to their critical regulatory functions in tumor initiation, progression and metastasis. Accumulating evidence highlights their involvement in multiple oncogenic and tumor-suppressive pathways, among them miRNA-2223-p has been implicated in tumor aggressiveness, treatment resistance and poor prognosis.

Objectives: this study aimed to evaluate serum miR-2223-p expression in (BC) patients compared with healthy controls (HCs) and to explore its association with clinic-pathological features.

Materials and methods: serum samples from 50 BC patients and 50 HCs were analyzed using RT-q PCR. Diagnostic performance was assessed by ROC curve analysis and statistical tests examined correlations with tumor characteristics.

Results: analysis of the differential expression of miR-2223-p suggested that the expression of the BC patients was higher than that of the normal control group (p=0.002), which were 5.916 ± 1.137 and 5.428 ± 0.85, respectively.

Elevated level of miRNA-222 was significantly associated with older age (>50), HER2-positive and triple-negative (TNBC) molecular subtypes, higher tumor grade and advanced disease stage by TNM staging system. Expression was inversely correlated with ER and PR positivity.

We further evaluate the discriminative power by ROC analysis which demonstrated strong discriminative ability (AUC = 0.827, sensitivity = 78.2%, specificity = 74.7%).

Conclusion: our study has provided evidence indicating that the miR-2223-p is frequently overexpressed in BC and correlates with adverse prognostic features, supporting its potential as a non-invasive biomarker for diagnosis, prognosis and therapeutic targeting in high-risk patients.

Keywords
Breast cancer, miRNA-2223-p, Tumor-biomarker, RT-q PCR.

Diagnostic Value of Bone Turnover Markers and Serum Cytokines in relation to Hematological Changes in patients of bone tumor

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Abstract

Background: Bone tumors are complex neoplasms that are likely to result in biochemical and hematological changes, and they are hard to diagnose in time. The detection of serum biomarkers that are reliable will help deal with limitations in early detection. The proposed study was aimed to examine the diagnostic usefulness of serum cytokines (TNF- 2, IL-6) and bone turnover (Collagen Type I, LDH, ALP) in relation to change of hematology in bone tumor patients.
Methods: On 90 participants, a case control trial was conducted. TNF- a, IL-6 and Collagen Type I serum levels were determined using Sandwich ELISA. The LDH, ALP, calcium, and phosphate were measured using conventional methods of colorimetry, and the hematological parameters (Hb, WBC, PLT) were measured using automated hematological analysis systems. Independent t-tests, ROC curve analysis were used in statistical analysis to define the diagnostic performance and correlation of markers.
Results: TNF-a, IL-6, Collagen Type I, LDH and ALP levels were found to be significantly higher in the patients ($p < 0.001$) than in the controls, which are an indication of higher levels of inflammation, cellular turnover and remodeling activity of the bones. There was a slight increase in phosphate levels and calcium was steady. The counts of hemoglobin and WBC had significantly decreased and indicated bone marrow suppression, but the counts of platelets had not significantly changed. The ROC analysis demonstrated high diagnostic performance with TNF- alpha, Collagen Type I, and IL- 6 having AUC values of 0.999, 1.000, and 0.981 respectively.
Conclusion: In combination with hematological parameters, serum cytokines and bone turnover markers are also seen to have high diagnostic value in the detection and follow up of bone tumor development. They can be incorporated into blood-based testing, which could lead to better detection of the disease early and help clinicians make decisions in practice of oncology and hematology.

Keywords
Bone tumors, Hematological changes, TNF- alpha, IL- 6, Collagen Type I, LDH, ALP, Biomarkers, Early diagnosi.

Oral squamous cell carcinoma in Erbil- Kurdistan region-Iraq

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Abstract

Background: Oral Squamous Cell Carcinoma (OSCC) is a significant global health concern, particularly due to its highly invasive and recurrent nature. The traditionally well-known underlying causes of OSCC which are mainly alcohol drinking, smoking tobacco and / or betel quid chewing are not very widely spread in Iraq-Erbil city due to the Islamic committing culture, however, there is an increasing number of OSCC, mainly among women.
Objectives: An Observational Study highlighting the underlying causes and preventive methods aimed for Analyzing the most underlying cause/ causes behind each case of OSCC in Erbil-Kurdistan region-Iraq, and the recommendations for prevention.
Methods: This retrospective study included 235 OSCC patients diagnosed between 2018 and 2025. Demographic data (age, gender, past medical history, past drug history and the presence of oral premalignant lesions were collected and analyzed.
Results: Among the 235 patients, 168 (71.5%) were female and 67 (28.5%) were male. The patients' ages ranged from 23 to 80 years. Of all cases, 161 (68.5%) were diabetic prior to their OSCC diagnosis, while 74 (31.5%) were non-diabetic at the time of diagnosis. Notably, among the diabetic patients, 85 (52.8%) developed OSCC at sites previously affected by oral erosive lichenoid drug reactions.
Conclusion: This study highlights a potential association between pre-existing diabetes, oral lichenoid lesions, and OSCC development. The high prevalence of OSCC in diabetic patients suggests a need for community education regarding diet, frequent investigations for HbA1C, and the need for regular scheduled dental appointments for exploring any eruption of new oral chronic mucosal pre malignant conditions.

Keywords
Oral Squamous Cell Carcinoma (OSCC), Diabetes, Oral Lichenoid Lesions, Erbil-Iraq, Risk Factors, Women

Elevated Bacterial Sepsis Risk from Inflammation and Iron Overload in Splenectomized Adults with β-Thalassemia Major: Prospective Cohort Findings

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Abstract

Background and Aim: When transfusion-dependent β-thalassemia major (β-TM) patients undergo splenectomy, a common surgical procedure, there is an increased likelihood of bacterial sepsis due to immunological dysfunction, chronic inflammation, and iron excess. This study compares splenectomized adults with β-thalassemia major to non-splenectomized controls in terms of the incidence of sepsis, the pathogens responsible, and related biomarkers.
Methods: From hematological centers in Baghdad, Iraq, we selected 170 adults (aged 18 years and above) who had β-thalassemia major (β-TM) after having their splenectomy at least six months ago. Group A, which consisted of 64 patients, was formed from this cohort after they were diagnosed with sepsis. Patients without splenectomy who were matched by age and transfusion history made up the control group (Group B; n=50). Inflammatory indicators, iron overload metrics, and organ damage indicators were evaluated through ELISA and electrochemiluminescent immunoassays. These biomarkers included high-sensitivity C-reactive protein (hs-CRP), procalcitonin (PCT), and interleukin-6 (IL-6). Other biomarkers included ferritin, serum iron, and hepcidin. A systemic inflammatory response and a blood culture-positive infection are the hallmarks of bacterial sepsis, the most common result. Disparities in biomarkers between the groups were included as secondary outcomes. A significance level of $\alpha=0.05$ was used in the statistical analyses performed in GraphPad Prism using unpaired t-tests.
Results: The most common bacteria in a group of 64 patients (Group A) were Streptococcus pneumoniae (41%), Escherichia coli (27%), Klebsiella pneumoniae (14%), and Acinetobacter baumannii and salmonella spp., each accounting for 6 cases (9%). Sepsis cases (Group A) had significantly greater levels of inflammatory biomarkers, such as high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and procalcitonin (PCT), as compared to non-splenectomized controls (Group B) ($P<0.001$ for all). Iron overload markers, including ferritin and hepcidin, showed significantly different patterns in splenectomized patients, with elevated ferritin and decreased hepcidin levels ($P<0.001$ for both). Compared to controls, splenectomized patients showed rather significant elevations in markers of organ damage, such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, and urea ($P<0.05$ for all).
Conclusion: Several pathogens, driven by increased inflammation and iron overload, greatly enhance the risk of bacterial sepsis after splenectomy in transfusion-dependent β-thalassemia major. In high-risk situations, these results highlight the immediate need for improved preventive measures and strict monitoring to reduce sepsis-related complications in β-TM patients who have had their splenectomies.

