BOOK OF ABSTRACT

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AI-Powered De Novo Antibiotics Discovery: Is It The Answer to Overcome Antimicrobial Resistance? A Systematic Review of Preclinical Evidence Across In Vitro and In Vivo Studies

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Introduction: Antimicrobial resistance (AMR) remains a critical global issue. By 2050, it is projected to cause around 10 million deaths if current trends persist. Traditional antimicrobial discovery struggles to keep up with rapidly evolving resistance due to its lengthy process, high cost, and high failure rate. Developing a single drug can take over a decade of research and cost millions of dollars. These challenges demand more efficient approaches, with artificial intelligence (AI) offering a promising path to accelerate and improve antibiotic development. Methods: GoogleScholar, PubMed, ScienceDirect, and Scopus were systematically searched following the PRISMA 2020, yielding 13 eligible studies. All included in vitro validation, and four extended to in vivoinvestigations. Risk of bias was evaluated using the QUIN (in vitro) and the SYRCLE (in vivo) tools.Discussion: Across studies, AI supported multiple stages of antibiotic discovery, including target identification, lead compound optimization, also enhancement of pre-clinical testing. In target identification, two studies revealed novel antibacterial targets distinct from classical pathways. During lead optimization, applied in most studies, AI-generated compounds demonstrated strong antimicrobial activity and low MIC values against broad-spectrum and multi-drug resistant bacteria. Four in vivo studies further showed that these de novo antibiotics exhibited superior antimicrobial efficacy to current standard therapies. Finally, in preclinical testing, AI models accurately predicted cytotoxicity and hemolysis, later confirmed experimentally. Conclusion: AI has markedly improved efficiency and accuracy in antibiotic development. While continued model refinement, validation, and ethical oversight remain crucial, AI-integrated pharmaceutical research indicates growing maturity and transformative potential.

Keywords: artificial intelligence, antibiotic discovery, antimicrobial resistance, preclinical evidence

Empowering Healthcare Through AI: The Development of Thalassemia NusaCare for Early Detection of Genetic Blood Disorders in Indonesia

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Introduction : Thalassemia is a prevalent inherited hemoglobinopathies in Indonesia, with an estimated carrier rate of 3-10% of the population. Under-resourced areas struggle with limited diagnostic services like genetic testing or hemoglobin electrophoresis. Prevention and clinical management by early screening and detection of potential thalassemia carriers are critical. This opens the opportunity to leverage computer vision and on-device machine learning to develop an iOS-based application, providing a digital anamnesis tool that is affordable and accessible for early thalassemia risk assessment. Methods : Large, diverse datasets were collected to compile the clinical reports and to conduct the AI training. The system architecture of Thalassemia NusaCare AI consists of three integrated computational modules: Vision-Based Analysis using MobileNetV3 for facial and blood image detection, CBC laboratory data Interpretation using OCR and decision-tree algorithms. Digital Anamnesis uses adaptive, federated learning for accurate, real time Thalassemia risk prediction. Results : Preliminary testing using a curated dataset (n=200 images, 120 lab entries, 80 questionnaire records) leads to a mean classification accuracy of 91.3% for detecting thalassemia major, minor, and non-thalassemic anemia, demonstrating high operational efficiency. Hybrid ensemble models result in an F1-score of 0.88 and enhanced sensitivity by 12% relative to single-input models. User experience testing with early adopters also suggested strong usability and intuitiveness (SUS = 89.2).Conclusion : Thalassemia NusaCare AI integrates edge AI and inclusive design to deliver adaptive diagnostics in low-connectivity areas. Combining visual, numerical, and behavioral data, enabling on-device screening that aligns with Indonesia's "Thalassemia-Free 2045" through federated learning and clinical collaboration.

Keywords: Thalassemia, Machine Learning, CoreML, Computer Vision, Mobile Health, iOS

PHARMACOGENOMIC REGULATION OF THE NF-KB-NRF2 AXIS BY CURCUMIN: A PRECISION MOLECULAR APPROACH TO INFLAMMATION AND OXIDATIVE STRESS

