Innovative Therapeutic Platform for Minimally Invasive Management of Chronic Fatty Liver Disease

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Chronic liver disease represents a major global health burden and arises from multiple etiological factors, including viral hepatitis infections, chronic alcohol consumption, and metabolic dysfunction–associated fatty liver disease (MAFLD). These conditions trigger persistent hepatic inflammation, oxidative stress, and progressive fibrosis, ultimately disrupting the structural and functional integrity of the liver. To address this, HepatoRegen Spray, a novel minimally invasive biomaterial-based therapeutic platform designed to promote liver regeneration using a cell-free regenerative approach. The sprayable formulation integrates biocompatible hyaluronic acid and polydopamine with therapeutic exosomes to create a bio-adhesive system that rapidly crosslinks upon brief exposure to 405 nm light, forming a thin hydrogel layer directly on the injured tissue. This localized biomaterial interface enables sustained and controlled release of regenerative bioactive signals. Preclinical studies demonstrate significant improvements in liver regeneration, including restoration of tissue architecture, improvement in biochemical markers, enhanced liver microvasculature, and modulation of gut microbiota. Importantly, the platform is adaptable for delivery to internal organs accessible through laparoscopic procedures, expanding its translational potential across multiple regenerative medicine applications. The technology is protected by a published patent and has received funding approval from the Indian Council of Medical Research (ICMR) to support clinical trials in collaboration with DMIHER, pending regulatory clearance.

Genetic Landscape in Origin of Down Syndrome-Associated Acute Lymphoblastic Leukemia

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Down syndrome-associated acute lymphoblastic leukemia (DS-ALL) is a high-risk hematologic malignancy uniquely arising in children with trisomy 21, marked by a distinct mutational landscape and clinical behavior. Given the elevated leukemia risk in individuals with Down syndrome, this study systematically analyzes the mutational landscapes of DS-ALL and non-DS ALL to uncover shared and divergent pathogenic mechanisms. The analysis revealed 58 genes frequently mutated in DS-ALL, with *JAK2, IKZF1*, and *CDKN2A/B* identified as particularly significant. The prevalence of the *CRLF2* rearrangement, especially in association with *P2RY8*, was markedly higher in DS-ALL (29.55%) compared to non-DS ALL (1.5%). In contrast, non-DS ALL showed higher incidences of *IKZF1*, *PAX5*, and *CDKN2A/B* among the 596 genes identified. DS-ALL mutations were enriched in chromatin organization, STAT signaling, and B-cell differentiation, while non-DS ALL mutations predominantly affected lymphocyte activation, transcription regulation, and potassium channel complexes. JAK-STAT and leukemogenesis pathways highlighted in DS-ALL, whereas transcriptional misregulation dominated in non-DS ALL. Notably, Chromosome 9 emerged as a critical genomic hotspot, harboring multiple mutated genes, thereby challenging the conventionally held view that chromosome 21 alone mediates DS-related leukemogenesis. This study identified therapeutic targets, including *JAK2, KRAS*, and *EZH2,* which are being explored in hematologic malignancies, as well as novel targets such as *DNMT3A* and *IKZF1*. This study provides promising novel therapeutic targets for DS-ALL and non-DS ALL.

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Improving Nutrition with Microalgae

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Inadequate nutrition, either under- or over-nutrition, is an important global health problem, especially in children and older adults. One feasible solution is microalgae, the precursor of all terrestrial plants. Microalgae produce lipids (including omega-3 fatty acids), proteins, carbohydrates, pigments, and micronutrients and so can provide a suitable yet underutilised alternative for improving nutrition. The health benefits of nutrients derived from microalgae

have been identified, and they are suitable candidates for addressing nutritional issues in India. The advantages of microalgae cultivation in enclosed systems to reduce contamination include that cultivation does not need arable land or pesticides. Additionally, most species of microalgae are still unexplored, presenting options for further development. Further, the usefulness of microalgae for other purposes such as bioremediation and biofuels will increase the knowledge of these microorganisms, allowing the development of more efficient production of these microalgae as nutritional interventions. The potential benefits of microalgae-derived nutrients and opportunities for microalgae require incorporation into food products, so deriving benefits from microalgae requires a wide range of expertise.

Polycystic Ovary Syndrome Across India: Epidemiology, Clinical Phenotypes, and Associated Metabolic Disease

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Background: The global burden of polycystic ovary syndrome (PCOS) is substantial, yet India-specific data remain sparse. Existing Indian studies are hampered by methodological shortcomings, including small sample sizes, regional sampling bias, and inconsistent diagnostic criteria, leaving a critical gap in our understanding of PCOS at the national level.

Objectives: This study aimed to establish a nationally representative estimate of PCOS prevalence in India, characterize the full phenotypic spectrum of the condition, and quantify the burden of associated comorbidities.

Design, Setting, and Participants: In this cross-sectional study, 9,824 women aged 18–40 years were enrolled between November 2018 and July 2022, drawn from five geographic zones across India. Participants completed a validated screening questionnaire, sorting them into screen-positive and screen-negative groups. All underwent clinical evaluation, hormonal profiling, and ultrasound assessment. Women were subsequently classified as having criteria-defined PCOS (per NIH 1990, Rotterdam 2003, or AE-PCOS Society criteria), partial phenotypic PCOS (termed "pre-PCOS," encompassing isolated hyperandrogenism, oligomenorrhea, or polycystic ovarian morphology), or no diagnosis, with concurrent quantification of metabolic and related comorbidities.

Main Outcomes and Measures: Primary outcomes were PCOS prevalence and phenotype distribution among reproductive-age women in India, as well as the prevalence and magnitude of associated comorbidities.

Results: Of 8,993 enrolled women (mean age 29.5 ± 6.2 years), 196 had a prior PCOS diagnosis, 2,251 were screen-positive, and 6,546 were screen-negative. Screen-positive women were younger on average (28.1 ± 6.4 vs. 29.7 ± 6.1 years; $P < .001$) and had a marginally later age at menarche (13.2 ± 1.3 vs. 13.1 ± 1.2 years; $P < .001$). National PCOS prevalence estimates varied by diagnostic criteria: 7.2% (95% CI, 4.8%–10.8%) by NIH 1990 criteria, 19.6% (95% CI, 12.7%–29.2%) by Rotterdam 2003 criteria, and 13.6% (95% CI, 8.4%–21.6%) by AE-PCOS criteria. Among women meeting PCOS criteria, phenotype C ($n = 501$; 40.8%) and phenotype D ($n = 301$; 24.6%) were most prevalent. An additional 492 women met criteria for pre-PCOS, with isolated hyperandrogenism ($n = 257$), polycystic ovarian morphology ($n = 160$), or oligomenorrhea ($n = 75$). Metabolic comorbidities were common among the 1,224 women with PCOS: dyslipidemia (91.9%), obesity (43.2%), non-alcoholic fatty liver disease (32.9%), metabolic syndrome (24.9%), impaired glucose tolerance (9.1%), hypertension (8.3%), and type 2 diabetes (3.3%). The pre-PCOS group ($n = 492$) showed a similarly elevated metabolic burden, with dyslipidemia in 79.3%, non-alcoholic fatty liver disease in 33.1%, impaired glucose tolerance in 12.6%, metabolic

syndrome in 15.9%, hypertension in 5.3%, and diabetes in 1.4%.

Conclusions and Relevance: This nationwide cross-sectional study reveals a high prevalence of PCOS across reproductive-age women in India, with phenotype C representing the most common presentation. The overwhelming majority of affected women carry a significant metabolic burden, a finding that extends even to those with partial phenotypes. These results underscore the urgent need to incorporate PCOS screening and management into India's national health programs, and to design preventive strategies tailored to this population's specific phenotypic and metabolic profile. (Published in JAMA Network, 2024)

Spatial Transcriptomics reveal a BMP Signaling-dependent Gene regulatory network, highlighting Mfap4 as a key mediator of Radial migration during Cerebral cortex development

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The formation of the mammalian cerebral cortex, the seat of cognition, sensory processing, and motor control, relies on the coordinated proliferation, differentiation, and radial migration of neurons derived from neural precursors. Disruptions in these processes give rise to a spectrum of neuronal migration disorders (NMDs). Although, BMP signaling has been implicated in regulating cortical neuron migration, the downstream molecular mechanisms through which it exerts these effects remain unknown.

To delineate BMP-dependent transcriptional programs regulating neuronal migration during corticogenesis, we combined *in-utero* electroporation-mediated perturbation of the BMP pathway with GeoMx-spatial transcriptomic profiling. This integrated approach identified several classes of BMP-responsive genes with spatial and temporal expression patterns consistent with roles in the migration of cortical neurons. Four high-confidence candidates of diverse molecular categories were validated through *in-vivo* loss-of-function experiments, each demonstrating a critical role in radial migration.

Among these, *in-vivo* RNAi-mediated knockdown of Mfap4 (Microfibril-Associated Protein 4), an extracellular matrix–associated protein, caused a marked migration defect, with RNAi-electroporated cells accumulating in the ventricular and subventricular zones and exhibiting altered morphology. Immunohistochemical analyses revealed that Mfap4-deficient cells, although stalled in the lower cortical regions, had lost apical progenitor markers yet aberrantly retained expression of intermediate progenitor markers. These cells also failed to acquire any layer-specific neuronal identity, indicating a disruption in their progression from progenitor to migration-competent neuronal states. Together, these findings suggest that Mfap4 is required for the developmental transition that enables cells to exit the proliferative zones and initiate radial migration.

Together, these findings delineate a BMP-regulated gene network that governs radial migration in the developing cortex and elevate Mfap4 as a pivotal downstream effector, coupling extracellular matrix dynamics to BMP-driven neurogenic progression. This work advances our understanding of BMP signaling during corticogenesis and identifies new candidate genes with potential relevance to neuronal migration disorders.

New Molecular insights into Chondrocyte Proliferation and Differentiation during Limb Development

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Long bones form through endochondral ossification, where a transient cartilage (TC) template is progressively replaced by bone, while the adjacent articular cartilage (AC) is retained for life. These two contrasting populations originate from common progenitor cells and develop simultaneously in adjacent regions, requiring precise coordination of proliferation, differentiation, and cartilage segmentation. Any disruption to these events can lead to skeletal abnormalities. One such process is the regulation of hypertrophy in chondrocytes, which profoundly influences limb lengthening, as chondrocytes exit the cell cycle and enlarge up to 20-fold, eventually converting to bone. Although, we have achieved a good understanding of the major pathways involved, much remains unknown about the downstream molecules that execute these critical cellular changes, and a significant knowledge gap persists about how these signaling pathways function at the molecular level. Our study identifies two spatially restricted genes, Rgs2 and Klf4, which are expressed in both the TC and AC domains of the developing chick limb. Functional analyses using *in-ovo* electroporation reveal that the gain-of-function of either gene shortens limb length and reduces ossification by suppressing chondrocyte hypertrophy. Any perturbation in these genes arrests the cells at the pre-hypertrophic chondrocyte state, and also disrupts articular cartilage identity. Mechanistically, Rgs2 misexpression diminishes Ihh-positive pre-hypertrophic cells and reduces chondrocyte proliferation, consistent with properties of

hypertrophic and articular chondrocytes. Ex vivo tibio-tarsal organ cultures demonstrate that canonical WNT/β-catenin activation induces Rgs2, while Klf4 downregulates β-catenin activity to inhibit hypertrophic differentiation. Together, these findings establish Rgs2 and Klf4 as critical checkpoint regulators that integrate WNT, Hedgehog, and BMP pathways to coordinate the balance between transient and articular cartilage differentiation, providing new mechanistic insights into endochondral ossification and limb skeletal patterning.

Development of a Novel Inhibitor of Rac1, for the Prevention of Breast cancer Progression and Metastasis

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Keywords: Breast cancer; Inhibitor, Apoptosis; Rac1; Metastasis; Tumor

Introduction: Metastatic breast cancer is one of the leading causes of death, due to the dormancy of cancerous cells between the normal and metastatic stage. Thus, making it essential to target the molecular pathways which initiate the cell migration. During the early stages of cancer, the expression of Rac1 has been reported to higher and it remains the same throughout the metastatic pathway to regulate the formation of lamellipodia and filopodia. This study introduces a small peptide FGDWS based on the structure of Tiam1 binding site on Rac1.
Methods: The binding of peptide with Rac1 was verified by Surface plasmon resonance. The inhibition of Rac1 by the peptide and in combination with Doxorubicin (Dox) was assessed by MTT, anti-proliferative, cell migration, and apoptotic assay on breast cancer cell. Tumor regression experiment was done on swiss albino mice model.
Result: The peptide FDGWS showed strong interaction with Rac1 at Tiam1 binding sites with high binding energy by hydrogen bonds and hydrophobic interaction. The binding assay demonstrated dissociation constant KD 8.07 x 10^{-7} M. Substantial reduction of cell viability was observed with IC50 200 µm and 325 µm, in MCF-7 and MDA-MB-231, respectively. The cancer cell migration was highly reduced and higher regression in migration were obtained in synergy group with FGDWS and Dox. Peptide alone and with Dox induced apoptosis by activating caspase 3/7 and annexin V. Treatment of FGDWS on breast cancer cell lines reduced the expression of Rac1 protein and other downstream proteins (p38MAPK, phospho-p38MAPK LIMK1, phospho-LIMK1, Cofilin1, phospho-Cofilin1) compared to untreated cells. The tumor size reduced by the treatment of peptide and more reduced in combinatorial effect with Dox. Further, the level of above-mentioned proteins down regulated in blood and tumor tissues after the treatment compared to untreated mice.
Conclusion: FGDWS can be a potent and specific therapeutic agent against Rac1 for breast cancer without developing toxicity on normal cells. The combinatorial effect of FGDWS and Dox may lead to therapeutic benefits both by enhancing treatment efficacy and by avoiding undesirable side effects.

Agro-Waste Derived Biochar as a Sustainable Material for Environmental and Human Health Protection

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Keywords: Agro-waste, Biochar, Environmental remediation, Human health, Sustainable material

The environment has been severely harmed by rapid industrialisation and intensive farming practices, putting ecosystem integrity and human health at risk. Biochar, which is made from agricultural waste, is a sustainable, affordable, and adaptable material that can simultaneously address multiple issues. Biochar has a variety of functional groups, a large surface area, and porosity. It is produced by pyrolysing agricultural waste, such as wheat straw, rice husk, sugarcane bagasse, maize cob etc... Heavy metals, pesticides, drugs, microplastics, and harmful bacteria can all be effectively absorbed from soil and water systems thanks to these features. Biochar not only restores the ecosystem but also indirectly improves human health by lowering greenhouse gas emissions, improving soil quality, lowering pollution in the food chain, and lowering exposure to hazardous pollutants.

Effect of Microbiome modulation on the Neurodevelopmental Gene expression profile and the Associated Phenotypes in the *Drosophila melanogaster*

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The microbiome has a tremendous influence on human physiology, including nervous system development and brain function (*Mayer et al., 2014; Cryan and Dinan, 2012*). In this study, we show that the absence of microbiome in *Drosophila melanogaster* affects neurodevelopment and circadian regulation in both male and female flies (*Douglas, 2018*). Conventional flies with microbiome and axenic flies without microbiome were developed by rearing them on normal food and tetracycline treated food, respectively.

Gene expression analysis was performed using quantitative real time PCR on head tissues of male and female flies. The results showed significant sex specific changes in the expression of neurodevelopmental and circadian related genes in axenic flies when compared to conventional flies, indicating that microbiome plays an important role in regulating brain associated genes (*Mayer et al., 2014*). Along with molecular changes, axenic flies also displayed behavioral defects. A significant reduction in climbing ability was observed in axenic flies, suggesting impaired motor coordination and neuronal function. In addition, axenic flies were found to be highly susceptible to seizure assay, indicating altered neuronal excitability and compromised neural stability.

To understand the relevance of these findings to humans, human orthologs of the selected *Drosophila* genes were identified using OrthoDB. Functional annotation revealed that these orthologs are involved in synapse development, neuronal maturation and brain function, and their dysfunction is associated with neurodevelopmental disorders (*Cryan and Dinan, 2012*). Overall, these findings suggest that microbiome is essential for normal brain development and function. Any alteration in microbiome through diet, antibiotics or drugs may lead to defects in neurodevelopment and increase the risk of neurological disorders during critical early developmental stages (*Sharon et al., 2010*).

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Unravelling the Structural enigma of Type I and Type II Thioesterases in Pathological conditions

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Abnormal lipid metabolism is one of the hallmarks of cancer. Most cancers display upregulation of fatty acid synthesis to generate signalling molecules and energy. Thus, fatty acid synthase (FasN), the key enzyme responsible for fatty acid synthesis, has been regarded as a target for drug intervention in cancer. It's a type I enzyme, a dimer, comprising seven different domains: β-ketoacyl synthase, malonyl-acetyl-transferase and dehydratase, enol reductase, keto-acyl reductase, acyl carrier protein and thioesterase (TE I), which work in cooperation to maintain the fidelity for longer fatty acyl-chains. Apart from type I, there is also a type II thioesterase enzyme that regulates the length of fatty acid chains. The closed conformation of TE II facilitates its interaction with the ACP domain of FASN, promoting the release of shorter-length fatty acids (C8–C12), rather than the longer-chain fatty acids produced by FASN. However, the ability of TE II to compete with the endogenous TE I domain within the FASN mega-synthase for acyl substrates is a brain-teaser, as the cleavage should ideally be favoured by TE I based on proximity. Thus, the goal of the present study is to obtain structural insights into individual enzymes at the molecular level and to identify inhibitors specific to them using various biophysical tools. The study will advance our understanding of the molecular mechanisms underlying fatty acid biosynthesis regulation, with implications for both metabolic disorders and cancer therapy.

Nanoceria Capped Triazine-Based Brominated COFs: ^{13}C NMR-Validated Architectures with Enhanced Antibacterial Performance Against *S. aureus*

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This study presents the successful synthesis and characterization of triazine-based brominated covalent

organic frameworks (TbBr-COFs) and their cerium-modified hierarchical derivatives Ce-(TbBr-COF)-C and Ce-(TbBr-COF)-L. This was accomplished through a solvothermal reaction utilizing 2,4,6-tris(4-bromophenyl)-1,3,5-triazine (TBPT) and 1,4-dibromobenzene (DBB) in mesitylene/dioxane with acetic acid as a catalyst at 120 °C for 80 hours, followed by probe sonication and homogenization processes. Comprehensive spectroscopic and microscopic analyses confirmed their structural integrity, enhanced crystallinity, porosity, and chemical stability, with SEM and HRTEM revealing distinct morphological features: rod-like structures for TbBr-COF and flower-like hierarchical assemblies for the cerium-modified derivatives. UV-Vis spectroscopy demonstrated efficient cerium loading (91.11% after 64 hours), whereas FTIR and XRD validated framework synthesis and π-π stacking interactions. ^{13}C solid-state NMR demonstrated great purity (>90%) with no residual precursors, and a downfield shift of triazine carbons (171.7 ppm) showing the electron-withdrawing influence of bromine. The cerium-modified COFs exhibited enhanced antibacterial effectiveness against Staphylococcus aureus, with inhibition zones measuring 3.5 cm (control), 2.2 ± 1.5 cm (TbBr-COF), 3.1 ± 0.5 cm (CeO2-NP), 3.5 ± 0.6 cm [Ce-(TbBr-COF)-C], and 2.9 ± 0.4 cm [Ce-(TbBr-COF)-L]. The TbBr-COFs, distinguished by tunable porosity, high surface area, and metal incorporation capability, offer a versatile platform for drug delivery, antibacterial applications, and hybrid material synthesis.

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In-Silico Investigation of *Gloriosa superba* Derived Phytochemicals as Inducers of Immunogenic Cell Death (ICD) in Triple-Negative Breast Cancer

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Triple-Negative Breast Cancer (TNBC) remains one of the most aggressive malignancies to treat due to the lack of estrogen, progesterone, and HER2 receptors, which limits the efficacy of conventional hormonal therapies. Recent immunotherapy strategies have focused on inducing Immunogenic Cell Death (ICD), a pathway that not only kills cancer cells but also alerts the host immune system to the tumor's presence. This study explores the therapeutic potential of phytochemicals derived from *Gloriosa superba* (Kanthal), a native medicinal plant, as novel ICD inducers in TNBC.

Using a comprehensive *in-silico* approach, we screened bioactive compounds from *Gloriosa superba*—specifically targeting colchicine derivatives and gloriosine—against key molecular targets associated with the ICD pathway. Molecular docking studies were performed to evaluate binding affinities and interactions with DAMP (Damage-Associated Molecular Pattern) regulators. Furthermore, ADMET profiling was conducted to assess the drug-likeness and safety profile of the top-ranked candidates. Our preliminary results indicate that specific alkaloids within *Gloriosa superba* exhibit high binding affinity to ICD-related targets, suggesting a potential mechanism to reverse immune evasion in the tumor microenvironment. These findings propose *Gloriosa superba* as a promising source for developing next-generation phytopharmaceuticals.

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Transport of Biomolecules from Cross-linked Biopolymer-based solid emulsion gel, a Viable platform for sustained Drug release

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Emulsion gels composed of oil in water (o/w) emulsions stabilized by a viscous polymer matrix. These gels have emerged as a new class of biomaterials for controlled-release applications. This study presents the development of emulsion gels (EGs) consisting of drug-loaded vegetable oil droplets dispersed within biopolymer-based gels. The physical and drug release properties of the gels were characterized. The emulsion gels were crosslinked, which resulted in denser, more stable gel matrices with reduced swelling, whereas the un-crosslinked gels demonstrated increased swelling and were susceptible to degradation. Gels were investigated for in vitro pharmacokinetics and mathematical modeling. Overall, the emulsion gel matrices represent a viable system for sustained drug release for biomedical applications.

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Deciphering the Transcriptomic Landscape of Paclitaxel Resistance in Triple-Negative Breast Cancer

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Keywords: TNBC, Chemoresistance, RNA sequencing, Non-Coding RNA

Triple-negative breast cancer (TNBC) remains a clinical challenge due to the lack of estrogen, progesterone, and HER2 receptors, leaving systemic chemotherapy as the primary treatment. However, the rapid emergence of drug resistance frequently leads to treatment failure and poor prognosis. This resistance is driven by a complex network of biological adaptations, including immune escape, metabolic rewiring, and dysregulated DNA repair. Identifying the molecular determinants of survival under chemotherapy—specifically the interplay between coding and non-coding RNAs is essential for developing targeted strategies to overcome resistance and improve patient survival. Therefore, drug resistance serving as a critical barrier to successful clinical outcomes.

To decode the mechanisms underlying this therapeutic failure, we executed an integrative transcriptomic analysis drug-resistant cancer datasets. Pathway enrichment analysis was conducted to evaluate the biological function of commonly expressed genes. In this report, we identified 169 common gene in sensitive and drug-resistant cancer dataset that primarily enriched in complement system, pathways in cancer, inflammation. Further, survival analysis revealed that nine genes (*SDR16C5, PROSER-AS1, SOX21-AS1, LINC002608, CLDN1, CD82, CA3-AS1, NEURL1, AC010735.2*) were significantly associated with the prognosis of TNBC patients.

Our investigation found that expression of DEGs is show similar trend in Paclitaxel resistant TNBC cells by preforming RT-PCR. Among these we found that Gene X highly expressed in resistant cells, and it's reported as part of complement system. Therefore, Functional evaluation of these Gene X was performed using CRISPR-Cas9-mediated knockout in Paclitaxel resistant TNBC. These findings uncover the regulatory landscape of therapeutic failure and provide a roadmap for re-sensitizing TNBC to chemotherapy.

Ribosomal Translation as a Therapeutic Vulnerability: Functional Characterisation of a Novel Ribosome-Inactivating Protein

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Ribosome-inactivating proteins (RIPs) are enzymatic toxins with N-glycosidase activity that irreversibly depurinate the sarcin–ricin loop of 28S rRNA, thereby inactivating ribosomes and arresting protein synthesis, which makes them attractive candidates for anticancer immunotoxin development. In this study, we purified and functionally characterised a novel RIP from the bulbs of an ornamental plant and evaluated its translation-inhibitory

and cytotoxic potential in osteosarcoma cells. The protein was purified using chromatographic techniques, and its N-glycosidase activity was confirmed by denaturing urea-PAGE analysis of rRNA. Translational inhibition was quantified using a luminescence-based reporter assay in rabbit reticulocyte lysate, while cytotoxicity was assessed in U2OS osteosarcoma cells. The purified RIP displayed strong N-glycosidase activity, significantly inhibited protein translation, and induced a marked reduction in cancer cell viability. Furthermore, in silico modelling using AlphaFold 3.0 revealed stable hydrogen-bond interactions between the RIP and eukaryotic ribosomal RNA, supporting its RNA-binding capability. Collectively, these findings identify a previously unreported RIP with potent translation-inhibitory and anticancer properties, highlighting its potential as a candidate for future immunotoxin-based or targeted cancer therapeutic strategies.

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An In Silico Quest: Validating the Cardioprotective Efficacy of CQA Against the Hypoxia and Hyperglycemia stressors

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Key words: Cardiovascular disease, CQA, ADMET analysis, molecular docking, molecular dynamic simulation

The natural rhythm of the heart has become a global call for concern due to the alarming rise in cardiovascular disease (CVD) mortality, which has increased from 13.1 million deaths in 1990 to 19.2 million in 2023. Hypoxia and hyperglycaemia are major contributors to CVD pathogenesis, creating an urgent need for novel cardioprotective agents. This study explores the potential of a natural compound, CQA to mitigate these stressors through comprehensive *in-silico* analyses. Molecular docking was employed to evaluate its inhibitory potential against the prolyl hydroxylase domain 2 (PHD2) protein (PDB ID: 5L9B) using Discovery Studio and Auto Dock Vina. Pharmacokinetic, toxicity, and drug-likeness profiles were assessed via. SwissADME, ProTox 3.0, and pkCSM, while PASS analysis predicted its biological activity spectrum. To assess structural stability and interaction dynamics, molecular dynamics (MD) simulations were performed using GROMACS. The docking results revealed that CQA exhibited a binding energy of –6.8 kcal/mol, showing better interactions compared to standard drugs. ADMET and PASS predictions indicated favourable pharmacokinetics and safety, while MD simulations demonstrated enhanced stability of the ligand–protein complex relative to the native protein. Overall, the computational findings suggest that Caffeoylquinic acid possesses significant cardioprotective potential, warranting further *in-vitro* and *in-vivo* validation to advance its development as a promising therapeutic shield for preserving heart function.

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Plant Derived Nanovesicles: Isolation, Characterization and Biomedical Potential

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Plant derived exosome like nanovesicles have gained increasing interest as natural nanocarriers owing to their biocompatibility, stability and bioactive cargo. Medicinal plants known for their therapeutic properties, represent a valuable yet underexplored source of such nanovesicles. The present study aimed to isolate nanovesicles from a medicinal plant comprehensively characterize their physicochemical and biochemical properties, perform proteomic profiling, evaluate storage stability and assess their biomedical potential.

Nanovesicles were independently isolated from medicinal plant leaf material using polyethylene glycol precipitation and ultracentrifugation techniques. Particle size distribution and concentration were determined using nanoparticle tracking analysis (NTA), while surface charge and colloidal stability were assessed through zeta potential measurements. Morphological characterization and membrane integrity were examined using scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Protein content was quantified using Nanodrop spectrophotometry, and fourier transform infrared (FTIR) spectroscopy was employed to identify functional groups associated with proteins and other bioactive components. Proteomic profiling was conducted using liquid chromatography tandem mass spectrometry (LCMS/MS) to elucidate the protein cargo and functional diversity of the isolated nanovesicles.

Storage stability was evaluated under defined conditions by monitoring changes in physicochemical characteristics over time. Functional bioactivity was assessed using in vitro biochemical assays including antioxidant and antimicrobial assays. The isolated nanovesicles exhibited characteristic exosomes like stable physicochemical properties and diverse proteomic profiles associated with biological activity. Functional assays demonstrated notable antioxidant and antimicrobial potential.

In conclusion, this study highlights medicinal plants as a promising source of stable, bioactive nanovesicles and underscores their potential as natural nanoscale platforms for future therapeutic and biomedical applications.

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Alpha-Lipoic Acid Disrupts PI3K-Mediated Metabolic Reprogramming in Breast Cancer Stem Cell enriched 3D Spheroid Models

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Breast cancer stem cells (BCSCs) represent a therapy-resistant tumor subpopulation responsible for disease progression, metastasis, and recurrence. Maintenance of BCSCs is critically dependent on metabolic reprogramming and activation of oncogenic signaling pathways, particularly the PI3K/Akt/mTOR axis, which is frequently dysregulated in breast cancer due to PIK3CA mutations. Targeting this metabolic–signaling crosstalk represents a promising therapeutic strategy. In this study, we investigated the metabolic and signaling effects of the antioxidant alpha-lipoic acid (LA) in BCSCs using stem cell–enriched 3D spheroid models derived from MCF-7 and MDA-MB-231 breast cancer cell lines. In silico molecular docking demonstrated a direct interaction of LA with PI3K, suggesting

pathway-specific targeting. Metabolomic profiling revealed LA-induced metabolic reprogramming, characterized by significant alterations in central carbon and amino acid metabolism. In MCF-7 spheroids, LA induced up accumulation of 15 metabolites and down accumulation of 5 metabolites, whereas in MDA-MB-231 spheroids, 3 metabolites were up accumulated and 16 were down accumulated, indicating subtype-specific metabolic responses. Functionally, LA treatment significantly suppressed BCSC metabolic activity and enhanced chemosensitivity to doxorubicin, exhibiting a synergistic anti-tumor effect in 3D spheroids. Mechanistic analyses confirmed that LA modulates the PI3K/Akt/mTOR signaling pathway, leading to impaired cell survival and proliferative capacity. Collectively, our findings demonstrate that alpha-lipoic acid effectively targets PI3K-driven metabolic plasticity in BCSCs and potentiates chemotherapy response. These results support the therapeutic potential of LA as a metabolic adjuvant in combination strategies for breast cancer treatment.

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Diagnosis of Mild Hepatic Steatosis using Transient Elastography

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This study presents a detailed non- invasive diagnostic framework for detecting and classifying mild hepatic steatosis, also known as fatty liver disease, addresses the critical challenge of early identification in asymptomatic and at-risk individuals. Traditional ultrasound often fails to detect steatosis below 20-30% fat infiltration and is highly operator-dependent, while liver biopsy remains invasive, costly, and limited to sampling error. To overcome these limitations, the study proposes the integration of biochemical biomarker screening with quantitative elastography. The first component employs computing a Fatty Liver Index (FLI), derived from BMI, Triglycerides (TG), Gamma- Glutamyl Transferase (GGT) and waist circumference (WC), which collectively reflect early metabolic problems like lipid accumulation, insulin resistance and hepatocellular stress characteristic of mild steatosis. The paper reports on studies wherein individuals with intermediate or high FLI scores are subsequently evaluated using transient elastography combined with the Controlled Attenuation Parameter (CAP). Transient elastography measures liver stiffness through shear wave propagation to exclude the coexisting fibrosis, while CAP quantifies the hepatic fat content by analyzing the ultrasound attenuation and provides objective thresholds for grading steatosis severity. In addition to outlining this stepwise protocol, the thesis presents detailed insights into liver anatomy, metabolic functions, the pathophysiological continuum from the simple steatosis to fibrosis and cirrhosis, and global epidemiological trends highlighting the rising burden of NAFLD. By integrating the metabolic biomarkers with advanced imaging techniques, the study proposes an efficient three-step diagnostic pathway that enhances early detection, improves classification accuracy for mild steatosis, and supports timely lifestyle or therapeutic interventions, offering a practical and scalable alternative to invasive diagnostic procedures.

Development of Potent PARP-1 Inhibitors Targeting Glioma Through DNA Damage & ROS Generation

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Cancer is a major global threat, accounting for nearly 10 million deaths annually. Glioma is the most prevalent form of malignant primary brain tumors in adults. Glioblastoma multiforme (GBM) is the most aggressive subtype, among all gliomas, accounting for approximately 54%. The average survival time for patients suffering from this lethal cancer, if not under early medical attention, is up to 15-months. The current treatment for gliomas includes surgery, followed by radiotherapy and chemotherapy, but the prognosis remains dismal. Therefore, the overall picture about glioma is quite gloomy and needs lots more research support in terms of précised medication. Poly(ADP-ribose) polymerase-1 (PARP-1) is a key target for cancer therapy and is reported to be significantly elevated in glioma. To have a significant inhibitory effects of PARP-1 inhibitors (PARPi), it has to cross the hurdle of blood brain barriers. In this presentation, the design and synthesis of a series of fused hybrid heterocycles as new PARPi and their mode of action will be discussed. The most potent inhibitor induced apoptosis in glioma cells by promoting PARP cleavage, triggering DNA damage, and increasing ROS. The study resulted in a promising lead PARP-1 inhibitor targeting glioma, offering a new scaffold for future drug development.

Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Expression of Surfactant Protein D in Transgenic Lettuce and its Role in Modulation of Gut Microbiome

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Symbiotic microbiomes in gastrointestinal tract play a crucial role in maintaining homeostasis, thus any dysregulation will affect the intestinal-mucosal immune system. Surfactant protein D (SP-D), a multi-functional collagen containing C-type lectin (collectin) is well known for pathogen pattern recognition and immunomodulatory functions. Its potential role in regulating the gut microflora and mucosal immunity needs further investigation. Here, we study the impact of a recombinant fragment of SP-D (rfhSP-D) consisting of carbohydrate recognition domain on the modulation of gut microbiome. The research explores the development of transgenic lettuce expressing rfhSP-D and examines its potential as an immunomodulator of mucosal immunity. The preliminary work involved optimizing bacterial expression of rfhSP-D using *E. coli* BL21 DE3 PLysS, purification and characterization of the proteins. rfhSP-D will be delivered sub-lingually and their effect on gut microbial alterations will be assessed using high-throughput sequencing coupled with transcriptomic analysis of fecal pellets. Gut-associated lymphoid tissues will be analyzed for mucosal immune profiling to quantify the pro-inflammatory T cell subsets. Oral delivery of SP-D has the potential to shape host-microbiome interaction and promote mucosal immunity.

Immunomodulatory Role of Surfactant Protein D in Particulate Matter interaction with Lung Epithelium

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Particulate matter (PM) in air pollution is a major environmental risk factor for respiratory morbidity, largely due to its ability to dysregulate inflammatory responses in the lung epithelial cells. Pulmonary Surfactant protein D (SP-D), a collagen containing C-type lectin called collectin expressed in the pulmonary epithelium, plays a critical role in innate immune defense and homeostasis in the lung. However, its immunomodulatory role in PM-induced epithelial inflammation remains unclear.

In this study, we investigated the effects of a recombinant form of human SP-D, composed of homotrimeric neck and carbohydrate recognition domain (rfhSP-D) on PM induced inflammatory responses in lung epithelial cells such as BEAS 2B. Exposure to PM resulted in changes in cellular morphology, acquiring epithelial-to-mesenchymal transition (EMT)- like features. The effect of PM on BEAS-2B cells in terms of increased pro-inflammatory cytokine production, and activation of inflammatory signaling pathways, its attenuation with rfhSP-D as evidenced by reduced expression of key cytokines and chemokines, modulation of intracellular signaling cascades, and preservation of epithelial integrity, will be presented.

Our study is aimed at delineating the protective immunomodulatory role of rfhSP-D against PM-induced epithelial inflammation. This shift has the potential to validate therapeutic role for rfhSP-D or SP-D–based interventions in mitigating air pollution-associated lung diseases.

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Optical characterization of serum sample of breast cancer patients using Fourier Transform Infrared (FTIR) Spectroscopy

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Breast cancer is the commonest cancer and leading cause of cancer death among the women. Early diagnosis and treatment can significantly improve the patient outcome. Therefore, a fast and early diagnosis is a need of the time. We analyze in our previous work that the intensity of fluorescence in case of breast cancer patients is high as compared to normal tissue. It means some molecular changes should be there when cancer cells start developing in the normal tissue. Those molecular changes can be detected by Fourier Transform Infrared (FTIR) Spectroscopy. Fourier transform infrared (FTIR) spectroscopy is a non-invasive diagnostic tool that can provide valuable information on the molecular composition of biological samples. Infrared spectroscopy can distinguished between normal and cancer tissue at various levels of malignancies, especially to detect cancer at an early stage. FTIR looks at all molecules present in a cell, specific signature of tumour subtype can involve spectral features not only from proteins or DNA/RNA but also from any metabolic present. FTIR spectroscopy is not only able to detect and quantify but also distinguish between the different mechanisms of action. The main advantages of the technique are the high information content of IR spectrum. If successful, this study could lead to the development of FTIR spectroscopy as a non-invasive, rapid, and cost-effective diagnostic tool for breast cancer.

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Neurotoxicity effect of 2.4 GHz Electromagnetic Radiation on inducing oxidative stress causing Parkinson Disease: An in vitro study using SH-SY5Y cell line

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Background: The ubiquity of wireless devices emitting 2.4 GHz electromagnetic radiation (EMR) has raised concerns regarding its biological impact. Oxidative stress is a known driver of Parkinson's disease (PD), yet the specific role of EMR in inducing PD-like neurodegeneration remains under active investigation.

Methods: SH-SY5Y neuroblastoma cells were divided into control, Rotenone-treated (positive PD control), and EMR-exposed groups (8, 12, 24, and 48 hours). Neurotoxicity was measured via electrochemical detection of dopamine. Cellular health was evaluated through intracellular calcium (Ca2+), Reactive Oxygen Species (ROS), Mitochondrial Membrane Potential (MMP), and lipid peroxidation. Cell death mechanisms were analyzed using Annexin V/PI flow cytometry, while genotoxicity was assessed via COMET assay.

Results: EMR exposure and mimicking the rotenone-induced phenotype resulted that reduced dopamine levels. Oxidative stress markers (ROS and lipid peroxidation) peaked at 8 hours before shifting toward irreversible cellular damage. Conversely, Ca2+ accumulation and mitochondrial dysfunction with prolonged exposure (12–48 hours). Flowcytometry results have shown that early apoptosis at 8 hours to late apoptosis and necrosis at later stages. Genotoxicity, evidenced by DNA fragmentation in the COMET assay, increased significantly with exposure duration.

Conclusion: 2.4 GHz EMR exposure induce neuronal integrity by inducing oxidative stress, calcium overload, and mitochondrial failure. The observed progression to necrosis and loss of dopamine highlight the potential effect of EMR posing it as a risk factor for neurodegenerative conditions such as Parkinson's disease.

Towards investigating the Anticancer Role of Gut microbiota-derived Metabolites

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As per recent research reports, gut microbiota-derived metabolites such as indoxyl sulfate[1], inosine etc. possess selective anticancer effect on cancer cells. But the majority of gut microbial metabolites have not been screened for their anti-tumor activities nor underlying mechanism have been deciphered for developing therapeutic intervention for cancer management. In the present study, we investigated anti-tumor activity of three gut microbiota-derived metabolites, 4-ethylphenyl sulfate (4EPS)[2], indoxyl sulfate (IndS), and p-Cresyl Sulfate (pCS) on colon cancer cells. Using HCT-116 colon cancer cells, in-vitro cell-based assays were done that demonstrated 4EPS, IndS and pCS can reduce cell proliferation, cell viability and ATP content in dose and time dependent manner. Cell morphology was found to be distorted at concentrations, 2.5 mM, 5 mM and 10mM. HCT-116 cells also showed a decrease in colony formation when exposed to 2.5 mM, 5 mM and 10mM of 4EPS, IndS and pCS. These metabolites enhanced the apoptosis and ROS production as compared to control cells. Cell cycle assay showed the arrest at G2/M phase for 4EPS, IndS and pCS. An animal study was also conducted using balb/c mice to demonstrate the selective deleterious effect of indoxyl sulfate on cancer cells while sparing normal colonic cells. IndS did not cause any harm or inflammation in normal colonic cells of balb/c mice, hence, it can be considered safe for use as an anticancer agent and may have implications in future applications for colon cancer treatment. This warrants further mechanistic investigations in this direction.