Keywords
β-Thalassemia Major, Splenectomy, Bacterial Sepsis, Inflammation, Iron Overload, Biomarkers

Histological study for the effect of gold nanoparticles in infected mice with mammary adenocarcinoma

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Abstract

Objective: One of the main causes of death in the globe is still cancer. In the sphere of medical applications, nanomaterials are being used more and more, particularly in the diagnosis and treatment of cancer. This study was done in Iraqi Centre for Cancer and Medical Genetic Research (ICCMGR), to evaluation the efficacy of gold nanoparticles (GNPs) in reduce tumor harmful effect, and other vital organs mice implanted with mammary adenocarcinoma.

Methods: Gold nanoparticles was preparing from Sigma Aldrich Company with 10nm, spherical shape and at concentration 6× 1012 particles/ml.Thirty laboratory mice bearing tumor were taken and divided into three groups, 1st group as control without tumor and treatment, 2nd group as control positive with tumor but without treatment, 3rd group bearing tumor and treatment with GNPs injection, after 28 days the animal were killed and sacrificed, so the tumor, kidney, liver and spleen are tested by histopathological procedure.

Results: The results showed several symptoms in 2nd group compare to the 1st group, these symptoms ranged between apoptotic and necrotic area, inflammatory infilteration cells in tumor and lobulation of glomerular tuft with necrosis in kidney to enlargement of hepatocyte with coagulative necrosis in liver and hyperplasia with megakaryocyte in spleen section, after treatment with GNPs in 3ed group, the histological changes were reducing to low effect.

Conclusion: The finding of this study suggests that GNPs is a good choice for reducing the effects of cancer, as well as GNPs have minimum toxic level with less disruption to vital organs.

Keywords
GNPs, Mammary adenocarcinoma, Histological changes, Tumor

Thymol nanocarriers inhibited proliferation of hepatocellular carcinoma (HCC) cells (3D in vitro model)

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Abstract

Niosomes as nanocarriers have been developed to improve treatment outcomes, enhance drug delivery to the targeted site, and reduce systemic side effects. Thymol is an FDA-approved natural phenolic compound that has anti-inflammatory, antimicrobial, and antioxidant properties. Recently, it has been shown that thymol also represents anti-tumoral effects toward many cancers, like gastric cancer, glioblastoma, and breast cancer. In the present study, hepatocellular carcinoma (HCC) microtissues were used in order to investigate the anti-cancer effects of niosome nanocarriers loaded with thymol (Thy-nio). Following fabrication of thymol-loaded niosomes using the thin-layer hydration method, particle size, polydispersity index (PDI), encapsulation efficiency (EE), and sustained drug release of nanocarriers were characterized. In vitro cytotoxicity of thymol-loaded niosomes towards HCC microtissues was investigated using the MTS assay. The expression of BAX and BCL2 genes was studied using quantitative real-time polymerase chain reaction (qRT-PCR).

MTS results indicated that (Thy-nio) effectively reduced HCC microtissues› viability and inhibited the proliferation of tumor cells ($P<0.001$). Moreover, gene expression results showed that the expression level of the BCL2 gene decreased significantly ($P<0.001$), while BAX expression ($P<0.001$) increased in thymol-loaded niosomes groups as compared with the control group.

Our study indicated that the thymol-loaded niosomes could effectively penetrate tumor cells and reduce cell proliferation in the HCC microtissues. In addition, thymol-loaded nanocarriers induced apoptosis in cancerous cells.

Keywords
Niosomes, Thymol, Hepatocellular Carcinoma (HCC), Nanocarriers, Apoptosis

Inhibition of MCT1 Reduces Lung Metastasis by Reversing Markers of Epithelial-to-Mesenchymal Transition (EMT)

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Abstract

Metabolic reprogramming contributes to the aggressiveness and metastatic potential of non-small cell lung cancer (NSCLC). Monocarboxylate transporter 1 (MCT1) facilitates lactate exchange between cancer and stromal cells, promoting tumor progression and survival. This study investigates the therapeutic potential of AZD3965, an MCT1 inhibitor, in reversing epithelial-to-mesenchymal transition (EMT) and suppressing lung metastasis in NSCLC models. Using both patient-derived xenografts (PDX) and cell-based assays, we demonstrate that MCT1 inhibition reduces metastatic burden, suppresses proliferation, and restores epithelial phenotype markers such as E-cadherin. These findings highlight the potential of MCT1 inhibition as a strategy to target cancer metabolism and metastatic behavior.

Methods:

• Animal Model: Mice were injected with NSCLC patient-derived xenografts (PDX; mx148). Once tumors became palpable, mice received AZD3965 (5 mg/kg) or vehicle (DMSO) for several weeks.
• Metabolic Tracing: Lung tissues were analyzed for ^{13}C-glucose enrichment in glycolytic and TCA metabolites. Fractional enrichments were normalized to glucose enrichment.
• Histology and IHC: Lung tissue was stained with H&E and Ki67 to evaluate tumor proliferation.
• Flow Cytometry: Lung cells were stained with human HLA antibody to quantify tumor-derived cells.
• Western Blotting: Protein lysates from subcutaneous tumors and cell cultures were analyzed for Slug, MCT1, and E-cadherin.
• Migration/Invasion Assays: HCC15 (MCT1-KO) and H1299 cells were used to assess the effect of MCT1 inhibition on cell motility.

Results: Figure 1. MCT1 Inhibition Suppresses Metastatic Progression

• A. AZD3965 treatment significantly reduced tumor growth in mice injected with mx148 PDX models.
• B. ^{13}C enrichment analysis showed decreased glycolytic and TCA metabolite flux in AZD3965-treated groups ($p < 0.05$).
• C. H&E and Ki67 staining revealed reduced tumor proliferation in AZD3965-treated mice.
• D. Flow cytometry confirmed reduced human HLA-positive cells in lung tissue following MCT1 inhibition.
• E. Western blot analysis demonstrated decreased Slug expression, indicating reversal of EMT.
• F. MCT1 knockout and AZD3965-treated cells showed increased E-cadherin levels.
• G. Migration and invasion assays revealed significantly reduced motility in treated and MCT1-deficient cells.

Conclusion: MCT1 inhibition through AZD3965 effectively suppresses metastatic behavior in NSCLC by altering lactate metabolism, reducing EMT markers, and impairing tumor cell invasiveness. These findings suggest that metabolic intervention targeting MCT1 could serve as a promising therapeutic strategy against aggressive lung cancer subtypes.

Keywords
Non-Small Cell Lung Cancer (NSCLC), Monocarboxylate Transporter 1 (MCT1), AZD3965, Metabolic Reprogramming, Epithelial-to-Mesenchymal Transition (EMT)

Metastasis-Step Vulnerability: NDV Blocks Spheroid Re-attachment and Outgrowth in Esophageal adenocarcinoma cells

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Abstract

Background: Esophageal adenocarcinoma continues to be deadly, with a high metastatic rate making it difficult to treat. Conventional 2D screening weakly predicts responses to complex metastatic behaviors. Three-dimensional (3D) spheroids and reattachment/dispersion assays better model early metastatic outgrowth. Newcastle disease virus (NDV) is a clinically promising oncolytic agent, but its efficacy across metastasis-relevant perspectives in esophageal cancer is undefined.

Methods: human esophageal adenocarcinoma SKGT4 cell line was evaluated in parallel 2D monolayers (10,000 cells/well), compact 3D engineered spheroids (50,000 cells/well), and a reattachment model (infect-before-attach vs. attach-then-infect). Cells were exposed to NDV (AMHA1; MOI 1, 3, 5, 10, and 20). Endpoints included 72-hr. dose–response and 24120--hr. time courses (crystal violet), dispersion-area quantification upon reattachment, viral entry/penetration monitored by PKH67-labeled fluorescent stain, infectious output (TCID50) from spheroid supernatants were measured, and the mechanism of killing studied through detection of caspase-3, p21/p27, and Ki-67 markers. Selectivity was tested in tumor–stromal co-spheroids (SKGT4 together with human adipose-derived mesenchymal stem cells, HAMSC).