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Introduction: Chronic inflammation and oxidative stress are major mechanisms in degenerative diseases, including cancer, diabetes, and cardiovascular disorders. The NF-κB and Nrf2 pathways play a role in maintaining redox balance and inflammatory response. Curcumin, the main bioactive compound of Curcuma longa L., can simultaneously modulate both pathways through pharmacogenomic mechanisms influenced by individual genetic variations. Methods: This study used the Systematic Literature Review method in accordance with the PRISMA 2020 guidelines. Searches were conducted in PubMed, Scopus, ScienceDirect, and Google Scholar until October 2025 using the keywords "Curcumin," "NF-κB," "Nrf2," "Oxidative Stress," and "Pharmacogenomics." Studies assessing the molecular modulation of NF-κB/Nrf2 by curcumin and gene-dependent effects were included. Results and Discussion: A total of 31 studies met the inclusion criteria, including in vitro, in vivo, in silico, and clinical studies. Curcumin suppressed NF-κB activation and activated Nrf2/HO-1, thereby reducing ROS and proinflammatory cytokines. Variations in the ERCC5 rs751402 gene, as well as the expression of SLC7A11 and ATAD3A/B, influenced the cellular response to curcumin. In silico and network pharmacology analyses revealed multigenic targets related to inflammation and oxidative stress. Nanoformulations enhance bioavailability and clinical immune response.
Conclusion: Curcumin acts as a dual-regulator pharmacogenomic agent that balances the NF-κB and Nrf2 pathways, reducing inflammation and oxidative stress in a gene-dependent manner. These findings support its potential as a natural biomolecule for the development of precision therapies for chronic diseases involving inflammation and oxidative stress.

Keywords: Curcumin, NF-κB, Nrf2, Oxidative Stress, Pharmacogenomics

Cardiovascular Adverse Event Risk in Rheumatoid Arthritis Patients Treated with JAK Inhibitor Tofacitinib versus TNF Inhibitors: a Systematic Review, Meta Analysis, and Meta Regression

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Rheumatoid arthritis (RA) is a chronic autoimmune disease, often requiring potent therapies like Tofacitinib or TNF inhibitors. Yet the comparative cardiovascular safety profile of these agents remains a critical and evolving concern. Previous meta-analysis revealed major adverse cardiovascular events (MACE) and thromboembolism was prevalent in tofacitinib treated patients. However, the impact of patient comorbidities on cardiovascular adverse events remains uncertain, requiring systematic assessment through meta-analysis and meta-regression. This study aims to assess the risk of cardiovascular adverse events in RA patients treated with tofacitinib versus TNF inhibitors and to evaluate the influence of baseline comorbidities through meta-regression. A comprehensive search of PubMed, Scopus, Scilit, and Epistemonikos identified RCTs and observational studies up to 2025. Random-effects meta-analysis in R estimated pooled OR and HR for MACE and thromboembolism, while patient comorbidities were evaluated through meta-regression. Four studies (n = 62,009) met inclusion criteria. Tofacitinib was associated with increased risk of MACE (HR = 1.33; 95% CI 1.08–1.65; p = 0.008; I^2 = 0%) and thromboembolism (HR = 1.79; 95% CI 1.23–2.60; p = 0.002; I^2 = 37.8%) compared with TNF inhibitors. Meta-regression revealed no significant effect of age, sex, hypertension, diabetes, smoking, heart failure, coronary artery disease, venous thromboembolism history, or corticosteroid use on these risks. Tofacitinib increases the risk of MACE and thromboembolism in RA patients compared with TNF inhibitors, independent of common cardiovascular comorbidities and baseline characteristics.

Keywords: MACE, Rheumatoid arthritis, Thromboembolism, Tofacitinib, TNF Inhibitors.

EXPLORING THE ROLE OF MITOCHONDRIA IN ALZHEIMER WITH NETWORK PHARMACOLOGY: A BIOINFORMATICS ANALYSIS

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Alzheimer's disease (AD) is a progressive neurodegenerative disease marked by the pathological accumulation of beta-amyloid peptide and hyperphosphorylated tau. Growing body of evidence indicates that mitochondrial dysfunction plays a pivotal role in AD pathogenesis, by inducing neurotoxicity through the formation of oxidative stress and reactive oxygen species (ROS). This study aims to investigate relevant mitochondrial proteins in Alzheimer by employing network pharmacology. Protein-coding genes associated with AD were identified from the GeneCards database, extracting only genes scoring >1 in relevancy. Datasets associated with mitochondria were extracted from the STRING database. 621 overlapping proteins from both keywords were further enriched and topologically analyzed. This study employed enrichment analyses using ShinyGO to identify relevant biological, cellular, and molecular processes, in addition to disease pathways. Topology analyses were conducted through STRING and Cytoscape by implementing eight different centrality parameters and clustering, the genes were further curated to obtain pivotal proteins in AD and their dysregulation. Aligned with our enrichment analyses, the proteins topologically relevant were components of the mitochondrial oxidative phosphorylation (OXPHOS) pathway, crucial to the respiratory electron transport chain and ATP synthesis system. This study provides a foundation for the discovery of multi-target drugs in AD therapy.

Keywords: Alzheimer, bioinformatics, mitochondria, network analysis, protein-protein interaction.