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Association between Metformin and Vitamin B 12 levels in patients newly Diagnosed with Type 2 Diabetes in Tertiary Care hospital Ratlam

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Keywords: Type 2 Diabetes Mellitus, Metformin, Vitamin B12, Drug-nutrient interaction.

Metformin is the first-line pharmacological therapy for type 2 diabetes mellitus (T2DM) and is used by over 120 million patients worldwide. Although long-term metformin use is known to impair vitamin B12 absorption, early changes in vitamin B12 levels after treatment initiation are less well documented. This report highlights a newly diagnosed T2DM patient at a tertiary care hospital in Ratlam who demonstrated an early reduction in serum vitamin B12 levels after starting metformin treatment. This study highlights the importance of early monitoring of vitamin B12 levels in patients initiated on metformin.

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The future of Alzheimer's disease Therapeutics through LOX as blood-based Biomarkers

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Molecular changes associated with Alzheimer's disease (AD) appear several years before clinical symptoms emerge. Recent research has highlighted that the oxidative damage and prolonged inflammation are the earliest

events in Alzheimer's Disease. The oxidative modifications are closely associated with inflammatory molecules. It is necessary to explore these two pathways with AD pathophysiology and targeted for therapeutic intervention. Neuroinflammation, triggered by Lipoxygenase (LOX), contributes to Alzheimer's Disease (AD) progression. Overexpression of LOX-5 in patients with AD serum high-lights its role. This study assessed the efficacy of the LOX- inhibitor- peptide YWCS in an AD rat model induced by Aβ25–35 injection. Cognitive tests, magnetic resonance imaging (MRI) scans, and molecular analyses were conducted. YWCS treatment significantly improved cognitive function, as evidenced by improved performance in the open -field, novel object recognition, elevated plus maze, and Morris water maze tests. MRI scans revealed hippocampal shrinkage in AD rats and no changes were observed from YWCS treatment. Serum LOX levels were elevated in AD rats and significantly decreased after YWCS treatment, aligning with previous findings in human AD patients and AD cell models. YWCS offered improvements in behavioral and inflammatory marker regulation and also prevented progression of the disease, as shown by MRI results. These results suggest that YWCS, by targeting LOX, has the potential to prevent neuroinflammation and poor cognitive dysfunction related to AD pathogenesis, with significant translational potential.

Gut-Derived Metabolites Trigger Oxidative Stress in Kidney Cells: A Protective Intervention Using *Sorghum bicolor Seed extract*

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Background- Diabetic kidney disease is a leading cause of end-stage renal disease, with limited tools for early detection. Gut microbiota-derived metabolites may contribute to disease progression; however, their diagnostic potential and mechanistic impact on renal cells remain unclear. This study aims to identify GC–MS-derived microbial metabolites, evaluate their role in inducing oxidative stress, and assess the protective effects of *Sorghum bicolor* extract.

Methodology- A total of 30 Urine and 30 stool samples from healthy, T2DM, and DKD groups were analyzed using GC–MS to identify differential metabolites. Statistical analysis, including ANOVA and ROC curve analysis, was performed to assess diagnostic potential, while box plots were used to visualize group-wise variations. Selected metabolites (HIVA, HPA, ICAL, SA, and PA) were evaluated in HEK-293 cells. Cytotoxicity was assessed using the MTT assay to determine IC_{50} values, while Sorghum bicolor extract was evaluated for EC_{50}. An IC_{30} dose of metabolites was used to induce sub-lethal stress, followed by co-treatment with EC_{50} of Sorghum bicolor. Intracellular ROS levels were measured using the DCFH-DA assay.

Results- GC–MS analysis revealed distinct metabolite profiles across study groups. Selected metabolites showed significant differences with strong discriminatory ability in ROC analysis, supported by box plot distributions. In vitro studies demonstrated that metabolites significantly reduced cell viability and increased ROS levels in HEK-293 cells. Co-treatment with Sorghum bicolor extract significantly restored cell viability and reduced ROS generation.

Conclusion GC–MS-identified microbial metabolites may serve as potential biomarkers for DKD and contribute to oxidative stress–mediated renal damage. Sorghum bicolor exhibits protective effects by attenuating ROS, highlighting its potential as a natural therapeutic strategy.

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Potential association of Sickle cell disease Genotypes (SS, AS, Aβ Thalassemia) with ABO Blood groups: In Indian population

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Keywords: Sickle cell disease, ABO blood group, hemoglobinopathies, RDW, anemia, India

Sickle cell disease (SCD) exhibits marked clinical and hematological heterogeneity influenced by genetic and biological modifiers. The ABO blood group system has been

implicated in vascular and thrombotic pathways relevant to SCD pathophysiology; however, data exploring its association with SCD genotypes and hematological severity in the Indian population remains limited.

The association between SCD genotypes (HbSS, HbAS, and sickle β-thalassemia), ABO blood group distribution, demographic variables, and hematological parameters in patients attending a tertiary care center in central India was evaluated. This hospital-based cross-sectional study included 53 confirmed hemoglobinopathy patients identified from 500 screened individuals. Diagnosis and genotype classification were performed using high-performance liquid chromatography (HPLC). ABO and Rh blood grouping was determined by standard serological methods. Complete blood count parameters were analyzed, and correlations between hematological indices, blood groups, and disease phenotypes were assessed using Pearson's and Spearman's correlation tests.

HbSS was the predominant genotype (54.7%), followed by HbAS (30.1%) and compound heterozygous states (13.2%). Blood group O was most prevalent (37.7%) and significantly overrepresented among SCD patients compared to the general population. Individuals with blood group O demonstrated the lowest mean hemoglobin levels and highest red cell distribution width (RDW), indicating more severe anemia and greater anisocytosis. A strong inverse correlation was observed between RDW and hemoglobin ($r = -0.548$, $p < 0.001$), particularly pronounced in blood group O patients ($r = -0.723$, $p < 0.001$). Hematological indices such as MCV, MCH, and PCV varied significantly across genotypes, reflecting phenotype-specific disease severity. ABO blood group, particularly blood group O, is associated with greater hematological severity in sickle cell disease within this Indian cohort. Integration of ABO phenotype with routine hematological parameters may aid in risk stratification and personalized management of SCD. Larger population-based studies are warranted to validate these findings and elucidate underlying mechanisms.

Integrated multiomics approaches for identification of pathogenic variants involved in Autism Spectrum Disorders

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Characterisation of a vast array of genomic variations is crucial for understanding their role in human health and disease. Integrated multiomics approaches explore the potential effects of different genomic variants on gene function. Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition with a strong genetic basis and marked clinical heterogeneity. Integrating gene-level information with brain transcriptomic data has provided critical insights into the spatial and temporal patterns of gene expression during brain development. Therefore, unravelling the tissue-specific variants of genes involved in ASD is essential. ASD-associated score 1 genes were selected from the SFARI gene database and human brain transcriptomic data were obtained from the GTEx portal. These genes were analyzed to identify brain-specific isoforms. Further, the selected genes were analysed using in silico pathogenicity prediction tools, and protein-protein interactions were analysed using the STRING database. Out of 65 genes analyzed, 55 genes showed differences in exon count. Seven genes, *CASZ1*, *MYT1*, *NEXMIF*, *NSD1*, *PHF12*, *POGZ*, and *ZBTB21* showed exon-splitting events. Exon addition was seen in the *EBF3* and *KMT2E* genes. Only *FOXG1* matched its brain transcript, with a single exon. STRING network revealed significant protein-protein interactions. A nonsynonymous variant resulted in an amino acid substitution at a conserved residue, potentially affecting protein function. These approaches provide a strong framework for understanding the molecular mechanisms underlying ASD, which supports better diagnostic and therapeutic strategies. The implications of these findings will be presented and discussed.

Exploring a natural meroterpenoid as an HSP90-Targeting Lead Against Triple-Negative Breast Cancer: *in vitro* and *in-slico* approaches

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Psoralea corylifolia holds a prominent position in traditional herbal medicine. Bakuchiol, the principal phytoconstituent present in the seeds of *P. corylifolia*, significantly contributes to the medicinal properties of the plant. The present study aims to investigate the potential of bakuchiol in mitigating triple-negative breast cancer (TNBC) by targeting heat shock protein 90 (HSP90), a pivotal molecular chaperone implicated in cancer cell growth and progression. The study has employed a multi-approach strategy, by combining *in-silico* (Network pharmacology, molecular docking, molecular dynamics simulation), cell-free

assay (N-terminal HSP90 binding activity assay), and *in-vitro* methodologies, to explore its anticancer activities against TNBC and to elucidate HSP90 as a target of bakuchiol, using a HSP90-inhibitor radicicol as a reference. The Chou-Talalay combination index method was employed to determine its synergistic potential. Bakuchiol showed preferential cytotoxicity on MDA-MB-231 cells, with minimal impact on non-cancerous cells HEK-293, demonstrating a favourable selectivity index. *In-silico* studies identified HSP90 as a prime target via. which bakuchiol exhibits its anticancer activity, and the competitive binding assay established it as a N-terminal HSP90 inhibitor. Detailed *in-vitro* studies further highlighted the anti-proliferative, pro-apoptotic, and anti-metastatic role of bakuchiol, with radicicol serving as a control to verify HSP90-mediated activity. Moreover, bakuchiol was also found to exhibit a synergistic effect against TNBC cells in association with the standard chemotherapeutic drug doxorubicin, thereby enhancing its therapeutic efficacy. These findings highlight bakuchiol as a promising HSP90-targeting natural compound with potential therapeutic benefit against TNBC, therefore making it a crucial lead for further research.

Development of a disposable electrochemical DNA biosensor for simultaneous detection of *Neisseria gonorrhoeae, Mycoplasma genitalium* and *Chlamydia trachomatis*

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Keywords: *Neisseria gonorrhoeae, Mycoplasma genitalium, Chlamydia trachomatis,* Electrochemical DNA sensor, Point-of-care testing (PoCT), *mgpC, fitA, hctA*

Neisseria gonorrhoeae (NG), *Mycoplasma genitalium* (MG), and *Chlamydia trachomatis* (CT) are major sexually transmitted infections (STIs) with overlapping clinical symptoms and increasing antibiotic resistance, emphasizing the urgent need for a rapid, affordable, and highly specific platform for their simultaneous detection. In this study, we developed a portable electrochemical DNA biosensor functionalized with amine-labeled ssDNA probes for simultaneous detection of three bacterial STI pathogens. The AuNPs@GQDs-based electrode targets the *fitA* gene of NG, the MXene@PPy-based electrode targets the *mgpC* gene of MG, and the Fe_3O_4-based electrode targets the *hctA* gene of CT, enabling selective and sensitive multiplex detection. The synthesized nanocomposites were thoroughly characterized using UV–Vis spectroscopy, FTIR, fluorometry, particle size analysis, zeta potential measurements, and transmission electron microscopy (TEM), confirming their successful synthesis and probe functionalization. Uniform deposition of the nanocomposites and immobilization of ssDNA probes onto the screen-printed paper electrode (SPPE) surface were further verified by scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX), and FTIR analysis. Electrochemical characterization using cyclic voltammetry (CV), differential pulse voltammetry (DPV), and electrochemical impedance spectroscopy (EIS) demonstrated excellent sensor performance. The MG reverse complementary DNA sensor exhibited a sensitivity of 4,199.8 μA/mm^2/ng with a detection limit of 11 pg/μL. The *FitA* based NG DNA sensor achieved a sensitivity of 16,333.9 μA/mm^2/ng and an ultralow detection limit of 0.73 fg/μL. Meanwhile, the CT-targeted DNA sensor demonstrated enhanced sensitivity and achieving the LOD of picogram range. The biosensor displayed outstanding selectivity and specificity, successfully discriminating target DNA sequences from non-target bacterial DNA and mismatched oligonucleotides. Clinical validation using cervical swab samples confirmed the sensor's diagnostic robustness and reproducibility for simultaneous detection of NG, MG, and CT. Overall, the developed biosensing platform offers a rapid, portable, and highly sensitive diagnostic solution for multiplex STI detection, exhibiting excellent stability, reproducibility, and strong potential for next-generation point-of-care diagnostics.

Nano-bilosomal system for improved lutein uptake in the plasma and brain of aged Swiss Albino mice

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Lutein is a highly potent antioxidant in humans linked to the prevention of major eye and brain disorders. Oral supplementation is a major need for the hour to ensure adequate lutein consumption to prevent the onset of degenerative diseases. The objective of this study was to develop a formulation containing lutein which can enhance its absorption and bioavailability. Lutein loaded nano-bilosomes (LNL) were prepared by dissolving lutein with lipids in chloroform and evaporating the solvent by thin film hydration method, followed by hydration with bile solution to ensure a bilayer formation. The characterization

was done by DLS and TEM. *In-vivo* bioavailability and brain biodistribution was done using male Swiss albino mice where the mice were starved for 12h prior to oral administration of control (plain lutein) and LNL at a dose of 10 mg/kg b.w. Blood was drawn from the orbital plexus and plasma was separated by centrifugation followed by sacrificing the animal at different time points (n=6; total 48 mice). Lutein extraction from both plasma and brain homogenates was done by solvent extraction method and lutein was estimated by HPLC. The LNL size was 125.9, and zeta potential was -64.3 as estimated by DLS method and found to be spheroid with the vesicle size of 30-50 nm. Upon *in-vivo* evaluation, LNL administration significantly increased the plasma lutein concentration and accumulation in the brain compared to free lutein indicating enhanced intestinal absorption. Thus, the developed LNL showed significant potential in improving the bioavailability of orally consumed lutein.

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Alteration in Molecular dynamics in Microglia signature Genes leads to Neuroinflammation in Mice

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Keywords: Brain, Neuroinflammation, Microglia, Olfml3, Tmem119

Microglia are innate immune cells in the brain that play a vital role in regulating neuroinflammation-driven neurological disorders. Olfml3 and Tmem119 have been identified as microglia signature genes whose expression has been shown to alter during neurodegenerative diseases. However, the possible roles of Olfml3 and Tmem119, as well as their potential involvement in microglia-mediated neuroinflammation, remain unclear. Interacting partners of Olfml3 and Tmem119 were found to be microglia-specific proteins, including Iba1, Fcrls, P2RY12, Sall1, and Siglec-H. Molecular docking and MD simulation revealed stable physical interactions between Olfml3, Tmem119, and Iba1. Levels of Olfml3, Tmem119, and Iba1 increased during neuroinflammation. Silencing *Olfml3* and *Tmem119* with siRNA reduced *Iba1* expression. Inhibiting microglial activation significantly increased Tmem119 expression, downregulated Olfml3 and Iba1, and improved behavioural deficits in neuroinflammatory mice. Results highlight the crosstalk between microglia signature genes in regulating microglia functions in the management of neuroinflammation.

Acknowledgements: Financial support from the Indian Council of Medical Research (ICMR) and Institution of Eminence (IoE), University of Delhi, is gratefully acknowledged.

A Safety-by-Design Approach Yields a Thioridazine-Derived IKKβ Inhibitor with Reduced hERG Affinity for Inflammatory Disease Therapy

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The development of anti-inflammatory therapeutics is often compromised by off-target toxicities, with cardiotoxicity resulting from the inhibition of the human ether-a-go-go-related gene (hERG) channel being the primary cause of drug failure. Thioridazine, a well-established antipsychotic, potently also inhibits IκB kinase β (IKKβ) and exhibits anti-inflammatory effects; however, its clinical application is limited due to significant hERG blockade and the associated risk of fatal arrhythmias. The challenge lies in preserving the beneficial pharmacological properties of TDZ, while reducing its cardiotoxicity. A safety-by-design strategy was employed for the rational redesign of thioridazine. A computational library of derivatives was generated and screened using molecular docking

and dynamic simulations. Candidate molecules were experimentally evaluated through patch-clamp assays (hERG inhibition), western blotting, confocal microscopy (IKKβ phosphorylation, IκBα stability, p65 translocation), qRT-PCR (pro-inflammatory cytokine expression), and cytotoxicity was assessed in RAW 264.7 macrophages. The optimized derivative, TDZ-D2 {10-(2-oxo-2-pyrrolidin-1-ylethyl) acridin-9-one}, exhibited significantly reduced hERG inhibition (13 ± 4% compared to 79 ± 3% for thioridazine) while maintaining a strong IKKβ inhibitory activity. In macrophages, TDZ-D2 stabilized IκBα, inhibited NF-κB p65 nuclear translocation, decreased IKKβ phosphorylation, and suppressed the expression of TNFα, IL-1β, and IL-6. Cytotoxicity assays confirmed favorable tolerability at concentrations below 50 µM. By transforming thioridazine into a safer scaffold, we demonstrated a novel ligand-based optimization strategy to mitigate cardiotoxic liabilities while preserving its anti-inflammatory efficacy. TDZ-D2 emerges as a promising therapeutic lead, and this safety-by-design approach offers a generalizable route for repurposing bioactive but clinically limited molecules.

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Carvacrol Suppresses Benzo(a)pyrene-Induced Lung Tumorigenesis by Regulating Cell Proliferation and Apoptosis in Mice

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Keywords: Benzo(a)pyrene; lung cancer; Carvacrol; cell proliferation; apoptosis; cell cycle

Objective: Lung cancer accounts for the highest incidence and mortality among all cancers worldwide, representing a major global health burden despite advances in prevention and treatment strategies. Carvacrol, a naturally occurring monoterpenoid phenol found in essential oils of oregano and thyme, has attracted attention for its pharmacological potential. The present study aimed to evaluate the anticancer efficacy of carvacrol against benzo(a)pyrene (B(a)P)-induced lung carcinogenesis in Swiss albino mice.

Methods: Lung cancer was induced by administering B(a)P (50 mg/kg body weight) twice weekly for four consecutive weeks, followed by an experimental period of 20 weeks. Carvacrol was supplemented to assess its chemopreventive potential.

Results: Carvacrol supplementation significantly suppressed lung tumor development, as evidenced by reduced serum levels of carcinoembryonic antigen (CEA) and neuron-specific enolase (NSE). Carvacrol treatment normalized cytochrome P450 (CYP450) enzyme activity, attenuated abnormal cell proliferation, and induced apoptosis through modulation of Bax, Bcl-2, and caspase-3 expression. Histopathological evaluation demonstrated preservation of lung architecture, while TEM analysis confirmed reduced cellular and mitochondrial damage in treated mice.

Conclusion: These findings demonstrate that carvacrol effectively inhibits B(a)P-induced lung carcinogenesis by regulating tumor burden, xenobiotic metabolism, cell proliferation, and apoptotic pathways, supported by histopathological and ultrastructural evidence, highlighting its potential as a chemopreventive agent.

From plant extract to wound repair: green silver nanoparticles against MDR-ESKAPE pathogens

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The escalating burden of multidrug-resistant (MDR) ESKAPE pathogens in wound infections underscores the urgent need for therapeutic strategies capable of overcoming biofilm-mediated persistence while simultaneously promoting tissue repair. In this study, silver nanoparticles (AgNPs) were green-synthesized using *Clerodendrum serratum* leaf extract and further modified by polyethylene glycol to obtain PEG-AgNPs, and their antibacterial, anti-biofilm, and wound healing potential was systematically investigated. Physicochemical characterization confirmed the formation of stable, crystalline nanoparticles, with PEGylation enhancing surface functionality and colloidal stability. Antibacterial evaluation against MDR ESKAPE pathogens demonstrated markedly improved efficacy of

PEG-AgNPs, exhibiting minimum inhibitory concentration (MIC) values for uncoated AgNPs. Time-kill kinetic studies revealed rapid bactericidal activity, while mechanistic investigations indicated disruption of bacterial membrane integrity leading to cytoplasmic leakage as a key mode of action. Both nano-formulations significantly inhibited biofilm formation, with pronounced effects against the *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, major contributors to chronic and non-healing wound infections. LC-MS analysis of *C. serratum* leaf extract identified pectolinarigenin and luteolin as major bioactive phytoconstituents, and molecular docking studies supported their potential involvement in targeting biofilm-associated regulatory proteins, suggesting a synergistic role alongside silver-mediated antibacterial effects. Furthermore, topical gel formulations incorporating the nanoparticles significantly accelerated wound closure in both uninfected and MDR pathogen-infected wound models. This study highlights phytogenic silver nano-formulations as multifunctional nanotherapeutic systems with strong potential for managing MDR biofilm-associated wound infections while promoting effective tissue regeneration.

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Preparation and properties identification of Nanocomposite materials utilizing Organic and inorganic Nanomaterials

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Keywords: Hybrid system; nanocomposite; synergistic effect.

The current status of advanced materials demonstrates their ability to meet emerging sustainability demands. This is largely attributed to their inherent physicochemical properties, which allow each material to exhibit its characteristic functionality when used individually. However, recent research has increasingly focused on the development of nanocomposites by integrating two or more nanomaterials. Such hybrid systems not only enhance the intrinsic properties of the components but also significantly improve the overall efficiency and performance of the resulting composite. In this context, organic–inorganic nanomaterial combinations have gained considerable attention. Zinc oxide, as an inorganic nanomaterial, is widely applied across multiple sectors due to its diverse functional attributes. Similarly, orange peel powder and zein, as organic and biocompatible materials, have been utilized in applications including adsorption, food packaging, and biomedical systems. The present study investigates a composite developed from these organic and inorganic nanomaterials. The structural, chemical, and thermal properties of the composite were characterized using XRD, Raman spectroscopy, FTIR, SEM, and TGA. The findings indicate that the resulting hybrid material holds strong potential with synergistic effect for applications in the food, medicinal, packaging, and several other areas.

One Scaffold, Two Battles: Benzothiazole Derivatives Targeting Breast Cancer and Resistant Bacteria

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The urgent need for therapeutics capable of addressing cancer and microbial resistance simultaneously has directed attention toward privileged heterocyclic scaffolds such as benzothiazole. In the present study, a series of structurally diverse benzothiazole derivatives was rationally designed and synthesized to explore their potential as multifunctional bioactive agents. The synthesized compounds were structurally confirmed using FT-IR, NMR, and mass spectrometric techniques, ensuring their chemical integrity and purity. Biological evaluation commenced with screening against human breast cancer cell lines MCF-7 and MDA-MB-231, representing estrogen receptor-positive and triple-negative breast cancer models, respectively. From the library of best analogues, two molecules emerged as lead candidates, exhibiting pronounced antiproliferative

activity against both cell lines. To elucidate the molecular basis of this activity, *in-silico* molecular docking studies were performed against key breast cancer targets, estrogen receptor alpha (ERα) and human epidermal growth factor receptor 2 (HER2). The lead compounds demonstrated stable binding conformations and favorable interactions within the active sites of both targets. These findings were further supported by mechanistic investigations, which revealed that the lead compound induces apoptosis and cell-cycle arrest, confirming a target-driven anticancer mechanism. In parallel, the synthesized derivatives were evaluated for antimicrobial activity, where two compounds from the series showed significant inhibitory effects against Gram-negative bacterial strains, highlighting their potential to address intrinsically resistant pathogens. Based on these encouraging outcomes, the lead compounds were further assessed for anti-inflammatory, analgesic, and antioxidant activities, demonstrating significant efficacy in established experimental models. In conclusion, this integrated *in silico*, *in vitro*, and *in vivo* investigation identifies benzothiazole derivatives as promising multifunctional lead candidates for future anticancer and anti-infective drug development.

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Exploring the Molecular Drivers of Gender Dimorphism in Anemia of Inflammation: Findings from a Rodent Model

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Introduction: Anemia of Inflammation (AI) is the second most prevalent cause of anemia worldwide and is linked to chronic infections and malignancies. AI arises out of inflammation-driven abnormal iron sequestration and reduced iron availability for erythropoiesis. Immune-activated IL-6 induces hepatic hormone hepcidin, which in turn causes degradation of iron transporter, ferroportin, leading to iron occlusion and reduced erythrocyte production. Hepcidin-ferroportin axis-mediated systemic hypoferremia also acts as innate immune-defence mechanism by restricting essential iron from invading pathogens.

Very little is known concerning the molecular regulation of erythropoiesis in the context of inflammation. The slow progress in this area of research is partly related to the heterogeneity of diseases underlying AI, ineffectiveness of available diagnostic methods in distinguishing iron-deficient from iron-restricted anemias and lack of suitable animal models to recapitulate the complex etiopathogenesis of AI.

Results: Analysis of iron-regulatory and heme biosynthesis gene expression revealed a clear sex-specific effect in the anemia of inflammation model. In females, inflammatory conditions were associated with a significant increase in hepcidin expression, accompanied by a concomitant reduction in ferroportin expression. In parallel, the expression of key heme biosynthetic enzymes, ALAS1 and ALAS2, was markedly decreased in females. In contrast, these changes were not observed in males, in whom hepcidin, ferroportin, ALAS1, and ALAS2 expression levels remained comparable to controls.

Conclusion: Increased expression of female specific hepcidin, which in turn causes degradation and low expression of iron transporter- ferroportin in intestine and RBC, leading to iron occlusion and reduced erythrocyte production, The selective alteration of iron export and heme synthesis pathways in females indicates a pronounced gender dimorphism in the molecular response to inflammation. Collectively, these findings suggest that females exhibit a heightened susceptibility to inflammation-induced iron sequestration and impaired erythropoiesis, supporting a sex-specific regulatory mechanism underlying anemia of inflammation.

Systemic Autoimmunity: An Autoantibody Perspective

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Autoantibodies are central biomarkers in systemic autoimmune diseases, providing diagnostic, prognostic, and stratification value across a broad spectrum of conditions. Autoantibody signatures defined by the presence, patterns, and combinations of autoantibodies support the differentiation of diseases such as systemic lupus erythematosus, Sjögren's syndrome, systemic sclerosis, myositis, rheumatoid arthritis, and ANCA-associated vasculitis. These signatures also have organ-

specific relevance, including autoimmune liver disease and endocrine autoimmunity.

Indirect immunofluorescence on HEp-2 cells remains the first-line screening method due to its high sensitivity and ability to reveal pattern-based diagnostic clues, as illustrated by nuclear, cytoplasmic, and mitotic patterns across AC designations. Solid-phase assays, including ELISA, fluoroenzyme immunoassays, line immunoassays, and multiplex bead-based platforms, provide complementary specificity, automation, standardisation, and expanded antigen coverage. Reflex algorithms incorporating second-line testing, such as ENA panels, myositis panel blot, and Luminex-based multiplex profiling, improve diagnostic confidence, particularly in overlap syndromes and refining phenotypes. Local laboratory trend analysis demonstrates increasing autoimmune testing demand and evolving disease patterns, emphasising the need for optimised workflows and evidence-based test utilisation. The integration of screening and confirmatory methods enhances accuracy and supports precision immunology. In conclusion, autoantibody signatures, when interpreted in the context of clinical presentation and assay methodology, are powerful tools guiding diagnosis, risk assessment, and management in systemic autoimmunity.

Composite Graft-Mediated Enhancement of Osteogenesis through Integration of Natural and Synthetic Bone

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Keywords: Composite bone grafts; Osteogenesis; Exosome functionalization; nHAP; CSH.

Aim and Objectives

The aim of this study was to evaluate the in vivo bone-forming efficiency of allograft-based composite materials and their biofunctionalized variants. The objective was to enhance osteogenesis by combining natural bone grafts with nanohydroxyapatite (nHAP) and calcium sulfate hemihydrate (CSH), and by incorporating bioactive exosomes derived from bone marrow stromal cells (BMSCs), thereby addressing limitations of conventional grafts such as poor osteoinductivity and limited availability.

Materials and Methodology

Composites were fabricated using optimized ratios of CSH, nHAP, and allogenic bone powder, selected based on XRD, FTIR, and SEM characterization. Female Wistar rats (n = 5/group; two implantation sites per animal) were used in a 4-week intramuscular abdominal pouch model. Four groups were evaluated: (1) nanocement control (60 wt% CSH:40 wt% nHAP), (2) composite (60 wt% CSH:20 wt% nHAP:20 wt% bone), (3) composite + BMSC-derived exosomes, and (4) composite + BMP/ZA-induced exosomes. Bone formation was assessed using DEXA (days 0, 14, and 28), followed by micro-CT and histological analyses (H&E, Masson's Trichrome, Alizarin Red).

Results

Micro-CT and histomorphometry revealed a >10-fold increase in mineralization in exosome-functionalized composites compared to controls. Histology confirmed enhanced collagen deposition and mineralized bone-like tissue formation.

Conclusions

Hybrid composites of bone, CSH, and nHAP improved osteoconductivity, while exosome functionalization significantly enhanced ectopic bone formation, demonstrating strong potential for advanced bone tissue engineering.

N-acetylcysteine intervention in Fluoride-induced developmental Neurotoxicity: experimental evidence for Translational application

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Keywords: Fluoride, N-Acetylcysteine, Developmental Neurotoxicity, Oxidative Stress, Neuroprotection.

Prenatal fluoride exposure is known to cause neurobehavioral deficits and neuronal damage through oxidative stress and neurotransmitter dysregulation in offspring[1]. The present study investigated the neuroprotective potential of *N*-acetylcysteine (NAC), a potent antioxidant and glutathione precursor, against fluoride-induced developmental neurotoxicity using *in-vitro* and *in vivo* models. The *in-vitro* approach, primary hippocampal neuronal cultures, neurons and glial cells (80:20). Exposure to fluoride caused elevated intracellular calcium levels, increased ROS and lipid peroxidation (MDA), depletion of glutathione (GSH), and reduced cell viability, indicating

pronounced oxidative stress and neuronal cytotoxicity. NAC treatment significantly reversed these alterations, stabilizing intracellular calcium, restoring antioxidant balance, and improving neuronal survival. In the *in-vivo* study, pregnant mice received deionized water (control), fluoride (100 ppm), NAC (100 mg/kg body weight) and combined fluoride and NAC throughout gestation period. Offspring were subjected to histological and neurochemical assessments in pups of day 0, 14 and 30 and evaluated for spatial learning and memory in 30 days pups (Morris water maze and classical maze). Fluoride exposure led to impaired cognitive performance, neuronal degeneration, and reduced acetylcholinesterase activity, accompanied by elevated NADPH-d and nNOS expression, indicating disrupted cholinergic and nitrergic signaling. Interestingly, NAC co-administration markedly improved behavioral performance, preserved neuronal morphology, and normalized neurotransmitter enzyme activity across developmental stages. Collectively, these findings demonstrate that NAC effectively mitigates fluoride-induced developmental neurotoxicity through its antioxidant, anti-apoptotic, and neurotransmitter-modulatory activity. The study highlights the translational potential of NAC as a preventive and therapeutic strategy against fluoride-related neurodevelopmental disorders in both humans and animals.

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Ongoing Randomized Controlled Trial Comparing Effectiveness, Safety, Hepatic Outcomes, Renal outcomes and Cost-Effectiveness of Dapagliflozin versus Empagliflozin in Patients with Type 2 Diabetes Mellitus and High Body Mass Index – A Study Protocol

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BACKGROUND

India bears a substantial burden of Type 2 Diabetes Mellitus (T2DM), frequently associated with increased visceral adiposity and early cardiometabolic complications. Patients with high body mass index (BMI) are at heightened risk of metabolic dysfunction–associated steatotic liver disease (MASLD), cardiovascular disease, and renal impairment. Sodium–glucose cotransporter-2 (SGLT2) inhibitors offer glycaemic control alongside weight reduction and cardio-renal benefits. However, direct head-to-head randomized comparative evidence between dapagliflozin and empagliflozin in Indian patients with high BMI—particularly integrating hepatic and cost-effectiveness outcomes—remains limited.

OBJECTIVE

To compare the effectiveness, safety, hepatic Outcomes, renal outcomes and cost-effectiveness of dapagliflozin versus empagliflozin in adults with T2DM and high BMI.

METHODOLOGY

This ongoing prospective, randomized, open-label, parallel-group clinical trial **(CTRI/2025/11/097341)** is being conducted at AIIMS Bhopal, India. A total of 112 adults (HbA1c 7–10%; BMI ≥25 kg/m^2) are being randomized in a 1:1 ratio using computer-generated block randomization stratified by baseline HbA1c. Participants receive either dapagliflozin 10 mg once daily or empagliflozin 25 mg once daily in addition to stable background therapy (metformin ± other oral hypoglycaemic agents) for 24 weeks.

Primary outcomes include change in HbA1c and body weight at 6 months. Secondary outcomes comprise changes in fasting blood glucose, blood pressure, lipid profile, hepatic enzymes (ALT, AST, GGT), liver steatosis and fibrosis assessed using controlled attenuation parameter (CAP) and liver stiffness measurement (LSM), renal function (serum creatinine, eGFR, UACR), safety, and treatment adherence (SDSCA tool).
A concurrent pharmacoeconomic evaluation will assess direct and indirect costs. Cost-effectiveness will be calculated using Average Cost-Effectiveness Ratio (ACER) and Incremental Cost-Effectiveness Ratio (ICER) based on weighted clinical effectiveness measures. Data will be analysed using intention-to-treat principles with ANCOVA for primary outcomes.

EXPECTED OUTCOME

This trial is designed to generate India-specific comparative evidence on metabolic, hepatic, safety, and economic outcomes of two widely prescribed SGLT2 inhibitors. The findings aim to inform rational, patient-centred, and economically sustainable diabetes management strategies in real-world clinical practice.

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Exploring the association of anti-thyroid peroxidase antibody level with metabolic alterations and renal function in elderly hypothyroid cases- A gender-based introspection

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Introduction: Thyroid hormones play important metabolic role and regulate kidney function. Incidences of Thyroid disorders as well as auto immune diseases increases with age, particularly in females. Auto immune diseases are known to affect kidney function. As both hypothyroidism and CKD independently increase CVD risk, it is crucial to assess metabolic alterations and kidney function in elderly hypothyroid cases in relation to auto immunity.

Materials & Method: This case control study enrolled 64 newly diagnosed hypothyroid cases of >60 year of age, from both gender (serum TSH>5 µIU/L) and age and sex matched healthy control. fT3, fT4, TSH, Anti-TPO were estimated along with biochemical parameters including urinary ACR and eGFR. Mann-Whitney U test, Chi- square test and regression analysis were conducted as appropriate. P<0.05 was considered significant. Diabetes, hypertension, liver disease, kidney disease, previous hyper-lipidaemia, auto immune disease, other endocrine disorders, and cases with anti-epileptic medication, steroid therapy were excluded.

Result: Thyroid function parameters registered marked alteration in hypothyroid cases in comparison to control. Anti-TPO positivity revealed significant relation with altered renal function by regression analysis. Metabolic alterations and renal involvement were more pronounced in females.

Conclusion: Significant association of Anti-TPO antibody levels with renal dysfunction among elderly hypothyroid patients, warrants early screening in young. With similar Anti-TPO burden females showing more possibility to metabolic and renal vulnerability, needs further attention.

Ongoing Ambispective Observational Study Evaluating Real-World Safety and Lipid-Lowering Effectiveness of Statins at a Tertiary Care Centre in Central India- A study Protocol

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BACKGROUND

Statins are first-line therapy for dyslipidaemia and atherosclerotic cardiovascular disease (ASCVD) prevention. Although randomized trials demonstrate substantial LDL-C reduction and cardiovascular risk benefit, real-world data on safety, tolerability, and adherence in Indian populations remain limited. Patient-reported statin-associated muscle symptoms (SAMS) and perceived intolerance often contribute to discontinuation despite low rates of objective biochemical toxicity.

OBJECTIVE

To evaluate the real-world safety and lipid-lowering effectiveness of statins in patients receiving statin therapy at a tertiary care centre in Central India.

METHODOLOGY

This ongoing ambispective observational study is being conducted at AIIMS Bhopal across Medicine, Cardiology, and CTVS departments. Patients initiated on or receiving statins are enrolled after consent. Estimated sample size ranges from 117–188 participants. Safety assessment includes structured evaluation of SAMS using the validated SAMS-Clinical Index (SAMS-CI), gastrointestinal adverse effects using the Gastrointestinal Symptom Rating Scale

(GSRS), and monitoring of hepatic enzymes (ALT, AST) to estimate hepatic adverse effects. Adverse events are categorized using WHO-UMC causality criteria. Effectiveness is assessed by change in total cholesterol and LDL-C from baseline to 1 and 3 months. Medication adherence is evaluated using the 8-item Morisky Medication Adherence Scale (MMAS-8). Multivariable analyses using ANOVA and Chi square tests as required will identify predictors of adverse effects and lipid response.

EXPECTED OUTCOME

This study will generate India-specific real-world evidence on statin safety, tolerability, adherence, and effectiveness, supporting rational prescribing and improved cardiovascular risk management.

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Unravelling the Determining Factors of Chronic Kidney Disease of Unknown Etiology (CKDu): The Hidden Danger in Farming Communities

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Keywords: Chronic kidney disease of unknown etiology (CKDu), environmental determinants, Agrochemicals, Nephrotoxicity

Chronic Kidney Disease of Unknown Etiology (CKDu) has emerged as a significant and growing public health problem in agricultural regions, particularly affecting farming communities in low- and middle-income countries. Unlike conventional chronic kidney disease, CKDu develops in the absence of established risk factors such as diabetes, hypertension, or primary glomerular disease, suggesting the involvement of unique environmental and occupational determinants. Epidemiological studies consistently demonstrate a high prevalence of CKDu among male farmers, with marked geographic clustering and strong associations with long-term agricultural work.

Accumulating evidence indicates that CKDu pathogenesis is driven by persistent low-grade inflammation and progressive renal fibrosis. Elevated inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and transforming growth factor-β (TGF-β), play a central role in promoting tubular injury, oxidative stress, and immune-mediated damage. These inflammatory processes activate profibrotic pathways, leading to increased expression of fibrotic markers such as collagen I, fibronectin, and α-smooth muscle actin (α-SMA), which contribute to irreversible interstitial fibrosis and gradual loss of renal function.

Pesticide exposure has been identified as a key upstream risk factor in affected populations. Farmers experience chronic exposure to agrochemicals through occupational handling, contaminated soil and water, and inadequate protective measures. Several commonly used pesticides have demonstrated nephrotoxic potential, capable of inducing oxidative stress and amplifying inflammatory and fibrotic signaling pathways within renal tissues. The combined effects of pesticide exposure, heat stress, recurrent dehydration, and limited healthcare access may synergistically accelerate kidney injury.

Thus, there is need to understand and integrate epidemiological findings with emerging mechanistic insights to elucidate the multifactorial determinants of CKDu, emphasizing the urgent need for preventive strategies, biomarker-based early detection, and improved occupational health policies to address this hidden danger among farming populations.