Results: NDV reduced SKGT4 viability in 2D with a steep dose–response; in 3D, susceptibility was right-shifted. Remarkably, NDV suppressed spheroid reattachment/dispersion, with larger effect sizes when infection coincided with or followed adherence, revealing a metastasis-step vulnerability. PKH67 tracking confirmed NDV entry and intratumoral spread in SKGT4 spheroids; supernatants contained infectious progeny by TCID50. Mechanistically, NDV increased caspase-3, p21,p27 and decreased Ki-67 in SKGT4 spheroids and co-spheroids, whereas HAMSC exhibited minimal changes, indicating safety and selectivity.

Conclusions: In SKGT4 esophageal adenocarcinoma, NDV oncolysis is shaped by the 3D architecture of tumor tissue. However, it has maximum effect at the reattachment/dispersion step, a clinically relevant window for preventing early metastatic outgrowth. These results nominate NDV as a candidate for peri-metastatic control strategies in esophageal cancer and establish reattachment assays as practical, mechanistically informative preclinical platforms.

Keywords
Esophageal Adenocarcinoma, Newcastle Disease Virus (NDV), Oncolytic Virus, Metastasis Model, 3D Spheroids

The Role of Tumor-Associated Macrophages (TAMs) in Cancer Progression and Immunosuppression

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Abstract

Tumor-associated macrophages (TAMs) are key immune components that play a pivotal role in shaping the tumor microenvironment, actively contributing to suppressing immune responses and promoting tumor growth and cellular proliferation. This study aimed to evaluate the functional, phenotypic, and molecular roles of TAMs in patients with solid tumors. This study analyzed blood and tissue samples using multiple methods, including flow cytometry, quantitative polymerase chain reaction (qPCR), and immunohistochemistry. Blood samples were collected from (30) patients clinically diagnosed with solid tumors, in addition to (20) healthy individuals as controls. Cytological analysis results showed a significant increase in the percentage of macrophages carrying the markers CD163 and CD204, with a decrease in the expression of HLA-DR, indicating cell polarization toward the M2 immunophenotype with immunosuppressive properties. Genetic analysis also revealed increased expression of IL-10, TGF-β, ARG1, CSF-1R, and MMP9, genes associated with enhanced immune and suppressive functions of the tumor environment. Histological examinations revealed a clear infiltration of macrophages in the tumor periphery, with increased expression of PD-L1, indicating the contribution of macrophages to regulating immune checkpoints and inhibiting effector T cells. Statistical analyses revealed an inverse correlation between PD-L1 and HLA-DR, and a direct correlation with IL-10, reinforcing the hypothesis of the multifaceted immunosuppressive role of macrophages. The results of this study highlight the essential role of tumor-associated macrophages in supporting tumor progression and immune suppression, making them a promising target for modern immunotherapeutic interventions. The study recommends the need for further research in this area, exploring the possibilities of reprogramming or therapeutically targeting these cells to improve the efficacy of immunotherapies in solid tumors.

Keywords
Tumor-associated macrophages, immune microenvironment, gene expression, CD163 PD-L1, immunosuppression, solid tumors.

Assessment of Immune parameters in Iraqi patients with acute myeloid leukemia

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Abstract

Background: Acute myeloid leukemia (AML) is a hematological malignancy characterized by abnormal proliferation of myeloid cells and an immunosuppressive tumor microenvironment. Immune checkpoint molecules, such as programmed cell death protein 1 (PD-1) and its ligand PD-L1, play a crucial role in immune evasion by leukemic cells. Interleukin-6 (IL-6) is another key immunomodulatory cytokine that may contribute to AML progression. Objectives: This study aimed to evaluate the expression levels of PD-1 and PD-L1 in AML patients and investigate their association with IL-6 levels, in order to clarify their potential role in immune suppression and disease pathophysiology.
Methods: The study included 80 AML patients and 40 age- and sex-matched healthy controls (aged 18–85 years). Quantitative reverse transcription polymerase chain reaction (qRT-PCR) was used to determine PD-1 and PD-L1 gene expression levels, while enzyme-linked immunosorbent assay (ELISA) was performed to measure serum IL-6 concentrations. Flow cytometry was used to determine the expression frequencies of myeloblast markers (CD13, CD33, CD117, CD64, and CD7).
Results: PD-1, PD-L1, and IL-6 levels were significantly elevated in AML patients compared to healthy controls. The cutoff values distinguishing AML patients from controls were 0.853 for PD-1 and 0.622 for PD-L1, indicating high diagnostic sensitivity. The expression frequencies of myeloblast markers were CD13 (91.25%), CD33 (85%), CD117 (70%), CD64 (47.5%), and CD7 (82.5%).
Conclusion: The upregulation of PD-1 and PD-L1, along with elevated IL-6 levels, suggests a synergistic role in promoting immune suppression and leukemic cell survival in AML. These findings highlight the potential of PD-1, PD-L1, and IL-6 as biomarkers for disease progression and treatment response, supporting their value as potential therapeutic targets in AML management.

Keywords
Acute Myeloid Leukemia, Interleukin-6, PD-1, PD-L1, Immune Checkpoint

Association Between IL-6 and TNF-α Gene Polymorphisms and Serum Levels in Iraqi Women with Breast Cancer

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Abstract

Background: Breast cancer (BC) is a heterogeneous disease influenced by genetic and inflammatory factors. Interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) are key pro-inflammatory cytokines implicated in tumor development, progression, and immune modulation. Single nucleotide polymorphisms (SNPs) in IL-6 and TNF-α genes may alter cytokine expression, thereby impacting disease behavior and patient outcomes.

Objective: To investigate the association between IL-6 (rs1800795) and TNF-α (rs1800629) gene polymorphisms and serum levels of their encoded cytokines in Iraqi women with breast cancer.

Methods: A total of 160 female participants were included in this study, categorized into four groups (40 for each group):

1. Breast cancer patients under active treatment (chemotherapy and/or hormone therapy).
2. Breast cancer patients post-mastectomy (total or partial).
3. Newly diagnosed breast cancer patients (treatment-naïve).
4. Healthy female controls.

Participants were aged between 30 and 65 years, with a mean age of (47.2 ± 8.5 years). All subjects were females, matched across the four groups in terms of age distribution. Venous blood samples were collected from all participants. Serum levels of IL-6 and TNF-α were quantified by ELISA, and SNP genotyping was performed using allele-specific PCR for IL-6 (rs1800795) and TNF-α (rs1800629). Associations between cytokine levels, genotypes, and clinical status were statistically analyzed using ANOVA, chi-square, and Pearson's correlation tests ($P \leq 0.05$ considered significant).

Results: Mean IL-6 levels were significantly elevated in newly diagnosed patients (45.7 ± 3.2 pg/mL) and those under active treatment (42.1 ± 2.8 pg/mL), compared to mastectomy patients (33.6 ± 2.7 pg/mL) and healthy controls (18.7 ± 1.4 pg/mL) ($P < 0.01$). TNF-α levels followed a similar trend: newly diagnosed (38.3 ± 2.6 pg/mL), active treatment (35.5 ± 2.4 pg/mL), mastectomy (29.1 ± 2.1 pg/mL), and controls (14.2 ± 1.1 pg/mL) ($P < 0.01$).

Genotypic distribution revealed a higher prevalence of mutant genotypes (CC for IL-6 and AA for TNF-α) among patients in groups 1 and 3, which strongly correlated with elevated serum cytokine levels ($r = 0.72$ for IL-6; $r = 0.69$ for TNF-α, $P < 0.001$). Conversely, the wild-type genotypes (GG for IL-6 and GG for TNF-α) were more frequent in the control group and associated with lower cytokine concentrations.

Conclusion: Our findings suggest that elevated IL-6 and TNF-α levels are associated with breast cancer activity, particularly in newly diagnosed and actively treated patients. These cytokines are further influenced by genetic polymorphisms, indicating that IL-6 and TNF-α SNPs may serve as predictive biomarkers for disease status and inflammatory response. Stratifying patients based on genotype and treatment stage offers valuable insights into tumor behavior and may guide personalized therapeutic strategies.