COMPARATIVE EFFICACY AND SAFETY OF LIMUS-ELUTING STENTS IN ACUTE CORONARY SYNDROME IN ASIAN PEOPLE: A NETWORK META-ANALYSIS AND BIOINFORMATICS STUDY

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Introduction: Evidence on the relative performance of limus-eluting stents (LES) in acute coronary syndrome (ACS) among Asian patients is mixed, and formal rankings with biological context are limited. We compared LES and examined drug-specific mechanisms. Methods: Randomized trials of ACS patients undergoing PCI with 12-month outcomes were identified systematically. A frequentist network meta-analysis combined 19 trials (n=25,642) to estimate odds ratios (ORs) for major adverse cardiovascular events (MACE) and mortality and to derive treatment ranks (P-scores). Bioinformatics included molecular docking to FKBP12/mTOR/VEGFR2, ADMET/toxicity prediction, protein-protein interaction networks, and KEGG/GO enrichment. Results and Discussion: All limus stents lowered 12-month MACE versus paclitaxel (ZES 0.46 [0.34-0.64]; EES 0.55 [0.41-0.71]; SES 0.58 [0.46-0.72]; BES 0.60 [0.42-0.86]). Differences within the limus class were small (ZES vs SES 0.80 [0.62-1.06]). Rankings favored zotarolimus (SUCRA 0.94), followed by everolimus (0.64) and sirolimus (0.50); biolimus (0.42) ranked below, and paclitaxel was lowest. Mortality did not differ. Docking indicated stronger binding of limus agents to FKBP12/mTORC1 than paclitaxel, and toxicity models suggested a wider safety margin for limus agents (everolimus LD50 2,500 mg/kg; paclitaxel 134 mg/kg). Enrichment analyses highlighted PI3K-Akt/mTOR pathways relevant to vascular healing. Conclusion: In Asian ACS, LES outperform paclitaxel at 12 months. Zotarolimus ranks first, with everolimus and sirolimus performing comparably. The clinical ranking aligns with predicted target engagement and toxicity profiles.

Keywords: Acute coronary syndrome, Bioinformatics, Drug-eluting stents, Network meta-analysis, Zotarolimus

POTENTIAL OF BIOACTIVE PEPTIDES FROM BLANAK FISH (Moolgarda seheli) AS MULTITARGET THERAPY FOR NON-SMALL CELL LUNG CANCER: A CANCER-INFORMATICS STUDY

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Non-Small Cell Lung Cancer (NSCLC) is the most common type of lung cancer with a high mortality rate and resistance to conventional therapy. Moolgarda seheli is known to produce bioactive compounds, but its potential against NSCLC still needs to be explored. This study aims to evaluate the pharmacokinetic profile, pharmacodynamics, and potential of M. seheli peptides as a multitarget agent for NSCLC through an in silico approach. Twelve M.seheli peptides were modeled using UCSF Chimera. Pharmacokinetic and pharmacodynamic predictions were performed using SwissADME, ProTox-3.0, and AllerTop. Membrane permeability was evaluated using PerMM. Target protein structures were obtained from PDBJ. Molecular docking was performed with MOE, then validated through molecular dynamics simulation (MD) using YASARA. Plasmid construction was performed in silico using ApE v2.0.36. Pharmacokinetic and pharmacodynamic profiles indicate the AVMAPIVA peptide has favorable distribution, metabolism, and excretion, as well as non-toxic and non-allergenic properties. The AVMAPIVA peptide exhibits strong affinity for CDK4 (-10.75 kcal/mol), BRAF (-11.60 kcal/mol), AKT1 (-10.79 kcal/mol), VEGFR2 (-10.73 kcal/mol), and EGFR (-10.47 kcal/mol). PerMM results indicate good membrane penetration ability. MD simulations confirm the stability of the complex. The results of the study indicate that the AVMAPIVA peptide is non-toxic, non-allergenic, stable in biological environments, and capable of penetrating cell membranes and inhibiting proliferation, migration, and angiogenesis in NSCLC. peptide from M. seheli has potential as a multitarget therapy for NSCLC with a good druglikeness profile. In vitro and in vivo experimental studies are needed for further validation of efficacy and safety.

Keywords: Moolgarda seheli, Multitarget, NSCLC, Peptide-based therapy, Bioinformatics.

ASSOCIATIONS BETWEEN GENETIC VARIANTS AND ADVERSE EFFECTS OF GEFITINIB IN NON-SMALL CELL LUNG CANCER: A SYSTEMATIC REVIEW