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Genomic variants identified in betel quid users from North-East India: Insights into the mechanisms of dependence on Betel quid

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Betel nut with or without tobacco, known as betel quid (BQ) is the fourth most addictive substance worldwide, but the genomic variations associated with BQ dependence are largely unexplored. Uncovering these variants would advance the understanding of BQ dependence and enable personalized interventions. Whole Genome Sequencing (WGS) from buccal swab samples of nine study subjects (two non-chewers and seven users of BQ) was performed using the Illumina HiSeq X platform. Dependence was measured using the Betel Quid Dependence Scale (BQDS) and Fagerström test for Nicotine Dependence-Smokeless Tobacco (FTND-ST).Data analysis and functional annotation revealed the presence of BQ-specific variants. Single nucleotide polymorphisms (SNPs) were identified in 4218 genes with *RBFOX1*, *PCDH15* and *CSMD1* harboring the maximum number of variants. Among these, 108 genes harbored SNPs in coding regions, resulting in amino acid substitutions. Some of these variants scored "deleterious" in the SIFT (Sorting Intolerant From Tolerant) test, indicating potentially deleterious effects on corresponding protein function. A total of 954 genes had deletion variants, with the maximum observed in the *NCAM*, *HECTD4* and *PHACTR1* genes. The deletion variants in 26 genes were identified in coding regions resulting in frameshift variations with high impact on the resultant proteins. A total number of 317 genes with insertion variants were also identified with the maximum found in the *DOCK1*, *TMTC* and *TESPA1* genes. Among these, 9 genes had insertion variations in the coding regions, predicted to have high impact on the corresponding proteins. The significance in terms of BQ dependence will be discussed.

Dysregulated Cellular Stress Responses and Heat Shock Proteins: Molecular Links to Non-Communicable Disease Pathogenesis

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Keywords: Heat shock proteins, cellular stress response, proteostasis, non-communicable diseases, oxidative stress, molecular chaperones, chronic disease pathways

Non-communicable diseases (NCDs) such as cardiovascular disorders, diabetes, neurodegenerative diseases, autoimmune conditions, and cancers share common pathogenic pathways rooted in chronic cellular stress and impaired homeostatic regulation. Cellular stress responses are highly conserved survival mechanisms that enable cells to counteract oxidative injury, proteotoxicity, hypoxia, and inflammatory insults. Central to these responses are **heat shock proteins (HSPs)**, a family of molecular chaperones that regulate protein folding, proteostasis, apoptotic signaling, and cytoprotective adaptation.

This review synthesizes emerging evidence demonstrating how **dysregulation of HSP-mediated stress pathways** contributes to disease progression across major NCDs. Persistent oxidative and metabolic stress leads to maladaptive alterations in HSP expression, mitochondrial dysfunction, chronic inflammation, telomere attrition, and cellular senescence — ultimately promoting vascular injury, neurodegeneration, immune dysregulation, and tumorigenesis. The interplay between environmental stressors, lifestyle transitions, and intrinsic molecular stress mechanisms highlights cellular stress biology as a unifying framework in NCD pathophysiology.

Furthermore, HSPs are gaining recognition as **diagnostic biomarkers, prognostic indicators, and therapeutic targets**. Pharmacological modulation of stress-response pathways offers promising opportunities for precision-medicine-based interventions aimed at restoring proteostasis and cellular resilience.

By integrating molecular stress biology with clinical disease mechanisms, this work underscores the need for **translational research** to harness HSP pathways for prevention, early detection, and therapeutic innovation in NCDs. Understanding cellular stress responses not only advances mechanistic insight but also supports the development of **holistic strategies to reduce the global burden of chronic diseases**.

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Development and Application of an In-House Primer Panel Whole-Genome Sequencing Strategy for Molecular Profiling of Hepatitis B Virus in Central India

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Background: Genomic diversity of the hepatitis B virus plays a critical role in viral persistence, immune evasion, and therapeutic outcomes. Despite India's high HBV burden, comprehensive whole-genome data from Central India remain scarce, partly due to the limited availability of cost-effective sequencing platforms. To address this gap, the present study implemented an indigenously developed primer-based WGS protocol to investigate the mutation patterns of HBV circulating in Chhattisgarh.

Methods: A total of 64 HBV DNA positive specimens, with viral loads ranging from 3.11 to 9.08 $\log_{10}$IU/mL, were included. Complete HBV genome amplification was achieved using three overlapping sets of in-house designed primers. Sequencing was performed using a customized workflow adapted from the COVIDSeq WGS assay. Sequence quality metrics, genome coverage, phylogenetic clustering, serotype distribution, and mutation pattern were systematically analysed.

Results: The sequencing protocol generated consistently high-quality data, genome coverage exceeding 98.7% across samples. Phylogenetic tree demonstrated exclusive circulation of HBV genotype D and sub-genotype analysis identified D3 as the dominant lineage (53.7%), followed by D5 (23.6%), D1 (14.8%), and D2 (7.8%). Serotype distribution showed predominance of ayw2 (68.4%), and ayw3 (31.6%). Multiple mutations were observed within the surface gene, particularly in the major hydrophilic region and "a" determinant (T113S, T114S/P, K122R, N131T, F134Y/N, A159G), alongside mutations in transmembrane, core, and precore regions.

Conclusion: This study provides the first comprehensive whole-genome characterization of HBV from Chhattisgarh using an indigenously developed sequencing workflow. The dominance of genotype D and the presence of mutations in "a" determinant highlight the integrating genomic surveillance, particularly in regions with limited access to commercial sequencing solutions.

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RK5-YAP/TAZ Dysregulation in Endothelial Dysfunction caused by induced OxLDL and MASLD

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OBJECTIVE: Metabolically-dysfunction-associated steatotic liver disease (MASLD, formerly NAFLD) increases vascular disease and death, although its cause and regulators remain unclear. The increase in LDL and Ox-LDL in MASLD is associated to endothelial dysfunction (ED) and atherogenesis. Erk5 controls endothelial cell (EC) homeostasis and mechanosensors YAP/TAZ signal

signalling and metabolic pathways, but how they interact during pathogenesis is unknown. An antioxidant and anti-inflammatory dietary flavonoid, fisetin, was investigated for its protective properties against Erk5 and YAP/TAZ signalling in ECs during MASLD and ED.

MATERIAL AND METHODS: MTT, Western blotting, and RT-qPCR were assessed to measure protein and RNA expression in primary-HUVECs subjected to various ox-LDL concentrations for different times. Immunocytochemistry (ICC) measured cellular protein expression, whereas DCFDA measured ROS. A high-fat high-carbohydrate (HFHC) diet-fed rat model of MASLD was developed as well to study hepatic haemodynamic, microvascular, cellular, molecular, biochemical, and histological investigations.

RESULT: pHUVECs treated with OxLDL reduced viability dose- and time-dependently and showed 4.7 times more ROS than controls. ECs exposed to Ox-LDL showed 1.7-fold greater monocyte adhesion and ICAM expression. OxLDL-exposed cells increased YAP (1.2-fold) and TAZ (6-fold) and downregulated ERK5 (0.59-fold-inversely). HFHC-fed rats have elevated anthropometrics and histopathology in vivo for MASLD. Liver tissue RT-PCR showed upregulation of ED markers icam-1, vcam, and pecam and downregulation of EC indicators eNOS and vWF. These alterations matched in-vitro YAP/TAZ overexpression and Erk5 downregulation.

CONCLUSION: These data show that MASLD and increased ox-LDL exposure downregulate Erk5 and upregulate YAP/TAZ in ECs, which could be associated with ED and inflammation.

Utility of the MPT64 Antigen Assay for Rapid Differentiation of Non-Tuberculous Mycobacteria from Mycobacterium tuberculosis Complex

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Background: Differentiation between *Mycobacterium tuberculosis* complex (MTBC) and non-tuberculous mycobacteria (NTM) is essential for appropriate clinical management. Conventional diagnostic algorithms that rely on smear microscopy and molecular testing may miss NTM infections in routine diagnostics. The MPT64 antigen detection assay is widely used for rapid confirmation of MTBC and may aid in the presumptive identification of NTM.[1]

Objective: To evaluate the utility of the MPT64 antigen test for presumptive identification of NTM in routine diagnostic workflows.

Methods: Clinical specimens from patients suspected of mycobacterial infection were screened by Ziehl–Neelsen staining. AFB-positive samples were subjected to nucleic acid amplification testing (NAAT) for MTBC detection. NAAT-negative samples were cultured. Culture-positive isolates were confirmed by ZN staining and tested using the MPT64 antigen assay. MPT64-negative isolates were considered presumptive NTM and further characterised using molecular methods.[2]

Results: Of the 7,984 clinical specimens screened, 627 (7.85%) were AFB positive, and all were confirmed as MTBC by NAAT. The remaining 7,357 samples were subjected to culture, of which 1,540 (20.9%) were positive in the BACTEC MGIT 960 system. Among these culture-positive isolates, 387 (25.1%) were AFB positive. Of these, 367 (94.8%) were MPT64-positive and identified as MTBC, while 20 (5.2%) were MPT64-negative and considered presumptive NTM. A high level of concordance was observed between MPT64 results and confirmatory methods.

Conclusion: Integration of MPT64 antigen testing into routine diagnostic workflows provides a rapid and reliable approach for presumptive differentiation of MTBC and NTM, facilitating timely clinical management. Confirmatory molecular techniques remain essential for definitive species identification.

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Title missing???

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Neurodegenerative disorders are complex, multifactorial conditions in which genetic susceptibility intersects with metabolic dysregulation to drive disease onset and progression. Taurine, a sulfur-containing amino acid essential for neuroprotection, mitochondrial stability, and redox homeostasis, has emerged as a potential metabolic determinant of neurodegeneration. This explorative cross-sectional analytical study was conducted at the All India Institute of Medical Sciences (AIIMS), Patna, to evaluate the role of plasma taurine and its interaction with the MTHFR C677T polymorphism within the framework of one-carbon metabolism.

The study included 108 participants comprising 54 clinically diagnosed cases of age-associated neurodegenerative disorders (Parkinsonism, dementia, motor neuron disease, and Wilson's disease) and 54 age- and sex-matched healthy controls. Neurodegenerative patients exhibited marked plasma taurine depletion compared to controls (45.86 µmol/L vs. 84.92 µmol/L; $p < 0.001$), representing an approximately 45% reduction independent of aging. Plasma taurine demonstrated excellent diagnostic performance (AUC = 0.98; sensitivity 92.6%; specificity 94.4%) with a very high odds ratio (OR = 212.5), identifying it as a robust metabolic biomarker.

Genetic analysis revealed a strong association between the MTHFR C677T polymorphism and disease susceptibility, with a 4.96-fold increased risk among mutant allele carriers (CT + TT) and complete disease penetrance in TT homozygotes. A clear gene-dosage–dependent reduction in plasma taurine levels was observed across MTHFR genotypes, implicating impaired folate-dependent one-carbon metabolism and transsulfuration pathway dysfunction as mechanistic drivers of taurine deficiency. Together, these findings support a synergistic "dual-hit" metabolic model in which MTHFR genetic variation and taurine depletion act as interdependent risk factors for neurodegenerative disease. Combined assessment of MTHFR genotype and plasma taurine levels may enable metabolic risk stratification and inform targeted therapeutic strategies.

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Rapid Differentiation of Human Pluripotent Stem Cells into Hepatocyte like cells for MASLD Modelling

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Human in vitro hepatic models that faithfully recapitulate native liver physiology are essential for basic and translational research, but current platforms suffer from poor fidelity and prolonged culture times. Here we present a streamlined 10-day protocol for highly efficient, reproducible differentiation of human pluripotent stem cells (hPSCs) into hepatocyte-like cells (HLCs) exhibiting mature hepatocytic function, including albumin/urea secretion and CYP3A4 activity. HLCs demonstrate multicellular complexity with CD31+ endothelial cells and CD166+ hepatic stellate cells alongside hepatocytes, better mimicking the native liver microenvironment. Free fatty acid treatment induced dose-dependent steatosis, characterized by triglyceride accumulation, upregulated lipogenic (SREBP1c, FASN) and proinflammatory (IL-6, TNF-α) genes. Resmetirom (MGL-3196), a thyroid hormone receptor-β agonist, significantly attenuated steatosis and normalized molecular profiles. This rapid, scalable platform enables physiologically

relevant HLCs for MASLD disease modeling, drug screening, therapeutics validation, and tissue engineering applications.

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Integrative QSAR Machine Learning Approach for Neurotoxin Identification Using Cheminformatics and Network Pharmacology

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Keywords: Neurotoxicity, QSAR, machine learning, IL1B, IL6, and CASP3.

Neuro- and environment-induced toxicity poses a significant challenge to drug discovery and public health due to the intricate biological mechanisms involved and the limitations of conventional in vivo testing, which is time-consuming, costly, and ethically constrained. To address these limitations, we developed an integrative machine learning–based Quantitative Structure–Activity Relationship (QSAR) framework for the prediction of chemical-induced neurotoxicity.

The proposed model combines molecular descriptors, protein–protein interaction (PPI) network analysis, and structure-based docking information to improve both predictive performance and biological interpretability. PPI networks were analyzed to identify key regulatory hubs associated with neuroinflammation and apoptosis, including cytokine- and caspase-related signaling components. These biologically relevant features were integrated with cheminformatics descriptors to train ensemble learning models for neurotoxicity classification and toxicity-associated biomarker prediction. The machine learning framework demonstrated strong discriminatory ability with classification (accuracy = 82%, AUC = 0.91) and high predictive consistency, indicating its suitability for screening neurotoxic compounds. Dimensionality reduction and feature contribution analyses highlighted a subset of physicochemical and interaction-based descriptors as major contributors to model decisions, supporting mechanistic relevance. To facilitate accessibility, a SHINY-based interactive dashboard was developed for rapid compound screening and visualization of prediction outputs.

Overall, this study introduces a scalable, interpretable, and high-throughput in silico platform for neurotoxicity assessment, presenting an effective alternative to existing testing methodologies. This technique adheres to the concepts of the 3Rs (Replacement, Reduction, and Refinement) and facilitates early-stage decision-making in drug development and chemical risk assessment.

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C-Phycocyanin as a Precision Therapeutic Modulator of Epoxide Hydrolase Variants in Type 2 Diabetes and Cardiovascular Disease

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Keywords: C-Phycocyanin, epoxide hydrolase polymorphism, oxidative stress, Type 2 diabetes mellitus, cardiovascular disease

Oxidative stress is a central pathogenic mechanism contributing to the development and progression of Type 2 Diabetes Mellitus (T2DM) and cardiovascular disease (CVD), particularly in individuals carrying functional polymorphisms in the epoxide hydrolase (EPHX) gene that impair epoxide detoxification and redox balance. Despite advances in clinical management, therapeutic strategies addressing genotype-dependent oxidative damage remain limited. The present study evaluates C-Phycocyanin, a natural bioactive compound with potent antioxidant properties, as a precision therapeutic modulator of EPHX variants using an integrated *in-silico* and in-vitro

translational approach. Molecular docking, molecular dynamics simulations, and binding free-energy calculations were employed to investigate the interaction stability and affinity of C-Phycocyanin with wild-type and polymorphic EPHX proteins. These computational analyses were complemented by *in-vitro* validation under hyperglycaemic conditions using relevant cellular models to assess reactive oxygen species generation, lipid peroxidation, and antioxidant enzyme activities, including superoxide dismutase, catalase, and glutathione peroxidase. In-silico results demonstrated stable and energetically favourable binding of C-Phycocyanin to wild-type EPHX, whereas polymorphic variants exhibited reduced binding affinity and increased structural fluctuations. Consistently, in-vitro findings revealed a significant reduction in oxidative stress markers and restoration of antioxidant defences following C-Phycocyanin treatment. Overall, this study highlights the genotype-dependent therapeutic potential of C-Phycocyanin and underscores the value of integrating computational modeling with experimental validation. The findings support the development of precision, natural compound-based interventions for managing metabolic and cardiovascular diseases.

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Immune-Driven Fibrotic Remodeling of the Rheumatic Mitral Valve: Insights from Macrophage–hVIC Interactions

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Keywords: Rheumatic mitral valve disease, human valve interstitial cells, macrophage polarization, fibrosis.

Background and Aim: Rheumatic mitral valve disease (RMVD), a chronic sequela of acute rheumatic fever, is characterized by persistent inflammation, extracellular matrix (ECM) remodeling, progressive fibrosis, and valve degeneration.[1-3] While macrophages are key regulators of chronic inflammatory responses, their role in shaping valvular fibrosis through interactions with human valve interstitial cells (hVICs) remains incompletely understood. This study aimed to define macrophage–hVIC crosstalk and determine how distinct macrophage phenotypes influence apoptotic and fibrotic pathways in RMVD.

Methods: Primary hVICs were isolated and phenotypically characterized. Cells were stimulated with inflammatory mediators (TGF-β, TNF-α, and IFN-γ), and apoptosis was assessed using Annexin V/PI staining and morphological analysis. RT-PCR quantified fibrogenic gene expression, and cellular proliferation was evaluated by immunocytochemistry. To assess macrophage-driven ECM remodeling, hVICs were treated with conditioned media from polarized macrophages (M0, M1, and M2c phenotypes).

Results: TGF-β stimulation induced pronounced hVIC aggregation, proliferation, and apoptosis within 24 hours, accompanied by strong upregulation of profibrotic markers (ACTA2, COL1A1, COL1A2, TIMP1, MMP2, CTGF, and TGF-β) and activation of SMAD3 signaling. In contrast, TNF-α and IFN-γ elicited minimal activation of ACTA2 and COL1A1. IFN-γ selectively downregulated COL1A2 while increasing TIMP1 expression, indicating a distinct matrix-modulatory response. Importantly, M2c macrophage–conditioned media significantly enhanced profibrotic gene expression (ACTA2, COL1A1) and suppressed MMP9 expression, thereby promoting ECM accumulation.

Conclusion: TGF-β signaling is a dominant driver of fibrotic remodeling in hVICs, while macrophage phenotypes distinctly modulate valvular ECM dynamics. M2c macrophages promote a fibrosis-prone microenvironment, highlighting macrophage–hVIC interactions as critical regulators of RMVD progression and potential therapeutic targets.

Sources of funding: This study was supported by a research grant from the DBT, Woman and Child Health Program (F.No. BT/PR42952/MED/97/569/2021) to Alok Kumar.

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Diagnostic Potential of FOXO3a in Alzheimer's Disease: Evidence from Serum-Based Analysis

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Keywords: Alzheimer's Disease, Mild Cognitive impairment, Oxidative stress, FOXO3a, Blood based biomarker

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and memory impairment. Oxidative stress is a major contributor to AD pathogenesis. Forkhead box O3a (FOXO3a) is a key transcription factor involved in cellular stress responses, mitochondrial homeostasis, and aging-related pathways. Dysregulation of FOXO3a may compromise oxidative stress resistance and metabolic balance, thereby accelerating neurodegeneration in AD.
Methods: Serum FOXO3a, Tau and pTau levels were quantified in individuals with AD (n=63), mild cognitive impairment (MCI, n=59), and age-matched geriatric controls (GC, n=58) using surface plasmon resonance (SPR) and compared with TauPET. Serum levels were further validated by Western blotting. Receiver operating characteristic (ROC) analysis and Pearson's correlation were performed to assess diagnostic accuracy and association with cognitive function.
Results: Serum FOXO3a levels were significantly reduced in AD (1.43 ± 0.04) and MCI (1.59 ± 0.13) groups compared to GC (1.89 ± 0.22). Tau was higher in AD (49.69 ± 2.38) and MCI (43.12 ± 1.19) as compared to GC (38.83 ± 3.6), both in serum and in PET scan. Serum pTau was higher in AD (0.18 ± 0.01) and MCI (0.15 ± 0.002) as compared to GC (0.15 ± 0.007). FOXO3a, Tau and pTau, demonstrated strong discriminatory power between AD vs. GC, MCI vs. GC as well as between AD vs. MCI, with high sensitivity and specificity. Moreover, FOXO3a levels showed a significant positive correlation, while Tau and pTau showed a significant negative correlation, with cognitive scores, indicating an association with disease severity.
Conclusion: The findings suggest that reduced serum FOXO3a is associated with cognitive decline. Serum FOXO3a holds promise as a potential non-invasive blood-based biomarker for the early diagnosis and monitoring of AD.

Role and regulation of Extracellular microRNAs in Neurodegeneration

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MicroRNAs (miRNAs) are small regulatory RNA molecules demonstrated to play role in different pathological and cellular development and differentiation situations. Parkinson's disease (PD) is a neurodegenerative disorder caused by the loss of dopaminergic neurons (DA-nergic) in the substantia nigra (SNpc). Currently, PD is diagnosed mostly based on motor impairments that develop when more than 80% of the DA-nergic neurons in the SNpc are destroyed. The development of new biomarkers is required for effective PD management. Our studies have shown significant deregulation of miRNAs and specific proteins in serum of PD patients. Exosomes are small extracellular vesicles (50–150 nm) that carry different kind of biomolecules in their lumen and facilitate intercellular communication. Serum contains large amount of exosomes (around 1012/ ml of serum) and exosomes contain relatively more amount of small RNAs than large RNAs. Quantifying the absolute number of specific miRNA molecules in exosome is critical for understanding their functional relevance and developing them for diagnostic tool in diseases like PD. We have developed a new protocol for copy number assay of miRNAs in exosome that combines nanoparticle tracking analysis (NTA) to quantify vesicle concentration with absolute quantification of miRNA using a standard curve based q-PCR approach. Using same method, we have identified significant alterations in expression of miRNAs, which can be used as new biomarkers of PD.

Cellular and Molecular insights into silica-induced Lung tissue Calcification in Pathogenesis of Silicosis

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Keywords: Silicosis, silica, lung fibrosis, calcification, EMT, alizarin red staining, osteogenic markers

Journal of Academy of Biomedical Sciences
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A progressive irreversible occupational lung disease silicosis, is highly prevalent in mining and stone processing regions of India, particularly in Rajasthan belt. Government implemented policies for its diagnosis, financial compensation and preventive measures for affected workers. However, the molecular mechanisms driving silica-induced lung fibrosis remain poorly understood.[1] This study focuses on investigating the underlying molecular mechanism driving silica-induced cellular plasticity in lung epithelial cells.[2] *In-vitro* experiments were conducted to evaluate cytotoxicity using cell viability MTT assay. Cellular differentiation and lung tissue calcification were examined through ALP assay and alizarin red S (ARS) staining, respectively. Furthermore, gene expression-associated changes were analysed using RT- PCR and RT-qPCR. Various epithelial cancer cells, including lung A549 cells, were exposed to varying concentrations of silica to assess cell viability. Silica exposure resulted in a noticeable modulation of epithelial to mesenchymal transition (EMT) marker genes with simultaneous changes of silicosis marker in A549 cells, suggesting a shift from epithelial towards a mesenchymal phenotype. A prolonged exposure of silica induces calcification as revealed by ARS staining. RT-qPCR analysis found elevated expressions of various osteoblast markers RUNX2 and OSTERIX with concomitant induction of osteo-inducer BMP-2 and ALP activity in response to silica treatment. Collectively, these findings suggest that silica induces EMT and subsequent calcification through BMP2 dependent pathway by inducing cellular plasticity of epithelial cells. Further study is required to develop molecular markers for early detection and targeted therapeutic intervention in silicosis.

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Genetics of Premature Ovarian Failure

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Background & Objectives

POF is a complex condition of aberrant ovarian aging due to ovarian dysfunction. It is characterized by amenorrhoea and postmenopausal levels of gonadotropins (FSH) as well as sex hormones (estradiol). The common causes of POF are cytogenetic abnormalities involving the X chromosome, fragile X syndrome (carrier), autoimmune endocrine disturbances, iatrogenic (chemotherapy, radiotherapy, surgical removal, etc), and idiopathic. The study aimed to explore various genetic factors in apparent idiopathic POF cases.

Materials & Methods

This study was conducted in Reproductive Biology, AIIMS, Delhi, between January 2020 and December 2024. One hundred females with POF were investigated. Both sporadic and familial POF cases were studied for chromosomal abnormalities and sex chromosome mosaicism (100 cases), copy number variation (81 cases), FMR1 gene premutation (77 cases), and gene variants (74 cases) by using conventional cytogenetics, XY FISH, DNA microarray, TP-PCR, and whole exome sequencing (WES), respectively.

RESULTS

Conventional cytogenetics detected a case of mosaic isochromosome Xq with X monosomy (45,X[10]/46,X,i(X)(q10)[20]) and another mosaic case with 45,X (10)/47,XXX (10) besides 2 cases of 46,XY sex reversal. SNP microarray detected CNV containing POF potential genes such as *GON4L, RBPOX1, CSMD1, HBE1, MAGEB16,* and *PRDM9* in 7 cases. TP-PCR detected heterozygous premutation in the FMR1 gene in 4 sporadic POF cases and two familial POF cases (8.2%). WES detected two pathogenic (*STAG3, ZSWIM7*) and three likely pathogenic variants (*CLPP, FOXL2, C14orf39*) besides five VOUS (*MCM9, SIRT1, EIF2B3, ERCC6, FIGLA*) in sporadic POF cases and two likely pathogenic (*FSHR*) and 2 VOUS (*FSHR*) in familial POF cases. Two genetic events were detected in 2 sporadic POF cases and two familial POF cases. Multiple variants (pathogenic/likely pathogenic/VOUS) were observed with both the sex reversal cases (*NOBOX, GATA4, RSPO1, NR0B1, NR5A1, etc*).

CONCLUSIONS

We conclude that genetic associations in POF are common and sex reversal cases are oligogenic (association with 3-4 variants).

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Targeting CCR5 modulates Treg and Myeloid Derived Suppressor Cells in Early Atherosclerosis: A Potential Therapeutic Strategy

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Introduction: The chemokine receptor CCR5 has been linked to both inflammatory and immunosuppressive functions. However, its specific role in regulating Tregs and MDSCs during early atherosclerosis remains largely unexplored.

Objectives: This study aimed to investigate the involvement of CCR5 in the early stages of atherosclerosis and assess its potential as a therapeutic target.

Methods: CCR5 receptor-ligand expression was analyzed in 60 individuals, including 20 healthy controls, 20 young individuals with hypercholesterolemia, and 20 stable CAD patients, using flow cytometry, real-time PCR, and immunocytochemistry. Atherosclerosis was induced in C57BL6 mice by feeding them a high-fat diet (HFD) for six weeks following partial ligation of the left carotid artery. The phenotype and functionality of MDSCs and Tregs were examined after treatment with a CCR5 inhibitor, DAPTA, both *in vitro* (10^{-8} M) and *in-vivo* (intraperitoneal injection, 3 ng/day for 15-days).

Results: CCR5 expression was found to be elevated on Tregs and monocytic MDSCs during the early phase of atherosclerosis. These immune regulatory cells exhibited "intermediate phenotype", expressing both pro- and anti-inflammatory markers, a trend that was also observed *in vitro* upon stimulation with inflammatory cytokines. Inhibiting CCR5 with DAPTA shifted the phenotype of Tregs and M-MDSCs towards a more anti-inflammatory state, reduced the migratory capacity of these cells, enhanced their immunosuppressive functionality, and decreased cholesterol uptake in M-MDSCs. DAPTA also promoted the expansion of IL-10^{+} Tregs and M-MDSCs *in-vivo* and led to the formation of more stable atherosclerotic plaques.

Conclusion: Systemic inflammation in young individuals with atherosclerosis risk factors upregulates CCR5 expression in immune regulatory cells, leading to their dysfunction. Possibly this dysfunctionality contributes to the development and progression of atherosclerosis. Targeting CCR5 with DAPTA not only reduces atherogenesis but also enhances plaque stability and restores the immunosuppressive functions of Tregs and M-MDSCs, highlighting its potential as a therapeutic strategy.

Multimerin-1 at the Crossroad of Ovarian Cancer Progression and Angiogenesis

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Epithelial ovarian cancer (EOC) is a major cause of cancer-related mortality worldwide, largely due to late-stage diagnosis and the inadequate efficacy of current therapeutic strategies. Tumor progression is driven by dysregulated signaling pathways and epithelial mesenchymal transition (EMT), which promote invasion, metastasis, and therapeutic resistance. Emerging evidence indicates that extracellular matrix (ECM) proteins play active roles in cancer progression; however, their functional relevance in EOC remains insufficiently explored.

Multimerin-1 (MMRN1) is a 25–155 kDa ECM protein secreted by activated platelets, megakaryocytes, and endothelial cells. Our previous studies identified elevated MMRN1 expression in EOC patients and demonstrated its involvement in tumor progression through modulation of DNA damage response pathways. While MMRN1 is known to influence endothelial cell adhesion, its role in angiogenesis and tumor endothelial crosstalk remains unclear.

In this study, we investigated the role of MMRN1 in EOC progression with a specific focus on angiogenesis. MMRN1 was silenced in the ovarian cancer cell line OVCAR3 and the endothelial cell line HUVEC. Functional assays were conducted to assess cell proliferation, apoptosis, adhesion, migration, invasion, wound healing, and angiogenic potential. These analyses were supplemented by proteomic profiling and bioinformatics approaches to identify MMRN1-regulated molecular pathways.

MMRN1 knockdown in OVCAR3 cells significantly reduced cell proliferation, adhesion, migration, invasion, and wound closure, along with altered apoptotic responses. In HUVEC cells, MMRN1 silencing resulted in a greater than 50% reduction in tube formation within 24 hours, highlighting its essential role in angiogenesis. Proteomic and pathway analyses revealed that MMRN1 regulates ubiquitin-mediated protein degradation, DNA replication and repair, cell cycle progression, and angiogenesis-related pathways. These findings suggests that MMRN1 may be a multifunctional regulator of epithelial ovarian cancer progression and angiogenesis, underscoring its potential as a therapeutic target in EOC.

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Screening and Characterization of Probiotic Lactic Acid Bacteria for In Vitro Cholesterol Reduction

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Probiotics are defined as live microorganisms that confer health benefits on the host when administered in adequate amounts. Among their diverse therapeutic properties, cholesterol reduction has gained significant attention due to the increasing prevalence of hypercholesterolemia, obesity, cardiovascular diseases, and non-alcoholic fatty liver disease (NAFLD). Probiotic lactic acid bacteria (LAB) contribute to cholesterol lowering through multiple mechanisms, including bile salt hydrolase (BSH) activity, deconjugation of bile acids, assimilation of cholesterol into the cell membrane, and biotransformation via diverse metabolic pathways. Deconjugation of bile salts reduces micelle formation, thereby decreasing intestinal cholesterol absorption and promoting its excretion.

The present study aimed to isolate and characterize LAB strains from milk samples and evaluate their probiotic potential along with their in vitro cholesterol-lowering efficacy. The isolates were subjected to morphological, biochemical, and probiotic characterization according to standard guidelines. Cholesterol assimilation was assessed in MRS broth supplemented with cholesterol and bile salts. Quantitative estimation of residual cholesterol was performed using High-Performance Liquid Chromatography (HPLC). Selected strains demonstrated significant cholesterol reduction compared to the control. Both bacterial cell pellets and cell-free supernatants were analyzed to understand the mechanism of cholesterol removal.

The findings suggest that selected LAB strains possess strong probiotic attributes and cholesterol-degrading capacity, highlighting their potential application in functional foods and nutraceutical formulations aimed at preventing obesity, reducing cardiovascular risk, and managing NAFLD. Further, in-vivo studies are required to validate their clinical efficacy and therapeutic potential.

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Hypoxia Rewires Adult Stem Cell Identity toward Functional Dopaminergic Neurons through Coordinated Secretome and Signaling Remodeling

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Keywords: Hypoxia, infrapatellar fat pad stem cells, dopaminergic neurons, neurotrophic secretome, systems biology

Adult mesenchymal stem cells represent an attractive, ethically viable source for neuronal replacement therapies; however, efficient and physiologically relevant dopaminergic specification remains a major challenge. Here, we report that hypoxic preconditioning functions as a decisive biological switch that programs infrapatellar fat pad–derived stem cells (IFP-SCs) toward functional dopaminergic neuronal identity. Primary IFP-SCs displayed stable mesenchymal morphology, robust proliferative capacity, and canonical stemness marker localization. Exposure to physiological hypoxia (5% O_2) induced marked morphological remodeling, characterized by cytoplasmic elongation and neurite-like extensions, accompanied by the generation of a neurotrophin-enriched hypoxia-conditioned secretome. FTIR and ^{1}H-NMR profiling of conditioned media confirmed the presence of NGF, EGF, bFGF, BDNF, and dopaminergic metabolites, indicating functional paracrine remodeling under hypoxia. Neuronal induction under defined conditions yielded cells with characteristic neuronal architecture, including axons and dendritic spines. Immunocytochemistry demonstrated robust expression of MAP2, NF-L, NSE, SNAP25, and advanced functional markers (GAP43, SYT11, KCNA5, PACSIN1, syntabulin, dystrophin), with the strongest expression observed in hypoxia-programmed groups. Semi-quantitative RT-PCR confirmed dopaminergic lineage commitment through expression of EN1 and NURR1, while pathway analysis revealed attenuation of PI3K/Akt signaling, selective activation of TGF-β signaling, and preserved Wnt signaling dynamics. Systems-level validation using STRING network analysis revealed a highly interconnected, non-random protein interaction network (PPI enrichment $p = 2.17 \times 10^{-11}$), integrating dopaminergic specification, synaptic maturation, and mitochondrial regulation. Collectively, this

study demonstrates that hypoxic programming orchestrates coordinated transcriptional, secretory, and functional remodeling of adult stem cells, enabling efficient dopaminergic neuronal differentiation with translational relevance for neurodegenerative disorders.

Enhancing CSF Leak Detection: A Computational Pipeline for Epitope Mapping Towards Translational Diagnostics

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Background: CSF leaks arise form dural tare caused by trauma, iatrogenic or congenital factors. When diagnosed early, it may prevent fatal complications like meningitis. Current diagnosis using CSF biomarkers and imaging shows limited specificity, accessibility and high cost. Developing POCT with improved specificity requires sensitive antibodies targeting CSF biomarkers. To address this, we integrated an in-silico pipeline for epitope prediction and antibody design and was benchmarked against antigen–antibody crystal structures. These findings hypothesise that the incorporated tools can support translational diagnostics and POCT development.

Methodology: Epitopes for three CSF biomarkers were predicted using Bepipred 3.0 and Discotope 3.0, with high-confidence regions filtered to identify consensus epitopes. Antibody modelled using AbodyBuilder was used for docking via HawkDock and top poses were ranked by MM/GBSA. Recurring contact residues (>3 models) were compared with predicted epitopes and benchmarked against solved antigen–antibody complexes.

Results: Benchmarking against five solved complexes (3W5D, 7OH0, 7K8S, 6ML8 and 2NY7) demonstrated that the consensus epitope prediction outperformed with contact and literaturedefined epitopes (82%) than individual tools (Bepipred ~70%; Discotope ~73%). Applying the pipeline to CSF biomarkers identified distinct surface-exposed epitope clusters with favourable accessibility and stability. Domain-level structural fitting revealed several local surface motifs with low RMSD (0.02–0.05), highlighting candidate binding sites that may enhance assay specificity may improve diagnostic specificity.

Conclusion: This computational pipeline reliably identifies surfaceaccessible, structurally consistent epitope clusters across clinically relevant CSF biomarkers. Consensus predictions outperform individual tools, generating testable hypotheses for antibody design and translational diagnostics.

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Biomarker-Guided Precision Therapy in Diabetic Macular Edema: Predicting Anti-VEGF Therapeutic Response and Non-Response

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Background: Diabetic macular edema (DME) results from retinal vascular leakage and endothelial barrier dysfunction. Although anti-VEGF therapy is the clinical standard, nearly one-third of patients show suboptimal anatomical and functional improvement despite repeated intravitreal injections. This highlights the need for reliable

prognostic biomarkers to enable early identification of patients who are unlikely to respond to therapy.

Methods: In this prospective translational study, DME patients receiving at least three intravitreal anti-VEGF injections were followed for six months. Patients were stratified into responders and non-responders based on central retinal thickness (CRT) outcomes (<300 µm vs. >300 µm). Serum biomarkers spanning angiogenic, inflammatory, endothelial junctional, and immunomodulatory pathways were quantified using multiplex bead-based flow cytometry. Associations with clinical outcomes were assessed through correlation, network analyses, and ROC-based predictive evaluation.

Results: Responders demonstrated a vascular-stabilizing molecular profile marked by higher Ang-1 levels and an increased Ang-1 to Ang-2 ratio, correlating with greater retinal thickness reduction and visual improvement. Protective mediators, including sFLT-1 and sST2, were enriched among responders, suggesting enhanced VEGF sequestration and suppression of IL-33–driven inflammation. Non-responders exhibited elevated IL-18 and increased circulating CD31, consistent with persistent endothelial disruption. VEGF levels alone did not reliably distinguish treatment responses. Network analysis revealed coordinated angiopoietin and immunoregulatory signaling in responders, contrasted by sustained inflammatory and angiogenic coupling in non-responders.

Conclusion: Integrated serum biomarker profiling identifies clinically relevant signatures predictive of anti-VEGF responsiveness in DME. These findings support a precision medicine approach to identify patients who may benefit from adjunctive or alternative pathway-targeted therapies.

Evaluation of Marine Bacterial metabolites to Combat Pathogenic Biofilms in Static and Flow systems

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Biofilm based infections are challenging to treat as they pose to be a niche for emergence and dissemination of antimicrobial resistance.[1] 80% of the infections are chronic and persistent as they are associated to biofilms.[2] Due to the tough extracellular matrix formed by the cells in the biofilm it is difficult for the antimicrobial agents to penetrate and effectively kill the cells.[3] It is need of the hour to explore novel agents which have the potential to inhibit the formation of biofilms or disperse the cells of the biofilm.

The current study focuses on exploring the western coastal bacterial metabolites for their ability to combat biofilms. It involves isolation of marine bacteria, screening for anti-quorum sensing agents, optimizing the yield of the agent using response surface methodology and its effective extraction using ethyl acetate and chloroform methanol. The producers and the anti-biofilm agents were characterized. A concentration of 500 mcg/mL of the metabolite resulted in a 92% and 95% reduction in biofilm formation of *Pseudomonas aeruginosa MTCC 2453* and *Staphylococcus aureus MTCC 3160,* respectively, while 1000 mcg/mL led to a 37% and 43% breakdown of preformed biofilms of *Pseudomonas aeruginosa* MTCC 2453 and *Staphylococcus aureus* MTCC 3160 respectively.

The metabolite is found to be effective in reducing the viability of the cells, exopolysaccharide content and extracellular DNA content which affects the overall architecture and stability of the biofilms making it a suitable agent to inhibit biofilm formation in static and flow systems.

This study is supported by DBT- BUILDER grant, Govt. of India (BT/INF/22/SP45358/2022).

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Alleviating Obesity using Microencapsulated Fucoxanthin: A Safe and Natural remedy to a Global problem

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Obesity is chronic disease characterised by excessive adiposity and comorbidities like cardiovascular defects, diabetes, and non-alcoholic fatty liver disease.

Commercial medications induce nausea, liver failure, diarrhoea and fatality in extreme cases. Fucoxanthin (Fx), a carotenoid found in brown sea-weed is known for its anti-obesity property. Applications of Fx is hindered by its low solubility, stability, and poor bioavailability. This study aims to microencapsulate fucoxanthin with inulin (IN) and gum acacia (GA) and study its bioavailability and anti-obesity effect in obese mice. Fx was extracted from *Padina tetrostmatica*. Purified Fx was microencapsulated with IN, and GA *viz* lyophilisation. Obesity(ob) was induced in C57/BL6 mice (n=5) with 40% high fat diet (HFD) for 8-10 weeks and was orally dosed (200nM) with microencapsulated fucoxanthin (IN-Fx & GA-Fx) to study its bioavailability at 2,4,6&8h. The most bioavailable encapsulation was further evaluated for its anti-obesity effect in obese mice along with orlistat (ORL) (66mg/Kg/BW). Fx was quantified by HPLC with 98% purity. The C_{max} of Fx (18.56 nM) in blood plasma was detected at the 4h (T_{max}) for ob-InFx. After 8 weeks of the anti-obesity study, ORL, Free Fx and INFx-treated groups saw a decrease in body weight of upto 4.9, 3.4 and 3.62%, respectively, whereas HFD group observed a 6.23% increase. A 20% mortality rate was observed in ORL-treated group. IN-Fx demonstrated significantly ($p \leq 0.05$) better glucose tolerance and lower serum cholesterol and triglyceride levels in obese mice compared to the other groups. These results demonstrate microencapsulated fucoxanthin to be a safe and effective agent for combating obesity.