Keywords
Breast Cancer, IL-6, TNF-α, SNP, Real-Time PCR, ELISA, Cytokines, Inflammation, Iraqi Women

Correlation Between Inflammatory and Tumor Markers in Colorectal Cancer: A Clinical Study of CRP, IL-6, and YKL-40 With CEA and CA19-9

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Abstract

Colorectal cancer (CRC) is the primary cause of Carcinoma-associated morbidity and death, emphasizing the urgent demand for dependable biomarkers to improve prognostic accuracy and guide treatment strategies. The purpose of the investigation was to evaluate the link between systemic inflammation. markers C-reactive protein (CRP), interleukin-6 (IL-6), and YKL-40, as well as classical Carcinoma indicators CEA and CA199- in CRC patients. A case-control design was employed, involving 30 patients with CRC and 30 matched healthy controls. Serum levels of all five biomarkers were measured using validated ELISA and immunoassay kits. Results revealed significantly elevated concentrations of CRP, IL-6, YKL-40, and Carcinoma indicators in CRC. There was a significant difference between sick and healthy persons. (ROC) curve analysis confirmed high Accuracy of tests for each biomarker, while combined evaluation improved discrimination between patients and controls. Correlation analysis showed strong positive associations among CRP, IL-6, CEA, and CA199-, whereas YKL-40 displayed an independent regulatory profile with negative correlations to the other markers. These findings support the growing evidence that systemic inflammation plays a pivotal role in CRC progression and prognosis. Elevated CRP and IL-6 were correlated with cancer development and decreased outcomes, while YKL-40 was established as a distinct predictive indicator. The combined use of multiple biomarkers provided greater clinical value than single markers, reinforcing the importance of multi-marker strategies in risk stratification, therapeutic decision-making, and long-term monitoring. In conclusion, integrating inflammatory biomarkers with classical tumor markers may enhance prognostic modeling and improve clinical management of CRC patients.

Keywords
Colorectal cancer; CRP, IL-6, YKL-40, CEA, CA199-, Biomarkers, Prognosis

The Cytotoxic and Genotoxic effects of Metformin on TM-4 Cell Lines

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Abstract

Metformin is a biguanide organic compound derived from the Galiga officinalis plant. Also, it is listed as the first line therapy to care for hyperglycemia in type II diabetes mellitus patients. Although the effects of metformin on metabolism have been well investigated, research on the drug›s impacts on reproductive health is still in its early stages. Examining its effects on testicular function and potential reproductive outcomes is essential, especially its effect on sertoli cells, which are essential for spermatogenesis and testicular function. The aim of the present study was use a mouse testicular sertoli cell line (TM-4 cells) to assess the reproductive toxicity and elucidate the molecular mechanisms by which metformin impacts on the proliferation of TM-4 cells in vitro. The anti-proliferative effect of metformin on TM-4 sertoli cell lines treated with 50 and 100µg/ml for 24, 48 and 72 h was detected using MTT assay and the dual staining assay (Acridine orange / Ethidium bromide), it was obtained that metformin exhibited anti proliferation effects in time and concentrations dependent manner. Western blotting and real time RT-qPCR are utilized to detect protein and gene expression. The results reveal that metformin restricts the proliferation of TM-4 cell lines via amplifying the expression of p21. The current results emphasize the ability of metformin to induce cytotoxicity and apoptosis in TM-4 Sertoli cells through altering the expression of genes that have an important role in cell cycle control and apoptosis and shed light on the impact of metformin on Sertoli cells and male reproductive function. As a result of growing usage of metformin among young populations, comprising those of reproductive age, additional study is important to fully understand its effects on reproductive health and fertility.

Keywords
Metformin; TM-4; CDK1, 4; CDK inhibitors (p21Cip1).

Exploring the Combined Cytotoxic Potential of Paclitaxel and p-Synephrine as a Novel Therapeutic Strategy against Glioblastoma: A Proof-of-Concept Study

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Abstract

Glioblastoma multiforme is one of the most aggressive forms of brain cancer. Treatment options remain limited, especially when resistance to temozolomide, the current standard chemotherapeutic agent, develops. Due to the blood–brain barrier, this study tests paclitaxel–synephrine synergy on Iraqi glioblastoma cells resistant to temozolomide. Cells were treated with synephrine and paclitaxel at 10, 100, and 150 µM, both individually and in 1:1 combinations, as well as with temozolomide (100 µM) combined with equivalent synephrine concentrations for 24 h. Cell viability was determined using the MTT assay; data were analyzed via one-way ANOVA followed by Tukey's post hoc test. Synephrine exhibited a strong dose-dependent antiproliferative effect, by 18%, 46%, and 83% at 10, 100, and 150 µM, respectively (IC_{50} = 128 µM, $p < 0.001$). Paclitaxel also showed potent inhibition—10%, 44%, and 77% at corresponding concentrations (IC_{50} ≈ 108 µM, $p < 0.001$). When combined, cytotoxicity was markedly enhanced, reaching 40% and 80% inhibition at 10 and 150 µM, respectively, with a reduced IC_{50} of 49.6 µM, confirming synergistic potentiation. According to the Bliss Independence model, synergy was strongest at 10 µM (observed 40% vs expected 26.8%), additive at 100 µM (63% vs 64.9%), and antagonistic at 150 µM (80% vs 96.9%). Synergy appears most pronounced at low doses, potentially due to synephrine's modulation of drug efflux or survival pathways. Additionally, synephrine + TMZ combinations yielded 40.96%, 57.71%, and 74.87% inhibition at increasing concentrations (IC_{50} = 63 µM), indicating a synergistic enhancement of TMZ efficacy.

Keywords
Glioblastoma multiforme, Temozolomide resistance, Paclitaxel, Synephrine, Drug synergy.

Anti-cancer effect of camptothecin and chloroquine on the inhibition of lung cancer and breast cancer cell proliferation

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Abstract

Introduction: Lung cancer and breast cancer are widespread and deadly types of cancer that have shown a significant impact on the mortality rate of affected people. Other research has demonstrated the efficiency of combination therapy methods.
Aim of study: The study aims to find a synergistic effect between chloroquine and camptothecin chemotherapy. Combination therapy can potentially reduce the destruction of healthy cells while effectively targeting cancer cells.
Methods: In this experiment, we exposed lung cancer cell line A549 to a combination of camptothecin and chloroquine. then, we made a cytotoxicity assay and colony formation assay. Our study shows that combining camptothecin and chloroquine can improve or reduce its toxicity, depending on the concentration used.
Results: The statistical analysis shows that combining camptothecin and chloroquine affects the lung cancer cell line A549 and the breast cancer MCF7 cell line
Conclusion: Our results indicated that the combined treatment increased cytotoxicity in tumor cells compared to the single treatment with camptothecin.

Keywords
Hardy-Weinberg equilibrium, genetic susceptibility, polymorphism, AML

The anticancer effect of essential oil from Salvia Palaestina grown in Iraq

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Abstract

The Salvia species, frequently referred to as "sage", has been long recognized as a medicinal herb. Salvia palaestina is native to a widespread area in the Eastern Mediterranean and Middle East, including Palestine, Turkey, Syria, Lebanon, Iraq, Iran, the Sinai Peninsula, and northeastern Egypt. its pharmacological actions have been studied and described, including the anticancer properties of its extract.

Objectives: This study aimed to isolate the essential oil of Salvia Palestina and assess its cytotoxic activity against SKG-T4 and A2780 cell lines.