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Introduction: Lung cancer remains the leading cause of cancer-related death worldwide, with non-small cell lung cancer (NSCLC) accounting for approximately 85% of cases. Gefitinib is a tyrosine kinase inhibitor frequently used in NSCLC with favorable outcome. However, many patients develop severe adverse effects which might be influenced by genetic variability. Therefore, we aim to systematically review the gene variants and its association with adverse effects of gefitinib in NSCLC patients. Methods: A systematic search was conducted according to PRISMA guidelines across PubMed, Scopus, and Cochrane. Studies investigating the association between genetic variations with adverse effects following gefitinib in NSCLC were included. Extracted data encompassed study and patient characteristics, adverse effects, and identified gene variations. Risk of bias was assessed using the RoB-2 for randomized trials and Newcastle-Ottawa Quality Assessment Scale for cohort and case-control studies. Results: Nineteen studies involving 2.087 patients were included, with Japanese populations being the most studied. Polymorphisms in EGFR and ABCG2 were among the most studied genes. Rash, diarrhea, and hepatotoxicity are the most common adverse effects reported. Poor metabolizers of CYP2D6 and CYP3A53/3, and variations in ABCG2, ABCB1, and EGFR were associated with higher incidence of adverse effects. However, several studies demonstrated no associations between gene variations with adverse effects. Conclusion: Genetic variations in ABCG2, ABCB1, CYP2D6, CYP3A53/3, and EGFR may influence gefitinib-associated adverse effects, highlighting the need of pharmacogenomic testing to guide personalized treatment and improved patient safety.

Keywords: Pharmacogenomics, Genetic Variants, Gefitinib, Non-Small Cell Lung Cancer, Adverse Effects

NOVEL OF TUBERCULOSIS VACCINE CANDIDATES THROUGH IN SILICO AND IN VIVO ANALYSIS OF SINGLE EPITOPE PROTEIN PE-PGRS MYCOBACTERIUM TUBERCULOSIS

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Tuberculosis (TB) is an infectious disease that remains a serious global health threat. The use of the Bacille Calmette-Guérin (BCG) TB vaccine has so far shown unsatisfactory results due to its inconsistent and limited effectiveness. In this study, a comprehensive preclinical study pipeline was developed to design a novel single-epitope subunit vaccine targeting the PE_PGRS protein family of Mycobacterium tuberculosis. VaxiJen screened antigenic proteins, IEDB and NetMHCpan predicted B- and T-cell epitopes. Selected epitopes were assembled with linkers and an adjuvant. The construct was expressed, purified, and tested in vivo in mice for antibody and cytokine responses. The construct result showed, which had a molecular weight of 35.1 kDa and an instability score of 16.58, was found to be stable, soluble, and somewhat hydrophilic by physicochemical examination. The three-dimensional model showed a tight and stable fold that was dominated by β-sheets and α-helices. Strong binding affinities with MHC class I (ΔG = -22.7 kcal/mol) and class II (ΔG = -10.9 kcal/mol) were confirmed by molecular docking and PRODIGY studies. In the in vivo test, the single epitope exposure group had an average value of 0.090 ± 0.017. This indicates that single epitope exposure provides a significant effective antigen presentation and T-cell activation and increase in the measured parameters compared to the control group. Collectively, these findings highlight the potential of the designed single-epitope construct as a safe, stable, and immunogenic vaccine candidate against M. tuberculosis, meriting further experimental validation.

Keyword: Myobacterium tuberculosis, PE_PGRS, Vaccine, Single Epitope, Preclinical Study

Efficacy and Safety of Tyrosine Kinase 2 Inhibitor Deucravacitinib in Psoriasis : A Systematic Review and Drug-Response Meta Analysis of RCTs

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Psoriasis is a chronic immune-mediated disease affecting 1-3% of the population worldwide and often impairs quality of life, with moderate-to-severe cases requiring systemic therapy. Deucravacitinib, a selective tyrosine kinase 2 (TYK2) inhibitor that modulates IL-23, IL-12, and type I interferon pathways, has emerged as a promising oral therapy. However, trial findings remain inconsistent, highlighting the need for systematic evaluation of its efficacy and safety versus placebo. A comprehensive literature search of PubMed, Scopus, Scilit, and ScienceDirect was performed to identify randomized controlled trials published up to 2025 comparing deucravacitinib with placebo in psoriasis. Risk of bias was assessed using the Cochrane RoB 2.0 tool, and meta-analysis was conducted with Rstudio with random effect model and REML estimator. Seven RCTs (n = 3,014) were included. Deucravacitinib significantly improved PASI-75 (OR = 9.85; 95% CI 5.11-19.01; $p < 0.0001$), PASI-90 (OR = 14.29; 95% CI 9.14-22.35; $p < 0.0001$), and PASI-100 (OR = 12.03; 95% CI 5.55-26.09; $p < 0.0001$), as well as sPGA 0/1 (OR = 14.28; 95% CI 9.30-23.62; $p < 0.0001$). Quality-of-life outcomes also improved: PSSD-0 (OR = 7.60; 95% CI 2.73-21.16; $p = 0.0001$) and DLQI 0/1 (OR = 6.27; 95% CI 4.68-8.41; $p < 0.0001$). Upper respiratory tract infection and acne were more frequent with deucravacitinib, while other adverse events were comparable to placebo. Meta-regression showed dose dependence for DLQI 0/1 ($p = 0.02$) and PSSD-0 ($p = 0.01$), but not for adverse events. Deucravacitinib demonstrates significant efficacy and acceptable safety in psoriasis treatment. Long-term studies are warranted to confirm its sustained safety profile.