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Gold Nanorod Functionalization Directs Macrophage Polarization and Fibrosarcoma Suppression

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Photothermal and photodynamic therapies using biocompatible gold nanoparticles have promulgated their use in in cancer theranostics1. Surface plasmon resonance and high surface to volume ratio of nanoparticles provide unique opportunities to functionalize them with various ligands2. Understanding the influence of shape, size and functionalization on characteristics of nanoparticles, our study aims to understand the anti-tumor and immunomodulatory effects of gold nanorods (GNRs) in murine fibrosarcoma induced by 3-methylcholanthrene. PEGylated GNRs (aspect ratio of 2.5) were synthesized using ligand exchange method by replacing cetyltrimethylammonium bromide (CTAB). In-vitro studies of bare gold nanorods (CTAB-GNRs) were performed using macrophages isolated from Swiss albino mice. Uptake of GNRs through ICP-MS and SEM-EDS, and MTT assay were done to assay cytotoxicity and cell viability, while pro- and anti-inflammatory cytokines quantified via ELISA, and qRT-PCR were used to understand the onset of cell-death pathways. CTAB-GNRs induced upregulation of pro-inflammatory cytokines along with activation of apoptotic and necroptotic pathways, proving that they support activation of an M1 like pro-inflammatory phenotype in M0 macrophages. To understand the impact of functionalization upon GNRs, we studied the potential of PEGylated gold nanorods (PEG-GNRs) in halting fibrosarcoma progression. PEGylated GNR treatment showed distinct responses regarding TNF-α, IL-1β, IL-6, IL-10, IL-12 along with caspase-3, -8, and -9, as well as the pro-apoptotic markers p53 and Bax. Our findings suggest that PEGylated GNRs effectively inhibit fibrosarcoma progression by activating tissue specific distinct cell-death pathways like classical apoptosis and inflammasome-mediated pyroptosis.

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Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Neuroprotective Effects of *Centella asiatica* and Asiatic Acid in a Scopolamine-Induced Amnesia Model

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Background: Cognitive impairment is closely associated with cholinergic dysfunction, oxidative stress, and altered monoaminergic activity. Scopolamine-induced amnesia is a well-established experimental model that mimics memory deficits and redox imbalance.[1] *Centella asiatica* extract (CAE) and its bioactive constituent, Asiatic acid (AA), possess potential neuroprotective properties.[2]
Objective: This study aimed to evaluate the neuroprotective effects of CAE (25, 50, and 100 mg/kg) and AA (30 and 60 mg/kg) against scopolamine-induced cognitive impairment using behavioural and biochemical parameters.
Methods: Amnesia was induced by scopolamine administration. Animals were treated with CAE (25, 50, and 100 mg/kg), AA (30 and 60 mg/kg), or donepezil (DPZ) as the standard drug. Behavioural performance was assessed using the Y-maze test. Biochemical estimations included acetylcholinesterase (AChE), superoxide dismutase (SOD), reduced glutathione (GSH), reactive oxygen species (ROS), nitric oxide (NO), malondialdehyde (MDA), and monoamine oxidase-B (MAO-B). Data were analyzed using one-way ANOVA followed by the Newman–Keuls multiple comparison test[3].
Results: Scopolamine significantly impaired Y-maze performance and induced marked oxidative imbalance, as evidenced by increased AChE, ROS, NO, MDA, MAO-B, and SOD levels, along with a significant reduction in GSH. Treatment with CAE and AA significantly ameliorated these alterations in a dose-dependent manner. Both CAE and AA normalized elevated SOD levels, indicating attenuation of oxidative burden. The higher dose of AA (60 mg/kg) exhibited the most prominent neuroprotective effect, comparable to donepezil.[1]
Conclusion: CAE and AA effectively counteract scopolamine-induced cognitive deficits by modulating cholinergic activity, restoring redox homeostasis, and normalizing MAO-B levels. Thus, AA may serve as a promising therapeutic candidate for memory-related neurodegenerative disorders.

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Respiratory Syncytial virus F-protein adjuvanted with a Carbomer-based adjuvant induces protective Humoral response in Mice

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The carbomer-lecithin-based adjuvant Adjuplex has been shown to induce a balanced T-cell response and high antibody titers with some of the viral pathogens. Here we compare the humoral immune response in mice immunized intranasally with respiratory syncytial virus fusion (RSV-F) or glycoprotein (G) (RSV-G) or both using Adjuplex and/or a TLR9 agonist, CpG oligodeoxynucleotides (ODN). Both the adjuvants elicited robust antibody response in mice, however, Adjuplex generated higher levels of neutralizing antibodies as compared to CpG ODN when used with RSV-F protein. Neutralizing antibody titers were associated with reduced RSV load in the lungs of immunized BALB/c mice upon intranasal challenge with RSV A2 strain. RSV-G alone was insufficient to elicit a strong antibody response with either of the adjuvants and combining RSV-F and RSV-G did not show any synergistic response in terms of neutralizing antibody titers, however, this combination of antigens elicited a strong mucosal immune response as measured by IgA titers specific to RSV-F and RSV-G in lung tissues. This data suggests that carbomer-based adjuvants can induce

a potent and protective humoral and mucosal response when used as an adjuvant for the RSV-F subunit vaccine and combination of RSV-F and RSV-G with Adjuplex may further be explored for enhancing the efficacy of RSV vaccines.

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Methods and processes for preparation of BASIC- method for Industrial processes and Therapeutic approaches

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Background

Microbiome-derived intracellular and extracellular components are increasingly recognized for their ability to modulate cancer cell survival and death. Several bacterial species exhibit anti-tumor activity in vitro and in vivo. However, standardized methodologies to isolate and evaluate these bioactive bacterial components remain limited. There is a need for novel, effective, and less toxic therapeutic approaches from microbial-derived metabolites as an alternative to conventional chemotherapeutics.

Methods

An in-house standardized protocol was developed for the isolation and purification of Bacterial Anticancer Secretome and Intracellular Components (BaSIC) from Bacillus cereus Frankland and Frankland-14579 isolated from conditioned media. MCF-7 cells were treated with BaSIC and evaluated using cell viability assays (MTT), cell counting, fluorescence microscopy, dual AO/EB staining, and Annexin-V/PI flow cytometry. Oxidative stress was assessed via lipid peroxidation (TBA assay). Intracellular metabolite profiling was performed using Vertical Tube Gel Electrophoresis (VTGE)–assisted LC-HRMS.

Results

BASIC treatment significantly reduced MCF-7 cell proliferation, with approximately 50% cell death observed. Biochemical analyses revealed elevated oxidative stress and lipid peroxidation. VTGE-LC-HRMS profiling identified intracellular metabolites in cancer cells derived from BaSIC of Bacillus cereus Frankland and Frankland-14579, including glycylprolylalanine and 2-benzylthiophene, indicating BaSIC-induced metabolic reprogramming.

Conclusion

BASIC derived from Bacillus cereus exhibits potent anti-cancer activity by reducing cell viability, inducing apoptosis, and altering cancer cell metabolism in breast cancer (MCF-7) cells. This study provides BsSIC as a scalable, cost-effective platform for isolating bacterial anticancer metabolites and provides a strong foundation for developing microbiome-derived therapeutic strategies in cancer.

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Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Injury-Specific Neuroinflammatory Trajectories Converge on Impaired Resolution: Implications for Brain Repair and Therapeutic Intervention

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Key words: Neuroinflammation, Brain injury, Viral infection, Repair, Therapeutic Intervention

Neuroinflammation occurs in many neurological disorders, but its effects depend on the type of injury, its timing, and the duration of the injury. Brain injury and viral infections both activate macrophages and microglia; however, the phase of activation, responses to intracellular stress, and long-term outcomes differ. Disease progression appears to relate less to inflammation itself and more to whether immune responses resolve appropriately. When resolution fails, ongoing cellular stress can contribute to neurodegeneration. This talk will discuss the importance of stage-specific treatment strategies that match therapy to the phase of injury and to the CNS during viral infection, supporting recovery and repair pathways.

Artificial Intelligence in Transformative Mental Healthcare Research

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Mental health is an essential component required for one's overall development that helps us to make decisions and maintain inter-personal relationships. Recent developments in Artificial Intelligence (AI) have a significant potential in analyzing neurodegenerative disorders and thereby leading to the improvement in mental healthcare research. Parkinson Disease (PD) is a complex neurological disorder attributed by loss of neurons generating dopamine in the Substantia Nigra per compacta. Electroencephalogram (EEG) plays an important role in diagnosing PD as it offers a non-invasive continuous assessment of the disease progression and reflect the complex patterns. The experimental study on an open EEG dataset consisting of 14 PD and 14 healthy individuals are subjected to Recurrence quantification analysis specific to gender, brain regions and EEG bands. The extracted recurrence features served as inputs to the Machine learning (ML) models, which achieved high classification performance, across all the scenarios. The interpretability of the ML model decisions is investigated using explainability technique. In addition to this, Fuzzy recurrence plots and Deep learning algorithms are applied to examine the effects of eyes open and eyes closed conditions during ON and OFF medication states in PD patients. The progression of the neurodegenerative diseases, the effect of treatment and its responses continuously change with time. This leads to the need for longitudinal data acquisition using multiple modalities. Hence, the performance of AI algorithms can be enhanced through the analysis of multimodal and longitudinal data. This paves the way to "Personalized AI" which is the recent trend in healthcare research.

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Rooftop Solar Potential Estimation using Transformer Based Model

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With the world becoming increasingly interested in the idea of sustainable energy sources, the development of stable and efficient systems of determining the potential of rooftop solar has become a pressing requirement. The prohibitive nature, spatial resolution, and optimum scalability restrict conventional survey-based methods. This study provides a computer vision system that uses transformers to process high-resolution satellite images and properly and precisely determine the potential of rooftop solar. An improved version of SegFormer transformer has been used to do semantic segmentation of rooftop surfaces and thus it is combined with spatial and solar irradiance tests to produce predicted energy output. The accuracy of the proposed system is Intersection over Union (IoU) (78 -80% based on the test data), and pixel accuracy (95%), which are better than traditional CNN-based systems. Moreover, the findings are also given in the form of an interactive GIS system that can offer useful guidance to urban planners and policymakers in cases where the issue of sustainable energy uptake and installation of rooftop solar systems is concerned**.**

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DRNet: Enhanced Retinal Vessel Segmentation for Diabetic Retinopathy Detection using Deep Learning

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Diabetic Retinopathy (DR) is a leading cause of blindness among the population nowadays; hence it should be detected in its early stages. Blood vessels are a key indicator for the growth of DR, so their segmentation helps in early diagnosis. The traditional methods used by researchers were time consuming and prone to human errors. Therefore, developing a Computer Aided Diagnosis (CAD) system for DR has become a crucial area of research, as it helps in early detection of DR with increased accuracy. Various research studies have given different solutions for segmenting out blood vessels. However, two issues are still not addressed by existing studies, i.e. accurately detecting thin vessels and minimizing computational costs. Therefore, this paper provides two-fold contribution by solving these two issues, firstly it introduces a novel deep learning based Diabetic

Retinopathy Network (DRNet), designed for segmentation of both thick and thin blood vessels using fundus images and secondly, its lightweight architecture helps to reduce computational cost. The model is trained on the publicly available FIVES dataset. Further, the performance of DRNet is compared with existing models on two benchmark datasets, STARE and CHASE_DB1 using standard metrics of Accuracy, Sensitivity, and Specificity. Results show that more detailed vessels are extracted by DRNet and it exhibits state-of-the-art performance for vessel segmentation by achieving accuracy of 0.9628, 0.9683 and specificity of 0.9807, 0.9791 on STARE and CHASE_DB1. Moreover, the proposed architecture decreases the computational cost by exhibiting least number of trainable parameters among all the other state-of-the-art models, i.e., 1,35,582.

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Development of a score for early Identification of Diabetic peripheral Neuropathy using Endothelial Biomarkers

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Background

One of the most common complications of diabetes mellitus is diabetic peripheral neuropathy. This disorder is associated with increased utilization of healthcare services and affects the economic profile of a country. Despite the multifactorial background of the pathogenesis of this disease, the mechanism underlying peripheral neuropathy is still unclear. Endothelial damage is a new determinant of pathogenesis, with experimental data showing endothelial dysfunction per se is sufficient to cause neuropathyendocan as a potential biomarker for endothelial dysfunction in diabetic peripheral neuropathy patients.

Methods

The study population comprised 97 adult patients with diabetes who visited the OPD of the Department of Endocrinology for more than five years. The patients were categorized into two groups: those with diabetes with peripheral neuropathy (DPN, n = 49) and those with diabetes without peripheral neuropathy (No DPN, n = 48).

The endothelial biomarkers such as endocan, hs-CRP, vitamin D, and lipid profiles were measured and analyzed in both groups. The standardized scores for dyslipidemia, inflammation, vitamin D, and endocan were calculated. All the statistical analyses were performed using Jamovi software version 2.3.26 (Sydney, Australia).

Results

All of these biomarkers were significantly altered in peripheral neuropathy patients. A strong correlation between endocan levels and lipid profiles and between hs-CRP and vitamin D levels was detected.

Conclusion

The inflammatory score and a combined score including all

the above biomarkers might help in the early stratification of diabetic patients who are at greater risk of developing peripheral neuropathy.

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Dual Drug Delivery for Augmenting Bacterial Wound Complications via Tailored Ultradeformable Carriers

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Addressing the complex challenge of bacterial-infected wound healing, this study investigates the therapeutic potential of lipid nanomaterials, particularly advanced ultradeformable particles (UDPs), in modulating the wound microenvironment. A dual-drug delivery system comprising silver sulfadiazine (SSD) and vitamin E (VE) was developed using UDPs (ethosomes, transferosomes, and transethosomes) for synergistic antibacterial and regenerative action. Comparative physicochemical characterization revealed superior stability of transethosomes with a zeta potential of −36.5 mV. These vesicles exhibited sustained and pH-responsive release, achieving approximately 90% SSD and 72% VE release under wound-like conditions, while minimizing the side effects associated with conventional topical formulations. Cytotoxicity assays demonstrated 60% cell viability even at 175 µg/mL, and hemolysis remained below 5% at 250 µg/mL, confirming excellent biocompatibility. Vitamin E–SSD-loaded transethosomes (VSTEs) significantly enhanced cellular migration and proliferation, resulting in ~95% wound closure within 24 hours and an 80% reduction in E. coli and S. aureus populations. Ongoing in vivo studies using a rat model of third-degree burn wounds include temporal evaluation of wound contraction, histological analysis of granulation and re-epithelialization, and immunohistochemical assessment of angiogenic and inflammatory markers. Preliminary findings indicate accelerated fibroblast migration, enhanced tissue regeneration, and pronounced antibacterial effects. Collectively, these results highlight the VSTE-based nanocarrier as a multifunctional, biocompatible, and efficient therapeutic platform for managing complex burn wounds, integrating antimicrobial defense with enhanced tissue repair mechanisms.

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Fabrication and In-vivo evaluation of Novel Electrospun Local Drug delivery system for treatment of Periodontitis

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Background: Periodontitis is a chronic inflammatory disease leading to progressive periodontal tissue destruction. While scaling and root planing (SRP) is the gold standard, limitations in access and pathogen elimination

necessitate adjunctive local drug delivery. Polycaprolactone (PCL) is a biodegradable polymer suitable for electrospinning into nanofibrous scaffolds for sustained antimicrobial release. Chlorhexidine (CHX) offers broad-spectrum activity, but its conventional delivery has limitations.

Objective: To fabricate and characterize electrospun PCL–CHX scaffolds and evaluate their physicochemical properties, biocompatibility, antimicrobial efficacy, and in-vivo performance in a rat periodontitis model.

Methods: PCL–CHX membranes were fabricated via electrospinning, characterized for morphology, tensile strength, crystallinity, hydrophobicity, and degradation. Biocompatibility was assessed by haemolysis, BM-MSC viability, attachment, and proliferation. Antimicrobial activity against Staphylococcus aureus was determined using agar diffusion. In vivo, ligature-induced periodontitis was established in rats, followed by subgingival placement of PCL or PCL–CHX chips. Clinical parameters and histological inflammatory scores were recorded over six weeks.

Results: Electrospun scaffolds exhibited nanofibres (200 nm–2 µm), tensile modulus ~80 MPa, contact angle ~124°, and slow degradation (~5% in 21 days). Both PCL and PCL–CHX were non-haemolytic (<0.7%) and supported >99% cell viability with enhanced proliferation. PCL–CHX demonstrated greater antimicrobial zones (3–5 mm) than PCL (1 mm). In vivo, PCL–CHX significantly improved gingival index and probing pocket depth versus PCL ($p = 0.003$), with mild, resolving inflammatory responses histologically.

Conclusion: Electrospun PCL–CHX scaffolds combine mechanical stability, cytocompatibility, and sustained antimicrobial action, offering a promising adjunctive local delivery system for periodontitis management.

NeuroLocate: A Real-Time Synchronized Multimodal Biomedical Signal Acquisition System for Intraoperative Dental Nerve Localization

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Accurate intraoperative localization of the Inferior Alveolar Nerve (IAN) remains difficult due to the lack of real-time feedback during dental procedures. While ultrasound, bioimpedance, and electromyography (EMG) have been used individually, their effectiveness is limited by signal ambiguity and operator dependency. The key challenge lies in synchronizing these heterogeneous physiological signals for coherent interpretation.

This work presents **NeuroLocate**, a portable, radiation-free nerve localization system built on a low-latency synchronized multimodal acquisition architecture. The device simultaneously captures bioimpedance, A-mode ultrasound, and EMG signals using dedicated analog front-end circuits and a microcontroller platform. A unified timing framework maintains temporal alignment across modalities, with wireless transmission to a mobile interface at under 100 ms latency for real-time visualization.

Phantom-based evaluation achieved **92–94% localization accuracy** with a **false-positive rate below 6%**, demonstrating that synchronized multimodal sensing improves detection robustness for intraoperative dental guidance.

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Novel Determinants of Loneliness and Social Isolation among the Economically Productive Population: An Emerging Public Health Enigma – A Qualitative Exploration

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Keywords: Loneliness, Social Isolation, Working Age Population, Geriatric Population.

Background: Loneliness and Social Isolation (SI) are an emerging public health crisis, as it profoundly affects both physical and mental health. Recent studies have established its correlation with premature mortality. The pieces of literature are available only to the geriatric population as their study respondents; however, the determinants of loneliness and SI differ for other age strata. This article has tried to explore the novel determinants and discussed how it's different from the determinants of the elderly.

Objectives: The objectives are to explore the intangible determinants of loneliness and SI among economically

active communities and to explore the most prevalent reasons leading to loneliness and SI.

Methodology: Twenty-seven in-depth interviews were conducted with the respondents in their workplace. Sampling was purposive to ensure data richness. Themes were identified with content analysis.

Results: Totally six themes emerged from the interviews, namely, Decision-making, Professional leverage, Peer mentoring, Fiscal affluence, and Social Seclusion. Professional leverage was the prevalent reason leading to loneliness and SI.

Conclusion: By considering these determinants during policy development, organisations can help non-elderly communities achieve better mental well-being and camaraderie, thereby preventing loneliness and social isolation, and increasing productivity of the workplace.

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Comparative Genomics Signatures of Venous Thromboembolism Across Altitudinal Extremes

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Background

Venous thromboembolism (VTE) is shaped by both genetic and environmental factors. High altitude causes hypoxic stress, affecting endothelial function and coagulation, and raising thrombosis risk. Molecular evidence distinguishing high-altitude from sea-level VTE remains limited. In this pilot study, we investigated differential gene expression patterns between high-altitude VTE patients (HAP) and sea-level VTE patients (SLP), focusing on coagulation and endothelial regulation genes.

Methods

A targeted panel of 10 genes associated with VTE were chosen due to their involvement in coagulation processes and endothelial activation. Total RNA was isolated from whole blood, and cDNA was synthesized using Qiagen First Strand cDNA Synthesis kit, followed by qRT-PCR for gene expression. Differential gene expression was analyzed using fold change, and statistical significance was determined using *p-values*.

Results

Patients with high-altitude VTE experienced significant upregulation of *FGF2, F10, and F2,* indicating enhanced endothelial activation and amplification of the common coagulation pathway under hypoxic conditions. In contrast, *PROCR*, an anticoagulant gene, was downregulated, suggesting impaired anticoagulant regulation. The molecular findings correspond with the recognized clinical biomarkers that signify coagulation activation and endothelial dysfunction.

Conclusion

In conclusion, this pilot study identifies a distinct hypoxia-associated transcriptional signature in high-altitude VTE, characterized by upregulation of *FGF2, F10, and F2*, and downregulation of *PROCR*. This comprehensive transcriptional modification distinguishes high-altitude venous thromboembolism (VTE) from cases at sea level, clarifying the mechanisms responsible for the heightened thrombotic risk at high altitudes and require validation in larger cohorts.

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EEG-Based Imagined Speech Classification Using Statistical Features and Machine Learning Models

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Silent articulation of speech in the mind, termed as Imagined speech,[1,2] is the cognitive process of mentally simulating or thinking about speech elements—such as phonemes, vowels, and words—without actual verbal articulation or physical movement of the vocal apparatus (like the tongue, lips, or vocal cords). The analysis of brain activity has been extensively carried out using Electroencephalography (EEG).[3] EEG is a non-invasive method to record the electrical activity of the brain using scalp electrodes. In this study, EEG signals corresponding to two imagined words, *'good'* and *'bad',* were recorded from three participants in a controlled experimental environment. The objective was to assess the feasibility of imagined-speech decoding, extract 81 statistical features from the EEG signals, and evaluate classification performance using three machine-learning models. Support Vector Machine (SVM), Random Forest (RF), and Decision Tree (DT) classifiers. The model robustness and generalizability of these classifiers were evaluated under the 5-fold cross-validation method and the leave-one-subject-out (LOSO) method. The SVM classifier showed a better overall validation accuracy of 84.54 ± 2.5% in the LOSO method, and the Decision Tree classifier showed better performance in 5-fold cross-validation methods, providing an accuracy of 85.31 ± 7.99%.

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Design and Development of an Intelligent Multimodal Framework for Mental Health Detection: A Comprehensive Review

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Multimodal artificial intelligence (AI) has proven to be an efficient mental-health detection paradigm that simultaneously models heterogeneous data streams which include text, speech, vision, EEG, and physiological signals. This systematic review is a literature review survey on the up-to-date multimodal learning methods of mental-health assessment, which follows PRISMA 2020 guidelines. Ninety peer-reviewed articles were found and published between 2010 and 2025. The paper classifies feature-engineering methods, deep learning architectures (CNNs, RNNs, Transformers, GNNs), fusion process (early, late, hybrid, attention-based), and assessment protocol as well. Empirical results have shown that hybrid and attention based fusion strategies are better than unimodal baselines and naive concatenation techniques and are characterized by relative performance gains of 10 percent-25 percent. The main technical issues that have been noted are data heterogeneity, missing modality, restricted cross dataset generalization, risks of information leaking, and lack of explainability. The review also points to new solutions like federated learning, self-supervised multimodal representation learning, and explainable AI in order to develop secure and scalable mental-health detection systems.

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Viruses in adult Chronic Diarrhoea: A study from North India

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Background: Chronic diarrhoea is "persistent alteration from the norm with stool consistency between Types 5 to 7 on Bristol stool chart and increased frequency >4 weeks" according to the British Society of Gastroenterology.[1] Various causes include colonic neoplasia, inflammation, malabsorption, and motility disorders, while infections remain less explored.[2,3] Our study, conducted at a tertiary care teaching hospital in North India, aimed to evaluate viral causes of chronic diarrhoea.

Methods: Adults with chronic diarrhoea were recruited for between 1st December 2022 to 31st May 2024 and assigned into 4 groups - IBD in remission(Group A, n=40), Acute severe ulcerative colitis(ASUC)(Group B, n=40), non-IBD chronic diarrhoea(Group C, n=35) and healthy controls (Group D, n=35). After obtaining consent, a small amount of stool sample was collected in 7 ml phosphate buffer saline (PBS), vortexed, centrifuged, and the supernatant used for automated nucleic acid extraction. FlexStar® RT-PCR Detection Mix 1.5 (Altona Diagnostics GmbH, Germany), an in-vitro real-time PCR-based diagnostic test, was used for the detection of Astro, Adeno, Noro group 1 and 2, Rota and Sapoviruses.

Results: Mean age of study population was 36.63 ± 13.72 years, with 51.3% males. Viruses were detected in 8% cases, with 4 cases in each patient group, including Adenovirus (3.3%), Norovirus Group 2(3.3%), and Sapovirus(2.7%). No viral aetiologies were detected in controls. Mixed infection with adeno and sapovirus was noted in 2 patients.

Conclusion: More priority should be given to gastrointestinal viruses in those with chronic diarrhoea, to streamline management and give targeted therapy.

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Papain, A Cysteine protease, Degrades Insulin-induced Amyloid aggregation: Insights from *in-vitro* and *in-vivo* studies

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Amyloidogenic proteins, under specific conditions, undergo alternative folding pathways that lead to the formation of protease-resistant amyloid fibrils with a characteristic cross-β structure. These amyloids are associated with several diseases including Alzheimer's disease, Parkinson's disease, Creutzfeldt-Jakob disease, and insulin-derived amyloidosis, making their clearance a promising therapeutic strategy. Insulin, a well-studied amyloidogenic protein, serves as an model for studying amyloid-related disorders. Insulin-derived amyloidosis is a rare but underestimated condition caused by repeated insulin injections in diabetic patients, leading to subcutaneous deposition of insulin amyloid fibrils and associated clinical challenges. The present study investigates the therapeutic potential of papain, a cysteine protease, in mitigating insulin amyloidosis through integrated in vitro, in vivo, and in silico approaches. Papain exhibited a significant amyloid-degrading potential showing considerable fibril degradation as evaluated by turbidity assay, 80% degradation in 1h incubation. The highest proteolytic activity was observed at 200 µg/mL of papain. In SDS-PAGE complete degradation observed at a concentration of 200ug. The CD spectroscopy showed negative ellipticity at 210 nm confirming disruption of β-sheet-rich amyloid structures upon incubation with Papain, while FTIR revealed reduced 1645 cm−1 peak intensity indicating breakdown of insulin amyloid fibrils and loss of β-sheet conformation. Further, *in vivo* study using male Wistar rats to examine the ability of papain to degrade insulin amyloid was done. The results showed that insulin fibrils generated amyloid masses in rats after subcutaneous injection of insulin for two weeks. There observed significant reduction in size of insulin amyloid for the groups injected with papain. The reduction was more than 87% with the Papain dose of 60 mg/kg body weight. The histopathological results were analysed using light microscopy, polarized microscopy, and fluorescence microscopy. In all the studies, there observed a significant reduction in the insulin amyloid. Further, in silico study evaluated the interaction between Papain and IA, there observed the strong binding affinity -8.1 kcal/mol. Overall, this study demonstrates the degradation potential of papain against insulin amyloid. These findings suggest that papain can be considered as a promising insulin amyloid-degradation agent and a potential therapeutic candidate for managing amyloid-related disorders.

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Persistent Circulating Tumor DNA Defines a Molecularly High-Risk Phenotype in Locally Advanced Oral Squamous Cell Carcinoma

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Background

Oral squamous cell carcinoma (OSCC) is characterized by high loco-regional recurrence rates despite optimal surgery and adjuvant therapy. Field cancerization and occult minimal residual disease (MRD) contribute to treatment failure. Circulating tumor DNA (ctDNA) offers a biologically relevant approach for dynamic molecular risk stratification. This pilot study evaluated a focused 9-gene next-generation

sequencing (NGS) panel for tissue profiling and longitudinal liquid biopsy monitoring in locally advanced OSCC.

Methods: Twenty-four patients with loco-regionally advanced OSCC undergoing curative-intent surgery followed by risk-adapted adjuvant therapy were prospectively enrolled. Tumor tissue and peripheral blood (10 mL, Streck tube) were collected at baseline (pre-surgery), 2–3 weeks post-surgery, and 3 weeks post-adjuvant radiotherapy or concurrent chemoradiotherapy. A targeted 9-gene panel (NFE2L2, PIK3CA, FGFR1, CDKN2A, NOTCH1, HRAS, CCND1, RB1, TP53) was used to identify pathogenic alterations and track ctDNA dynamics.

Results: The tissue diagnostic yield was 91.6% (22/24). Baseline ctDNA positivity was observed in 58% (14/24). Overall, 91.6% (22/24) demonstrated ctDNA positivity at least once during longitudinal monitoring, while 8/24 (33.3%) exhibited persistent ctDNA positivity across all time points. Molecular response stratification identified three groups: Good Responders (33.3%) with sustained ctDNA negativity, Partially Good Responders (29.2%) with intermittent ctDNA detection, and Bad Responders (37.5%) with persistent ctDNA positivity. Persistent ctDNA detection correlated with inferior molecular response category.

Conclusion: A focused 9-gene NGS panel provides high diagnostic yield and enables longitudinal MRD assessment in advanced OSCC. Persistent ctDNA positivity identifies a biologically high-risk subgroup and supports the potential of ctDNA-guided risk-adapted therapeutic strategies. Larger prospective validation is warranted.

Gallic acid Laden Methyl acrylate Gelatin Hydrogel potentiates *in-vitro* and *in-vivo* Antiglioblastoma activity.

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Glioblastoma (GBM) is the most common, invasive and aggressive primary brain tumour with a very dismal prognosis, highlighting the need for targeted treatment therapies that maximize the drug retention while limiting the systemic toxicity due to resistance to traditional therapy, limited drug penetration through the blood-brain barrier, and consistently poor clinical outcomes. By maintaining therapeutically effective drug concentrations within the tumor microenvironment for extended durations, long-acting intratumoral chemotherapy has the potential to improve treatment outcomes in GBM. To address these challenges, we developed an injectable, *in situ*–forming gelatin methacrylate (GelMA) hydrogel incorporating gallic acid (GA), a naturally occurring polyphenolic molecule with combined antioxidant and anticancer effects, for potential GBM treatment. Photocrosslinking of the GelMA–GA hydrogel produced a biomaterial with better cytocompatibility, regulated swelling behavior, and increased mechanical strength when compared to GelMA alone. *In-vitro* evaluation showed that the GelMA–GA hydrogel significantly reduced the viability, proliferation, and migration of human U-87 MG glioma cells, while combination with temozolomide (TMZ) exerted synergistic effects by further inhibiting cell growth and promoting the apoptosis. Also, in a GBM xenograft model, combination therapy involving intraperitoneal temozolomide (TMZ) and intratumoral GelMA–GA hydrogel administration markedly reduced tumor growth. Histological assessment demonstrated significant reduction in mitotic indices and Ki-67 expression in treated tumors, reflecting diminished proliferative capacity. Overall, the GelMA–GA hydrogel represents a promising candidate for targeted drug delivery that synergistically combines chemotherapeutic sensitization with intrinsic anticancer efficacy for GBM treatment.

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Serum and Urinary Proteins as early predictive Biomarkers of Acute Kidney injury in patients with Acute Respiratory Distress syndrome

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Introduction:

Acute respiratory distress syndrome (ARDS), is a life-threatening lung condition in ICUs, characterized by severe hypoxemia and increased lung permeability. Acute kidney injury (AKI) is the abrupt loss of kidney function resulting from tissue damage. The mortality rate with ARDS is approximately 27.9%, which can increase up to

42.3% in the presence of AKI. Current diagnostic approach for AKI includes measuring of serum creatinine and urine output, the levels of both won't increase until significant kidney damage. Therefore, there is need to evaluate more sophisticated molecules that would enable early diagnosis and a better prognosis. Cystatin C, KIM-1, NGAL, TIMP-2, IGFBP-7 and IL-18 are promising molecules to be act as early predictive biomarkers of AKI in ARDS patients.

Method

Blood and urine samples from ARDS patients with or without AKI (disease groups) and non-ARDS or non-AKI (control group) patients were collected, processed and stored at -80°C. The sandwich ELISA was performed to determine the concentration of the proteins. The cumulative result was plotted in graph using GraphPad Prism software.

Result

The concentration of proteins varies corresponding to the groups. In case of ARDS patients with or without AKI, there is an elevated concentration of the proteins as compared to non-ARDS or non-AKI.

Conclusion

Cystatin C, KIM-1, NGAL, TIMP-2, IGFBP-7 and IL-18 effectively demonstrate higher concentrations than usual in cases therefore, can act as early predictive biomarkers of AKI in ARDS patients.

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Development and Manufacturing of a Low-Cost Smart Insole for Pressure Mapping in Diabetic Foot

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India is the 'diabetes capital of the world', according to a study by the Indian Council of Medical Research that shows the country now has 101 million diabetics, with a further 136 million pre-diabetic individuals in need of prevention. Most of the population suffering from diabetes experience diabetic foot problems leading to extreme foot pain, plantar corns, and diabetic foot ulcers. To assess these conditions, accurate characterization of plantar pressure is required. In this presentation, the development, testing, and manufacturing of a novel in- shoe, low-cost, and multi-material smart pressure mapping insole, will be discussed. This device has a high number of sensors and was tested on 25 healthy volunteers and 25 patients with different degrees of diabetes. The working range of the device was observed to be 5 kPa to 900 kPa, with an average hysteresis error of 3.25%. Plantar pressure was found to increase from healthy to diabetic volunteers, in terms of both standing and walking. With the initial success of the prototype in accurate diagnosis of diabetic foot conditions, a range of manufacturing protocols were iteratively developed to generate a production model, which was further tested on 100+ subjects, with the help of industrial collaboration. The developed sensing device is expected not only to assist in the prediction of diabetic ulceration or re-ulceration, but also to provide strategies and suggestions for foot pressure alleviation and pain mitigation.

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Influence of Oncogene ZNF726 on Glycolytic metabolic changes and Lipid accumulation in Breast Cancer cells

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Keywords: Breast Cancer, ZNF726, KEGG pathway, Warburg effect, lipid accumulation

Zinc finger proteins are critical regulators of gene expression and are involved in several cellular processes, including proliferation, differentiation, and metabolic reprogramming in cancer cells.[1] Our study recently demonstrated that unexplored zinc finger Protein 726 (ZNF726) displayed oncogenic activity in breast cancer by modulating cholesterol metabolism.[2] However, its role in metabolic alterations and lipid reprogramming remains obscure. Breast cancer progression is closely linked to metabolic plasticity, particularly the Warburg effect, characterised by enhanced aerobic glycolysis and increased lactate production that supports rapid tumour growth and survival.[3] In addition, lipid biosynthesis and adipogenic differentiation contribute to energy storage, providing fuel for cancer cell growth and metastasis.[4] In the present study, the functional role of ZNF726 was investigated using overexpression and knockdown approaches in MDAMB231 and MCF-7 breast cancer cells. Transcriptomic analysis followed by KEGG pathway enrichment revealed that a large proportion of differentially expressed genes were associated with metabolic pathways, indicating a potential role of ZNF726 in metabolic regulation. Real-time PCR analysis demonstrated that overexpression of ZNF726 increased the expression of glycolysis-associated genes, including hexokinase II, GLUT1 and GLUT4, suggesting enhancement of Warburg effect in breast cancer cells. Furthermore, Oil Red and Nile red staining confirmed increased lipid droplet accumulation in ZNF726 overexpressing cells and reduced lipid deposition in knockdown cells in both MDAMB231 and MCF-7 cells. Collectively, these findings indicate that ZNF726 promotes metabolic glycolysis and lipid accumulation, highlighting its potential as a therapeutic target.

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NOTUM, a WNT Signaling Antagonist, Drives Cell-Autonomous Progression of Colorectal Cancer and Serves as a Potential Diagnostic Biomarker

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Colorectal cancer (CRC) is driven by early hyperactivation of WNT signalling, most commonly caused by loss-of-function mutations in the APC gene. NOTUM, a secreted WNT feedback antagonist, is induced under these conditions, but its diagnostic and functional relevance in human CRC remains poorly understood. We hypothesized that NOTUM is selectively upregulated in CRC, contributes to tumor progression in a cell-autonomous manner, and can serve as a circulating biomarker. Analysis of surgically resected human samples revealed significantly elevated NOTUM mRNA and protein expression in CRC tumors compared with matched peritumoral tissues across all disease stages, whereas no differential expression was observed in inflammatory bowel disease, indicating CRC-specific upregulation. Importantly, serum ELISA demonstrated markedly increased circulating NOTUM levels in CRC patients relative to healthy controls and IBD patients, supporting its potential as a non-invasive diagnostic biomarker. Functional studies using colorectal cancer cell lines showed that doxycycline-inducible NOTUM overexpression significantly enhanced cell proliferation, while shRNA-mediated knockdown suppressed proliferation

and clonogenic survival. Consistently, pharmacological inhibition of NOTUM using the selective inhibitor ABC99 resulted in a dose-dependent reduction in CRC cell growth and long-term clonogenic potential, phenocopying genetic depletion. These effects were observed in APC/β-catenin–mutant cells and therefore were independent of extracellular WNT ligand availability, demonstrating a cell-autonomous pro-tumorigenic role for NOTUM. Collectively, our findings identify NOTUM as a CRC-specific biomarker detectable in patient serum and establish it as a functional driver of colorectal cancer progression, highlighting its promise as both a diagnostic and therapeutic target.

Polydopamine-Based Surface Modification of Hemoglobin Particles for Enhanced Antioxidant Properties and Reduced Heme Release in Oxygen Carriers

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The development of hemoglobin-based oxygen carriers (HBOCs) is limited by several challenges, including free heme release, auto-oxidation of hemoglobin to nonfunctional methemoglobin, oxidative side reactions, tetramer instability, nitric oxide scavenging, and a short circulatory half-life. To mitigate free heme release and reduce oxidative toxicity, we synthesized polydopamine (PDA) coated hemoglobin nanoparticles using a simple one-step method. Owing to the excellent adhesive and antioxidant properties of PDA, we investigated its effect on the structural stability and functional integrity of hemoglobin. UV–visible spectroscopy demonstrated that PDA coating does not compromise heme stability and preserves reversible oxygen binding. Furthermore, circular dichroism and fluorescence analyses revealed no significant alterations in the secondary or tertiary structure of hemoglobin upon PDA coating. Notably, PDA-coated β-F41K exhibited significantly enhanced $ABTS^{\bullet+}$ radical scavenging activity and ferric-reducing capability compared to the uncoated β-F41K. Importantly, PDA-coated recombinant hemoglobin showed a markedly reduced release of free heme into solution relative to uncoated hemoglobin. The nanoparticles also displayed good hemocompatibility and biocompatibility with blood and human embryonic kidney cells, respectively. Collectively, these results highlight PDA-coated recombinant hemoglobin as a promising platform for the development of artificial oxygen carriers with reduced toxic side effects.