Methods: The aerial parts of the plant were air-dried and ground, then submitted for water-distillation using a Clevenger-type apparatus for 3 hours, The oil obtained was dried over anhydrous sodium sulphate and stored sealed at +4 °C in the dark until tested. subsequently a colorimetric MTT reduction assay was conducted to assess its effect on human cancer cell lines and its cancer selectivity, utilizing cell lines esophageal SKG-T4 and ovarian A2780 cancer cell lines as well as normal human fibroblast (NHF) as control. Each cell line was treated with serial concentrations (100, 50, 25, 12. 5, 6. 25, 3. 12) µl/ ml of salvia palaestina essential oil for 72 hours. MTT dye solution 28 µL of (2 mg/ml) was added to each well. The incubation continued for three hours. A total of 100 µl of DMSO was added to each well and incubated for 15 min. The optical density was measured at 492 nm using a microplate reader. Analysis of data done using GraphPad Prism software version 8.

Results: The results showed a decrease in cell viability; cytotoxicity of the highest dose used (100µl/ml) of essential oil in SKG-T4 was 62.8% and in A2780 was 52.3%. IC50 of Salvia Palaestina essential oil in SKG-T4 cell line was 57.9» µl/mL» and in A2780 cell line 72.9 µl/mL, indicating the essential oil's potential anti-cancer properties. The essential oil showed concentration dependent inhibition of cell proliferation. It was slightly more potent in SKG-T4 than A2780 cells, with much less cytotoxicity against normal human fibroblast (NHF) cells, where 100µg/ ml of essential oil resulted in 27.2% cytotoxicity with IC50 value of 492.1 µl/mL.

estimation of safety index ($SI = \frac{IC_{50}^{nocancercell}}{IC_{50}^{cancercell}}$) of salvia essential oil in SKG-T4 cells was 8.5, while in A2780 cells 6.8. Showing more selectivity towards cancer cells. Morphological observation of cells under microscope showed cell shrinkage, membrane blebbing, and formation of apoptotic bodies indicating cell apoptosis.

Conclusion: the essential oil of Salvia Palestina possesses potential anticancer activity in vitro, based on its concentration dependent cytotoxic effect on cancer cells with a favorable safety index.

Keywords
Salvia palaestina, Essential Oil, Cytotoxicity, SKG-T4, A2780, Apoptosis

Evaluation of the biological activity of Echinococcus granulosus Hydatid Cyst Antigens on HRT-18 Colon Cancer Cells: selective Cytotoxicity and DNA Damage

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Abstract

Cystic echinococcosis (CE) is a zoonotic infection caused by the larvae of Echinococcus granulosus. Studies have indicated a direct or indirect relationship between infection with these parasites and cancer. They may have anticancer effects capable of inhibiting the development of some types of cancer in different cell cultures or animal models. This study aimed to evaluate the biological efficacy of different antigens extracted from the fluid, wall, and primary heads of the hydatid cyst (larval stage) of the nematode Echinococcus granulosus on the growth and proliferation of cancer cells compared to normal cells. In this study, a cytotoxicity test (MTT assay) was performed. This test primarily aims to evaluate the potential toxic effects on cancer cells by assessing the cell viability in response to different concentrations of antigens. To determine the half-maximal inhibitory concentration (IC50) for each antigen on both the HRT-18 colon cancer cell line and the normal NHF cell line, normal fibroblasts derived from adipose tissue, the cells were exposed to a range of concentrations (100, 50, 25, 12.5, 6.2, 3.1, or 0.0 µg/ml). The results showed a significant decrease in the viability of cancer cells with increasing concentration for all antigens, while the effect was less on normal cells. The IC50 values for the antigens on cancer cells were for the capsular antigen IC50 = 29.93 µg/ml, for the wall antigen IC50 = 24.00 µg/ml, and for the cyst fluid antigen IC50 = 24.09 µg/ml. As for the IC50 values for normal cells, they were for the capsular antigen IC50 = 119.4 µg/ml, for the wall antigen IC50 = 100.8 µg/ml, and for the cyst fluid antigen IC50 = 25.95 µg/ml. To evaluate the mechanism of cell death, a DNA damage test was performed in this study. The severity of programmed cell death was measured in infected cell lines using (AO/PI). Treatment with the hydatid cyst fluid antigen gave high cytotoxicity in the MTT test. The results showed the occurrence of programmed death and DNA damage. These results indicate the occurrence of programmed cell death and DNA damage. Although antigens possess toxic and selective properties against cancer cells, possibly due to their ability to induce apoptosis and damage DNA, they can be considered promising sources for the development of natural antitumor agents.

Keywords
Echinococcus granulosus, antigens, cytotoxicity, apoptosis, HRT-18, DNA damage

In Vitro Evaluation of Anticancer Activity for Benzothiazine Derivatives and for Hydrazine-1-carbothioamide Derivatives in Multiple Myeloma

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Abstract

Introduction: Multiple myeloma is plasma cells tumor. The disease is the second-ranking hematological malignancy. Disease clinical manifestations are anemia, renal failure, bone pain and fracture. Its incidence in Iraq at 2023 was 406 cases.
The clinical problems of many approved antimyeloma drugs and treatment relapse urge to test new compounds. In the current study five novelly compounds synthesized at Baghdad University / College of pharmacy, (three sulfonyl-hydrazides denoted as S1, S2, and S4), and two hydrazine-1-carbothioamides, denoted as N5b and A5an), and NS6180, were tested.
Methods: Plasmacytoma cell line was exposed to the novel compounds in comparison to two standard compounds; bortezomib and melphalan. The study was conducted at the Cell Technologies Laboratories /Harithya/Baghdad/Iraq, during the period of June to November 2025.
The statistical analysis was done by ANOVA test and multiple t-tests, accomplished by the software GraphPad prism 10.
Results: The IC50 of the tested compounds indicate that compound NS6180 is the most potent one (IC50 =194.38µM), followed by S1 (207.78µM), A5an (216.18µM), as compared to Bortezomib (94.186µM) and melphalan (148.07µM). There is a high significant difference between the treated groups and the untreated one ($P < 0.001$).
Discussion: NS6180 is an inhibitor of intermediate-conductance Ca2+-activated K+ channel (KCa3.1 channels) potency is related to the remarkable role of that channel in multiple myeloma.
A5an anticancer effect is related to its inhibition of histone deacetylase (HDAC) whereas that of N5b is due to epidermal growt factor recptor (EGFR) inhibition.
Whereas S4 is better than S1 against the lung and breast tumor, the opposite is true regarding multiple myeloma due to the difference in the nature of such tumors.
Conclusions: KCa3.1 channels have strong role in tumorigenesis and therapy resistance of multiple myeloma.
The superiority of A5an over N5b indicate the more association of HDAC than EGFR in multiple myeloma. The high IC50 of the standard drugs on plasmacytoma cell line indicates that this cell line belongs to a resistant strain. S1 is effective more on the pathways of a hematology tumor than that of solid tumors.

Keywords
multiple myeloma, Plasmacytoma cell culture, benzothiazines, hydrazine-1-carbothioames, IC50.

Advantages and Challenges of Using 3D Culture System for Mouse Cancer Cell Lines to Generate Physiologically Accurate Mouse Tumor Models

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Abstract

The most system used in traditional in vitro culture system in cancer research is the two-dimensional (2D) on a flat support. Though, this system is not representing the real in vivo physiological conditions of the natural tumor microenvironment. The 2D culture system lacks cell-cell communication and interaction. One of the main approaches to overcoming these limitations is the use of the three-dimensional (3D) culture systems. 3D culture system is most used in cancer research and tissue engineering for mimicking the structure and function of real tissues in vivo. This study investigates the formation and growth dynamics of three-dimensional (3D) tumor spheroids using the AMN3 mouse mammary tumor cell line in vitro. Cells were cultured in RPMI medium and transferred to Petri dishes to facilitate spheroid formation under standard incubation conditions. Spheroid development was monitored over nine days using inverted microscopy and quantified using ImageJ software. Results demonstrated that spheroid size and number increased steadily, with a significant peak observed on day five, reflecting active proliferation and aggregation. Morphological analysis revealed early formation of compact spheroids, followed by the development of necrotic cores in later stages, mimicking in vivo tumor physiology. Notably, a decline in both spheroid size and number was observed post-day five, likely due to nutrient depletion, hypoxia, metabolic waste accumulation, and structural instability. These findings highlight the utility of 3D culture models for studying tumor microenvironments, growth kinetics, and treatment resistance. The study underscores the need for optimized culture protocols and additional time-point analyses to better understand spheroid behavior and improve the relevance of in vitro tumor models for cancer research and drug screening.