Keywords: Deucravacitinib, Psoriasis, TYK2 Inhibitor, Efficacy

EFFECTIVENESS OF Bacillus Calmette-Guérin (BCG) VACCINE AS POST-EXPOSURE PROPHYLAXIS AGAINST LEPROSY AMONG HOUSEHOLD CONTACTS: A SYSTEMATIC REVIEW

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Introduction: Indonesia remains one of the top three countries with the highest leprosy burden. Current prevention focuses mainly on early detection. However, limited public awareness allows continued transmission, especially among household contacts (HHCs). Considering WHO's 2030 "Toward Zero Leprosy" goal, post-exposure prophylaxis (PEP) with vaccines represents a promising strategy. Although no specific leprosy vaccine exists, Bacillus Calmette-Guérin (BCG) provides cross-protection due to antigenic similarity with Mycobacterium leprae. Its effectiveness is assessed through new leprosy cases and IgM anti-phenolic glycolipid-1 (PGL-1) antibody levels. Therefore, this systematic review aims to evaluate the effectiveness of BCG vaccination as post-exposure prophylaxis against leprosy among household contacts. Methods: Databases including PubMed, Springer, Nature, Frontier, Epistemonikos, ScienceDirect, BMJ, Sage, and Karger were searched. From 6,303 records, seven studies met inclusion criteria. Eligible studies were RCTs and cohort studies (2015-2025) on BCG-based PEP among household contacts. Non-English, in vitro, review, and non-field case reports were excluded. Study quality was assessed using JBI Critical Appraisal tools. Results and Discussion: Seven studies showed that BCG vaccination reduced leprosy incidence by 57-75%. The strongest protection occurred with BCG revaccination (59-95%), while combining BCG with single-dose rifampicin (SDR) achieved about 80% efficacy. Immunologically, vaccinated contacts showed lower IgM anti-PGL-1 levels, indicating a protective immune response. This indicates the vaccine's ability to simulate a protective immune response that suppresses the humoral response against Mycobacterium leprae. Conclusion: BCG vaccination provides substantial protection as post-exposure prophylaxis against leprosy, while its revaccination or combination with SDR further strengthens preventive efficacy among household contacts.

Keyword
Bacillus Calmette-Guérin (BCG), Household contacts (HHCs), Leprosy, Postexposure prophylaxis (PEP), Vaccine.

THE EFFECTIVENESS OF POLYDEOXYRIBONUCLEOTIDE FROM SALMO SALAR ADMINISTERED VIA MICRONEEDLING VERSUS TOPICAL SERUM FOR ANTI-AGING THERAPY

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The use of polydeoxyribonucleotide (PDRN) has recently gained attention as an anti-aging skin treatment. Initially, PDRN treatments were more commonly performed in aesthetic clinics using microneedling techniques. However, the beauty industry has recently developed PDRN-based moisturizers that are easier for daily use and are often promoted as products containing salmon-derived DNA. PDRN is known to activate the adenosine A2A receptor, which promotes collagen synthesis, accelerates tissue repair, and provides anti-inflammatory effects. This study aimed to compare the efficacy and safety of PDRN administration through microneedling and topical application for anti-aging purposes. A systematic review was conducted of experimental and clinical studies reporting outcomes on wound healing, skin texture, elasticity, and side effects. The analysis showed that both methods effectively improved skin quality with minimal adverse reactions. Microneedling enhanced intradermal penetration, accelerated tissue regeneration, and stimulated collagen and elastin synthesis more rapidly; meanwhile, topical PDRN reduced oxidative stress and improved skin tone, with effects being particularly significant when combined with vitamin C or niacinamide. Overall, both methods are safe and effective for anti-aging therapy. Microneedling offers faster collagen regeneration, whereas topical PDRN serum provides a practical and non-invasive alternative. The choice of treatment should be tailored to patient preference, skin condition, and pain tolerance.