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Ketoconazole and Zingerone Synergistically Inhibit *Candida albicans* Growth and Virulence Factors

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Keywords: Anti-biofilm, *Candida albicans*, combination, drug resistance, phytochemical, virulence,

Topical fungal infections caused by *Candida albicans* remain a significant clinical concern, particularly due to increasing resistance and adverse effects associated with prolonged antifungal therapy. Ketoconazole, a widely used azole antifungal agent, exhibits broad-spectrum activity against *C. albicans* but is limited by reduced efficacy and potential toxicity when used alone. Zingerone, a bioactive phenolic compound derived from Zingiber officinale (ginger), has demonstrated notable antifungal, anti-inflammatory, and antioxidant properties. The present study explores the synergistic antifungal potential of a ketoconazole–zingerone combination against *Candida*

albicans in the context of topical fungal infections.[1]

The study intended to evaluate the *anti-Candida* activity of Zingerone alone and with Ketoconazole (KTZ), particularly against the biofilms. Results revealed the concentration-dependent activity of Zingerone against the planktonic growth and virulence factors of *C. albicans*. Significant ($p < 0.05$) inhibition of the biofilms was evident at ≤1 mg/ml concentrations of Zingerone. Notably, a combination of 0.125 µg/mL of KTZ and 0.062 mg/mL of zingerone prevented the biofilm formation. Similarly, the preformed biofilms were significantly ($p<0.05$) inhibited by the Zingerone - Ketoconazole combination. The fractional inhibitory concentration indices ranging from 0.132 to 0.375 indicated the synergistic activity of Zingerone and KTZ against the biofilm formation and the preformed biofilms. Zingerone was found to potentiate ketoconazole activity, by disrupting fungal cell membrane integrity, increasing drug permeability, and inhibiting virulence factors such as biofilm formation.[2]

The synergistic combination also suggests potential benefits in reducing ketoconazole dosage, thereby minimizing adverse effects while maintaining therapeutic effectiveness. These findings support the development of a novel topical antifungal formulation incorporating ketoconazole and zingerone as a promising strategy for the management of *C. albicans*–associated skin infections. Further *in-vivo* and clinical studies are warranted to confirm safety, efficacy, and formulation stability for clinical application.[3]

Acknowledgment : Authors are thankful to DY Patil Education Society, Deemed to be University, Kolhapur, Maharashtra, India for providing infrastructure facility and funding support (DYPES/DU/R&D/2025/3035).

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Cellular and Acellular Approaches in Cardiac Repair: Comparative Assessment of c-Kit$^+$ Amniotic Fluid Mesenchymal Stem Cells versus Their Secretome

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c-Kit (CD117) positive amniotic fluid mesenchymal stem cells (AF-MSC) demonstrate promising cardiomyogenic potential in myocardial injury models. However, the administered cells exhibit limited differentiation and homing capacity at injury sites, suggesting cardio-protection could occur primarily through paracrine mechanisms rather than direct cellular integration. While cell-free therapies have emerged as promising alternatives, direct comparative studies evaluating c-Kit$^+$ AF-MSCs and their secretome remain absent. Here, we have compared the cardioprotective efficacy of c-Kit$^+$ AF-MSC versus their secretome using in-vitro ischemia-reperfusion injury models and in-vivo isoproterenol (ISO)-induced myocardial injury in rats. In-vitro assessments measured cell survival and apoptosis in injured cardiomyocytes at days one and three post-treatment. The in-vivo evaluation employed cardiac function analysis, including 2D-echocardiography and electrocardiography, alongside assessment of infarct size, fibrosis, apoptosis, oxidative stress, and inflammatory markers. Both c-Kit$^+$ AF-MSC and their secretome improved cardiomyocyte survival and reduced apoptosis, with the secretome showing significantly superior outcomes at both time points. In the ISO-induced rat model of myocardial injury, both therapeutic approaches exhibited cardioprotective efficacy; however, secretome therapy consistently outperformed cell-based treatment across all evaluated parameters. These findings establish that, while both modalities provided cardio protection, cell-free secretome therapy demonstrates superior efficacy compared to cell-based approaches in myocardial injury. Overall, this study highlights that the c-Kit$^+$ AF-MSC-derived secretome is a compelling candidate for advancing cardiac

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Investigating histone post-translational modification towards epigenetic therapeutics of Alzheimer's disease

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Post-translational modification and epigenetic changes can cause long-term gene silencing or over-expression in a context-dependent manner and are related to various disease conditions, including major Neurological Disorders such as Alzheimer's Disease (AD). Due to high complexities in chromatin architecture and dynamic context-specific cross-talks between chromatin and modifying protein partners, many of these areas are still largely unaddressed due to the difficulty in constructing appropriate experimental protocols.

Our target, the G9a, is a Lysine Methyltransferase that mainly dimethylates the H3K9 of chromatin, triggering the repression of genes epigenetically, leading to Alzheimer's disease (AD). Over the last few decades, considerable G9a inhibitors were reported, such as BIX-01294, UNCO224, UNC0321, UNCO638, UNC0642, E72, as potential anti-cancer agents. However, these inhibitors were troubled in clinical trials, and the involvement of G9a in neurological disease was overlooked (gap area).

Therefore, we have ventured to bridge the gap by exploring the role of G9a in neurological disorders and to find novel leads against G9a as potential epigenetic therapeutics of Alzheimer's disease (AD). Purposefully, we used an interdisciplinary chemical biology approach in combination of AI/ML-based design, medicinal chemistry, and pharmaceutical science. Our G9a inhibitors reduced the Aβ aggregates, an important hallmark in AD, in the C elegans CL2006 worms up to 47% in a concentration-dependent manner, highlighting their potential in AD treatment.[1-2]

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Metabopsy of Inherited Metabolic Disorders: Discard to Diagnosis Approaches

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Background: Inherited Metabolic Disorders (IMDs) are genetic disorders caused by deficient enzymes leading to defective metabolism. Recently, notable forms of IMDs, including organic acidurias and amino acidurias has grown substantially, highlighting the need for timely diagnosis, as many IMDs are treatable. However, the approach to detecting IMDs using non-invasive, affordable methods in children is limited. Also, an *in-silico* approach that can alleviate clinical implications due to different IMDs is not emphasized.

Methods: We have developed a novel methodology for detecting IMDs using non-invasive biological samples by employing an in-house designed Vertical Tube Gel Electrophoresis (VTGE) system and 96-well plate colorimetric assays. LC-HRMS analysis was used for the metabolic profiling and validation. Further, we extended our research to develop mimetics of metabolites computationally

against pathway-associated enzymes by using molecular docking and MD simulations.

Results: IMD suspected samples showed three folds elevated levels of methylmalonic acid in tears, 2-3 fold increased hydroxyglutaric acid in nail, urine and 4-5 folds increased hydroxyproline in milk teeth, compared to the healthy controls, after performing 96-well plate colorimetric assays. LCHRMS analysis validated these findings. Furthermore, we designed the mimetics of metabolites as potential inhibitors of respective enzymes and studied their interactions using docking and MD simulation.

Conclusion: This research provides the first and novel method to use non-invasive samples for early detection of IMDs such as organic aciduria and amino acidurias by employing VTGE and 96-well plate colorimetric assays. Also, development of mimetics is a beneficial approach to overcome metabolic conditions in patients.

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Artificial Intelligence Unveils Temporal Cytokine Dynamics in Myocardial Injury: Analysis of c-Kit+ Amniotic Fluid Mesenchymal Stromal Cell Secretome

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Acute myocardial infarction (AMI) triggers complex, time-dependent inflammatory and reparative responses that critically determine patient outcomes. While conventional biomarkers like cardiac troponins provide diagnostic snapshots, they fail to capture the dynamic temporal evolution of myocardial healing. This study employs artificial intelligence to characterize phase-specific cytokine patterns from c-Kit+ amniotic fluid-mesenchymal stromal cell (AF-MSC) secretome across myocardial injury progression. Using a reproducible computational pipeline in Google Colab, we analyzed 15 cytokines, chemokines, and growth factors across 9 post-injury time points (0-72 hours) with 1,350 total observations. Long short-term memory (LSTM) neural networks achieved 92% accuracy in temporal classification, while SHAP explainability analysis identified IL-1β as the dominant early-phase predictor (27% contribution). Three distinct temporal phases emerged: an early inflammatory phase (0-12h) dominated by IL-1β, TNF-α, and CXCL8; a mid-reparative phase (24-48h) characterized by IL-10, VEGF, and FGF-2; and a late remodeling phase (60-72h) featuring TGF-β, TIMP-1, and SDF-1. Hierarchical clustering, principal component analysis (73% variance explained), and Spearman correlation analysis validated these temporally distinct cytokine modules with strong intra-phase correlations (ρ=0.82-0.91) and reciprocal inter-phase regulation (ρ=-0.68 to -0.71). These findings demonstrate that AF-MSC secretome exhibits adaptive, time-dependent responses reflecting host pathophysiological states rather than static cytokine release. This AI-driven temporal framework enables identification of phase-specific therapeutic targets and provides a foundation for precision medicine approaches in myocardial injury management.

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Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
www.iabsjournal.com

In-Vitro Analysis of *Candida albicans*–Host Cell Interactions

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Candida albicans is an opportunistic fungal pathogen that can cause mucosal infections by adhering to, invading, and damaging host epithelial cells. Understanding these early and late interaction events is crucial for elucidating mechanisms of fungal pathogenesis. In the present study, *in-vitro fungal–host* interactions between *C. albicans* SC5314 and human epithelial cells were investigated to characterise adhesion, invasion, and host cell damage.

Fungal adhesion to epithelial cells was assessed following short-term co-incubation, allowing quantification of surface-associated fungal cells. Invasion was evaluated by differential staining approaches to distinguish invading hyphae from non-invading fungal cells. Host cell damage was assessed using lactate dehydrogenase (LDH) release assays following prolonged exposure to the fungus. The results demonstrated efficient adhesion of *C. albicans* to epithelial cells, followed by active invasion and significant host cell damage at later stages of interaction.

Collectively, these findings highlight the dynamic nature of *C. albicans*–host cell interactions and underscore the role of fungal adhesion and invasion in epithelial damage. The study provides experimental insight into key stages of fungal pathogenesis and establishes a foundation for further investigation into virulence mechanisms and functional validation of interaction-associated genes.

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Appetite modulator Quercetin enhances antioxidant defence and neuroprotection in induced aging Rat model

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This study investigated the neuroprotective and antioxidant effects of a potent appetite modulator Quercetin in a d-galactose-induced accelerated aging model using male Wistar rats. Animals were assigned to four groups: control, Quercetin-treated, d-galactose-induced aging, and d-galactose and Quercetin treatment. Quercetin was administered orally (100 mg/kg) and d-galactose subcutaneously (300 mg/kg) for 28 days. Biochemical analyses included measurement of ferric reducing antioxidant power (FRAP), glutathione (GSH) content, malondialdehyde (MDA), protein carbonyl (PCO) formation, and activities of superoxide dismutase (SOD) and catalase in brain tissue homogenates. Levels of appetite regulatory hormones leptin, ghrelin and insulin were also measure in serum. Gene expression of Beclin-1, ULK-1, SIRT1, NSE, TNF-α, IL-6, GSHR, and GLP-1 was assessed by RT-PCR. Histopathological evaluation of hippocampal architecture was performed, and statistical significance was determined by ANOVA with Bonferroni post-hoc analysis. D-galactose significantly reduced FRAP, GSH, SOD, and catalase activities while increasing MDA and PCO levels, alongside downregulation of autophagy and neuroprotection-related genes and elevation of inflammatory cytokines. Quercetin treatment effectively restored antioxidant markers, reduced oxidative stress indices, improved enzymatic activity, upregulated neuroprotective and autophagy-associated genes, and attenuated inflammation. Histopathological assessment confirmed preservation of neuronal structure in treated rats. Quercetin supplementation robustly enhances cerebral antioxidant defenses, mitigates oxidative damage, modulates gene expression related to neuron survival and inflammation, and confers histological neuroprotection in experimental aging.

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A Network-based framework connecting Cancer cell lines and patients for personalized Drug response prediction in Lung cancer

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Cancer treatment remains challenging due to the strong molecular heterogeneity observed across patients, which often leads to variable drug responses and resistance. To improve the translation of experimental findings into clinical applications, it is essential to better connect cancer cell lines with real patient tumour data. In this study, we present a network-based framework that integrates lung cancer gene expression profiles from both GDSC cell lines and TCGA patient samples to support personalized drug response prediction. To do this, we minimize batch effects between datasets, data homogenization was performed using the ComBat algorithm. Next, patient-specific and cell line-specific gene interaction networks were constructed for every individual sample using the LIONESS algorithm, incorporating protein-protein interaction (PPI) information to generate personalized gene-gene correlation networks. This approach captures unique molecular network signatures for each patient and each cell line, reflecting their distinct biological states. To quantify the similarity between patient tumours and cell lines, we computed the Jaccard similarity index between each patient-specific network and all cell line networks. This resulted in a comprehensive patient-cell line similarity matrix across all combinations. Notably, the highest similarity score reached 0.45, indicating a meaningful level of similarity between cancer cell lines and patient tumours. By identifying the most similar cell line counterparts for each patient, this framework provides a meaningful basis for transferring drug sensitivity knowledge from cell lines to patients and improving drug response prediction in clinical settings. Overall, this study offers a systematic strategy for selecting patient-relevant cancer cell lines, advancing precision oncology, and enabling more accurate personalized cancer treatment.

Salivary Uric Acid as a Non-Invasive Predictor of Pregnancy Complications: Findings from a Nested Case–Control Study

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Keywords: Salivary biomarkers; uric acid; pregnancy complications; preeclampsia; gestational diabetes mellitus; non-invasive diagnostics; maternal health

Background

Pregnancy-related complications such as preeclampsia, gestational diabetes mellitus (GDM), and miscarriage remain major contributors to adverse maternal and fetal outcomes. Early identification of women at risk is essential, yet current screening approaches rely largely on invasive blood-based investigations. Salivary biomarkers offer a non-invasive, easily accessible alternative for early risk assessment. Uric acid (UA), a marker of oxidative stress and metabolic dysregulation, has been implicated in several pregnancy complications, but its utility in saliva remains underexplored.

Objective

To evaluate the potential of salivary uric acid as a predictive biomarker for pregnancy complications and associated adverse outcomes.

Methods

This exploratory nested case–control study was conducted among 132 healthy pregnant women enrolled at ≤20 weeks of gestation. Saliva and serum samples were collected at recruitment and stored for subsequent analysis. Participants were prospectively followed for the development of pregnancy-related complications. For biomarker evaluation, 24 women were selected—12 who developed complications (cases) and 12 who had uncomplicated pregnancies

(controls). Salivary uric acid levels were quantified using the uricase-based spectrophotometric method on the Cobas 8000 platform.

Results:

Mean salivary uric acid levels were significantly higher in cases compared to controls (1.1 ± 0.4 mg/dL vs. 0.5 ± 0.3 mg/dL; p = 0.004). Although salivary cortisol levels were higher in cases than controls (0.125 ± 0.03 µg/mL vs. 0.10 ± 0.05 µg/mL), this difference was not statistically significant (p = 0.4). These findings suggest that salivary uric acid may be a useful biomarker for predicting pregnancy complications, though further validation is needed.

Conclusion:

Salivary uric acid demonstrates potential as a non-invasive biomarker for the early prediction of pregnancy complications, including preeclampsia, miscarriage, and GDM. While salivary cortisol did not show significant discriminatory ability in this cohort, the findings support further investigation of salivary biomarkers in maternal risk stratification. Larger, prospective studies are required to validate the clinical applicability of salivary uric acid in routine antenatal screening.

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Total Laboratory Automation: Transforming Clinical Laboratories through Integrated, Intelligent, and Standardized Workflows

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Keywords: Total laboratory automation, Laboratory workflow, Artificial intelligence, ISO 15189, Sustainable diagnostics

Background:

Modern clinical laboratories face increasing test volumes, demand for rapid turnaround time, and stringent quality and accreditation requirements. Total Laboratory Automation (TLA) has emerged as a comprehensive technological solution that integrates pre-analytical, analytical, and post-analytical processes into a single, continuous workflow, enabling reliable and efficient diagnostic services.

Description:

Total Laboratory Automation encompasses automated sample reception, barcode-based identification, centrifugation, decapping, aliquoting, analytical processing, storage, and retrieval, all connected through conveyor-based systems and middleware. Integration with laboratory information systems enables real-time sample tracking, auto-verification, and intelligent rule-based result validation. Artificial intelligence and data-driven algorithms further enhance decision support, anomaly detection, workload balancing, and predictive maintenance of analyzers.

Quality and Compliance: TLA supports compliance with NABL and ISO 15189 standards by minimizing manual interventions, reducing pre-analytical errors, ensuring traceability, and standardizing processes. Automated documentation, quality indicator monitoring, and audit-ready data improve laboratory governance and accreditation preparedness.

Sustainability and Workforce Optimization:

Automation contributes to sustainable laboratory practices by optimizing reagent usage, reducing repeat testing, minimizing sample wastage, and improving energy-efficient operations. TLA also enables optimal utilization of skilled laboratory personnel by shifting focus from manual tasks to quality assurance, data interpretation, and clinical consultation.

Conclusion:

Total Laboratory Automation represents a paradigm shift in laboratory medicine, offering an integrated, intelligent, and sustainable approach to diagnostics. Its adoption is essential for future-ready laboratories aiming to deliver high-quality, standardized, and patient-centric services in evolving healthcare systems.

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Comprehensive Profiling of Neutrophil Metabolism During Sepsis

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Sepsis is a life-threatening condition defined by a dysregulated host immune response to infection, in which neutrophils play a central role. Early sepsis is triggered by pathogen- and damage-associated molecular signals that drive a burst of inflammatory mediators and rapid neutrophil mobilization.[1] This acute response frequently causes transient neutropenia and defective pathogen clearance. To compensate, the host initiates emergency granulopoiesis, increasing the production and release of mature and immature neutrophils with altered functions.[2] These dynamic shifts in neutrophil abundance and activity strongly shape sepsis progression and outcome, however excessive or prolonged activation can worsen tissue damage, increasing mortality. Because neutrophil effector mechanisms are highly energy dependent, sepsis induces profound metabolic reprogramming. Understanding neutrophil metabolism alongside function may therefore reveal therapeutic opportunities.[3,4] Using the cecal ligation and puncture model of polymicrobial sepsis in C57BL/6 mice, we identified time-dependent changes in neutrophil number, function, and metabolism. High bacterial burden and marked neutrophil activation, including sustained NETosis, coincided with neutropenia at 12 and 24 hours after sepsis. By 48 hours, neutrophil counts rebounded and bacterial clearance occurred, consistent with emergency granulopoiesis. Despite infection control, mortality rose between 48 and 54 hours. Elevated liver enzymes and persistent NETosis at this stage indicated that NET-mediated organ damage, rather than ongoing infection, drove lethality. Metabolomic profiling revealed dynamic alterations in pathways governing inflammation, reactive oxygen species production, energy metabolism, nucleotide turnover, lipid remodeling, and glutathione balance. Together, these results suggest that while neutrophil expansion is required for bacterial control, unresolved inflammatory and metabolic stress promotes immunopathology in sepsis.

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Development and Evaluation of a Lytic Bacteriophage Cocktail for Combating Multidrug-Resistant *Salmonella*

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Salmonella remains a leading cause of foodborne and enteric infections worldwide, with the increasing prevalence of multidrug-resistant (MDR) strains posing a serious threat to public health. The limited efficacy of antibiotics against these pathogens highlights the urgent need for alternative antimicrobial strategies. In this study, we report the development and evaluation of a lytic bacteriophage cocktail targeting clinically and environmentally relevant *Salmonella* spp. Individual phages were isolated from the River Ganga and selected for their broad host range, strong lytic activity, and genetic safety. Detailed characterization included plaque morphology, adsorption kinetics, latent period, burst size, and stability under varying pH and temperature conditions. Whole-genome sequencing confirmed the absence of lysogenic genes, virulence factors, and antibiotic resistance determinants.

The optimized phage cocktail demonstrated superior antibacterial activity compared to individual phages, achieving rapid and sustained reduction of *Salmonella* growth *in-vitro*. The cocktail also significantly disrupted established *Salmonella* biofilms and effectively delayed

the emergence of phage-resistant bacterial populations. Additionally, enhanced antibacterial efficacy was observed when the phage was combined with selected antibiotics, suggesting phage–antibiotic synergy.

Overall, this study highlights the promise of a rationally designed *Salmonella*-specific bacteriophage cocktail as a viable therapeutic and biocontrol strategy for combating MDR *Salmonella* infections. These findings support further preclinical development and translational evaluation of phage-based interventions for *Salmonella* control.

Unmasking Hidden Drug Resistance: A Whole Genome Sequencing-Based Evaluation of Molecular TB Diagnostics in Central India

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Keywords: Whole Genome Sequencing, GeneXpert, Line probe Assay, Discordance, DR-TB

Background: Rapid molecular diagnostic tools such as GeneXpert and Line Probe Assays (First-Line and Second-Line LPA) are routinely used for detecting drug-resistant tuberculosis (DR-TB) in India. However, their probe-based design restricts mutation coverage and may cause discordant resistance profiles when compared with whole genome sequencing (WGS). This study evaluated diagnostic discordance between routine assays and WGS-based resistance profiling in clinical isolates from All India Institute of Medical Sciences Bhopal (AIIMS Bhopal).

Methods: Five *Mycobacterium tuberculosis* clinical isolates from AIIMS Bhopal underwent WGS and were compared with GeneXpert, FL-LPA, and SLPA results. Lineage classification, and resistance-associated mutations across first- and second-line anti-tubercular drugs were systematically analysed.

Results: Among the 5 isolates, rifampicin resistance was detected in one case by GeneXpert and in a different case by FL-LPA. In contrast, WGS classified 4 isolates as pre-XDR-TB and 1 as isoniazid mono-resistant. Of the 4 pre-XDR isolates, three belonged to Lineage 3 (East-African-Indian) and one to Lineage 4 (Euro-American). The isoniazid mono-resistant isolate belonged to Lineage 1 (Indo-Oceanic). All pre-XDR isolates harboured mutations in rpoB, inhA, gyrA, and katG. Additional resistance-associated mutations affecting ethambutol, pyrazinamide, ethionamide, and streptomycin were identified.

Conclusion: Substantial discordance was observed between routine molecular assays and WGS-based resistance profiling in this Central Indian cohort. These findings highlight the limitations of probe-based diagnostics in detecting complex and evolving resistance patterns, particularly within predominant regional lineages. Integration of WGS into TB diagnostic and surveillance frameworks may enhance treatment individualization, prevent inappropriate therapy, and reduce transmission of undetected drug-resistant strains.

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Surface-decorated Extracellular Vesicles Derived from Human Cells for Targeted Drug Delivery

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Extracellular Vesicles (EVs) have been widely explored as drug delivery systems due to their favourable biophysical and biochemical properties. However, the

limited targeting ability of EVs and the lack of strategies to engineer their surfaces make the clinical translation of EV-based therapeutics more difficult. Conventionally, the surface functionalisation of EVs primarily relies on tetraspanin protein scaffolds or the chemical conjugation of targeting moieties. However, recent efforts have been made to explore single-pass membrane proteins as a scaffold, thereby reducing the genetic payload required for parent cell modification.

Through literature screening, an ideal single-pass transmembrane protein was identified as a suitable scaffold for engineering the EV surface. Using *in-silico* tools, we designed a truncated protease-resistant variant of the protein to enhance its biochemical stability under proteolytic conditions. For the ligand display, Enhanced Green Fluorescent Protein (EGFP) was fused to the N-terminal domain of the single-spanning protein. For EGFP expression, a lentiviral construct encoding EGFP fused to the engineered protein in the 5′ to 3′ orientation was cloned into a pGenLenti vector and was co-transfected into Human Embryonic Kidney 293FT cells along with third-generation packaging and envelope plasmids. The HEK293 FT cells were transduced and selected using puromycin. The results demonstrated successful membrane presentation of the fusion protein, and EVs derived from these cells also display EGFP on their surface. Surface Green Fluorescent Protein–decorated EVs can be passively or actively loaded with the drug of interest and can be readily tracked within cellular systems.

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Regulation of altered Synaptic Transmission by Semaphorin in Temporal Lobe Epilepsy

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Temporal lobe epilepsy (TLE) is associated with altered regulation of glutamatergic synaptic activity in the hippocampus and extra-hippocampal structures, which contributes to generation of distributed networks. Semaphorins are known to regulate neuronal excitability by influencing the surface expression of glutamate receptors. We investigated the role of semaphorin 3F in regulating glutamatergic activity in the animal model of TLE. mRNA and protein expression of semaphorin 3F and glutamate receptor subunits were measured in Li-pilocarpine rat model TLE after inhibiting semaphoring 3F using intra-hippocampal administration of siRNA. TLE rats demonstrated EEG patterns indicative of spontaneous epileptic seizures, conversely, TLE rats treated with semaphorin 3F siRNA exhibited EEG patterns similar to control group. Expression of semaphorin 3F, Plexin A3, and GLUR4 receptor subunits were significantly increased in the TLE rats. Golgi-Cox staining of brain samples showed a reduction in the length of apical dendrites and spine density in TLE rats, and not in TLE rats injected with Sema 3F siRNA. Whole-cell patch clamp recordings indicated an increase in the frequency and amplitude of glutamatergic activity in the brain samples of TLE rats, but such changes were not observed in siRNA-treated TLE rats. Further, we observed that the magnitude of alteration post semaphorin 3F inhibition was different in the hippocampus as compared to extra-hippocampal samples in TLE rats. Our findings suggest that semaphorin 3F differentially regulates the AMPA receptor-mediated glutamatergic activity in the hippocampus & extra-hippocampal structure of TLE rats, which may be responsible for the development of independent networks in these regions.

Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Decoding Metabolic rewiring in Retinoblastoma using NMR-based Serum metabolomics

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Keywords: Retinoblastoma, metabolic rewiring, NMR, serum metabolomics, diagnostic markers.

Retinoblastoma (RB) is a rare and aggressive form of ocular malignancy that mostly affects children under 5-years of age. Delayed diagnosis of RB results in vision loss and metastasis, underscoring the need to develop diagnostic and prognostic markers for RB. Although metabolic rewiring is a well-recognized hallmark of all cancer cells, it has yet to be explored in RB. This study aims to develop a non-invasive screening strategy for early detection of RB using NMR-based serum metabolomics. A total of 70 metabolites belonging to classes of amino acids, organic acids, carbohydrates, and others were qualitatively and quantitatively profiled in serum samples from 24 RB patients and 26 controls. PLS-DA model depicted distinct clustering of RB patients and controls, highlighting key discriminatory metabolites. Metabolic fingerprints unique to unilateral and bilateral RB patients were observed, which might be an outcome of their distinct mutational backgrounds. 11 metabolites displayed consistent alterations in both groups, with the effect being heightened in bilateral RB, indicating greater disease severity. Metabolic discrepancies among non-invasive and invasive unilateral patients were also observed, with the more pronounced alterations in invasive RB. Additionally, assessment of patients with active RB and regressed tumors revealed the suppression of metabolites in the regressed group that were elevated in active disease and vice versa. Altogether, these findings reveal profound metabolic rewiring in RB, implying the potential of serum metabolites as non-invasive diagnostic and prognostic markers for RB.

Engineering Controlled Destabilization: The "Magic Methyl" Effect in RNAi Enhancement

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siRNAs silence genes via endogenous RNAi pathways and hold promise as therapeutics. We report the synthesis of 2′-alkoxy/fluoro-m^3C phosphoramidites and their incorporation into siRNAs to probe the role of thermodynamic destabilization in gene silencing. We showed that incorporation of N^3-methyl-uridine (m^3U) into siRNA duplexes selectively destabilizes Watson–Crick base pairing, leading to improved thermodynamic asymmetry and enhanced guide-strand selection. This results in significantly increased RNAi activity at the intracellular level when these modifications were incorporated at cleavage or 3′-overhang of passenger strand.

We further combine m^3U modification with 2′-O-hexadecyl (C16) conjugation. siRNA duplexes containing 2′-alkoxy/fluoro-N^3-methylpyrimidines displayed significant thermal destabilization due to disrupted Watson–Crick hydrogen bonding and reduced base stacking. RNAi assays showed that incorporating 2′-alkoxy-m^3U/m^3C at the sixth position of passenger-strand enhanced RNAi activity significantly.

Furthermore, using site-specific incorporation of 2′-fluoro-m^3U as a sensitive ^{19}F NMR probe, we directly map local loop environments within a parallel NG16 G-quadruplex. Importantly, loop modification suppresses complementary strand invasion, thereby stabilizing the G-quadruplex against duplex formation.

These findings demonstrate that deliberate destabilization through 2′-functionalized N^3-methyl pyrimidines can fine-tune siRNA structure, enabling enhanced and safer RNAi activity, and G4 folding dynamics.

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Unlocking Minerals through Fermentation: Mechanistic Insights from Kerala Red Rice

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Keywords: Kerala red rice, fermentation, phytate degradation, mineral bioavailability, micronutrient deficiencies.

Kerala red rice (*Oryza sativa* L. subsp. *indica*) is an indigenous Indian whole-grain variety with a red pericarp, high bran retention, and relatively low glycemic index. It is rich in dietary fiber, micronutrients, and antioxidants. Like many cereals, it contains phytate, an antinutrient that chelates essential minerals—including iron, zinc, calcium, magnesium, and manganese—into insoluble complexes, limiting gastrointestinal bioavailability. Fermentation is a traditional South Asian practice enhancing digestibility and nutritional quality, yet biochemical and functional properties of fermented Kerala red rice remain largely unexplored. Microbial communities in fermented red rice broth may improve mineral accessibility through phytase-mediated phytate degradation.

To investigate this, phytate–mineral complexes of calcium, iron, zinc (1:1 molar ratio) were synthesized to model dietary chelation and incubated in 18-hour fermented red rice water. Structural and compositional changes were analyzed using Fourier-transform infrared spectroscopy (FTIR), X-ray fluorescence (XRF), and scanning electron microscopy with energy-dispersive X-ray spectroscopy (SEM-EDX). Mineral release kinetics were quantified via. ICP-MS, and phytase activity was measured using the Fiske–Subbarow assay, interpreted in the context of microbial taxa identified in parallel analyses, including *Bacillus* and *Enterobacter*. Fermentation enabled enzymatic dephosphorylation of phytate, releasing minerals in patterns consistent with stability constants, with calcium mobilizing most rapidly. Elevated phytase activity highlighted the functional role of microbial communities in mineral liberation. By bridging culinary tradition with modern nutrition science, these findings validate fermentation of Kerala red rice as a strategy to improve mineral accessibility, which could help address micronutrient deficiencies in cereal-dependent populations.

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From DOTS to NTEP: Two Decades of Policy Transitions and Their Impact on Tuberculosis Indicators in India-An Interrupted Time-Series Analysis

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Background: To examine the long-term, phase-specific effects of national tuberculosis (TB) program transitions on key TB indicators in India using interrupted time-series analysis to inform future TB policy and program design.
Methods: Thirteen TB indicators were analysed using data from the India TB Report and World Health Organization estimates (2000–2023). Interrupted time-series analysis with linear generalised estimating equations quantified level and trend changes across program phases: DOTS (2000–2005), Revised National Tuberculosis Control Programme (2006–2011), National Strategic Plan (NSP) 2012–2017, NSP 2017–2025, and the National Tuberculosis Elimination Programme (NTEP) (2020–2023).
Results: Observed outcomes diverged substantially from model-derived counterfactual trajectories, with marked heterogeneity by phase. TB incidence showed minimal deviation during DOTS, a large cumulative reduction during NSP 2017–2025 (–48%; –2.57 million cases), and the greatest excess during NTEP (+474%; +2.33 million cases). TB–HIV co-infection remained below counterfactual expectations from NSP 2012–2017 onward, with sustained

reductions exceeding 110% during NTEP. Bacteriologically confirmed pulmonary TB declined under NSP 2017–2025 (–18%) and increased during NTEP (+44%). Extrapulmonary TB showed phase-specific reversals, while drug-resistant TB declined during NSP 2017–2025, but increased during NTEP. Household contact tracing declined during NSP 2017–2025 (–24%) and rebounded during NTEP (+73%). TB mortality declined most during DOTS (–43%) and again during NTEP.

Conclusions: Program transitions were associated with substantial and uneven changes across TB indicators. Earlier strategies achieved durable mortality and TB–HIV reductions, whereas later phases revealed vulnerabilities in incidence control, drug-resistant TB, and service continuity. Strengthened surveillance, uninterrupted services, and adaptive, phase-specific policies are essential for sustained TB control.

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Smart Bioimpedance Signal Analysis for Functional Localization of the Inferior Alveolar Nerve in Mandibular Surgery

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Accurate identification of the Inferior Alveolar Nerve (IAN) during mandibular surgery is essential to avoid unintended contact with nerve tissue. Conventional surgical guidance relies on anatomical estimation and preoperative imaging, which cannot confirm nerve presence in real time. This study presents an Artificial Intelligence (AI)–driven bioimpedance analysis framework designed to detect whether nerve tissue is present or absent during mandibular surgical procedures.

The proposed system employs multi-frequency Electrical Impedance Spectroscopy (EIS) to measure tissue electrical properties. A tetrapolar electrode configuration improves measurement accuracy and reduces electrode–tissue interface effects. Bioimpedance signals are recorded over a controlled frequency range, and parameters such as resistance, reactance, impedance magnitude, and phase angle are extracted. Signal preprocessing techniques including digital filtering and normalization enhance signal quality.

For intelligent tissue classification, a Convolutional Neural Network (CNN) is used to automatically learn complex patterns from processed impedance signal representations, while a Deep Neural Network (DNN) performs high-level feature learning and classification of tissues into nerve-present or nerve-absent categories. When nerve-specific impedance characteristics are detected, the system provides an immediate indication to the surgeon, functioning as a real-time decision-support tool.

This work demonstrates a novel integration of bioimpedance sensing and deep learning–based tissue classification, contributing toward smart surgical assistance and improved safety in mandibular procedures.

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Phenotypic Characterization of Extracellular Vesicles in a MASH-Induced Mouse Model

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Metabolic dysfunction-associated steatohepatitis (MASH) involves progressive hepatic steatosis and inflammation and is linked to extracellular vesicle (EV)-mediated signaling. To investigate EV phenotypes in the murine MASH model, C57BL/6 mice were divided into control and MASH groups (n=6). The MASH group received a Western diet, while the control group was fed normal chow for 12 weeks. In addition, the MASH group received sugar solution supplementation and intraperitoneal CCl4 injections at a dose of 0.32 µg/g body weight. Body weight over time and the liver-to-body weight ratio at sacrifice were measured to monitor disease progression. Pathological changes associated with MASH were evaluated by histological characterization of the liver using hematoxylin and eosin, Oil Red O, Masson's trichrome, and periodic acid–Schiff staining. EVs were isolated by size-exclusion chromatography (SEC) and characterized by nanoparticle tracking analysis (NTA) and Western blotting.

MASH animals showed a distinct pattern of body weight over time, along with a highly significant liver-to-body weight ratio. Histopathological analyses revealed marked steatosis, inflammation, structural alterations with lipid deposition, fibrosis, and the absence of glycogen deposition. SEC-based isolation yielded reproducible EV preparations, and NTA analysis showed a higher EV concentration in the MASH group than in controls; however, the difference was not statistically significant. EV size also did not differ significantly among the groups. Although EV size and concentration did not differ significantly with disease status, EV cargo profiling may reveal molecular signatures associated with MASH severity and progression.

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Vision Transformer-Based Automated Detection of Pulmonary Tuberculosis from Chest X-Rays: A Multi-Source Dataset Study with Grad-CAM Interpretability

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Background: Tuberculosis (TB) remains a critical global health burden, with chest X-ray (CXR) being the most widely used screening modality in resource-limited settings. Accurate and interpretable automated detection systems are urgently needed to support radiologists, particularly in high-burden regions. Recent advances in Vision Transformers (ViT) offer a compelling alternative to conventional Convolutional Neural Networks (CNN) by capturing long-range spatial dependencies through self-attention mechanisms, enabling detection of TB lesions distributed across diverse pulmonary regions.
Methods: A total of 7,994 CXR images were curated from four publicly accessible datasets: 700 TB-positive images from the Belarus TB Portal and NLM datasets, 2,800 TB-positive DICOM images from the NIAID TB Portal Program Dataset obtained under a formal data-sharing agreement, and 3,500 Normal CXR images sourced from NLM and RSNA repositories. An additional independent test cohort comprising 2,494 TB and 514 normal images was incorporated for external validation. All images underwent CLAHE-based contrast enhancement and standardized preprocessing. A pretrained ViT-Base/16 model was fine-tuned and systematically benchmarked against established CNN baselines including ResNet-50, DenseNet-121, and EfficientNet-B0, using five-fold stratified cross-validation. Gradient-weighted Class Activation Mapping (Grad-CAM) was applied to provide clinical interpretability of model predictions.
Results: The proposed ViT-based model achieved a training accuracy of 98.87% with a validation accuracy of 95.95%. On the independent test cohort, the model achieved an overall accuracy of 93.0%, with a precision of 0.96, recall of 0.63,

and F1-score of 0.76 for the TB class, demonstrating robust discrimination capability against class imbalance.

Conclusion: The Vision Transformer architecture demonstrated superior performance over CNN baselines for automated TB detection, with Grad-CAM visualizations confirming clinically meaningful attention to pathological lung regions. This framework offers a scalable and interpretable solution for TB screening in low-resource clinical environments.

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Phytochemical, Biological, and Computational Evaluation of *Aegle marmelos* Unripe Fruit Extract Against HER2-Driven Breast Cancer

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Keyword Classification: Biochemistry & Molecular Biology; Bioinformatics & Computational Biology; Drug Screening & Pharmacodynamics.

Breast cancer is the most common type of cancer in women around the world, and it is still one of the main causes of cancer deaths. Overexpression of the human epidermal growth factor receptor 2 (HER2), found in approximately 20–25% of breast cancers, correlates with aggressive tumor progression and a poor prognosis. This study assessed the anticancer efficacy of a hydroalcoholic extract from unripe fruits of Aegle marmelos L. using both in vitro and in silico methodologies focused on the HER2 receptor. The extract was prepared and underwent phytochemical screening and cytotoxicity assessment against MCF-7 breast cancer cells using the MTT assay. Using GC-MS and LC-MS to do a full phytochemical profile, we found 26 bioactive compounds, such as flavonoids, phenolic acids, terpenoids, and alkaloids. The extract exhibited notable cytotoxicity against MCF-7 cells. Among the identified constituents, naringenin, limonene, and marmelosin exhibited significant anticancer potential. Molecular docking demonstrated that naringenin displayed the highest binding affinity (-9.2 kcal/mol) for HER2, establishing stable hydrogen bonds and hydrophobic interactions within the receptor's active site. Molecular dynamics simulations lasting over 80 ns verified the stability of the naringenin–HER2 complex, exhibiting an average RMSD of 2.1 Å. ADMET and toxicity evaluations indicated advantageous pharmacokinetic and safety profiles. Overall, these results show that Aegle marmelos unripe fruit extract has strong anticancer properties, and naringenin may be a good candidate for HER2-targeted therapy. The study shows that natural products can be useful in treating breast cancer and calls for more research in both the lab and the clinic.

Polystyrene Microplastics Induce Oxidative Stress–Driven β-Cell Failure: Implications for Diabetes Pathogenesis

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Pollution has escalated into a severe global environmental crisis, with microplastics (MPs) now recognized as pervasive contaminants across all ecosystems.[1] Among the polymers constituting MPs, polystyrene (PS) is consistently detected at high frequencies in human-associated environments, including metabolically relevant tissues.[2] The pervasive and unavoidable nature of PS-MP exposure raises critical concerns regarding its long-term consequences for human health, particularly the escalating global burden of diabetes.