Keywords
3D Spheroid Culture, Tumor Microenvironment, Necrotic Core, AMN3 Cells, In Vivo Mimicry

Machine Learning-Based Identification of Candidate Circular RNA Biomarkers for early breast cancer diagnosis

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Abstract

Circular RNAs (circRNAs) are a stable and abundant type of non-coding RNAs characterised by tissue-specific expression, and they can be detected in blood and tissues. Their unique features make them promising non-invasive biomarkers for cancer detection. However, identifying reliable circRNA biomarkers for early breast cancer is challenging due to the complexity and high dimensionality of transcriptomic data. This study presents a machine learning framework for discovering and validating circRNA biomarkers for early breast cancer detection using the GSE210790 dataset. This dataset includes circRNA expression profiles from breast cancer and matched normal tissues, obtained through high-throughput sequencing of 12 samples (6 tumor and 6 normal), providing a balanced basis for differential expression analysis and classification. Feature selection was conducted with Random Forest in order to identify the most relevant circRNAs. Three machine learning models—Support Vector Machine (SVM), Random Forest (RF), and XGBoost—were trained and validated with 5-fold cross-validation. The XGBoost classifier achieved the highest performance, reaching 93.4% accuracy, 92.1% precision, 91.8% recall, and 92.0% F1-score, demonstrating the potential of circRNAs as reliable biomarkers for early detection. Overall, this study underscores the importance of machine learning in circRNA biomarker discovery and lays a foundation for future clinical validation. The methodology supports the development of non-invasive diagnostic tools that can improve early detection, reduce diagnostic costs, and enhance patient outcomes.

Keywords
Circular RNAs, breast cancer, early diagnosis, machine learning, blood biomarkers, non-invasive detection

Machine Learning-Based Single-Cell RNA-Seq Analysis in Drug Response: A Hybrid Multi-Stage Gene Selection and Soft Voting Approach

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Abstract

Background: Oral squamous cell carcinoma is the most common type of oral cancer, where cisplatin is the widely used chemotherapeutic agent as a first-line drug. Resistance to chemotherapeutic agents, is a significant challenge in the treatment of Oral squamous cell carcinoma. The development of chemo resistance is influenced by various molecular mechanisms and is further compounded by the interactions within the tumor microenvironment. Novel high-throughput sequencing techniques, such as single-cell RNA sequencing (scRNA-seq), enable the examination of gene expression at the single-cell level. This provides insight into the complex intra-tumoral heterogeneity and enables the development of more targeted and effective therapies. However, the massive data generated by scRNA-seq poses challenges for traditional statistical methods, a limitation that advancements in machine learning have successfully addressed.
Method: In this study, we developed a Hybrid Multi-Stage Gene Selection and Soft Voting Classifier for cancer drug response prediction at the single-cell level by integrating large-scale bulk cell-line data.
Result: 100 significant genes were selected as identifiers for training the developed Soft Voting Classifier. The results demonstrated the effectiveness of our machine learning model, achieving an accuracy of 97.9%, precision of 98.9%, recall of 96.9%, and an F1-score of 97.9% in predicting cisplatin response in Patient-Derived Oral squamous cell carcinoma at the single cell level.
Conclusion: The proposed model consistently outperformed all other classifiers across multiple performance metrics, demonstrating its robustness and reliability. Notably, it achieved significantly higher accuracy and F1-score compared to previous studies using the same dataset. While earlier approaches employing Deep Transfer Learning reported accuracy and F1-scores in the mid-80s to low-90s, our model surpassed these benchmarks by achieving nearly 98% in both metrics. Another comparative method that incorporated gene selection techniques showed considerably lower accuracy, highlighting the superior effectiveness of our approach.

Keywords
Cisplatin Sensitivity and Resistance, Gene Selection, Machine Learning, Oral Squamous Cell Carcinoma, Single-Cell RNA-Seq

Comprehensive Pan-Cancer Bioinformatics Analysis Identifies DHX58 as a Promising Therapeutic Target and Prognostic Biomarker Across Multiple Tumor Types

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Abstract

This study comprehensively investigated the multifaceted role of DHX58 as a potential therapeutic target and prognostic biomarker across various tumor types using an extensive pan-cancer bioinformatics analysis. Leveraging publicly available datasets from platforms such as GEPIA2, TIMER 2.0, UALCAN, and starBase, we analyzed DHX58 expression patterns, prognostic significance, drug sensitivity, functional enrichment, genomic alterations, protein-protein interactions, and DNA methylation profiles. Our findings reveal consistent differential expression of DHX58 across numerous cancers, with context-dependent upregulation or downregulation. Notably, DHX58 expression was found to significantly influence patient overall survival, acting as both a favorable and unfavorable prognostic indicator depending on the cancer type. Furthermore, low DHX58 transcript levels were associated with increased sensitivity to specific chemotherapeutic agents, suggesting its potential as a predictive biomarker for therapeutic response. Functional enrichment analysis emphasized DHX58›s established role in innate immunity and antiviral responses, with its co-expressed genes implicated in viral defense pathways. Genomic profiling identified various alterations, including mutations and copy number variations, contributing to DHX58 dysregulation. Protein-protein interaction mapping solidified its central role in immune signaling, while DNA methylation analysis highlighted epigenetic regulation as another layer of control. Collectively, these findings provide a comprehensive understanding of DHX58›s intricate involvement in cancer biology, suggesting its promise as a novel biomarker and a potential target for therapeutic intervention. Further experimental validation is warranted to translate these bioinformatics insights into clinical applications.

Keywords
DHX58, Pan-cancer analysis, Prognostic biomarker, Therapeutic target, Innate immunity

Machine Learning-Based Detection with AI-Powered Lifestyle Guidance for Parkinson's Disease

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Abstract

Early identification of Parkinson›s disease (PD), a progressive neurological disease with both motor and non-motor symptoms, is essential to slowing the disease›s course and enhancing its quality of life for patients. In this study, we provide an integrated artificial intelligence (AI) system that can analyze multimodal inputs, including speech signals, handwriting patterns, ECG recordings, and MRI scans, to forecast the stage of Parkinson›s disease. Convolutional Neural Networks (CNN) and hybrid machine learning models are used in the core detection framework to extract and categorize both temporal and spatial information, allowing for precise stage prediction even in the disorder›s early stages. In order to minimize disease development and minimize side effects, the system integrates an AI-based recommendation engine in addition to diagnostic classification. This engine offers individualized meal plans, exercise regimens, and preventive lifestyle alterations.In order to ensure accessibility for both patients and professionals, the architecture also incorporates a chatbot interface for interactive symptom reporting and patient advice. In order to increase confidence and clinical interpretability, the experimental design focuses on improving explainability through visualization approaches (Grad-CAM, SHAP/LIME). All things considered, the suggested approach offers a comprehensive AI-assisted healthcare solution that covers not only Parkinson›s disease detection but also prevention and management.

Keywords
Parkinson's Disease,Artificial Intelligence (AI),Convolutional Neural Networks (CNN),Transfer Learning,Early Diagnosis,Stage Prediction,Multimodal Data (ECG, MRI, Voice, Handwriting),Personalized Recommendations,Food and Exercise Guidance,Preventive Healthcare..