Keywords: Salmon DNA, PDRN, Microneedling, Skin regeneration, Anti-Aging appearance

STEM CELL-BASED THERAPEUTIC APPROACHES FOR THALASSEMIA: A SYSTEMATIC REVIEW

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Thalassemia is a hereditary hematologic disorder characterized by defective hemoglobin synthesis, resulting in chronic anemia and rekated systemic complications,which are often managed through lifelong blood transfusions and iron chelation therapies. Recent advances in cell-based therapeutic strategies, particularly hematopoietic stem cell (HCS) gene therapy, have demonstrated substantial potential in addressing the underlying genetic defects and improving erythropoiesis. This systematic review evaluates preclinical and clinical studies, from PubMed, ScienceDirect, SCOPUS, focusing on the efficacy of HSC gene therapy and other immunomodulatory cellular approaches in thalassemia models. Studies involving thalassemic mice indicated that HCS-based gene therapy significantly enhanced β-globin expression and restored normal red blood cell phenotypes,suggesting functional hematologic improvements.Complementary strategies involving regulatory T cells (Tregs) and engineered immune cells, including CAR-T and NK cells, offer additional promise for immune modulation, transplant tolerance,and the reduction of therapy-related complications. Despite these advances, challenges including limited cell availability, complex ex vivo culture conditions, immune rejection, and scalability remain. Innovations in genome editing,engineered TCR/CAR technology and CRISPR/Cas-edited iPSC-derived cells may further improve specificity, stability, and efficacy. Collectively, cell-based therapies offer a transformative approach for thalassemia by correcting the underlying genetic defect and modulating immune responses, with the potential to reduce dependence on conventional transfusions and enhance quality of life. Further clinical studies are required to establish long-term safety, feasibility and therapeutic efficiency in human patients.

Keywords : Thalassemia,Hematopoietic Stem Cell,Gene Therapy,Regulatory T Cells,Cell-Based Therapy

From Promise to Proof: Revealing the Comparative Performance of RSV Vaccines Through Network Meta-Analysis

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Introduction: There is no consensus on the optimal vaccine platform for preventing respiratory syncytial virus (RSV) infection. Recent advances in RSV vaccine development aim to improve efficacy and safety across various platforms. This study aimed to compare the efficacy and safety of available RSV vaccines using a network meta-analytic approach to identify the most effective strategy for RSV prevention. Method: A systematic search was performed in PubMed, ScienceDirect, Cochrane, and Scopus up to November 2025 to identify randomized controlled trials (RCTs) of RSV vaccines in healthy populations. Ten RCTs were included, evaluating adenovirus vaccine, subunit vaccine, mixed subunit and adenovirus vaccine, subunit vaccine with AS01E, and placebo controls were included. Analyses were conducted in RStudio using the netmeta package. Risk of bias was appraised using RoB 2.0 and certainty of evidence was assessed with CINeMA and the GRADE frameworks. Result: This analysis demonstrated that the subunit vaccine with AS01E possesses superior efficacy in reducing RSV-related respiratory illness compared to placebo (RR = 0.22, 95% CI: 0.16 -- 0.31). This finding was reinforced by ranking analysis, which identified this intervention as the most effective (P-score = 0.916). No significant differences in safety profiles were observed across interventions, although precision was limited by wide confidence intervals and substantial heterogeneity. Conclusion: Subunit vaccines with AS01E demonstrated the highest efficacy for RSV prevention. However, their safety profile has not yet been clearly defined, and further research is needed to assess long-term effectiveness and monitor potential late adverse effects.

Keywords: Efficacy, Respiratory Synctial Virus, Respiratory Illness, Vaccines, Safety

HOW GUT MICROBIOME SIGNATURES SHAPE METFORMIN RESPONSE AND GI INTOLERANCE IN TYPE 2 DIABETES

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Metformin is first-line therapy for type 2 diabetes mellitus (T2DM), yet interindividual variability in glycaemic response and frequent gastrointestinal (GI) intolerance are not fully explained by pharmacogenomics alone. This review synthesised evidence that links baseline gut microbiome composition to metformin effectiveness and tolerability. English-language, open-access Human observational studies from the past decade were identified in PubMed, ScienceDirect, and Google Scholar if they reported stool- or rectal sample derived microbiome profiles alongside glycaemic outcomes (e.g., HbA1c change) or GI adverse events, dose modification, or discontinuation, with standardised extraction of design, population, -omics methods, and outcome definitions. Few eligible studies met criteria; across prospective and cross-sectional cohorts, higher alpha diversity and specific taxa ncluding Akkermansia and Streptococcus were associated with increased GI adverse events to metformin, while distinct microbial signatures differentiated glycaemic responders from non-responders. A small multi-omic analysis suggested that shifts in bile acid-related bacteria together with down-regulation of anti-inflammatory host genes may underlie intolerance. Integrative models combining pharmacogenomic variants with microbiome features were rarely evaluated, and head-to-head comparisons with pharmacogenomics-only models are lacking. Overall, baseline gut microbiome signatures correlate with variability in metformin responses and GI intolerance in T2DM, underscoring the need for larger, standardised multi-omic cohorts to quantify the incremental predictive value of microbiome data for personalised metformin theraphy.