Recent research has begun to bridge the mechanistic gap linking PS-MP exposure to diabetes pathogenesis. In this study, we investigated the cellular and functional consequences of PS-MP exposure in pancreatic β-cells using the MIN6 cell line. We demonstrate that 1 µm PS-MPs are efficiently internalized and predominantly localize within cytoplasmic and perinuclear regions. PS-MP exposure induced a dose- and time-dependent increase in mitochondrial superoxide and intracellular reactive oxygen species,[3] accompanied by marked suppression of antioxidant gene expression. This oxidative stress was associated with pronounced necrotic cell death. Furthermore, metabolic

viability assays revealed a progressive decline in β-cell viability and suppression of key β-cell identity markers such as PDX1 and MAFA, consistent with established mechanisms of oxidative stress–mediated β-cell failure in diabetes. These converging defects culminated in early β-cell failure, a hallmark event in diabetes initiation.

Collectively, our findings provide mechanistic evidence that PS-MPs induce oxidative stress–driven cytotoxicity, necrosis, and functional impairment in pancreatic β-cells, highlighting a plausible environmental pathway through which chronic microplastic exposure may contribute to β-cell dysfunction, reduced insulin production, and increased susceptibility to diabetes.

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Assessment of Antinuclear antibody IIFA Pattern: Antigen Correlation Using ENA Immunoblot in Suspected SARD Patients

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Background: Antinuclear antibody (ANA) testing by indirect immunofluorescence assay (IIFA) remains the gold-standard screening tool for systemic autoimmune rheumatic diseases (SARDs). ANA(IIFA) interpretation alone is insufficient and requires confirmation with antigen-specific assays.[1,2]
Objective: To evaluate the correlation between ANA-IIFA patterns and specific autoantigen reactivity on ENA immunoblot in suspected SARD patients
Methods: Laboratory-based observational study evaluated 60 SARD patients with ANA (IIFA) and ENA immunoblot (Tulip Diagnostics). IIFA pattern interpretation was performed as per International Consensus on ANA Patterns (ICAP),[3] and antigenic associations were evaluated on ENA immunoblot against observed patterns. Data was managed and analyzed in Microsoft Excel.
Results: Out of 60 samples, 54 (90%) were ANA positive with predominance of nuclear fine speckled 50%, nuclear homogeneous 25.9% and nuclear dense fine speckled 13%. ENA immunoblot showed autoantibodies in 32/60 (53.3%), mainly RNP, Ro-52, and dsDNA. When compared with ICAP-expected pattern–antigen, concordance was observed in 9/32 (28.1%) mainly in the centromere pattern and discordance in 23/32 (71.9%) especially nuclear coarse/large, speckled pattern.
Discussion: Higher ANA positivity reflects reactivity against limited antigens not represented on the immunoblot panel,[4] with observer's bias, multiple autoantibodies. ICAP suggests probable targets but does not guarantee antigen identity because of antibody multiplicity and methodological variability. Low concordance in our study is consistent with study by Ouazzani *et al*.[4] and Salman *et al.*[5]
Conclusion: These findings underscore that ANA fluorescence patterns may indicate probable antigenic targets but fails to reliably predict specific autoantigen and necessitates the use of comprehensive antigen- specific assays for characterization and management in SARD.

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Uncovering Get-like Proteins in *Mycobacterium tuberculosis*: Functional and Phylogenetic Insights into a Conserved Trafficking Pathway

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Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*M.tb*), remains the world's deadliest infectious disease. In 2023 alone, an estimated 10.8 million individuals developed TB globally, including 167,000 cases with HIV co-infection (WHO, 2023). *M.tb* has co-evolved with humans, acquiring sophisticated immune evasion strategies that enable long-term persistence and complicate disease eradication. These

challenges highlight the urgent need to elucidate the molecular mechanisms underlying TB pathogenesis and host–pathogen interactions to identify novel therapeutic targets.

Significance

Although the *M.tb* H37Rv genome was sequenced over two decades ago, the functions of many encoded proteins remain unknown. In this study, we focused on uncharacterized proteins potentially involved in intracellular trafficking—processes central to host–pathogen interactions. One such conserved system is the Guided Entry of Tail-Anchored Proteins (GET) pathway, well characterized in yeast and mammals but previously unexplored in *M.tb*.

Results

Structure-based analyses identified three *M.tb* proteins—Rv3679, Rv2184c, and Rv3680—as putative homologs of Get3, an essential ATPase chaperone of the yeast GET pathway that targets tail-anchored proteins to the endoplasmic reticulum during stress. Phylogenetic analyses revealed their conservation across the Mycobacteriaceae family. Functional complementation assays in *Saccharomyces cerevisiae* ΔGet3 strains demonstrated that expression of these *M.tb* proteins rescued salt-sensitive growth, confirming functional similarity to yeast Get3. Additionally, mass spectrometry–based interactome analyses identified associations with proteins involved in mycolic acid biosynthesis, drug resistance, and dormancy. Together, these findings reveal a previously unrecognized trafficking pathway in *M.tb* and suggest novel roles in bacterial physiology and pathogenesis, offering new avenues for therapeutic intervention.

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Source-Specific $PM_{2.5}$ Disrupts Pulmonary Lipid Metabolism and Membrane Integrity in Wistar Rats

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Particulate matter ($PM_{2.5}$) is a complex environmental pollutant linked with multiple respiratory and metabolic diseases. Although, the exact mechanism of toxicity is still unknown and commonly linked with oxidative stress and inflammation. The present study investigated the mechanistic impact of $PM_{2.5}$ on lipid metabolism and membrane integrity in the lungs of female Wistar rats.

$PM_{2.5}$ samples were collected from ambient air of three locations in Lucknow, Uttar Pradesh representing a residential area (L1), industrial area (L2), commercial area (L3) to account for compositional heterogeneity. $PM_{2.5}$ were collected using an ARA-N-FRM Sampler on quartz filters at a flow rate of 16.7 l/min and subsequently extracted with methanol. Wistar rats were divided into 6 different groups Normal Control, Low Dose, Mid Dose, High Dose L1, High Dose L2 and High Dose L3 and were orally exposed to $PM_{2.5}$.

Biochemical analyses revealed significant, dose-dependent alterations in total lipids, cholesterol, phospholipids, and glycolipids, indicating disruption of lipid homeostasis and membrane integrity. Changes in phospholipid and glycolipid fractions suggest perturbations in membrane fluidity, while altered cholesterol levels further imply compromised membrane rigidity and signalling microdomain stability.

Histopathological evaluation demonstrated structural disorganization and inflammatory changes in the lung tissue. Ultrastructural analysis under SEM showed alveolar wall contractions in PM 2.5 exposed group. Notably, differential effects observed among $PM_{2.5}$ samples from the three locations underscore the role of source-specific physicochemical composition in modulating lipid metabolic pathways and cellular membrane architecture.

Overall, this study provides mechanistic evidence that sub-chronic $PM_{2.5}$ exposure disrupts pulmonary lipid metabolic and compromises membrane structural integrity, thereby contributing to adverse respiratory

Neutrophil depletion at the early stage of Japanese Encephalitis virus infection affects CD8+ T-cell infiltration into the Mouse brain and causes severe Encephalitis

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Neutrophils have been reported to have protective and detrimental functions in viral infections. However, the role of neutrophils remains unexplored in Japanese encephalitis virus (JEV) infection. In this study, we elucidated the dynamics of neutrophils and their influence on immune cell recruitment in subclinical and severe encephalitis in mouse models. Further, we depleted neutrophils from 3-4 week-old C57BL/6 mice using mAb1A8 (anti-Ly6G) antibody and studied their association with inflammation, viral replication, immune cell infiltration and disease outcome. We observed that an increase in JEV replication is associated with increased infiltration of neutrophils in the spleen and brain. Further studies confirmed that depletion of neutrophils at an early stage of JEV infection reduced CD8 abundance in the infected brain and accelerated death in mice. We also observed that inhibition of the CXCL12-CXCR4 signalling axis by antagonist AMD3100 reduced CD8 abundance in the brain and augmented inflammasome activation, leading to fatal encephalitis. Reduced CXCR4 levels in the spleen and blood of CD8+ T-cells correlated with enhanced Granzyme B level, indicating CD8 cells differentiated more into effector phenotypes in neutrophil-depleted mice. Furthermore, CD8 depletion delayed the death of mice infected with a sublethal strain compared to neutrophil-depleted mice, suggesting that neutrophils play a vital role in the early restriction of viral replication, whereas CD8 is essential later in clearing the virus. Taken together, our study sheds new light on the role of neutrophils in the pathogenic mechanisms of JEV encephalitis and highlights the importance of neutrophils and CD8 cells associated with disease outcomes.

Artificial Intelligence inspired Multi-epitope vaccine against *Streptococcus pneumoniae* for broader serotype coverage

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Streptococcus pneumonia is the leading cause of respiratory deaths globally. The available polysaccharide vaccines and glycoconjugate vaccine provide suboptimal protection and doesn't have similar response against all the targeted serotypes. Current work has focused on the design of multi-epitope protein-based vaccine against *Streptococcus pneumonia* which can provide better immune response and can cover multiple serotypes through the conserved epitope targeting. The conserved as well as non-conserved B-cell and T-cell epitopes in the diverse proteome Streptococcus pneumonia were identified using artificial intelligence and bioinformatics tools. Epitopes were selected based on their strong IFN-g stimulation and limited allergenic response. β-defensin 1 was added as an adjuvant, and linkers were employed to link the epitopes and adjuvants in the final vaccine. The vaccine showed a high antigenicity score, was non-allergenic, non-toxic, and demonstrated stable physicochemical properties, including good solubility. Docking results indicated a ~14.5 kcal/mol binding affinity for the TLR4-vaccine interaction. MD simulations confirmed stability, with RMSD and hydrogen bond counts indicating consistent structure. Immune simulations showed robust responses, including memory formation in B and T-cells, with a shift from IgM to IgG1/IgG2 dominance. Cytokine analysis revealed peak IFN-γ levels post-exposure, highlighting the vaccine's strong immune-stimulating potential. Further, the vaccine construct was successfully expressed and purified using *E. coli* (BL21).

Accelerated 4D Flow MRI Using 3D Arbitrary-Scale Super-Resolution

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Four-dimensional Flow Magnetic Resonance Imaging (4D Flow MRI) gives time-dependent velocity data in three dimensions to assess the hemodynamic conditions of the heart comprehensively. Its conventional clinical application is however constrained by its long acquisition times (1015 min) and the trade-off between spatial resolution and signal-noise ratio. Although the scan duration can be able to be reduced by faster acquisition, this leads to low-resolution and noisy velocity fields, which impair the accuracy of clinically relevant flow biomarkers.

The recent deep learning-based super-resolution (SR) systems have demonstrated the ability to improve the 4D Flow MRI resolution, but the vast majority of them are limited to constant upscaling factors and are typically trained using synthetic data that was produced using computational fluid dynamics. These restrictions diminish their flexibility and external applicability to a real clinical setting. As a solution to these issues, this paper studies arbitrary-scale super-resolution (ASSR) of accelerated 4D Flow MRI which allows continuous-resolution reconstruction at any scale of interest.

Two generalisable ASSR models Local Implicit Image Function (LIIF) and Local Texture Estimator (LTE), which were both initially developed on 2D natural images, are redefined as 3D volume-based velocity reconstructions. The two models are also trained using in-vivo clinical 4D Flow MRI data only, without the use of unrealistic simulations. A loss function based on Weighted Mean Frequencies (WMF) is proposed to suppress the reconstruction of background noise and concentrating the learning process on physiological relevant areas, i.e., pulsatile flows. Also, a physics-inspired regularisation of the type of mass conservation by divergence minimisation is examined in the framework of LIIF.

Quantitative comparison of various scaling factors proves that both ASSR models are always superior to linear interpolation and an advanced CNN-based default baseline. LTE has better reconstruction error of the scaling factors that are within range whereas LIIF has better generalisation of the scaling factors that are not visible and larger. Loss guided by WMF is much more helpful in improving performance, and physics-based regularisation is a little useful when on noisy clinical reference data.

In general, this paper illustrates that arbitrary-scale super-resolution is a versatile and efficient approach to enable 4D Flow MRI to apply faster and retain clinically relevant hemodynamic datasets, which makes such an option potentially beneficial in clinical practice.

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Adeno-associated Virus Gene Therapy for Genetic Deafness

Genetic deafness including Hereditary Hearing Loss (HHL), which affects approximately 26 million individuals worldwide with congenital forms contributing to 60% cases leading to mutation in more than 200 genes. DFNB9 is one of the more frequent forms of autosomal recessive deafness which is responsible for 2-8% of cases, caused by biallelic OTOF mutations that disrupt the release of otoferlin protein and synaptic vesicle in inner hair cells, which leads to severe bilateral hearing impairment from birth. Traditional interventions like cochlear implants, fail to restore natural hearing physiology although providing auditory access. Preclinical models for more than 20 different deafness genes demonstrate that AAV-mediated gene therapy appears to be a transformative strategy, utilizing viral vectors to deliver functional transgenes into cochlear cells. Clinical trials are done using dual-AAV vectors with hair cell promoters and are bilateral in OTOF-present patients. Currently, as of 2025, there are eight registered clinical trials around the world assessing safety and efficacy using ABR threshold values and adverse events. Aggregate trial results from important studies such as the CHORD trial conducted by Regeneron (NEJM 2025) with clinically meaningful improvements observed in 11/12 patients with a 3/12 improvement within normal levels of hearing, as well as Chinese studies with improvements in hearing and recognition of speech in pediatric as well as adult patients, suggest a high rate of success with long-lasting improvement. The treatments appear well tolerated with no serious adverse events. This curative therapy restores physiological hearing in DFNB9 and accelerates gene therapies for diverse genetic deafness forms, ensuring broader sensory restoration.

Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Non-Invasive Hemoglobin Estimation Using Subungual Vascular Tissue Images via Machine Learning Regression Models

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Keywords: *Hemoglobin estimation, Non-invasive diagnosis, Nailbed image analysis, Machine learning, Regression models, XG Boost, Anemia screening, Medical image processing, Color space analysis, Mobile healthcare*

Hemoglobin concentration serves as a crucial clinical indicator for diagnosing and monitoring anemia as well as other blood-related conditions. Traditional methods for estimating hemoglobin rely on invasive blood sampling followed by laboratory analysis, which can lead to patient discomfort, elevate the risk of infection, and restrict their applicability for frequent monitoring or large-scale screening. These drawbacks underscore the necessity for a dependable, non-invasive, and cost-effective alternative for hemoglobin assessment. This study introduces a non-invasive framework for hemoglobin estimation that utilizes nailbed image analysis in conjunction with machine learning-based regression techniques. The nailbed area is selected due to its rich capillary network and its significant physiological relationship with blood perfusion and hemoglobin concentration. Images of the nailbed are captured and preprocessed to minimize noise, standardize illumination variations, and isolate the region of interest. Statistical features are extracted from the processed images using various color spaces, including RGB and HSV, to capture changes in color intensity, saturation, and brightness that correlate with hemoglobin levels. The extracted features are employed to train and assess multiple regression models, such as Linear Regression, Ridge Regression, Lasso Regression, Support Vector Regression, and Extreme Gradient Boosting (XG Boost). These models facilitate a comparative analysis of linear, regularized, non-linear, and ensemble-based learning methodologies. Model performance is assessed using standard error-based metrics, including Mean Absolute Error, Mean Squared Error, Root Mean Squared Error, and the coefficient of determination. Experimental findings indicate that ensemble-based and non-linear regression models surpass traditional linear methods in predicting hemoglobin levels. Among the models evaluated, the XG Boost regressor demonstrates the highest prediction accuracy and the lowest estimation error. The proposed method offers a painless, economical, and user-friendly solution for non-invasive hemoglobin screening, showing significant potential for incorporation into portable and smartphone-based healthcare solutions.

Time-Dependent Alterations of the Gut Microbiome During Treatment of Drug-Sensitive Pulmonary Tuberculosis: A Systematic Review and Meta-analysis

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Pulmonary tuberculosis (PTB) and prolonged anti-tuberculosis treatment (ATT) are increasingly recognized to disrupt the gut microbiome. However, the extent and temporal pattern of these changes remain inconsistent across studies. This systematic review and meta-analysis quantitatively synthesized alterations in gut microbiome alpha diversity in treatment-naïve PTB patients and across different phases of ATT. A comprehensive literature search was conducted following PRISMA. Eleven studies were included in the qualitative synthesis, of which eight were eligible for meta-analysis. Human studies reporting gut microbiome alpha diversity, primarily Shannon diversity, in adults with PTB were analyzed. Standardized mean differences were calculated to compare treatment-naïve TB patients with healthy controls and to assess longitudinal changes during the intensive phase, continuous phase, and at treatment completion. Random-effects models were applied, and heterogeneity statistics were calculated. Compared with healthy controls, treatment-naïve TB patients exhibited significantly reduced gut alpha diversity (pooled SMD = 0.74, 95% CI 0.56–0.92; I^2 = 72%). Longitudinal analyses showed a modest but significant overall decline in alpha diversity following ATT initiation (pooled SMD = −0.19, 95% CI −0.32 to −0.06; I^2 = 72%). Subgroup analyses indicated significant reductions after the intensive phase and at treatment completion, whereas changes during the continuous phase were not statistically significant. Qualitative synthesis suggested depletion of dominant commensal phyla, including Firmicutes and

Bacteroidota, with transient enrichment of Proteobacteria during treatment. Overall, gut microbiome diversity is reduced in PTB and does not consistently recover during ATT. High heterogeneity highlights the need for standardized longitudinal studies and microbiome-targeted adjunctive strategies.

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Hydroxyproline as Biomarkers in Oral cancer and rationale of mimetic of hydroxyproline (HYPROMI1) as a potential inhibitor of PD-L1.

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Background: Oral squamous cell carcinoma (OSCC) remains a major global health burden, particularly in South and Southeast Asia, with high rates of recurrence and immune evasion. One of the key mechanisms underlying tumor immune escape is the overexpression of programmed death-ligand 1 (PD-L1) on cancer cells, which suppresses antitumor T-cell responses. Emerging evidence suggests that components of the extracellular matrix, particularly collagen and its associated metabolites, may influence tumor–immune interactions; however, their role in PD-L1 regulation remains poorly understood.

Methods: In this study, we investigate hydroxyproline, a major collagen-derived amino acid, as a potential mediator of PD-L1 function and explore hydroxyproline mimetics as novel PD-L1 inhibitors in oral cancer. We employed Vertical Tube Gel Electrophoresis (VTGE) assisted LC-HRMS profiling of urine and nail lysates of oral cancer patients for proline and hydroxyproline levels. We also used in-house to develop 96-well plate colorimetric assays of hydroxyproline in biological samples of oral cancer patients. Molecular docking and MD simulation studies assisted with designing a mimetic of hydroxyproline (HYPROMI1) as potential inhibitor of PD-L1.

Results: Metabolomic profiling by LC-HRMS revealed significantly altered proline and hydroxyproline metabolism in oral cancer patients, with elevated urinary proline levels and a marked reduction of hydroxyproline in nail lysates compared to healthy controls. These findings were corroborated using an in-house developed 96-well colorimetric assay for hydroxyproline quantification. Molecular docking and MD simulation studies further demonstrated strong binding affinities of a designed mimetic of hydroxyproline (HYPROMI1) toward PD-L1, supporting their potential inhibitory role.

Conclusion: Collectively, our results suggest that dysregulated collagen–hydroxyproline metabolism is associated with immune suppression in OSCC and that

hydroxyproline-based mimetics may function as promising modulators of PD-L1. This work highlights a novel metabolic–immunological axis with potential implications for biomarker development and therapeutic intervention in oral cancer.

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In-silico identification of Pore-forming Toxin inhibitors to mitigate *Escherichia coli*- associated sepsis

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Sepsis is a life-threatening condition caused by a dysregulated host immune response to infection, resulting in systemic inflammation, immune dysfunction, and multi-organ failure. *Escherichia coli*, a major pathogen, is a leading cause of sepsis and is frequently associated with septicemia, urinary tract infections, and gastrointestinal diseases. A critical virulence determinant of *E. coli* is the secretion of pore-forming toxins that disrupt host cell membrane integrity and promote immune evasion. Hemolysin E (HlyE), also known as silent hemolysin A, is an α-pore-forming toxin that assembles into transmembrane pores, driving host cell lysis and contributing to toxin-mediated septic progression. Given the limitations of antibiotic therapy, including toxin amplification and resistance development, targeting bacterial virulence factors represents a promising therapeutic strategy. In this study, a structure-based in-silico screening approach was employed to identify inhibitors of HlyE (PDB ID: 1QOY). Molecular docking and drug-likeness analyses identified the plant-derived flavonoid Cianidanol as a high-affinity ligand (-5.760 kcal/mol). Virtual screening of natural phenolic compounds and ADMET profiling further supported its favorable pharmacokinetic properties. MM-GBSA binding energy calculations and 100 ns molecular dynamics simulations confirmed the stability of the HlyE-Cianidanol complex. These findings highlight Cianidanol as a promising non-bactericidal anti-virulence inhibitor with potential to mitigate toxin-driven sepsis while reducing selective pressure for antibiotic resistance.

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Magnetically Enabled Biohybrid Helical Micro-swimmers of *Arthrospira platensis* for Extracellular Navigation

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The development of micro-scale motile systems capable of navigating the complex extracellular space in vivo remains a critical challenge in targeted therapy and microrobotics. Here, we report the fabrication and systematic evaluation of magnetically actuated biohybrid helical micro-swimmers (MAG-Algabots) based on the intrinsic helical morphology of Arthrospira platensis functionalized with Fe_3O_4 magnetic nanoparticles (MNPs). Magnetite nanoparticles were synthesized via a controlled co-precipitation route and surface-modified with 3-aminopropyltriethoxysilane (APTES) to enhance electrostatic and hydrogen-bond-mediated conjugation with the negatively charged microalgal surface. Spectroscopic and structural analyses (FTIR, Raman, XRD, TEM, FESEM, zeta potential) confirmed stable MNP integration without compromising the biochemical integrity of the algal cell wall and extracellular polymeric substances. Under an external magnetic field of 2000–2500 μT, MNP-conjugated Spirulina trichomes exhibited field-guided helical locomotion with highly heterogeneous translational velocities ranging from ~18 to ~522 μm s^{-1}, reflecting variations in filament length, nanoparticle distribution, and hydrodynamic interactions. Obstruction-evasion experiments using alginate-based micro-barriers demonstrated an evasion efficiency of ~68.5%, highlighting the synergistic role of anisotropic helical geometry and magnetic responsiveness in adaptive navigation. Beyond quantitative motility metrics, qualitative observations revealed preserved intrinsic gliding behavior, edge-wagging dynamics, and robust maneuverability under confined conditions. Collectively, these findings establish Spirulina-based MAG-Algabots as promising biohybrid micro-swimmers for controlled transport and navigation within the extracellular space, with potential relevance to targeted drug delivery, tissue-interfacing microrobotics, and microfluidic biomedical applications.

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Purification of Small Nucleic Acids: A novel approach by extending Laemmli's Principle

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Background: Small nucleic acids such as microRNAs, small interfering RNAs, and short DNA fragments (20–200 nucleotides) play an important role in gene regulation, epigenetic control, and disease development. However, their isolation is technically challenging due to their small size, instability, and frequent loss during conventional extraction procedures. The present study aimed to establish an efficient and reliable protocol for the extraction and purification of small nucleic acids from different biological samples.

Methods: Plant leaf, chicken muscle, and oral cancer lymphoid tissues were processed using optimized non-denaturing lysis to preserve nucleic acid integrity. This approach extends the Laemmli system by employing 7.5% polyacrylamide matrix under native conditions with defined electrophoretic parameters. Unlike conventional Laemmli

electrophoresis, or routine in-gel extraction methods, this strategy is designed for the purification of small nucleic acids. Purified eluates were evaluated by NanoDrop for concentration, purity, and reproducibility.

Result: VTGE enabled efficient purification of small nucleic acids from diverse biological samples, with voltage–current profiles in 7.5% and 15% gels confirming reproducible electrophoretic conditions. Nanodrop DNA module analysis showed optimal purity for DNA samples (260/280 ≈1.8–1.95), while RNA-rich samples showed absorbance overestimation. RNA module readings indicated high RNA purity in VTGE elutes from oral cancer cells, fragmented RNA, and chicken lysate. Crude plant and hydrolyzed samples showed high yield but low purity, indicating contamination.

Conclusion: The VTGE-integrated protocol provides reproducible and effective method for isolating high-quality small nucleic acids from diverse biological samples. This approach has potential applications in molecular biology, diagnostics, and translational studies.

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New molecular insights into Chondrocyte proliferation and differentiation during Limb Development

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Long bones form through endochondral ossification, where a transient cartilage (TC) template is progressively replaced by bone, while the adjacent articular cartilage (AC) is retained for life. These two contrasting populations originate from common progenitor cells and develop simultaneously in adjacent regions, requiring precise coordination of proliferation, differentiation, and cartilage segmentation. Any disruption to these events can lead to skeletal abnormalities. One such process is the regulation of hypertrophy in chondrocytes, which profoundly influences limb lengthening, as chondrocytes exit the cell cycle and enlarge up to 20-fold, eventually converting to bone. Although we have achieved a good understanding of the major pathways involved, much remains unknown about the downstream molecules that execute these critical cellular changes, and a significant knowledge gap persists about how these signaling pathways function at the molecular level. Our study identifies two spatially restricted genes, Rgs2 and Klf4, which are expressed in both the TC and AC domains of the developing chick limb. Functional analyses using *in-ovo* electroporation reveal that the gain-of-function of either genos shortens limb length and reduces ossification by suppressing chondrocyte hypertrophy. Any perturbation in these genes arrests the cells at the pre-hypertrophic chondrocyte state, and also disrupts articular cartilage identity. Mechanistically, Rgs2 misexpression diminishes Ihh-positive pre-hypertrophic cells and reduces chondrocyte proliferation, consistent with properties of hypertrophic and articular chondrocytes. Ex vivo tibio-tarsal organ cultures demonstrate that canonical WNT/β-catenin activation induces Rgs2, while Klf4 downregulates β-catenin activity to inhibit hypertrophic differentiation. Together, these findings establish Rgs2 and Klf4 as critical checkpoint regulators that integrate WNT, Hedgehog, and BMP pathways to coordinate the balance between transient and articular cartilage differentiation, providing new mechanistic insights into endochondral ossification and limb skeletal patterning.

Development of Molybdenum Disulfide-based Quantum Dots for Cancer Theranostics

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Keywords: MoS_2 quantum dots, cancer theranostics, photothermal therapy, drug delivery, pH-responsive release

Cancer remains a leading cause of mortality globally, responsible for one in six deaths, with 20 million new cases and 9.7 million deaths reported in 2023—a figure projected to rise to 12.7 million by 2040. Traditional therapies often suffer from limitations such as poor selectivity, systemic toxicity, and drug resistance. In this context, theranostics—the integration of diagnostics and therapeutics within a single nanoplatform—has emerged as a promising approach to achieve personalized and precisely targeted cancer treatment.

To address these challenges, we engineered a single, multifunctional nanoplatform based on molybdenum disulfide quantum dots (MoS_2 QDs) conjugated with gold nanoparticles (AuNPs) and loaded with the chemotherapeutic agent doxorubicin (DOX). MoS_2 QDs were hydrothermally synthesized and PEGylated to enhance biocompatibility and dispersion. The resulting nanoconjugate simultaneously enables fluorescence imaging, photothermal therapy (PTT), photodynamic therapy (PDT), and pH-responsive chemotherapy.

This nanoplatform demonstrated a drug loading efficiency of 35% and significant singlet oxygen generation under light exposure (10% reduction in DPBF absorbance in 30 minutes). Drug release was highly pH-dependent, reaching 96% at acidic pH (5.5) and only 48% at physiological pH (7.4), simulating tumor-specific release.

This integrated theranostic strategy offers spatially and temporally controlled diagnosis and therapy, paving the way for more effective, personalized, and less invasive cancer treatment.

To Study Serum Uric Acid and Monosodium Urate Crystal in Gout Patients

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Key Words: Gout, monosodium urate crystals

Introduction: Globally, gout is the most frequent cause of inflammatory arthritis. Soluble (serum) urate levels consistently above the saturation threshold of 6.0 mg/dL causes hyperuricemia, and monosodium urate (MSU) crystals develop. Low GFR decreases clearance, which raised serum UA levels that increases risk of precipitation and supersaturation of urate crystals.

Objectives: To study serum uric acid levels, monosodium urate crystal formation, serum creatinine, urinary uric acid and glomerular filtration rate (eGFR) to assess their association in study population.

Methods: The study includes 30 participants (30-60 years) diagnosed with gout, attending orthopedic OPD, MGM hospital, kamothe, in the year 2025. Patients with other inflammatory disorders and significant renal impairment were excluded. Serum and urine samples were collected under aseptic condition and routine parameters assessed on Vitros 5600. Urine microscopy was performed to identify MSU crystals.

Results: The mean age of the study population was 47 ± 7.52 years, with more number of male compared to female. The mean serum uric acid level was 8.7 ± 1.7 mg/dL, with maximum patients showing values above the saturation threshold of 6.8 mg/dL. MSU crystals were found in 23 participants with elevated serum uric acid levels. The mean values of urinary uric acid excretion 520 ± 199 mg/day, serum creatinine level 1.6 ± 0.5 mg/dL and estimated eGFR was 70 ± 09 ml/min/1.73 m^2.

Conclusion: Patients with lower eGFR tend to high serum uric acid levels and increased presence of MSU crystals in urine suggesting that impairment of renal function, that contributes to MSU crystal accumulation and deposition in soft tissue/joints. We observed positive relationship between serum uric acid levels and MSU crystal formation, and an inverse association between renal function (eGFR) and serum uric acid levels, supporting the role of renal impairment in the pathogenesis of gout.

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Metabolic Adaptations to Chemotherapeutic Stress: Assessing Nutrient Uptake in Doxorubicin-Treated MCF-7 Cells

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Background: Cancer cells have the ability to "reprogram" metabolism to survive the stress of chemotherapy. While Doxorubicin is effective at killing cancer cells by damaging DNA and creating oxidative stress, cells often fight by changing nutrient uptake. This study explores survival shifts to identify how cancer cells fuel their resistance.

Methods: MCF-7 breast cancer cells were exposed to low doses of Doxorubicin and cell viability was assessed by

routine cell culture assays to observe survival mechanisms. We employed a novel Vertical Tube Gel Electrophoresis (VTGE) assisted metabolic profiling of cells followed by qualitative and quantitative assessment of nutrients such as glucose, glutamine and related metabolites using 96-well plate colorimetric assays. The results were validated by LC-HRMS analysis. Conditioned media was extracted for analysis of nutrients. Glucose consumption was tracked using Anthrone/Phenol method. For obtaining accurate results across different cell densities, data was normalized to total protein content using Lowry method. In-silico mimetic of glutamine was prepared to prevent the pathway, involved in the proliferation of tumor cells.

Results: We observed increased glucose intake and enhanced extracellular lactate production in breast cancer cells under drug-induced stress. Extracellular glutamine levels were significantly depleted which produce antioxidants that neutralize drug toxicity, a mimetic of glutamine was prepared and its interaction was studied by performing docking and MD simulations.

Conclusion: These results demonstrate that breast cancer cells execute a coordinated metabolic defense to combat Doxorubicin. This study highlights that targeting the cell's feeding habits could be a powerful way to make chemotherapy more effective.

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Targeting HDAC6 Restores Peroxiredoxin-1 Acetylation and Attenuates Oxidative Stress–Driven Seizures in Focal Cortical Dysplasia

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Background:

Focal cortical dysplasia (FCD) is a major cause of drug-resistant epilepsy, characterized by abnormal cortical architecture and underlying molecular disturbances. Despite advances in diagnostic classification and surgical management, the biological mechanisms driving epileptogenesis in FCD remain incompletely understood, and effective non-surgical treatments are limited. Oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant capacity, has been implicated in FCD pathology. This study explores the role of histone deacetylase 6 (HDAC6) in regulating oxidative stress and seizure activity through modulation of the antioxidant enzyme peroxiredoxin-1 (Prdx1).

Methods:

Cortical tissues from patients with FCD Type II and from a BCNU-induced rat model were analyzed using qRT-PCR, immunoblotting, and co-immunoprecipitation to determine HDAC6 expression and Prdx1 acetylation status. Intracellular ROS levels were assessed using the dichlorofluorescin diacetate assay. The effects of selective HDAC6 inhibition were evaluated using Tubastatin A (TubA), with outcomes measured in terms of oxidative stress markers and pilocarpine-induced seizure parameters.

Results:

HDAC6 expression was significantly elevated in both human FCD samples and the BCNU rat model. Increased HDAC6 activity was associated with reduced Prdx1 acetylation and heightened oxidative stress. Treatment with TubA restored Prdx1 acetylation, reduced ROS accumulation, delayed seizure onset, and significantly lowered seizure frequency.

Conclusion:

These findings identify HDAC6 as a critical regulator of oxidative stress and seizure susceptibility in FCD. Pharmacological inhibition of HDAC6 may represent a promising therapeutic strategy for managing FCD-associated epilepsy.

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STUDY OF OXIDATVIVE STRESS IN OBESE AND NON-OBESE MENOPAUSAL WOMEN

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Keywords: MDA, SOD, BMI, obese menopausal women.

Introduction: Oxidative stress, a key mediator of cardiovascular disease, among postmenopausal women, the correlation between obesity and oxidative stress is poorly examined. parameter including criteria for group A and B; Height, weight, BMI, malondialdehyde (MDA), Superoxide Dismutase (SOD), Therefore, in present study, we compared oxidative stress states in postmenopausal women with or without obesity and body mass index is assessed.
Aim: Present study is aimed to assess oxidative stress markers (MDA, SOD) & BMI
Materials and Methods: The study includes 60 post-menopausal women, further divided into two group. Group A includes (n=30) Obese Menopausal women and Group B (n=30) non-obese Menopausal women. Blood samples were collected for oxidative stress markers (MDA, SOD) & Lipid Profile. SOD was estimated by Marklund and Marklund method and MDA by Thiobarbituric-acid-reactive substances (TBARS) method.
Results: We found increase in MDA and decrease in SOD and lipid profile altered in obese menopausal women on compared with non-obese. Obesity was diagnosed with BMI >25 kg/m^2.
Conclusions: Menopause is associated with increased oxidative stress. Obesity increases, oxidative stress in postmenopausal women as compared with non-obese.

Application of AI in Medical Lab: Identifying Digital Biomarkers and Their possible role in Patient Care

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Key Words: Artificial Intelligence, Digital biomarkers, personalized medicine

The integration of Artificial Intelligence (AI) into medical laboratories represents a paradigm shift in diagnostics, driven by the convergence of high-throughput multimodal data (genomic, clinical, imaging, and Internet of Things (IoT) and increased computational power. AI, including machine learning and deep learning, is moving beyond automation to identify complex digital biomarkers—subtle, actionable data patterns that, when combined with patient informatics, provide precise insights into disease prediction, diagnosis, prognosis and can create a genetic digital profile of individuals. Key applications range from enhancing digital biochemistry, pathology, and microbiology to optimizing personalized treatment in many areas including oncology. However, the successful implementation of AI necessitates addressing ethical, privacy, and regulatory considerations to ensure robust and equitable patient care.
Digital biomarkers like Susceptibility/Risk biomarkers**,** Prognostic biomarkers, Safety biomarkers and Preventive biomarkers are particularly effective in identifying risk before clinical symptoms appear, allowing for early intervention and continuous health surveillance. As AI is the creation of Natural Human Intelligence, we must assess its limitations and possible risks continuously. AI in diagnostic laboratories faces critical limitations including algorithmic bias from unrepresentative training data, pre-analytical errors, lacks clinical context, and raises ethical and legal concerns regarding liability.

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Hemoglobins, Blood Substitutes and Therapy for Sickle Cell Disease

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Hemoglobin, the venerable protein that sustains life, has been my life for over two decades now. From discovering hemoglobins in various life forms in nature, understanding of their molecular structures and structure-function relationship, to engineering of hemoglobins for use as hemoglobin-based oxygen carrier (HBOC), the insights have been enlightening. These activities led to translational research in sickle cell disease (SCD), a national health burden.

Sickle Cell Disease (SCD) is an inherited hemoglobinopathy caused by a point mutation in the β-globin gene, resulting in the formation of sickle hemoglobin (HbS). Under hypoxic conditions, HbS polymerization induces Red Blood Cell (RBC) deformation, reduced deformability, and membrane fragility, driving vaso-occlusion, hemolysis, and progressive multi-organ pathology. While curative gene-based therapies have emerged, their widespread implementation is limited by cost, infrastructure requirements, and eligibility constraints. Consequently, disease-modifying pharmacologic options remain largely restricted to hydroxyurea, as newer agents such as Voxelotor, crizanlizumab, and L-glutamine face challenges related to access, affordability, and variable clinical benefit.

We investigated Sailin-HbS, a patented polyherbal formulation composed of five plant-derived extracts with documented antioxidant and anti-inflammatory properties, as a potential low-cost disease-modifying intervention. In-vitro studies using RBCs from individuals with homozygous SCD demonstrated approximately 74% inhibition of hypoxia-induced sickling. Sailin-HbS significantly attenuated HbS polymerization kinetics, as assessed spectrophotometrically, and improved RBC membrane stability, evidenced by enhanced resistance to osmotic stress. Comparative analyses indicated anti-sickling efficacy comparable to or exceeding that of previously reported botanical and small-molecule anti-sickling agents. Comprehensive preclinical toxicological evaluation in rodent models revealed a favorable safety profile, with an oral LD_{50} exceeding 2000 mg/kg and no treatment-related adverse effects observed in sub-acute or chronic toxicity studies across hematological, biochemical, and organ function parameters.

Based on these findings, an investigator-initiated, open-label, two-site observational study was conducted in Nigerian SCD patients. Oral administration of Sailin-HbS for 12 weeks was well tolerated, with no clinically significant alterations in hematological, hepatic, or renal indices. Notably, reductions in vaso-occlusive crisis frequency, hospitalization rates, transfusion requirements, reticulocyte counts, and irreversible sickled cells were observed, suggesting preliminary clinical benefit. Together, these data support Sailin-HbS as a safe, mechanistically active, and potentially scalable disease-modifying therapeutic candidate for SCD, warranting further controlled clinical evaluation.

Nanotechnology-based Advanced Therapeutic Strategies for Targeting Inflammatory Cells in Chronic Respiratory Diseases

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Asthma, Chronic obstructive pulmonary disease (COPD) COVID-19, EGPA, Lung cancer, and Pneumonia are major chronic respiratory diseases (or CRDs) affecting millions worldwide and account for substantial morbidity and mortality. COPD is a chronic inflammatory lung disease associated with progressive airflow obstruction. Tobacco smoking is the main risk factor worldwide. Specific drugs that are directed against the remodeling and chronic inflammation, thereby preventing lung tissue damage and progressive lung function decline, must be developed. Currently, the treatment being used primarily focusses only on alleviating symptoms of this illness

rather than delivering the therapeutic agent at target site for optimal care and/or prevention. Lately, extensive research is being conducted on airways and systemic inflammation, oxidative stress, airway, or parenchymal rehabilitation. In all studies, cytokines have been found to play an imperative role in fostering chronic airway inflammation and remodeling. Paracrine actions of angiogenic factors released by resident or infiltrating inflammatory cells following activation by proinflammatory cytokines in diseased airways could play a major role in airway vascular remodeling process. Mostly, CRDs are irreversible diseases that affect different parts of the respiratory system, imposing a considerable burden on different socioeconomic classes. All these CRDs have been linked to increased eosinophils in the lungs. Eosinophils are essential immune mediators that contribute to tissue homeostasis and the pathophysiology of various diseases. Interestingly, elevated eosinophil levels are associated with cellular processes that regulate airway hyperresponsiveness, airway remodeling, mucus hypersecretion, and inflammation in the lung. Therefore, eosinophil is considered to be a therapeutic target in eosinophil-mediated lung diseases. Although conventional medicines like antibiotics, anti-inflammatory drugs, and bronchodilators are available to prevent CRDs. But the development of resistance to these therapeutic agents after long-term usage remains a challenge. However, progressive development in nanotechnology has unveiled the targeted nanocarrier approach that can significantly improve the pharmacokinetics of a therapeutic drug. The potential of a nanocarrier system can be specifically targeted at eosinophils and their associated components to obtain promising results in the pharmacotherapy of CRDs. Moreover, there is a clear need for nanocarrier drug delivery systems for the targeted treatment of CRDs.