Molecular Docking and Anticancer Evaluation of 6-aminopenicillanic Acid derivatives Targeting 1OZ3 in Glioma Cells

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Abstract

Background: Glioblastoma multiforme (GBM) is one of the most aggressive and treatment-resistant brain cancers, with poor survival rates despite the use of temozolomide as a standard therapy. Developing new, selective, and less toxic agents is therefore a major goal in neuro-oncology. Compounds derived from 6-aminopenicillanic acid (6-APA), the core of the penicillin family, have recently attracted interest due to their versatile biological potential, particularly when modified as Schiff bases.
Objective: This study aimed to synthesize and characterize a series of 6-APA Schiff base derivatives (P1–P6), evaluate their cytotoxic activity against glioma (AMGM5) cells compared with normal rat fibroblasts (REF), and investigate their molecular interactions with the cancer-related protein 1OZ3 using docking analysis.
Methods: Six Schiff base derivatives were synthesized by condensing 6-APA with various aldehydes and characterized through FT-IR and ^1H-NMR spectroscopy. Cytotoxicity was tested using the CCK-8 assay after 72 h exposure at concentrations ranging from 10 to 60 µM. Molecular docking was performed with GOLD Hermes 2021 to evaluate ligand–protein interactions and binding energies. Statistical significance was determined using ANOVA ($p < 0.05$).
Results: The synthesized compounds demonstrated concentration-dependent cytotoxicity, with P5 and P6 showing the lowest IC_{50} values (23.5–24.5 µM) against AMGM5 cells while maintaining higher IC_{50} values in REF cells, indicating selectivity toward cancer cells. Docking studies revealed strong binding affinities for P6 (60.62 kcal/mol) and P3 (59.73 kcal/mol) with the 1OZ3 active site, forming multiple hydrogen bonds (GLN250, TYR275, GLN304). A clear correlation was observed between docking affinity and cytotoxic potency.
Conclusion: The study demonstrates that Schiff base derivatives of 6-APA possess significant anticancer potential against glioma cells, particularly compound P6, which exhibited superior binding energy and selective cytotoxicity. These findings support further in-depth investigations into 6-APA derivatives as promising candidates for developing novel therapies targeting resistant brain tumors.

Keywords
DHX58, Pan-cancer analysis, Prognostic biomarker, Therapeutic target, Innate immunity

Detection of unique translocations in Philadelphia chromosome of CML Iraqi patients

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Abstract

Debatable issues include the molecular basis of translocation and prognosis in unique chronic myeloid leukemia (uCML). While some cytogenetic studies predict a poor response to imatinib mesylate, other research show that both classical and uCML exhibit a similar illness trajectory. Additionally, numerous investigations have established a conclusive relationship between tyrosine kinase region (TKR) mutations and severe clinical signs and symptoms. We cytogenetically characterized 20 uCML patients with the objectives of identifying the third partner chromosome, investigating the molecular causes of translocation, and providing information about the development of the disease and its clinical result. We also compared uCML cases with and without TKR mutations to more accurately describe the clinical outcome and identify the significant contributor to treatment resistance. Results: Conventional and molecular cytogenetic were used to define the third partner chromosome in unique translocation. Even while the majority of the cases in our analysis had clinical responses that were insufficient due to TKR mutations rather than unique translocations, when chromosome 5 was the third partner, we saw a deterioration of the situation. Thus, we draw the conclusion that cytogenetic analysis will help us better understand the syndrome if new examples of unusual translocations involving numerous separate chromosomes as third partners (with different breakpoints) are characterized and reported. Few research have been conducted on the cytogenetically defined Ucml.

Keywords
TKR, Cytogenetic, Karyotype, Philadelphia chromosome.

The association of +252 A/G polymorphism in the lympho-toxin –α gene and the risk of non-Hodgkin lymphoma

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Abstract

Non-Hodgkin is one of the wide ranges of blood malignancies that are affecting on the lymphatic system. The genetic variations in immune –related genes have been connecting with NHL susceptibility. The +252 A/G variation is located in the promoter region of the LT-α gene this polymorphism can effect on the transcription and consequently, the expression of the LT-α gene is a cytokine which involved in the immune system response,

Methods: The studied groups were conducted on 62 non-Hodgkin lymphoma patients divided into 37 females and 25 males collected from Hematology department at Baghdad teaching hospital from period from March 2024 to August 2024, and 54 apparently people without any symptoms 32 females and 22 males used as control group. The DNA was extracted by a specific kit manufactured in Geneaid/Taiwan, it used to extract DNA from entire blood samples from both studied groups. Utilizing the Restriction Fragment Length Polymorphism–PCR technique, and sequencing the LT-α gene (+252 A/G rs: 909253) was identified.

Result: The findings demonstrated that non-Hodgkin lymphoma patients had considerably higher levels of the LT-α gene +252 G>A, heterozygous AG genotype, and G allele ($P<0.05$) than the control group. A site of diversity that appears in the CCATGA sequencing and switches to the CCATGG sequencing when a nucleotide change (from A to G) actually takes place indicates the restriction site of the restriction enzyme, according to the sequence of the region under study. Our results suggest that the polymorphism in the LT-α gene (+252 G>A, rs909253) may be associated with the susceptibility of Iraqi patients to non-Hodgkin lymphoma.

Conclusion: The development of non-Hodgkin lymphoma was found to be significant associated between the +252 G>A polymorphism of the LT-α gene and non-Hodgkin lymphoma. Carriers of the G allele , G/G and A/G genotype were likely to developing risk in non-Hodgkin lymphoma than carriers of the A allele and the A/A genotypes.

Keywords
+252A/G polymorphism, Iraqi patients, LT-α gene, Non-Hodgkin lymphoma

Case report: An Iraqi family with hereditary methemoglobinemia

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Abstract

Methemoglobinemia is a rare life-threatening condition that can be hereditary or acquired mainly related to certain chemicals like nitrites and dapsone. Clinical cyanosis and low oxygen saturation in the presence of normal arterial oxygen tension was highly suggestive of methemoglobinemia, methylene blue is the usual antidote in the proper dose (12-mg/kg) with ascorbic acid.
Congenital methemoglobinemia is further classified into two main types with one due to methemoglobin reductase enzyme deficiency and the other due to an abnormal oxygen affinity hemoglobin termed hemoglobin M.
Methemoglobin reductase enzyme deficiency is either type I or type II; type I: demonstrable only in the erythrocytes, presents as uncomplicated, benign methemoglobinemia, and associated with a normal life expectancy with only fatigue and dyspnea being the most commonly reported symptoms. Hereditary type II methemoglobinemia, is global (affects both red and white blood cells) and is associated with severe neurologic dysfunction and reduced life expectancy. The enzyme's activity is less than 20% of normal. The family includes the symptomless father who is 56 years of age while has 2 sons and daughter who were symptomatic with neurological symptoms (type 2 disease) the age of the patients was 7, 6, 4 years the daughter is the oldest, the mother is normal.

Keywords
Methemoglobinemia, Congenital Methemoglobinemia, Methemoglobin Reductase Deficiency, Hereditary Type II, Methylene Blue, Cyanosis

Detection of 18 cystic fibrosis mutations and allele homogeneity for children patients suffering of pulmonary and gastrointestinal diseases in Baghdad- Iraq by Real time-PCR

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Abstract

The Real time PCR is a straight forward way, rapid, and reliable for the detection of any mutations involving changing in amino acid, insertion deletions. We have confirmed the previous study (ARMS-PCR) about using applied PCR- Real time PCR technique in detecting of mutation in transmembrane conductance regulator (CFTR) gene for the cystic fibrosis disease. Ready mix reaction in real time -PCR for cystic fibroses showed better than ARMS-PCR test (Monoplex) especially in time, and more feasible in mutational detection of cystic fibrosis disease .The Real time PCR reactions for the most common mutations have been multiplexed to give a test which will detect the presence of 18 following mutation site in CFTR gene : G542X,F508Delta,W1282X, E92K, DelTA1677, G>A52789+, K68E, R334W, delTATT4010, F1052V, AA—G2181, S4X, , I148T, G551D, N1303K, Y1032C, R560T, C>T103849+.
According to mutations sites, they were classified into 5 different classes depending on severity of mutation and according to global history database by analysis of over 60 different children ages (2-13 years) of collected samples found in the Baghdad –Iraq.
This study has investigated rapid detection of the most common mutations and facilitated early molecular confirmation detection of cystic fibrosis disease in neonates and determined mutational typing (homogeneity) in cystic fibrosis patients and their relatives in Baghdad -Iraq.