Keywords: Gastrointestinal intolerance; Gut microbiome; Metformin; Pharmacomicrobiomics; Type 2 diabetes mellitus

GENETIC DETERMINANTS OF HELICOBACTER PYLORI VIRULENCE AND GASTRIC CANCER SUSPECTIBILITY: A SYSTEMATIC REVIEW

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Introduction: Gastric cancer (GC) remains a leading cause of cancer mortality, with Helicobacter pylori (H. pylori) infection recognized as a major carcinogen. Virulence genes such as cagA, cagE, and vacA, along with specific cag pathogenicity island (PAI) polymorphisms, are implicated in gastric mucosal injury and malignant transformation. This systematic review aimed to identify H. pylori genotypes associated with increased GC risk. Methods: Following PRISMA 2020 guidelines, a systematic search was conducted in PubMed, ProQuest, and ScienceDirect. Eligible studies included case-control or cross-sectional designs assessing H. pylorivirulence genotypes among GC and non-GC patients. Data were extracted and summarized descriptively based on odds ratios (ORs) and genotype distributions. Results and Discussion: From 4,359 screened records, five studies met inclusion criteria. The vacA c1 allele was linked to a higher GC risk (OR = 3.14, 95% CI 1.08–9.09), and cagA+cagE co-expression increased susceptibility (OR = 0.46, 95% CI 0.24–0.86). In Japan, East-Asian cagA with vacA s1m1 showed the strongest association (OR = 6.68, 95% CI 1.73–25.8), while multiple cagA EPIYA-C motifs in Brazilian isolates tripled GC risk (OR = 3.08, 95% CI 1.74–5.45). Latin American data identified cagA and cagC variants significantly enriched in GC isolates. These findings indicate that cagA and vacA synergistically drive epithelial disruption and inflammation, underpinning their oncogenic potential. Conclusion: CagA, vacA, and cagE genotypes represent key H. pylori virulence predictors of GC. Integrating genotypic profiling into clinical risk assessment could improve early detection and targeted prevention strategies.

Keywords: Gastric cancer, Helicobacter pylori, Virulence gene

IN SILICO DESIGN AND IMMUNOINFORMATICS EVALUATION OF A MULTI-EPITOPE VACCINE CANDIDATE AGAINST *Mycobacterium tuberculosis*

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Tuberculosis, caused by Mycobacterium tuberculosis, continues to be a major global health threat, causing 1.3 million deaths annually despite the availability of the Bacillus Calmette-Guérin (BCG) vaccine, which offers variable efficacy in adults. The emergence of multidrug-resistant strains further highlights the need for novel vaccine strategies. In this study, an in silico immunoinformatics approach was employed as a cost-effective and safe method to design a multi-epitope vaccine candidate with enhanced immunogenic potential.
Epitope prediction was performed for major M. tuberculosis antigens (Ag85 complex, CFP-10, HspX, TB10.4) using IEDB servers, yielding 95 CTL and 39 HTL epitopes. Epitopes were screened for high antigenicity (VaxiJenv2.0 > 0.4), non-allergenicity (AllerTOPv2.1), and non-toxicity (CSM-Toxin). Selected epitopes were combined using suitable linkers to construct the vaccine, and physicochemical properties were assessed with ProtParam. The 3D model was predicted and refined using I-TASSER and GalaxyRefine, validated by SAVESv6.1.The construct displayed global and Southeast Asian HLA coverages of 58.57% and 49.21%, respectively, indicating sufficient potential for global vaccine deployment. Structural analysis indicated high stability (instability index 33.27) and thermostability (aliphatic index 65.94). Molecular docking with TLR4 displayed stable interaction (lowest energy weighted score -976.8) and immune simulation displayed efficient humoral and cellular response, indicated by peak IgM and IgG titers following simulated injections, adequate activations of CTLs and HTLs, and progressive memory cell development. This study presents a promising multi-epitope vaccine candidate against M. tuberculosis. Further in vitro and in vivo validation is necessary to confirm its immunogenic potential.

Keywords: sMycobacterium tuberculosis, Multi-epitope vaccine, Immunoinformatics, Molecular docking, In silico analysis

Development of an Artificial Intelligence-Based Portable Prototype for Early Tuberculosis Detection Using Exhaled Breath Analysis and IoT Integration: A Feasibility Study

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Introductions: Tuberculosis (TB) remains a major global health problem and has become one of the world's leading infectious diseases, particularly affecting populations in low- and middle-income countries. Despite advancements in molecular testing, the accessibility, cost, and time requirements of conventional diagnostics limit early case detection. Exhaled breath analysis provides a promising non-invasive approach through the identification of volatile organic compounds (VOCs) produced during TB infection. This study aimed to develop and evaluate a portable diagnostic system that integrates VOC sensing, Artificial Intelligence (AI), and Internet of Things (IoT) technologies to enhance early TB screening in community and primary healthcare settings. Methods: A metal oxide semiconductor gas sensor array connected to an ESP32-S3 microcontroller was employed to capture VOC profiles from 33 participants (17 TB-confirmed patients and 16 healthy controls). The acquired data were preprocessed, reduced, and classified using Principal Component Analysis. Several machine learning algorithms, including Support Vector Machines (SVM), Random Forest, Gradient Boosting, and Artificial Neural Networks (ANN), were trained and validated to develop a TB recognition model. Results and Discussion: The ANN achieved the best performance, with an accuracy of 79%, sensitivity of 78%, specificity of 80%, and an AUC of 0.84. IoT integration enabled real-time data transfer and cloud-based visualization, demonstrating scalability and potential use in resource-limited settings. Conclusion: This portable AI-based breath analysis system offers a rapid, affordable, and non-invasive approach for early TB detection. With further validation, it might complement existing diagnostics and strengthen global TB elimination efforts.