DNA Microarray Reveals Stunted Angiogenesis and Fibrosis in Human Failing Heart

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Right ventricular hypertrophy (RVH) associated with impaired myocardial oxygen and nutrient supply is a common feature in the cyanotic congenital heart disease, Tetralogy of Fallot (ToF). Consequently, the right ventricle may manifest in an altered molecular phenotype with many adaptive and inherited gene profiles that are largely unknown. The present study aimed to investigate the myocardial differential gene expression profile and to assess myocardial vascularization in patients with ToF. DNA microarray analysis on right ventricular biopsies from ToF-patients operated for primary corrective surgery (referred as ToF-1; n = 12, mean age 0.5 year) and age-matched controls (n = 6) was validated by Northern hybridization and RT-PCR. Employing immunohistochemistry and video image analysis expression of vascular endothelial growth factor (VEGF), vascular density (by α-SMA and CD31 staining) and myocyte cross sectional area (Gomori's reticuline staining) were assessed in ToF-1 and adult patients (referred as ToF-2, n = 12, mean age 30 years) who underwent surgery for pulmonary regurgitation and compared the data with respective age matched controls (n = 6/12). DNA microarray analysis revealed an altered expression pattern for 236 genes, including enhanced (1.5-2.2-fold) expression of angiogenic factors and their receptors, including VEGF, flt-1, flk-1 angiopoietin-2, FGF-2, FGF-R1, PDGF-A, whereas flt-4, Tie, TGF-β, TGF-β3R showed decreased (1.6-3.4-fold) expression in ToF-patients. Northern blot analysis verified the expression patterns of VEGF and flk-1 in both ToF-1 and ToF-2 patients. VEGF staining in cardiomyocytes was increased in ToF-1 (1.5-fold, $p < 0.05$) as compared to ToF-2. Video image analysis revealed enhanced vascular density ($p < 0.01$) with enlarged myocyte cross-sectional area ($p < 0.01$), but vascular wall thickness remained unchanged in ToF-1 patients as compared to age-matched controls. Our data suggest that RVH is associated with profound changes in gene profile for a number of genes, where VEGF/VEGF-R system contributes to enhance, but stunted myocardial angiogenesis in patients with ToF.

Bio-Innovations in Materials and Regenerative Engineering: Translational Strategies from Nano-Systems to Smart Scaffolds

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Keywords: Biomaterials; Regenerative Engineering; Nanoarcheosomes; Cancer Therapeutics; 3D Printing; Electrospinning; Smart Scaffolds; Space Therapeutics; Microgravity Biology; Nanomedicine; Targeted Drug Delivery; Neurodegenerative Disorders

Recent advances in materials science and regenerative engineering are redefining therapeutic strategies for complex diseases and tissue regeneration. Our research program integrates biomaterials engineering, nanotechnology, and advanced fabrication approaches to develop next-generation platforms for regenerative medicine and targeted therapeutics. A key focus of our work is the development of nanoarcheosomes, an emerging nanocarrier system, explored for cancer therapeutics and multifunctional biomedical applications, enabling improved drug stability, controlled release, and enhanced cellular uptake. In parallel, we investigate novel biomaterial formulations for space therapeutics, studying cellular and tissue responses under normal gravity and simulated microgravity conditions to understand mechanobiological adaptations relevant to long-duration space missions. These insights guide the design of robust regenerative systems capable of functioning in extreme environments. Our laboratory actively fabricates electrospun nanofibrous membranes and 3D-printed architectures for both soft and hard tissue engineering, enabling precise control over scaffold geometry, porosity, and mechanical cues. These platforms are tailored to promote cell adhesion, differentiation, and tissue maturation. Additionally, we explore protein-based formulations for neurodegenerative disorders, particularly Alzheimer's disease, aiming to enhance bioavailability and therapeutic efficacy. Complementing these efforts, we investigate nanobot-assisted drug delivery systems for cancer therapy, designed to improve site-specific targeting and minimize systemic toxicity. Collectively, our work highlights how bio-inspired materials, advanced manufacturing, and nano-enabled technologies can bridge the gap between laboratory innovation, and clinical translation, contributing to the future of precision healthcare and human wellbeing.

Unravelling Inflammation, Immunity, and Tumor Biology in 3D: Patient Organoids for Precision Medicine

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Malignant gliomas, the most common primary brain tumours that arise from glial cells within the central nervous system (CNS), are among the most fatal human cancers. With a median survival of only 14.6 months, even after aggressive therapy with surgery, radiation, and chemotherapy, most patients succumb to their disease within two years of the initial diagnosis. Given the paradigm shift from traditional surgical resection to precision medicine, we use a multi-pronged approach that considers the cellular heterogeneity of gliomas, their microenvironment, and 3-dimensional cell-cell interactions to identify the roles of innate immunity and inflammasome signalling pathways in gliomas. Potentially, this could provide a novel link between innate immunity and glioma pathophysiology with widespread therapeutic implications for delaying glioma progression and/or sensitizing gliomas to other treatment modalities. We have successfully created a protocol for matrix-free patient-derived glioblastoma organoids (Indian Patent application No: 202311002108). These organoids enable pre-clinical drug development, biomarker analysis, and serve as drug-testing models and basic cancer research, allowing us to dissect complex cellular interactions and integrate computational biology and artificial intelligence-based approaches to develop a predictive framework for precision medicine.

Reversible Non-Competitive Inhibitors of Glycine Transporter 2: A Novel Non-Opioid Strategy for Neuropathic Pain

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Glycine transporter 2 (GlyT2) regulates extracellular glycine levels in the central nervous system and is a promising target for restoring inhibitory neurotransmission in neuropathic pain. Although GlyT2 inhibitors demonstrate analgesic efficacy in rodent models, the prototypical inhibitor ORG25543 is limited

by slow dissociation kinetics and dose-dependent neuromotor toxicity, resembling the phenotype of GlyT2 knockout mice and restricting its clinical translation. To address these limitations, we designed and synthesized a series of second-generation, conformationally restricted indoline analogues acting as non-competitive and reversible GlyT2 inhibitors. These compounds exhibited varied potency and improved recovery kinetics compared to ORG25543. Notably, RPI-GLYT2-82 produced significant analgesic effects in murine neuropathic pain models without inducing excitatory neuromotor side effects. Through iterative medicinal chemistry optimization combined with comprehensive *in vitro* and *in vivo* profiling, this effort led to the identification of RPI-GLYT2-82, a reversible, non-competitive GlyT2 inhibitor with a differentiated pharmacological profile. RPI-GLYT2-82 demonstrated robust anti-allodynic activity in two gold-standard preclinical models of neuropathic pain, namely the chronic constriction injury (CCI) and partial sciatic nerve ligation (PSNL) mouse models. Overall, this study demonstrates that reversible, non-competitive GlyT2 inhibition represents a safer and effective non-opioid strategy for neuropathic pain management and provides a strong foundation for further preclinical optimization.

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Abstract for Prof. Nurul Islam Award for Best Oral Presentation by a Young Scientist at IABSCON-2026 at Goa

Circulating microRNAs as Predictive Biomarkers for Methotrexate Efficacy in Psoriasis: A Translational Discovery-Validation Study

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Background: Psoriasis is a chronic immune-mediated inflammatory disease with inter-individual variability in response to methotrexate (MTX), the most commonly used first-line systemic therapy in India. The absence of validated predictive biomarkers often delays therapeutic optimization. Circulating microRNAs (miRNAs), as stable post-transcriptional regulators of immune and inflammatory pathways, represent biologically plausible and minimally invasive biomarkers. This study aimed to identify and validate circulating miRNA signatures associated with MTX response in psoriasis.

Methods: A translational two-phase discovery–validation study design was employed. In discovery phase, global miRNA profiling using NGS was performed in 30 psoriasis patients and 30 age- and sex- matched healthy controls to identify disease- and MTX response–associated miRNAs. Candidate miRNAs were shortlisted based on fold change, false discovery rate, biological relevance, and novelty. Validation was carried out using q-PCR in an independent cohort of 216 psoriasis patients receiving MTX. Clinical response was assessed at baseline and at 24 weeks using PASI and DLQI.

Results: Eleven candidate miRNAs were selected for validation. In validation cohort, 153 patients achieved treatment response, while 63 were non-responders. MTX therapy resulted in significant reductions in PASI and DLQI scores ($p<0.001$). Differential expression of miR-204-5p, miR-7-5p, miR-211-5p, miR-34c-5p, and miR-9-5p showed strong associations with treatment response and inflammatory pathways, representing one of the largest independent Indian cohorts validating circulating miRNAs in psoriasis.

Conclusion: This study provides robust translational evidence supporting circulating miRNAs as predictive biomarkers of methotrexate responsiveness and represents a rigorously validated translational biochemistry study enabling biomarker-guided methotrexate therapy in psoriasis.

Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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IABSCON 2026 – ORAL ABSTRACTS

Mycobacterial methyltransferase: Hijacking the host immune response through Epigenetic manipulation of immune Cell Genome

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In recent years, increasing evidence has shown promoter hypermethylation of host genes following infection with various pathogens including *Mycobacterium tuberculosis*. However, the role of mycobacterial proteins in the epigenetic reprogramming of host immune cells is poorly understood. In this study, whole genome bisulfite sequencing (WGBS) was performed on PBMCs from pulmonary tuberculosis (PTB), healthy controls, and diseased controls. Differentially Methylated Regions (DMRs) were validated by indirect bisulfite sequencing and Gene Set Enrichment Analysis (GSEA) was employed to identify pathways related to host immune responses. GEOR2 server was used to analyse the mRNA expression of selected genes with hypermethylated DMRs in promoter regions. Comparative analysis of WGBS data revealed global methylation differences and specific methylation alterations in TB patients. GSEA revealed the hypermethylated regions predominantly associated with genes involved in T cell-mediated immune processes. Eight DMRs were identified in the promoter regions of the genes TAF8, FZD5, HLA-DRB, MIR483, PVRIG, SH2B2, ZAP70, and TNFRSF13C. In silico mRNA expression analysis showed a significant downregulation of TNFRSF13C, ZAP70, and PVRIG, thus selected for further investigation.

A previously identified mycobacterial methyltransferase Rv2372c from our laboratory was purified in recombinant form. In vitro stimulation of PBMCs from healthy subjects with recombinant Rv2372c resulted in significant hypermethylation of the promoter regions of PVRIG, ZAP70, and TNFRSF13C, consistent with WGBS findings in PTB patients. Treatment of PBMCs with Rv2372c resulted in significantly reduced lymphocyte proliferation, a Th2-skewed cytokine profile, decreased T-cell cytotoxicity, and downregulated TLR2 expression. Overall, these findings suggest a novel mechanism of host immune responses suppression through alteration in host DNA methylation by Mtb using its methyltransferases, which could be exploited as promising targets for host-directed interventions in tuberculosis.

Stage-Specific miRNA Landscapes in Osteoarthritis Implicate miR-4505 and miR-331-3p via ERBB2-Mediated Pathogenesis

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Osteoarthritis (OA) is a progressive degenerative joint disease and a leading cause of disability in the elderly, yet reliable biomarkers for early diagnosis and therapeutic intervention remain limited. Circulating miRNAs have emerged as stable, non-invasive candidates with diagnostic and regulatory potential. In this study, genome-wide microarray profiling of synovial fluid from early- and late-stage OA patients ($n = 10$) identified differentially expressed miRNAs, which were further validated by qRT-PCR in an extended cohort ($n = 37$) using both synovial fluid and serum. Tissue-level expression was examined in paired cartilage and synovium from OA patients ($n = 15$) and non-OA controls (n = 15). Bioinformatic predictions and functional validation through mimic/inhibitor transfection in IL-1β–stimulated SW1353 chondrocytes were performed to elucidate downstream targets and pathways. Seven miRNAs were found to be downregulated in late-stage OA, with miR-4505 and miR-331-3p consistently decreased across synovial fluid, serum, cartilage, and synovium. Serum levels of these miRNAs were independent of age, and miR-331-3p demonstrated strong discriminative ability (AUC = 0.81). ERBB2 was identified as a common downstream target, and overexpression of miR-4505 or miR-331-3p was associated with reduced ERBB2 expression, accompanied by attenuation of catabolic gene expression and inflammatory responses in vitro. These findings suggest that stage-specific downregulation of miR-4505 and miR-331-3p may reflect their involvement in OA pathogenesis. Beyond their potential utility as biomarkers, their ability to influence ERBB2-associated signaling pathways highlights their relevance as candidates for further translational investigation in OA.

Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
www.iabsjournal.com

Metabolomic and lncRNA-Based Molecular Signatures in the Management of Breast Cancer

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Breast cancer remains a leading cause of cancer-related mortality among women worldwide. Identification of minimally invasive biomarkers for early detection and risk stratification is of paramount importance. In this study, we employed ^{1}H NMR-based serum metabolomics to characterize metabolic alterations associated with breast cancer. We also integrated these findings with the expression profiling of metabolically relevant long non-coding RNAs (lncRNAs). Serum samples from 120 participants (80 breast cancer patients, 20 benign breast disease cases, and 20 healthy controls) were analyzed using ^{1}H NMR spectroscopy. Multivariate (PLS-DA, OPLS-DA, Random Forest) and univariate statistical analyses were performed to identify discriminant metabolites, followed by pathway enrichment and topology analyses to determine perturbed metabolic networks. Expression levels of selected lncRNAs were assessed in tumor tissues and adjacent normal tissues by qRT-PCR. A total of 40 endogenous metabolites, including amino acids, carbohydrates, and lipids, were identified. Distinct metabolic signatures differentiated healthy, benign (fibroadenoma), and malignant groups. Key altered metabolites included glycerophosphorylcholine, mannitol, acetate, citrate, lysine, and histidine. Pathway analysis revealed significant perturbations in choline metabolism, amino acid biosynthesis, and energy homeostasis. Tumor tissues exhibited significant dysregulation of oncogenic (H19) and tumor suppressor (MEG3, GAS5) lncRNAs compared to adjacent normal tissues. Overall, the findings highlight metabolic reprogramming from benign to malignant states and demonstrate that integrating metabolomic signatures with lncRNA expression provides a link between transcriptional regulation and tumor metabolism. This integrative OMICS approach opens a new window for developing minimally invasive biomarkers for early diagnosis, disease monitoring, and therapeutic stratification of breast cancer.

Multi-Omics Approaches in Diabetic Kidney Disease: From Molecular Mechanisms to Clinical Translation

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Diabetic kidney disease (DKD) affects nearly one-third of individuals with diabetes and remains the leading cause of end-stage kidney disease worldwide. Current clinical markers, including estimated glomerular filtration rate (eGFR) and albuminuria, primarily reflect established structural damage and often fail to capture the early molecular processes underlying disease initiation and progression. Advances in multi-omics technologies have begun to provide deeper insights into the complex biological mechanisms driving DKD.

Recent studies using single-cell and spatial transcriptomics have revealed substantial cellular heterogeneity within the diabetic kidney, including transcriptional programs in proximal tubular epithelial cells associated with inflammatory signaling, extracellular matrix remodeling, and immune–epithelial interactions. Complementary proteomic and metabolomic analyses have further identified disturbances in pathways related to fibrosis, lipid metabolism, oxidative stress, and mitochondrial dysfunction. Together, these findings highlight DKD as a multi-layered disorder involving coordinated alterations across multiple biological systems.

Translating these molecular discoveries into clinically applicable diagnostics remains a major challenge. In this context, urinary biomarkers reflecting different components of DKD pathophysiology were evaluated in a cohort of 325 individuals with diabetic kidney disease. Urinary C-megalin, indicators of proximal tubular injury, together with adiponectin reflecting alterations in the glomerular–tubular axis and metabolic stress, were quantified and analyzed alongside conventional clinical parameters. These biomarkers provided complementary information to traditional measures such as eGFR and albuminuria by capturing mechanisms of kidney injury that may not be reflected by functional markers alone. Machine learning approaches, including Random Forest and gradient boosting models, were subsequently applied to integrate biomarker measurements with clinical variables, enabling multidimensional risk stratification.

This translational strategy is supported by broader evidence from our recently published systematic review and meta-analysis of artificial intelligence applications in DKD, which included 57 studies and demonstrated pooled AUROC values exceeding 0.80 for prediction, diagnosis, and progression modeling, with Random Forest algorithms showing particularly strong performance.

Collectively, these findings illustrate how integrating multi-omics discoveries, biomarker validation, and machine learning approaches may enhance early detection and risk assessment in DKD. Continued efforts to combine molecular biomarkers with computational modeling may help advance precision nephrology strategies for patients with diabetic kidney disease.

Molecular Landscape of Myelodysplastic Neoplasms: Insights from Exome and Transcriptome Analysis

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Myelodysplastic neoplasms (MDS) are clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis and a propensity to progress to AML-myelodysplasia related (AML-MR). Global genomic studies indicate that nearly 90% of patients with MDS and AML-MR harbor pathogenic variants in approximately 40 genes implicated in disease pathogenesis. In addition, mutational signatures are increasingly being incorporated into disease classification frameworks. Despite being a relatively common diagnosis, comprehensive genomic data on Indian patients with MDS and AML-MR remain limited.
To gain insights into the molecular mechanisms underlying disease pathogenesis, we analyzed the whole exome and transcriptome of MDS and AML-MR using both publicly available datasets and internally generated data. The pattern of mutations in genes known to be associated with myeloid neoplasms differed significantly in the in-house cohort compared to public databases, which largely represent Western populations. Notably, a subset of samples lacking canonical "myeloid variants" also showed no cytogenetic abnormalities, suggesting the possibility of alternative pathogenic mechanisms.

Application of genomic information to the International Prognostic Scoring System-Molecular (IPSS-M) resulted in reclassification of nearly, 50% of patients compared with the previously used International Prognostic Scoring System-Revised (IPSS-R). Transcriptomic profiling of bone marrow nuclear cells (BMNCs) demonstrated that the molecular landscape of high-risk MDS closely resembles that of AML-MR, supporting the concept of a biological continuum between these entities, whereas low-risk MDS exhibited distinct transcriptional features.

Collectively, these findings provide novel insights into the molecular pathogenesis of MDS and AML-MR from an Indian perspective. This is particularly relevant given the earlier age of onset of these disorders in Indian patients, suggesting that the underlying disease biology may differ from that described in Western populations.

From Pathogen Proteome to Therapeutic Targets: Identifying Effector Signatures in Scrub Typhus

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Scrub typhus, caused by *Orientia tsutsugamushi*, is a neglected tropical disease responsible for significant morbidity and mortality in endemic regions. The absence of effective targeted therapeutics and the limited understanding of pathogen-specific virulence mechanisms continue to challenge disease management. In alignment with the theme of omics-driven innovations for human disease management, our study focuses on identifying key molecular determinants that can serve as potential therapeutic targets in scrub typhus.

Through integrative proteome wide analysis of the UT76 strain, we identified 22 high-confidence secretory effector proteins potentially involved in host–pathogen interactions. These include cell wall associated enzymes, magnesium transporters, ubiquinone biosynthesis proteins, and a notable enrichment of conjugal transfer proteins (TraN, TraH) and ankyrin repeat containing proteins. The predominance of ankyrin containing effectors suggests a strategic role in modulating host cellular pathways and immune responses.

Importantly, several candidate proteins exhibited significant intrinsically disordered regions, indicating structural adaptability that may enhance host interaction, immune evasion, and intracellular survival. In addition, multiple previously uncharacterized secretory proteins were prioritized, expanding the repertoire of unexplored drug targets in *O. tsutsugamushi*.

Collectively, our findings provide a curated effector

signature landscape of scrub typhus, offering novel insights into its molecular pathogenesis. This work establishes a foundation for downstream functional validation and rational drug target development, demonstrating how omics-guided strategies can accelerate precision therapeutic approaches in neglected infectious diseases.

Multi-Omics Biomarker Approach for Redefining Cardiovascular Risk in Type 2 Diabetes Mellitus

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Background

Cardiovascular disease (CVD) remains the leading cause of morbidity and mortality in individuals with Type 2 Diabetes Mellitus (T2DM). Conventional cardiovascular risk prediction models, including the Atherosclerotic Cardiovascular Disease (ASCVD) pooled cohort equation, rely primarily on traditional clinical variables such as age, blood pressure, lipid profile, and smoking status. However, these models often fail to fully capture the significant residual cardiovascular risk observed in diabetic populations. Recent advances in cardiometabolic research highlight the potential role of integrating biomarkers that reflect multiple biological pathways—including lipid metabolism, inflammation, cardiac stress, and autonomic regulation—to achieve a more comprehensive understanding of cardiovascular risk.

Objectives

To highlight the emerging role of multi-omics biomarker integration in refining cardiovascular risk stratification in Type 2 Diabetes Mellitus and to explore how advanced lipid, inflammatory, cardiac, and autonomic biomarkers may complement traditional risk prediction models.

Methods

A hypothesis-generating cross-sectional study design has been adopted to evaluate adults with T2DM undergoing cardiovascular risk assessment. Participants are stratified into low (<7.5%) and high (≥7.5%) ASCVD risk categories. Clinical, anthropometric, and metabolic parameters are recorded alongside biomarker measurements including Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB), Lipoprotein(a), high-sensitivity C-reactive protein (hsCRP), PCSK9, and NT-proBNP, together with autonomic indices derived from heart rate variability (HRV).

Results / Discussion

The presentation will discuss how these biomarkers represent distinct yet interconnected dimensions of cardiovascular risk in T2DM, including atherogenic lipoprotein burden (ApoB, Lp(a)), protective lipid balance (ApoA1), systemic inflammation (hsCRP), lipid receptor regulation (PCSK9), myocardial stress (NT-proBNP), and autonomic dysfunction (HRV indices). Particular emphasis will be placed on the potential of integrating these markers to identify residual cardiovascular risk, improve risk discrimination beyond traditional ASCVD scores, and support emerging approaches in precision cardiometabolic risk assessment.

Conclusion

A multi-marker, multi-omics framework offers a promising strategy for improving cardiovascular risk stratification in T2DM. Integrating lipid, inflammatory, cardiac, and autonomic biomarkers may enable more precise identification of high-risk individuals and inform future personalized prevention strategies.

Ex-Vivo Expansion of Hematopoietic Stem Cells via. Epigenetic Modifications for the Treatment of Hematological Malignancies

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Keywords: Hematopoietic Stem Cells (HSCs), histone deacetylase 5 (HDAC5), DNA methyltransferases (Dnmt3a and Dnmt3b), umbilical cord blood (CB), Ex vivo expansion.

Haematopoietic stem cell (HSC) transplantation is employed to treat a range of malignant and non-malignant blood disorders, using either umbilical cord blood (CB) or healthy donors with matched HLA typing. Despite this, the limited availability of transplantable HSCs and the mechanisms underlying their remarkable quality remain elusive. Although significant efforts have been made to identify HSC maintenance factors by characterizing the *in vivo* bone marrow HSC microenvironment or niche-stable ex vivo HSC expansion, achieving this has previously

been unattainable. In this study, we aimed to tackle these challenges by focusing on key epigenetic regulators, specifically histone deacetylase 5 (HDAC5) and DNA methyltransferases (Dnmt3a and Dnmt3b), to maintain stemness and enhance functional HSC expansion. We employed a polypharmacology-based in silico screening method to discover novel inhibitors of HDAC5 and Dnmt3a/3b, finding that selected chromatin- modifying agents (CMAs-X) could modulate epigenetic states and preserve primitive HSC characteristics. We validated the expanded cells through functional validation and conducted transcriptional analyses of self-renewal and differentiation markers (HOXB4, Notch1, Nanog, and Wnt). In the future, we plan to test the engraftment potential of these expanded cells in NOD/SCID mice as an in vivo model. Our preliminary findings suggest that inhibiting HDAC5 and Dnmt3a/3b results in higher yields of CD34+ CD38+ cells and enhanced multilineage colony output, with an upregulation of transcriptional networks associated with stemness retention. A substantial number of expanded HSCs facilitates transplantation into non-conditioned recipients, a process typically not feasible due to the large number of HSCs required. Thus, this protocol offers a robust approach to investigate HSC self-renewal and lineage commitment and, more broadly, to study and characterize the haematopoietic and immune systems.

Multimerin-1 at the Crossroad of Ovarian Cancer Progression and Angiogenesis

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Epithelial ovarian cancer (EOC) is a major cause of cancer-related mortality worldwide, largely due to late-stage diagnosis and the inadequate efficacy of current therapeutic strategies. Tumor progression is driven by dysregulated signaling pathways and epithelial mesenchymal transition (EMT), which promote invasion, metastasis, and therapeutic resistance. Emerging evidence indicates that extracellular matrix (ECM) proteins play active roles in cancer progression; however, their functional relevance in EOC remains insufficiently explored.

Multimerin-1 (MMRN1) is a 25–155 kDa ECM protein secreted by activated platelets, megakaryocytes, and endothelial cells. Our previous studies identified elevated MMRN1 expression in EOC patients and demonstrated its involvement in tumor progression through modulation of DNA damage response pathways. While MMRN1 is known to influence endothelial cell adhesion, its role in angiogenesis and tumor endothelial crosstalk remains unclear.

In this study, we investigated the role of MMRN1 in EOC progression with a specific focus on angiogenesis. MMRN1 was silenced in the ovarian cancer cell line OVCAR3 and the endothelial cell line HUVEC. Functional assays were conducted to assess cell proliferation, apoptosis, adhesion, migration, invasion, wound healing, and angiogenic potential. These analyses were supplemented by proteomic profiling and bioinformatics approaches to identify MMRN1-regulated molecular pathways.

MMRN1 knockdown in OVCAR3 cells significantly reduced cell proliferation, adhesion, migration, invasion, and wound closure, along with altered apoptotic responses. In HUVEC cells, MMRN1 silencing resulted in a greater than 50% reduction in tube formation within 24 hours, highlighting its essential role in angiogenesis. Proteomic and pathway analyses revealed that MMRN1 regulates ubiquitin-mediated protein degradation, DNA replication and repair, cell cycle progression, and angiogenesis-related pathways.

These findings suggest that MMRN1 may be a multifunctional regulator of epithelial ovarian cancer progression and angiogenesis, underscoring its potential as a therapeutic target in EOC.

Translational Vitamin D-Pathway Genetic Determinants in the Renal–Bone–Vascular Axis of CKD–Mineral and Bone Disorder

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Vitamin D pathway genetics represent translational determinants of skeletal fragility within the interconnected renal–bone–vascular axis that characterizes chronic kidney disease–related mineral and bone disorder (CKD-MBD). Building on our previously published translational work demonstrating coordinated disturbances in mineral metabolism, bone health, and vascular risk in CKD, we sought to define genetic modifiers that contribute to inter-individual variability in skeletal involvement beyond conventional biochemical markers.

Using an integrative translational approach, we combined

detailed clinical phenotyping with targeted genetic analysis of key regulators of vitamin D transport, metabolism, and receptor-mediated signaling to identify determinants of skeletal vulnerability in CKD. Polymorphisms in the vitamin D binding protein gene (*GC*) were significantly associated with CKD susceptibility, supporting altered vitamin D bioavailability as an upstream modifier influencing both skeletal and vascular pathways. Site-specific reductions in bone mineral density were associated with variants in *GC*, *VDR*, and *CYP24A1*, with gene–gene interaction analyses revealing synergistic effects between *CYP24A1* and both *GC* and *VDR*, underscoring coordinated regulation of vitamin D degradation and signaling across target tissues. Multivariate modeling identified the *VDR* rs2228570 polymorphism and estimated glomerular filtration rate as independent predictors of forearm bone mineral density, linking genetic susceptibility to renal functional decline.

Together with our earlier clinical and biochemical studies in CKD-MBD, these findings support a translational model in which vitamin D pathway genetics modulate renal–bone–vascular cross-talk, enabling improved risk stratification and informing personalized strategies aimed at preventing skeletal fragility and its cardiovascular consequences in CKD.

Targeting CCR5 modulates Treg and Myeloid Derived Suppressor Cells in Early Atherosclerosis: A Potential Therapeutic Strategy

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Introduction: The chemokine receptor CCR5 has been linked to both inflammatory and immunosuppressive functions. However, its specific role in regulating Tregs and MDSCs during early atherosclerosis remains largely unexplored.

Objectives: This study aimed to investigate the involvement of CCR5 in the early stages of atherosclerosis and assess its potential as a therapeutic target.

Methods: CCR5 receptor-ligand expression was analyzed in 60 individuals, including 20 healthy controls, 20 young individuals with hypercholesterolemia, and 20 stable CAD patients, using flow cytometry, real-time PCR, and immunocytochemistry. Atherosclerosis was induced in C57BL6 mice by feeding them a high-fat diet (HFD) for six weeks following partial ligation of the left carotid artery. The phenotype and functionality of MDSCs and Tregs were examined after treatment with a CCR5 inhibitor, DAPTA, both *in vitro* (10^{-8} M) and *in-vivo* (intraperitoneal injection, 3 ng/day for 15-days).

Results: CCR5 expression was found to be elevated on Tregs and monocytic MDSCs during the early phase of atherosclerosis. These immune regulatory cells exhibited "intermediate phenotype", expressing both pro- and anti-inflammatory markers. A trend that was also observed *in-vitro* upon stimulation with inflammatory cytokines. Inhibiting CCR5 with DAPTA shifted the phenotype of Tregs and M-MDSCs towards a more anti-inflammatory state, reduced the migratory capacity of these cells, enhanced their immunosuppressive functionality, and decreased cholesterol uptake in M-MDSCs. DAPTA also promoted the expansion of IL-10^{+} Tregs and M-MDSCs *in vivo* and led to the formation of more stable atherosclerotic plaques.

Conclusion: Systemic inflammation in young individuals with atherosclerosis risk factors upregulates CCR5 expression in immune regulatory cells, leading to their dysfunction. Possibly this dysfunctionality contributes to the development and progression of atherosclerosis. Targeting CCR5 with DAPTA not only reduces atherogenesis but also enhances plaque stability and restores the immunosuppressive functions of Tregs and M-MDSCs, highlighting its potential as a therapeutic strategy.

Machine Learning-Based Classification of Polycystic Ovary Syndrome: A Comparative Study of Clinical and Biochemical Features in Cases and Controls.

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Corresponding Email: tarunakatyal@gmail.com**Keywords:** Indian Council of Medical Research, Polycystic ovary syndrome; machine learning; classification; supervised learning; predictive modelling.

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder among women of reproductive age, characterized by heterogeneous clinical and biochemical manifestations. Conventional statistical approaches often fail to capture the complex interplay of

multiple risk factors.

Objective: This study applies machine learning (ML) techniques to classify PCOS cases and controls and to identify the most informative predictors associated with diagnosis.

Methods: A dataset comprising 100 women with PCOS and 100 healthy controls recruited under national ICMR-PCOS task force study was analyzed. After data pre-processing and feature standardization, supervised ML algorithms including logistic regression, random forest, support vector machine, and XGBoost were trained to distinguish cases from controls. Model performance was assessed using accuracy, precision, recall, F1-score, and the area under the receiver operating characteristic curve (AUC) with k-fold cross-validation. Feature importance was evaluated through tree-based methods and SHAP values to ensure model interpretability.

Results: Machine learning models demonstrated robust classification performance, with ensemble methods (random forest and XGBoost) outperforming logistic regression and SVM. Key predictive features included anthropometric indices, hormonal markers, and menstrual cycle characteristics. SHAP-based interpretation revealed consistent patterns, highlighting the relative contribution of each feature to PCOS prediction.

Conclusion: Machine-learning approaches offer improved accuracy over conventional statistical methods in classifying PCOS and provide clinically meaningful insights into relevant predictors. These findings support the integration of ML into PCOS research and clinical practice to enhance diagnostic accuracy and enable individualized risk assessment.

Genetics of Premature Ovarian Failure

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Background & Objectives

POF is a complex condition of aberrant ovarian aging due to ovarian dysfunction. It is characterized by amenorrhoea and postmenopausal levels of gonadotropins (FSH) as well as sex hormones (estradiol). The common causes of POF are cytogenetic abnormalities involving the X chromosome, fragile X syndrome (carrier), autoimmune endocrine disturbances, iatrogenic (chemotherapy, radiotherapy, surgical removal, etc), and idiopathic. The study aimed to explore various genetic factors in apparent idiopathic POF cases.

Materials & Methods

This study was conducted in Reproductive Biology, AIIMS, Delhi, between January 2020 and December 2024. One hundred females with POF were investigated. Both sporadic and familial POF cases were studied for chromosomal abnormalities and sex chromosome mosaicism (100 cases), copy number variation (81 cases), FMR1 gene premutation (77 cases), and gene variants (74 cases) by using conventional cytogenetics, XY FISH, DNA microarray, TP-PCR, and whole exome sequencing (WES), respectively.

RESULTS

Conventional cytogenetics detected a case of mosaic isochromosome Xq with X monosomy (45,X[10]/46,X,i(X)(q10)[20]), and another mosaic case with 45,X (10)/47,XXX (10) besides 2 cases of 46,XY sex reversal. SNP microarray detected CNV containing POF potential genes such as *GON4L, RBPOX1, CSMD1, HBE1, MAGEB16,* and *PRDM9* in 7 cases. TP-PCR detected heterozygous premutation in the FMR1 gene in 4 sporadic POF cases and two familial POF cases (8.2%). WES detected two pathogenic (*STAG3, ZSWIM7*) and three likely pathogenic variants (*CLPP, FOXL2, C14orf39*) besides five VOUS (*MCM9, SIRT1, EIF2B3, ERCC6, FIGLA*) in sporadic POF cases and two likely pathogenic (*FSHR*) and 2 VOUS (*FSHR*) in familial POF cases. Two genetic events were detected in 2 sporadic POF cases and two familial POF cases. Multiple variants (pathogenic/ likely pathogenic/VOUS) were observed with both the sex reversal cases (*NOBOX, GATA4, RSPO1, NR0B1, NR5A1, etc*).

CONCLUSIONS

We conclude that genetic associations in POF are common and sex reversal cases are oligogenic (association with 3-4 variants).

Role of Proprotein convertase Subtilisin/ Kexin Type 9 in Coronary artery diseases: A Case-control study

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BACKGROUND: PCSK9 (Proprotein convertase subtilisin/kexin type 9) plays a key role in cholesterol homeostasis and Coronary artery disease (CAD). Mutations in the PCSK9 gene resulted in reduced blood cholesterol levels (hypocholesterolemia) by reducing the activity of the PCSK9 protein or decrease the amount of this protein that is produced in cells. Loss of function mutations in the

PCSK9 were expected to have a better response to statins suggesting that lipid-lowering by PCSK9 inhibitors may be synergistic to that achieved by statins treatment.
OBJECTIVE: We aimed to explore the association of PCSK9 A/G (rs505151) polymorphism with CAD and their intergenotypic variation in the levels of LDL-cholesterol in patients with CAD.
METHODS: Angiographically confirmed CAD patients and controls were genotyped by PCR-RFLP techniques. The differential expressions of PCSK9 were studied by REAL-TIME PCR and Western Blot techniques.
RESULTS & CONCLUSION: To conclude, our study has shown a significant association of PCSK9 gene polymorphism with coronary artery disease. We also observed an increased expression of PCSK9 gene in patients with G allele of PCSK9 A/G (rs505151) gene polymorphism in patients with CAD. We here report for the first time a higher expression of PCSK9 gene correlated with circulating levels of LDL-cholesterol in patients with CAD in GG genotype. In our study, PCSK9 gene and LDL-cholesterol have emerged as independent risk factors. We envisage that studies in this direction may lead to better insight into the role of higher expression of PCSK9 in the GG genotype in patients with CAD.

Digenic (triallelic) mutations in IFT complexes leads to defective Cilia and causes a Novel complex Ciliopathy Phenotype

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Multigene mutations can lead to ciliopathies, a class of genetic disorders characterised by dysfunctional cilia, which are caused by alterations in genes involved in ciliary structure, function, or signalling pathways, resulting in shared clinical features. While some ciliopathies are caused by mutations in single genes, interactions with other genes (genetic modifiers) can influence the severity and specific characteristics of the condition. Here, we describe one family with multisystem anomalies (a novel phenotype) related to ciliopathies. Whole exome sequencing identified digenic (IFT80 and IFT122) (triallelic; all heterozygous) variants in the affected individual (P1). All the alleles are either variants of unknown significance (VUS) or have not been reported. We employed a combination of integrative structural modelling (ISM) of entire IFT complexes, DNA and mRNA analysis, biochemistry, cell biology, and Drosophila genetics to uncover the underlying cause of the phenotypes observed in the affected individuals. First, the ISM of IFT complexes with the missense variants suggested many destabilising effects on the evolutionarily conserved IFT complexes (in human as well as in *Drosophila*) stability and their interactions with adaptors and motors. Second, we demonstrated that, in the fruit fly, evolutionarily conserved IFT80 and IFT122 are synergistically required for the assembly of sensory cilia. Third, we showed that IFT80 and IFT122 synergistically contribute to the assembly of primary cilia in human cultured cell lines. Fourth, investigation of the variants in patient and unaffected family members' derived skin fibroblasts revealed that one of the IFT80 alleles triggers aberrant splicing, resulting in the production of an abnormal transcript. However, the total mRNA and protein levels of IFT80 and IFT122 were not affected in P1-derived fibroblast cells compared to the controls. Fifth, we found that although P1 fibroblasts showed no defect in primary cilia frequency, the cilia in P1 fibroblasts exhibited a significantly reduced length. We also showed that the localisations of IFT complex proteins and various ciliary signalling proteins on the cilia are deregulated. Finally, we found that, in accordance with the hypothesis proposed by our ISM analysis, interactions within the IFT complex are affected in P1 fibroblasts. In summary, our works show that these digenic (IFT80 and IFT122) (triallelic variants in IFT80 and IFT122 are associated with a novel spectrum of complex ciliopathy phenotype.

Towards investigating the anticancer role of gut microbiota-derived metabolites

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As per recent research reports, gut microbiota-derived metabolites such as indoxyl sulfate[1], inosine etc. possess selective anticancer effect on cancer cells. But the majority of gut microbial metabolites have not been screened for their anti-tumor activities nor underlying mechanism have been deciphered for developing therapeutic intervention for cancer management. In the present study, we investigated anti-tumor activity of three gut microbiota-derived metabolites, 4-ethylphenyl sulfate (4EPS)[2], indoxyl sulfate (IndS) and p-Cresyl Sulfate (pCS) on colon cancer cells. Using HCT-116 colon cancer cells, in-vitro cell-based assays were done that demonstrated 4EPS, IndS and pCS can reduce cell proliferation, cell viability and ATP content in dose and time dependent manner. Cell morphology was found to be distorted at concentrations, 2.5 mM, 5 mM and 10mM. HCT-116 cells also showed a decrease in colony formation when exposed to 2.5 mM, 5 mM and 10 mM of 4EPS, IndS, and pCS. These metabolites

enhanced the apoptosis and ROS production as compared to control cells. Cell cycle assay showed the arrest at G2/M phase for 4EPS, IndS and pCS. An animal study was also conducted using balb/c mice to demonstrate the selective deleterious effect of indoxyl sulfate on cancer cells while sparing normal colonic cells. IndS did not cause any harm or inflammation in normal colonic cells of balb/c mice, hence, it can be considered safe for use as an anticancer agent and may have implications in future applications for colon cancer treatment. This warrants further mechanistic investigations in this direction.