Keywords
CFTR, ARMS, Chloride Pump,18 mutations

Association Analysis of EGFR L858R and T790M Polymorphisms in Non-Small Cell Lung Carcinoma Patients

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Abstract

Background: Lung cancer represents one of the most prevalent malignancies worldwide, with non-small cell lung carcinoma (NSCLC) constituting nearly 85% of all cases. Mutations in the epidermal growth factor receptor (EGFR) gene are considered key molecular determinants of tumor progression and therapeutic response. This study aimed to evaluate the association between two EGFR polymorphismsL858R (rs121434568) and T790M (rs121434569) and susceptibility to NSCLC among the Kurdish population in Erbil, Iraq.
Methods: A total of 51 NSCLC patients and 50 healthy controls were recruited from Rizgari Teaching Hospital in Erbil, Iraq. Peripheral blood samples were collected, and genotyping for EGFR L858R and T790M polymorphisms was performed using the allele-specific polymerase chain reaction (AS-PCR) technique. Statistical analysis was conducted using the Chi-square test to determine genotype and allele frequency associations.
Results: The mean ages of NSCLC patients and controls were 41.22 ± 1.23 and 40.45 ± 2.34 years, respectively, with no significant difference in demographic distribution ($p > 0.05$). Both EGFR L858R (rs121434568) and T790M (rs121434569) variants showed no statistically significant association with NSCLC risk ($p > 0.05$). The calculated odds ratios ($OR < 1$) indicated a non-significant protective trend.
Conclusion: The current findings suggest that EGFR L858R and T790M polymorphisms are not associated with an increased risk of NSCLC among patients from Erbil. Further large-scale molecular and pharmacogenetic studies are warranted to confirm these observations and explore other EGFR pathway variants in the Iraqi population.

Keywords
Non-Small Cell Lung Carcinoma; EGFR gene; Polymorphism; Allele-Specific PCR; Genetic susceptibility; Lung cancer biomarkers

High-Sensitivity Detection of DNA Fragmentation in Lymphocytes Using Plasmonic Microfluidics and Laser-Induced Fluorescence

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Abstract

Rapid and accurate Detection of DNA Fragmentation in Lymphocytes is critical for the Early diagnosis of Breast Cancer. Optical biosensing technologies, such as laser-induced fluorescence detection (LIFD), offer high sensitivity and specificity for biomolecular analysis. In this study, we investigated the use of LIFD, coupled with a plasmonic gold-coated Y-shape polymethyl methacrylate (PMMA) microfluidic chip, for detecting DNA fragmentation in lymphocytes isolated from healthy individuals and breast cancer patients. Acridine Orange (AO) dye used to stain the DNA, and a 450 nm blue laser at varying powers (10, 15, 20 mW) served as the excitation source. Fluorescence signals were analyzed to compare spectral shifts and emission intensities between healthy and cancerous cells. Cancerous lymphocytes exhibited a red-shifted emission peak (~595 nm) relative to healthy cells (~515 nm), attributed to AO binding to denatured DNA. Enhanced fluorescence intensity was observed in microfluidic systems due to laminar flow, reduced photobleaching, and increased AO-DNA interaction time. The inclusion of gold nanolayer further amplified fluorescence via metal-enhanced fluorescence (MEF), improving detection sensitivity. The integration of LIFD with a plasmonic microfluidic chip provides a sensitive and cost-effective platform for detecting DNA fragmentation. This approach holds promise for early breast cancer screening and broader applications in molecular diagnostics.

Keywords
DNA Fragmentation, Laser-Induced Fluorescence Detection, Plasmonic Microfluidic Chip, Acridine Orange, Metal-Enhanced Fluorescence.

Genetic variations of recql gene in Iraqi breast cancer patients

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Abstract

Background: Identifying genetic contributors to BRCA12-/negative breast cancer is crucial for improving diagnosis and personalized care. This study examined single nucleotide polymorphisms (SNPs) in the RECQL gene, a key DNA repair helicase.
Method: FFPE tissue samples were collected from 50 Iraqi women with early-stage breast cancer and 50 healthy controls (ages 40–60). DNA from exon 2 of RECQL was sequenced and compared with controls and NCBI references.
Results: A novel single nucleotide polymorphism (TA) was identified in exon 2 of the RECQL gene. Among breast cancer patients, the genotype frequencies were TT (4.0%), TA (79.0%), and AA (17.0%), whereas the control group exhibited 100% TT genotype. The TA genotype was associated with a significantly increased risk of breast cancer (OR=79.21), while the TT genotype appeared to have a protective effect (OR=0.04). The differences in genotype distribution between patients and controls were statistically significant ($p<0.05$).
Discussion: The findings suggest that the newly identified TA polymorphism in exon 2 of the RECQL gene may play a significant role in breast cancer susceptibility among women in Baghdad. While RECQL variants have been reported in European populations, the Iraqi context is distinct due to higher consanguinity rates, younger age at onset, and different environmental exposures. These factors may explain the high prevalence of the TA genotype in Iraqi patients and emphasize the importance of population-specific studies.

Keywords
RECQL gene, Single Nucleotide Polymorphism (SNP), Breast Cancer Susceptibility, TA Genotype, Iraqi Women

Thermal and Chemical Effect on DNA Extracted from Blood

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Abstract

Background: One of the most valuable pieces of evidence used in an investigation is the blood found at crime scenes. Detectives use blood samples to connect possible criminals with victims. The identification of a suspect's DNA can be impaired or made more difficult when these traces are burnt by murderers or cleaned up with common household cleaning products, which frequently contain bleaching agents or active oxygen. Environmental conditions and temperature variations can also impact the quality of blood remains at the crime scene, thereby influencing the DNA. On the other hand, pieces of the victims' and assailants' clothes found at the crime scene can be holding important evidence to be used in court.
Results: Our results showed that extracting dry blood from a piece of cloth is significantly affected when compared to direct DNA extraction from fresh blood; however, there was no significant difference between three types of fabric. Hot weather up to 50ºC had a highly significant effect on the quantity of DNA extracted from different fabrics when compared to the positive control, but the TH01 gene could still be detected. Burning the blood sample and cleaning it with bleach showed the most adverse impact on the capacity to obtain entire DNA profiles by PCR. On the other hand, hydrogen peroxide H2O2 showed different effects on DNA depending on the cloth material; still, samples on gauze and satin were affected, and the gene was undetectable. PCR of the sample on leather showed many bands of different molecular weights, which indicate non-specific binding.
Conclusions: Positive identification of DNA extracted from a burnt or cleaned crime scene is less precise and dependable than fresh blood stains. Burning or cleaning the crime scene makes it more difficult to solve crimes.

Keywords
DNA extraction, PCR, TH01 gene, Bleach, Hydrogen Peroxide, Burn, Forensics.

Detection of the role of IL-17A gene polymorphism (rs2275913) in Iraqi infertile males by using HRM real-time qPCR technique

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Abstract

One of the most serious social problems facing developed countries today is infertility which is a multifactorial syndrome encompassing a wide variety of disorders, IL-17 A is a pro-inflammatory cytokine and plays an important role in the pathogenesis of many diseases, including infertility. Due to the lack of previous studies on the polymorphism of the IL-17A gene in sterile men despite the high serum level of this gene in them, the current study was designed to reveal the role of genetic variations of the IL-17A gene located in the promoter region and its relationship to the occurrence of infertility in Iraqi men. The study included collecting semen samples and dividing them into two or more sterile groups, and the second group samples were collected from Kamal Al-Samarrai Hospital. DNA was extracted and HRM technology was used to find genetic variants of the IL-17A gene. The results of the current study showed that the heterogeneous genotype may be associated with the prevention of infertility, with a significant difference of 0.004, while the A allele was the most common in Iraqi society, according to the results of this study. The conclusion is that the genotypes of the IL-17A gene may be associated with an increased risk of infertility in men due to the deviation of the patient group from the normal balance equation (Hardy-Weinberg equation).

Keywords
Interleukin-17 A gene, infertility, SNPs.