Keywords: Artificial Intelligence, Breath Analysis, Early Diagnostic, Machine Learning, Tuberculosis

COMPARING GENOTYPE-GUIDED, PLATELET-FUNCTION-GUIDED, UNIVERSAL POTENT, AND UNIVERSAL CLOPIDOGREL ANTIPLATELET THERAPY STRATEGIES POST-PCI: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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Optimal P2Y12 inhibitor selection after percutaneous coronary intervention (PCI) is pivotal, yet high-quality evidence remains limited, creating uncertainty for routine practice. This paper synthesizes evidence comparing four post-PCI antiplatelet therapy strategies: genotype-guided (CYP2C19-directed), platelet-function-guided, universal potent P2Y12 inhibition, and universal clopidogrel. Comprehensive searches of three databases were conducted to identify eligible randomized controlled trials. Study quality was appraised using Cochrane RoB 2.0, while evidence certainty was assessed with the GRADE framework. A frequentist NMA was performed using a random-effects model. Interventions were compared using risk ratios (RRs) with 95% confidence intervals (CIs) for binary clinical outcomes (major adverse cardiovascular events, bleeding, and stent thrombosis) and mean differences (MDs) with 95% CIs for the continuous pharmacodynamic outcome of platelet reactivity. Cost outcomes, when reported, were synthesized narratively. The comparative performance of each intervention was summarized and ranked using the Surface Under the Cumulative Ranking Curve (SUCRA). Findings revealed a distinct hierarchy among antiplatelet therapy strategies. The universal potent P2Y12 inhibitor strategy consistently ranked highest for preventing ischemic events but was associated with a significantly increased risk of major bleeding. Conversely, the universal clopidogrel strategy demonstrated the most favorable safety profile for bleeding but the lowest ischemic efficacy. This analysis confirms that while universal potent and clopidogrel strategies represent extreme ends of the efficacy-safety spectrum, guided strategies bridge the gap by delivering the ischemic protection of potent therapy while reducing the risk of bleeding, demonstrating superior clinical benefit.

Keywords: CYP2C19, Genotype-Guided Therapy, P2Y12 Inhibitors, Percutaneous Coronary Intervention, Platelet Function Testing

Causal Inference Between Metabolic Traits and Ovarian Cancer Subtypes from Genome-Wide Association Data: A Mendelian Randomization Analysis

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Metabolic disorders have been linked to ovarian cancer risk, but the causality and subtype specificity remain unclear. This study applied a computational genetics approach using two-sample Mendelian randomization (MR) to identify potential causal effects of metabolic traits on distinct ovarian cancer histotypes. Genome-wide association summary statistics for adult female body mass index (BMI), fasting glucose, glycated hemoglobin (HbA1c), LDL, and HDL cholesterol were obtained from the IEU OpenGWAS database. Summary-level data for ovarian cancer subtypes (endometrioid, mucinous, clear cell) were analyzed as outcomes. MR analyses were conducted to assess causal relationships using inverse variance weighted, MR-Egger, weighted median, and weighted mode methods, with sensitivity tests for pleiotropy and heterogeneity. Higher BMI was causally associated with increased risk of endometrioid ovarian cancer (MR-Egger OR = 5.56, p = 0.0009; IVW OR = 1.65, p = 0.0056). Elevated fasting glucose increased the risk of mucinous ovarian cancer (OR = 2.10, p = 0.035), and higher HbA1c showed a positive association (OR = 1.32, p = 0.015). LDL cholesterol was modestly associated with mucinous ovarian cancer (OR = 1.25, p = 0.041). Interestingly, higher HDL cholesterol was also linked to increased risk of endometrioid (OR ≈ 1.27, p = 0.035) and clear cell ovarian cancers (OR = 1.20, p = 0.040). Our analysis revealed significant findings, highlighting distinct metabolic pathways contributing to ovarian cancer subtypes. These results utilize genetic epidemiology and computational biology approaches in uncovering mechanistic links between metabolism and oncogenesis, supporting future precision prevention strategies.

Keyword: Mendelian randomization, metabolic traits, ovarian cancer, causal interference, genome-wide association study

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