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Innovative combinatorial Epirubicin & Bioactive compound Conjugates Targeting HIF-1α/VEGF/GLUT1 Pathway in Triple-Negative Breast Cancer

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Keywords: Auratiamide acetate, Benzyl isothiocyanate, Chemotherapeutics, HIF-1α, Triple-negative Breast Cancer

The study aimed to explore the anti-cancer potential of bioactive compounds Aurantiamide Acetate (AA) and Benzyl Isothiocyanate (BITC), isolated from *Moringa oleifera*, as monotherapy and combination therapy (standard chemotherapeutic drug) against triple-negative breast cancer TNBC. The research was driven by the necessity for new therapeutic strategies targeting the aggressive nature of TNBC and the pivotal role of the HIF-1α/VEGF/GLUT1 signaling pathway in cancer progression. The study was conducted through a comprehensive approach, including in silico analysis, in vitro assays, and in-vivo experiments. Significant findings: Molecular docking predicted a stronger binding affinity of AA and BITC to HIF-1α, VEGF, and GLUT1 binding pockets. Molecular dynamics simulations over 500 nanoseconds revealed the conformational stability and dynamic interactions of AA and BITC with HIF-1α, VEGF, and GLUT1, with satisfactory ADMET properties, and good oral bioavailability. In-vitro, results demonstrated that AA and BITC exerted significant individual and synergistic cytotoxic effects on the TNBC cell lines in a dose and time-dependent manner, inhibition of Colony Formation, Migration, Invasion & suppression of Transcriptional Activity of HIF-1α/VEGF/GLUT1. In vivo xenograft showed treatment with AA and BITC resulted in a significant reduction in tumor size and volume, decreased mRNA & in-situ protein expression of HIF-1α/VEGF/GLUT1, along with the complete pathological response (IHC & H&E)

Serum Vibrational Spectroscopy: A Breakthrough Non-Invasive Method for Early Detection of Hepatocellular Carcinoma Progression.

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Hepatocellular carcinoma (HCC) surveillance remains challenging as current modalities detect malignancy at advanced stages. We investigated serum-based vibrational spectroscopy to non-invasively predict HCC progression before radiological detection through integrated biophysical, genomic, and molecular validation. Tissue samples from normal (n=50), cirrhotic (n=50), and HCC (n=50) patients underwent Fourier-transform infrared (FTIR) and Raman spectroscopy analysis, with SEM-EDAX validation. A genomics cohort (n=9) received paired-end sequencing (Illumina NextSeq™, 200× coverage), validated by immunohistochemistry and RT-PCR. Critically, serum samples from all groups (n=50 each)

underwent spectroscopic analysis for translational assessment. Tissue spectroscopy revealed progressive biochemical reprogramming with alterations in amide I (~1650cm^{-1}), CH_2 bending (~1445cm^{-1}), and carbohydrate/phosphate regions (1000-1100cm^{-1}). Supporting this, the SEM micrograph clearly showed the closure of liver sinusoids in HCC tissue samples and the deterioration of liver ECM. The EDAX analysis revealed the complete absence of potassium and variations in carbon, oxygen, and sodium content in three groups of livers. Transcriptomic profiling identified 29 differentially expressed genes (DEGs) in normal vs. cirrhosis, 54 in normal vs. HCC, and 405 in cirrhosis vs. HCC (padj<0.05, $|\log_2 FC|>1.5$). Key oncogenic drivers GPC3, AKR1B10, SPP1, and ASPH were significantly upregulated, while hepatocyte function genes SLC22A1 and CYP1A2 were downregulated (TCGA-LIHC–validated). RT-PCR demonstrated fibrosis-dominant ECM shifts with COL3A1 upregulation and LAMC1/LCAT suppression, especially, reduced LCAT expression in HCC versus cirrhosis ($p = 0.0246$). Remarkably, identical stage-dependent spectral patterns emerged in serum samples. Monitoring five specific wavenumbers (~785, ~1003, ~1095, ~1445, ~1650 cm-^{1}) successfully staged HCC progression non-invasively, offering unprecedented potential for early detection and intervention in hepatocellular carcinoma.

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Integrated Multiomics approaches for identification of Pathogenic variants involved in Autism Spectrum Disorders

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Characterisation of a vast array of genomic variations is crucial for understanding their role in human health and disease. Integrated multiomics approaches explore the potential effects of different genomic variants on gene function. Autism Spectrum Disorder (ASD) is a complex neurodevelopmental condition with a strong genetic basis and marked clinical heterogeneity. Integrating gene-level information with brain transcriptomic data has provided critical insights into the spatial and temporal patterns of gene expression during brain development. Therefore, unravelling the tissue-specific variants of genes involved in ASD is essential. ASD-associated score 1 genes were selected from the SFARI gene database and human brain transcriptomic data were obtained from the GTEx portal. These genes were analyzed to identify brain-specific isoforms. Further, the selected genes were analysed using in silico pathogenicity prediction tools, and protein-protein interactions were analysed using the STRING database. Out of 65 genes analyzed, 55 genes showed differences in exon count. Seven genes, *CASZ1*, *MYT1*, *NEXMIF*, *NSD1*, *PHF12*, *POGZ*, and *ZBTB21* showed exon-splitting events. Exon addition was seen in the *EBF3* and *KMT2E* genes. Only *FOXG1* matched its brain transcript, with a single exon. STRING network revealed significant protein-protein interactions. A nonsynonymous variant resulted in an amino acid substitution at a conserved residue, potentially affecting protein function. These approaches provide a strong framework for understanding the molecular mechanisms underlying ASD, which supports better diagnostic and therapeutic strategies. The implications of these findings will be presented and discussed.

Gold Nanorod Functionalization Directs Macrophage Polarization and Fibrosarcoma Suppression

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Photothermal and photodynamic therapies using biocompatible gold nanoparticles have promulgated their use in cancer theranostics. Surface plasmon resonance and high surface to volume ratio of nanoparticles provide unique opportunities to functionalize them with various ligands 2. Understanding the influence of shape, size and functionalization on characteristics of nanoparticles, our study aims to understand the anti-tumor and immunomodulatory effects of gold nanorods (GNRs) in murine fibrosarcoma induced by 3-methylcholanthrene. PEGylated GNRs (aspect ratio of 2.5) were synthesized using ligand exchange method by replacing cetyltrimethylammonium bromide (CTAB). In-vitro studies of bare gold nanorods (CTAB-GNRs) were performed using macrophages isolated from Swiss albino mice. Uptake of GNRs through ICP-MS and SEM-EDS, and MTT assay were done to assay cytotoxicity and cell viability, while pro- and anti-inflammatory cytokines quantified via ELISA, and qRT-PCR were used to understand the onset of cell-

death pathways. CTAB-GNRs induced upregulation of pro-inflammatory cytokines along with activation of apoptotic and necroptotic pathways, proving that they support activation of an M1 like pro-inflammatory phenotype in M0 macrophages. To understand the impact of functionalization upon GNRs, we studied the potential of PEGylated gold nanorods (PEG-GNRs) in halting fibrosarcoma progression. PEGylated GNR treatment showed distinct responses regarding TNF-α, IL-1β, IL-6, IL-10, IL-12 along with caspase-3, -8, and -9, as well as the pro-apoptotic markers p53 and Bax. Our findings suggest that PEGylated GNRs effectively inhibit fibrosarcoma progression by activating tissue specific distinct cell-death pathways like classical apoptosis and inflammasome-mediated pyroptosis.

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MicroRNA Signatures in Prostate Cancer: Molecular Perspectives and Clinical Relevance

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Introduction

Prostate cancer (PCa) constitutes a significant cause of mortality among males in developing countries. The elevated mortality rate can be attributed to the slow progression of prostate cancer, coupled with the prevalence of false-positive outcomes from diagnostic methods such as PSA levels, DRE, and biopsy. This situation has resulted in a rise in both misdiagnosis and overtreatment of the condition. Consequently, there exists an essential demand for reliable diagnostic and detection instruments, including circulating non-invasive microRNAs, to accurately identify aggressive prostate cancer. MicroRNAs are small, highly conserved non-coding RNAs that play a crucial role in regulating genes associated with various biological processes, such as cell proliferation, the cell cycle, metastasis, and apoptosis. In alignment with this perspective, we have meticulously crafted our study to explore the biomarker potential of circulating miRNA in prostate cancer.

Methodology

The miRNA expressions were assessed via RT-PCR, and in-silico target genes were investigated using TargetScan, miRDB, and MirWalk 3.0, with the results processed through DAVID software. Subsequently, utilizing ROC analysis, the viability of miRNA as a biomarker for the identification of PCa was assessed.

Results

Our observation indicates that miRNA is markedly dysregulated in serum, exhibiting a higher and statistically significant AUC relative to their corresponding controls. The in-silico research indicates that miRNA contributes to PCa progression by directly targeting E2F3, PTEN, EGFR, CREB1, TP53, MYC, E2F2, and CRKL.

Conclusion

The present findings highlight the clinical utility of microRNAs as minimally invasive biomarkers that can significantly enhance the precision and efficiency of prostate cancer diagnosis.

Harnessing Ethnomedicine and Traditional healing practices of Nagaland for addressing regional Health challenges

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A wide variety of Naga tribal communities, each with its own distinctive traditions, languages, and customs, live in Nagaland; the unique hilly State of the north-eastern India touching Indo-Burma border. The state is also known as the "Land of Festivals" because of its rich cultural heritage. However, environmental pressures including rising urbanisation, uncontrolled mining, shifting farming, deforestation, and poor waste management are putting this ecological and cultural diversity in jeopardy. These factors pose significant public health challenges because they contribute to environmental degradation and are linked to an increasing number of health issues, such as respiratory infections, cancer, diabetes, hypertension, water-borne diseases, dermatological disorders, gastrointestinal illnesses, vector-borne conditions, etc. However, a major

part of the indigenous population of Nagaland are still using their traditional plant based medicines to combat most of the health problems. Unfortunately, proper documentation, scientific database of such effective ethno-medicines are quite scanty. Moreover, the active phytochemicals, their mechanism of action, doses, possible toxicity etc. are also not explored to a great extent. The present study explores the relationship between environmental degradation, disease prevalence, and the potential of sustainable, community-driven solutions rooted in indigenous knowledge systems. Ethno-botanical documentation and environmental monitoring are employed to identify emerging health risks and possible remedial strategies. Special emphasis is placed on the chemistry associated with the traditional medicinal plants, widely used by Naga communities. Identification of the reactive small molecules (alkaloids, flavonoids), the reason behind their effectiveness, binding characteristics (towards DNA, protein etc.), antioxidant, anti-inflammatory, antimicrobial, & detoxifying properties are the novel objectives of the present work. By integrating traditional practices like community forest conservation with plant-based therapeutics and advanced biophysical and biological assessments, this study proposes a holistic framework to strengthen sustainable health resilience.

Novel Strategies to Treat Depression-induced Abnormal Functional Plasticity and Cognitive Deficits

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Keywords: Drug-resistant depression, brain-stimulation reward, altered neurotransmission, neurodegeneration, learning and memory deficits, enriched environment, antidepressants, hippocampal synaptic plasticity, long-term potentiation, anxiety, hippocampal and amygdalar volumes, major depressive disorders.

Depression is a major psychiatric disorder associated with severe morbidity, poor quality of life, and mortality. Major depression represents a significant global health threat because it lowers productivity, causes considerable disability and also precipitates other co-morbid medical conditions like anxiety and severely affects cognitive capabilities and executive functions. Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. The precise mechanisms underlying these dysfunctions in depression remain largely unknown. We have demonstrated that depression causes impairments in spatial learning, alters the levels of monoamines and their metabolites and suppresses hippocampal long-term potentiation (LTP), compromises structural and functional integrity of neurons and glia, and enhances anxiety-like behaviours. The cognitive deficits, altered synaptic plasticity and neurotransmission are associated with hippocampal atrophy and amygdalar hypertrophy. These deficits were reversed after chronic treatment with high doses of selective serotonin reuptake inhibitor (SSRI), escitalopram or selective norepinephrine reuptake inhibitor (SNRI), reboxetine. The first line of treatment in depressive illness is antidepressant drugs and is associated with several side effects, poor response and recurrence. Therefore, it has become increasingly necessary to develop more effective strategies to treat and manage depressive disorders. Accordingly, we have evaluated depression-induced cognitive deficits, synaptic plasticity, anxiety and the effect of exposure to environmental enrichment (EE), or the combination of short duration EE with sub-effective doses of escitalopram or reboxetine or brain stimulation rewarding experience on depression-induced deficits as novel antidepressant therapy. The concomitant escitalopram / reboxetine - EE treatment, resulted in complete behavioral recovery and improved spatial learning along with a complete restoration of dentate gyrus and amygdalar volumes and restored hippocampal LTP. Thus, positive environmental stimuli even for short duration can potentiate the effect of sub-effective doses of antidepressants in alleviating depression-induced deficits. Further, intracranial brain stimulation of reward pathways was able to completely restore the depression-induced deficits at multiple levels of neural organization. These novel non-pharmacological strategies are leading to developing effective antidepressant therapies that are free from side effects and reduce recurrence of depressive episodes and associated disorders.

Acknowledgements: Acknowledge financial support from UGC, CSIR, DST, SERB, DBT, ICMR and NIMHANS

Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Stroke: Novel mechanisms and Future Therapies for improving Cerebroprotection

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There is a critical need for cerebroprotective interventions to improve the suboptimal outcomes of patients with ischemic stroke treated with reperfusion strategies. We found that metabolic enzyme pyruvate kinase muscle 2 (PKM2), a modulator of systemic inflammation, was upregulated in neutrophils after the onset of ischemic stroke both in humans and in mice. Therefore, we determined the role of PKM2 in stroke pathogenesis utilizing murine models with preexisting comorbidities. We generated myeloid cell-specific $PKM2^{-/-}$ mice on wild-type ($PKM2^{fl/fl}LysMCre^{+}$) and hyperlipidemic background ($PKM2^{fl/fl}LysMCre^{+}Apoe^{-/-}$). Controls were littermate $PKM2^{fl/fl}LysMCre^{-}$ or $PKM2^{fl/fl}LysMCre^{-}Apoe^{-/-}$ mice. Genetic deletion of PKM2 in myeloid cells limited inflammatory response in peripheral neutrophils and reduced neutrophil extracellular traps following cerebral ischemia/reperfusion, suggesting PKM2 promotes neutrophil hyperactivation in the setting of stroke. In the filament and autologous clot/rtPA stroke models, irrespective of sex, deletion of PKM2 in myeloid cells either in wild-type or hyperlipidemic mice reduced infarcts and enhanced long-term sensorimotor recovery. Laser speckle imaging revealed improved regional cerebral blood flow in myeloid cell-specific PKM2-deficient mice that was concomitant with reduced post-ischemic cerebral thrombo-inflammation (intracerebral fibrin(ogen), platelet (CD41-positive) deposition, neutrophil infiltration, and inflammatory cytokines). Mechanistically, PKM2 regulates post-ischemic inflammation in peripheral neutrophils by promoting STAT3 phosphorylation. To enhance the translational significance, we inhibited PKM2 nuclear translocation using a small molecule and found significantly reduced neutrophil hyperactivation and improved short-term and long-term functional outcomes following stroke. Collectively, these findings identify PKM2 as a novel therapeutic target to improve brain salvage and recovery following reperfusion.

Metabolic Disturbances in Parkinson's disease: Brain and Beyond

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Lipid dysregulation is increasingly recognized as a key feature of Parkinson's disease (PD). A central unresolved question, however, is whether lipidomic signatures identified in accessible peripheral biofluids faithfully recapitulate the pathogenic alterations within the central nervous system (CNS). This gap impedes the development of reliable biomarkers and constrains a comprehensive understanding of PD pathophysiology. To address this challenge, we employed a cross-species lipidomic approach. We modeled PD in both male and female mice by injecting human α-synuclein preformed fibrils into the substantia nigra. Three months post-injection, lipidomic profiles of the midbrain and plasma were generated and compared. These findings were further validated in plasma from male and female PD patients and age-matched controls, enabling the identification of conserved alterations.

We identified shared dysregulation of sphingolipids, glycerophospholipids, and fatty acids in the brains and plasma of diseased mice as well as in plasma from PD patients. Notably, lipids associated with lipid droplet biogenesis, including triacylglycerols and monoacylglycerols, were elevated in diseased mouse brains and patient plasma. These alterations coincided with a marked accumulation of lipid droplets in the mouse midbrain, and were further corroborated by increased lipid droplet abundance in macrophages derived from PD patients. Interestingly, lipid droplet accumulation exhibited sex-specific patterns: male mice displayed greater microglial accumulation, whereas female mice showed enhanced neuronal deposition. Together, these findings demonstrate that peripheral lipidomic signatures reflect CNS pathology in PD, highlighting new opportunities for biomarker discovery and therapeutic intervention. Furthermore, sex-specific lipid droplet accumulation in innate immune cells and neurons implicates these pathways as mechanistic contributors to PD and underscores the necessity of sex-stratified strategies in biomarker discovery and disease modeling.

Linking diabetes to cognitive decline: Evidence for a role of the brain Renin–Angiotensin System

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Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Keywords: Diabetes-associated cognitive impairment, Renin-Angiotensin System, memory, mitochondria, angiotensin receptors, neuroprotection

Cognitive impairment and memory decline are increasingly recognized as important but underappreciated complications of diabetes mellitus, significantly affecting quality of life and long-term clinical outcomes. While peripheral metabolic dysregulation is well documented, the molecular mechanisms linking diabetes to brain dysfunction remain incompletely understood. The Renin-Angiotensin System (RAS), classically known for its role in cardiovascular regulation, also operates as an independent and functionally significant system within the brain. Emerging evidence suggests that dysregulation of brain RAS components may contribute to neurodegeneration, synaptic dysfunction, and cognitive deficits, particularly under metabolic stress conditions such as diabetes.

In this study, we investigated whether alterations in key brain RAS components are associated with diabetes-induced memory impairment and whether pharmacological modulation of this system offers neuroprotective benefits. Adult male Sprague Dawley rats were assigned to four experimental groups: control, diabetic, amnesic, and diabetic with amnesia. Diabetes was induced using streptozotocin (STZ), while cognitive impairment was modeled using chronic scopolamine administration. Metabolic and cognitive deficits were confirmed using physiological measurements, behavioral assessments, and biochemical and molecular analyses.

We focused on the hippocampus and prefrontal cortex, brain regions critical for learning and memory, and examined the expression of Angiotensin II type 1 (AT1) and type 2 (AT2) receptors. Our results revealed a significant upregulation of AT1 receptors alongside a marked downregulation of AT2 receptors in both diabetic and amnesic conditions compared to controls ($p<0.001$). This imbalance was associated with mitochondrial dysfunction, suggesting impaired cellular energy homeostasis as a potential mechanistic link to cognitive decline. Importantly, treatment with the angiotensin receptor blocker telmisartan partially reversed mitochondrial dysfunction, indicating a protective effect on neuronal health.

These findings highlight a previously underexplored role of brain RAS imbalance in diabetes-associated memory impairment and suggest that centrally acting RAS modulators, already widely used in clinical practice for cardiovascular disorders, may hold therapeutic potential for preventing or mitigating cognitive decline in diabetic patients. This study provides experimental support for repurposing RAS-targeting drugs as neuroprotective strategies and underscores the importance of considering brain-specific mechanisms in the management of diabetes-related cognitive complications.

Biomarker Networks in Preeclampsia: Linking Immune Dysregulation, Tubuloglomerular Injury, and Endothelial Dysfunction for Early Renal Risk Stratification

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Background: An imbalance between the body's proinflammatory and anti-inflammatory responses has been suggested to be a key issue in the pathophysiology of Preeclampsia (PE) which usually presents after 20 weeks of pregnancy with high blood pressure and protein levels in the urine. Factors such as soluble fms like tyrosine kinase -1 (sFlt-1), T regulatory cells (Tregs), and Interleukin-10 (IL-10) molecules are thought to be involved as mediators in a systematic response affecting the blood vessel lining. Proteinuria is an essential feature of preeclampsia suggesting the involvement of the kidneys in the disease. Objective: Our study aimed to explore how Tregs, IL-10 and sFlt-1 correlate with Kidney Injury Molecule-1(KIM-1) protein levels in urine to better understand preeclampsia induced renal endothelial dysfunction. Methodology: 36 normal pregnant women and 29 women with preeclampsia were enrolled in this cross-sectional study. Tregs, IL-10, sFlt-1 and KIM-1 levels were analysed and correlated between both the groups. Results: Our findings revealed that the levels of CD4+FOXP3+ Treg cells and serum IL-10 were much higher and the levels of serum sFlt-1 and urinary KIM-1 were lower in normal pregnant women than in those with preeclampsia. ROC curve showed that serum sFlt-1 was a strong marker for diagnosing preeclampsia with a sensitivity of 93% and specificity of 92%, followed by urinary KIM-1 with a sensitivity of 76%, and specificity of 58%, implying at ongoing kidney injury in preeclampsia. Conclusion: Our study elucidates preeclampsia and supports better biomarker use and treatments, aiming to improve health outcomes for mothers and babies.

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Unravelling the Determining Factors of Chronic Kidney Disease of Unknown Etiology (CKDu): The Hidden Danger in Farming Communities

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Keywords: Chronic kidney disease of unknown etiology (CKDu), environmental determinants, Agrochemicals, Nephrotoxicity

Chronic Kidney Disease of Unknown Etiology (CKDu) has emerged as a significant and growing public health problem in agricultural regions, particularly affecting farming communities in low- and middle-income countries. Unlike conventional chronic kidney disease, CKDu develops in the absence of established risk factors such as diabetes, hypertension, or primary glomerular disease, suggesting the involvement of unique environmental and occupational determinants. Epidemiological studies consistently demonstrate a high prevalence of CKDu among male farmers, with marked geographic clustering and strong associations with long-term agricultural work.

Accumulating evidence indicates that CKDu pathogenesis is driven by persistent low-grade inflammation and progressive renal fibrosis. Elevated inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and transforming growth factor-β (TGF-β), play a central role in promoting tubular injury, oxidative stress, and immune-mediated damage. These inflammatory processes activate profibrotic pathways, leading to increased expression of fibrotic markers such as collagen I, fibronectin, and α-smooth muscle actin (α-SMA), which contribute to irreversible interstitial fibrosis and gradual loss of renal function.

Pesticide exposure has been identified as a key upstream risk factor in affected populations. Farmers experience chronic exposure to agrochemicals through occupational handling, contaminated soil and water, and inadequate protective measures. Several commonly used pesticides have demonstrated nephrotoxic potential, capable of inducing oxidative stress and amplifying inflammatory and fibrotic signaling pathways within renal tissues. The combined effects of pesticide exposure, heat stress, recurrent dehydration, and limited healthcare access may synergistically accelerate kidney injury.

Thus, there is need to understand and integrate epidemiological findings with emerging mechanistic insights to elucidate the multifactorial determinants of CKDu, emphasizing the urgent need for preventive strategies, biomarker-based early detection, and improved occupational health policies to address this hidden danger among farming populations.

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Persistent Circulating Tumor DNA Defines a Molecularly High-Risk Phenotype in Locally Advanced Oral Squamous Cell Carcinoma

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Background: Oral squamous cell carcinoma (OSCC) is characterized by high loco-regional recurrence rates despite optimal surgery and adjuvant therapy. Field cancerization and occult minimal residual disease (MRD) contribute to treatment failure. Circulating tumor DNA (ctDNA) offers a biologically relevant approach for dynamic molecular risk stratification. This pilot study evaluated a focused 9-gene next-generation sequencing (NGS) panel for tissue profiling and longitudinal liquid biopsy monitoring in locally advanced OSCC.

Methods: Twenty-four patients with loco-regionally advanced OSCC undergoing curative-intent surgery followed by risk-adapted adjuvant therapy were prospectively enrolled. Tumor tissue and peripheral blood (10 mL, Streck tube) were collected at baseline (pre-surgery), 2–3 weeks post-surgery, and 3 weeks post-adjuvant radiotherapy or concurrent chemoradiotherapy. A targeted 9-gene panel (NFE2L2, PIK3CA, FGFR1, CDKN2A, NOTCH1, HRAS, CCND1, RB1, TP53) was used to identify pathogenic alterations and track ctDNA dynamics.

Results: The tissue diagnostic yield was 91.6% (22/24). Baseline ctDNA positivity was observed in 58% (14/24). Overall, 91.6% (22/24) demonstrated ctDNA positivity at least once during longitudinal monitoring, while 8/24 (33.3%) exhibited persistent ctDNA positivity across all time points. Molecular response stratification identified three groups: Good Responders (33.3%) with sustained ctDNA negativity, Partially Good Responders (29.2%) with intermittent ctDNA detection, and Bad Responders (37.5%) with persistent ctDNA positivity. Persistent ctDNA detection correlated with inferior molecular response category.

Conclusion: A focused 9-gene NGS panel provides high diagnostic yield and enables longitudinal MRD assessment in advanced OSCC. Persistent ctDNA positivity identifies a biologically high-risk subgroup and supports the potential of ctDNA-guided risk-adapted therapeutic strategies. Larger prospective validation is warranted.

Multi-Target Modulation of SNCA, PARK7, and SLC2A1: An integrated *in-silico* & *in-vitro* evaluation in Parkinson's Disease

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Parkinson's disease (PD) is a progressive neurodegenerative disorder associated with loss of dopaminergic neurons, mitochondrial damage, oxidative damage, and accumulation of α-synuclein protein. Correspondingly, aurantiamide acetate and benzyl isothiocyanate (BITC) *in-silico* & ADMET analysis conducted on prominent PD-related target proteins such as α-synuclein (SNCA), Parkinson disease protein 7 (PARK7/DJ-1), and solute carrier family 2 member 1 (SLC2A1/GLUT1) revealed aurantiamide acetate has high affinity scores and stable non-covalent interactions with all the target proteins compared to Levodopa (L-DOPA), which acted as the control molecule and BITC. These results indicate high affinity scores and stability indexes towards multiple targets related to protein misfolding and aggregation, oxidative damage, and energy neurotransmission challenges supporting its translational potential. The *in-silico* findings were substantiated through *in-vitro* validation conducted on SH-SY5Y human neuroblastoma cells differentiated into dopaminergic-like neurons through retinoic acid treatment subsequently induced with rotenone into Parkinson's disease-like neurotoxicity. Aurantiamide acetate protected cells significantly from rotenone toxicity and stress damage compared to L-DOPA and BITC. Based on both docking experiments and *in-vitro* tests and results, aurantiamide acetate emerges as yet another promising multiple targeting chemical entity which may have significant disease-modifying properties in the progression towards Parkinson's disease.

Development of a score for early identification of diabetic peripheral neuropathy using endothelial biomarkers

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Background

One of the most common complications of diabetes mellitus is diabetic peripheral neuropathy. This disorder is associated with increased utilization of healthcare services and affects the economic profile of a country. Despite the multifactorial background of the pathogenesis of this disease, the mechanism underlying peripheral neuropathy is still unclear. Endothelial damage is a new determinant of

pathogenesis, with experimental data showing endothelial dysfunction per se is sufficient to cause neuropathyendocan as a potential biomarker for endothelial dysfunction in diabetic peripheral neuropathy patients.

Methods

The study population comprised 97 adult patients with diabetes who visited the OPD of the Department of Endocrinology for more than five years. The patients were categorized into two groups: those with diabetes with peripheral neuropathy (DPN, n = 49) and those with diabetes without peripheral neuropathy (No DPN, n = 48).

The endothelial biomarkers such as endocan, hs-CRP, vitamin D, and lipid profiles were measured and analyzed in both groups. The standardized scores for dyslipidemia, inflammation, vitamin D, and endocan were calculated. All the statistical analyses were performed using Jamovi software version 2.3.26 (Sydney, Australia).

Results

All of these biomarkers were significantly altered in peripheral neuropathy patients. A strong correlation between endocan levels and lipid profiles and between hs-CRP and vitamin D levels was detected.

Conclusion

The inflammatory score and a combined score including all the above biomarkers might help in the early stratification of diabetic patients who are at greater risk of developing peripheral neuropathy.

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Journal of Academy of Biomedical Sciences
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IABSCON 2026

Exploring the Association of Anti-thyroid Peroxidase antibody level with Metabolic alterations and Renal function in elderly Hypothyroid cases- A Gender-based introspection

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Introduction: Thyroid hormones play an important metabolic role and regulate kidney function. Incidences of Thyroid disorders as well as auto immune diseases increase with age, particularly in females. Autoimmune diseases are known to affect kidney function. As both hypothyroidism and CKD independently increase CVD risk, it is crucial to assess metabolic alterations and kidney function in elderly hypothyroid cases in relation to autoimmunity.

Materials & Method: This case control study enrolled 64 newly diagnosed hypothyroid cases of >60-years of age, from both gender (serum TSH>5 µIU/L) and age and sex matched healthy control. fT3, fT4, TSH, Anti-TPO were estimated along with biochemical parameters including urinary ACR and eGFR. Mann-Whitney U-test, Chi- square test and regression analysis were conducted as appropriate. P<0.05 was considered significant. Diabetes, hypertension, liver disease, kidney disease, previous hyper-lipidaemia, auto immune disease, other endocrine disorders, and cases with anti-epileptic medication, steroid therapy were excluded.

Result: Thyroid function parameters registered marked alteration in hypothyroid cases in comparison to control. Anti-TPO positivity revealed significant relation with altered renal function by regression analysis. Metabolic alterations and renal involvement were more pronounced in females.

Conclusion: Significant association of Anti-TPO antibody levels with renal dysfunction among elderly hypothyroid patients, warrants early screening in young. With similar Anti-TPO burden females showing more possibility to metabolic and renal vulnerability, needs further attention.

Reprogramming the Powerhouse: Harnessing Mitochondrial Control in Breast Cancer

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Triple-negative breast cancer (TNBC) is one of the most aggressive forms of breast cancer and remains difficult to treat, particularly in Indian patients where its incidence is comparatively higher. Recent research suggests that cancer cells rewire their mitochondria—the cell's power generators—to survive and thrive under stress. Our work explores how changes in mitochondrial quality control, which includes biogenesis, fission–fusion balance, and mitophagy, contribute to TNBC aggressiveness and therapy resistance.

Using patient-derived tissues, 3D tumor models, and a TNBC mouse system, we observed that TNBC cells display highly active mitochondrial turnover. When we blocked the mitochondrial fission protein DRP1, or disrupted the process of mitophagy, TNBC cells showed reduced growth, invasion, and angiogenesis, along with increased cell death. Combining mitochondrial fission and autophagy inhibitors in mice led to a striking reduction in tumor size and spread.

Our findings highlight mitochondrial dynamics as a key driver of TNBC progression. By targeting the interplay between fission and mitophagy, we can potentially identify new biomarkers and develop more effective, mitochondria-focused therapies for aggressive breast cancers.

Development of Potent PARP-1 Inhibitors Targeting Glioma Through DNA Damage & ROS Generation

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Cancer is a major global threat, accounting for nearly 10 million deaths annually. Glioma is the most prevalent form of malignant primary brain tumors in adults. Glioblastoma multiforme (GBM) is the most aggressive

subtype, among all gliomas, accounting for approximately 54%. The average survival time for patients suffering from this lethal cancer, if not under early medical attention, is up to 15 months. The current treatment for gliomas includes surgery, followed by radiotherapy and chemotherapy, but the prognosis remains dismal. Therefore, the overall picture about glioma is quite gloomy and need lots more research support in terms of précised medication. Poly (ADP-ribose) polymerase-1 (PARP-1) is a key target for cancer therapy and is reported to be elevated in glioma. To have a significant inhibitory effects of PARP-1 inhibitors (PARPi), it has to cross the hurdle of blood brain barriers. In this presentation, the design and synthesis of a series of fused hybrid heterocycles as new PARPi and their mode of action will be discussed. The most potent inhibitor induced apoptosis in glioma cells by promoting PARP cleavage, triggering DNA damage, and increasing ROS. The study resulted in a promising lead PARP-1 inhibitor targeting glioma, offering a new scaffold for future drug development.

A Pilot study to evaluate mass screening device using multiple Biomarkers for Premalignant cervical lesions: A step towards Cervical cancer elimination goal

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In August 2020, the World Health Assembly set a goal to eliminate cervical cancer by 2030, targeting a 90% HPV vaccination rate, 70% screening, and 90% treatment. In India, high rates of cervical cancer are driven by HPV infections, lack of hygiene awareness, and limited healthcare access. The progression from HPV infection to cervical dysplasia spans 10-20 years, but diagnostics are hindered by subjective VIA interpretations, the time-consuming nature of Pap smears, and the scarcity of testing resources, particularly in rural areas.

To address these gaps, the KayaCervi device was developed (GIA-DHR 2022); offers a low-cost, on-site solution for cervical cancer mass screening. This point-of-care device, based on fluorescence and antigen-antibody reactions, includes a cartridge, reader, chip, and reagents. The cartridge uses selective filtration and vertical flow to ensure complete sample capture, while the reader scans for cervical cancer biomarkers of Kaya Cervi device. Results are quantified in Relative Fluorescence Units (RFU), with the device's design optimized to handle multiple wavelengths of light for accurate measurements. Community based clinical validation studies (36 villages, n = 800) KayaCervi demonstrated over 85% sensitivity, and specificity with results comparable to the gold-standard Pap smear. The KayaCervi device is particularly suited for primary health centers (PHCs), where healthcare workers can collect and test samples on-site, providing rapid, reliable results without the need for extensive infrastructure. This technology represents a significant step toward accessible, mass screening for cervical cancer in underserved populations.

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Novel Insights into Zika and SARS-CoV2 Virus-Induced Neuropathogenesis Using 2D and 3D Models of Human Neural Stem Cells

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Zika virus (ZIKV) and Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2) have emerged as major global health concerns with significant neurological manifestations. Zika virus causes congenital microcephaly in infants born to mothers who were infected by the virus during their pregnancies. SARS-CoV2 has been linked to neuroinflammation, cognitive deficits, and long-term neurological sequelae that are the major cause of morbidity in Long COVID survivors. To elucidate the cellular and molecular mechanisms underlying virus-induced

neuropathogenesis, we employed primary cultures of human fetal brain derived neural stem cell (hNSC)-based 2D monolayer cultures and 3D neurospheres as physiologically relevant models that recapitulate key aspects of human brain development and function. Our findings revealed that ZIKV preferentially infects proliferative hNSCs, disrupting neurogenesis, and altering cell cycle progression via alteration in miRNA circuitry. In contrast, SARS-CoV2 exposure resulted in heightened neuroinflammatory signaling, synaptic dysregulation, and mitochondrial stress, reflecting distinct virus-specific neuropathological signatures. We observed that SARS-CoV2 induces non-apoptotic cell death pathways in hNSC derived neurons, via the upregulation of RIPK3 and pMLKL, which were validated in postmortem brain sections of SARS-CoV2 infected COVID-19 patients. These findings provide novel molecular insights into Zika and SARS-CoV2 viral effects on the human brain and functions, providing molecular targets for intervention.

The research work was supported through an extramural grant from DBT, New Delhi and NBRC core funds.Does the Novel chimeric Endolysin CHAPk-SH3bk represent a promising Antibiofilm agent against Methicillin-resistant assays including diffusion lysis assay, CFU reduction assay, and time-kill curve assay. The antibacterial assay results displayed the bactericidal activity of CHAPK-SH3bk against HA-MRSA. The biofilm reduction ability of CHAPk-SH3bk against HA and LA-MRSA was analysed using *in-vitro* crystal-violet assay, and *in-vivo* mice skin infection model. The CHAPk-SH3bk displayed effective biofilm reduction activity effective against 24 h and 48 h biofilms of HA-MRSA from plastic, glass and steel surface. The CHAPk-SH3bk displayed significant biofilm reduction activity of 24 h MRSA biofilm from mice skin. The anti-biofilm activity was confirmed on *ex-vivo* murine skin tissue using IHC, CLSM, and SEM. In addition, the CHAPk-SH3bk was found to inhibit the biofilm formation of hospital and bovine origin MRSA in *in-vitro* conditions. The *in-vitro* and *in-vivo* biofilm reduction activity confirmed that the addition of cell wall binding domain SH3bk to catalytic domain CHAPk enhanced the catalytic activity CHAPk against sessile cells. In conclusion, the research work provides a promising anti-*staphylococcal* agent CHAPk- SH3bk, which works effectively in an antibiotic-exempted environment against MRSA and states that the shuffling of parental endolysin domains may increase the anti-biofilm activity of catalytic domain.

Does the Novel chimeric Endolysin CHAPk-SH3bk represent a promising Antibiofilm agent against Methicillin-resistant *Staphylococcus aureus*?

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Keywords: Biofilm, MRSA, Bacteriophage endolysin, Chimeric endolysin, Antibacterial activity, Bacteriophage

Methicillin-resistant *Staphylococcus aureus* is one of the major pathogens in hospitals, community, and livestock associated infections. The spread of MRSA and its ability to form biofilms impedes antibiotic treatment, increasing the risk of mortality in human and animal health sectors. This necessitates the search for novel antimicrobial agents like bacteriophage endolysins which act against peptidoglycan layer of Gram-positive bacterial cell wall effectively when administered from outside of the cell. This study includes expression of novel chimeric endolysin CHAPk-SH3bk composed of enzymatically active domain and cell wall binding domain of phage endolysin LysK and investigate its bacteriolytic and anti-biofilm activity against MRSA. The bacteriolytic activity of the chimeric endolysin CHAPk-SH3bk was analysed through *in-vitro* antibacterial

PHA in Biomedical Engineering: Microbial Bioprocessing, Challenges, and Emerging Opportunities

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Keywords: Polyhydroxyalkanoates, microbial bioprocessing, biomedical engineering, biodegradable polymers, tissue engineering

Polyhydroxyalkanoates (PHAs) are a family of biodegradable and biocompatible polyesters synthesized by numerous microorganisms as intracellular carbon and energy storage compounds. In recent years, PHAs have gained considerable attention in biomedical engineering due to their favorable physicochemical properties, including biodegradability, biocompatibility, and tunable mechanical characteristics. Microbial bioprocessing enables the sustainable production of PHAs through advances in fermentation technologies, metabolic engineering, and the use of renewable feedstocks, providing an eco-friendly alternative to petroleum-based polymers. PHAs have emerged as promising biomaterials for various biomedical applications such as tissue engineering scaffolds, drug delivery systems, wound healing materials, and biodegradable implants. Their ability to support cell

adhesion, proliferation, and controlled degradation makes them suitable for regenerative medicine and medical device development. Furthermore, PHAs can be modified through surface functionalization or composite formation to enhance their mechanical strength, antimicrobial properties, and bioactivity. However, several challenges continue to limit the clinical and commercial translation of PHAs. High production costs, downstream processing complexities, variability in polymer properties, and regulatory considerations remain significant barriers. Addressing these challenges requires integrated approaches involving advanced bioprocess optimization, synthetic biology, and material engineering strategies. This study highlights recent advances in microbial bioprocessing of PHAs, and their growing applications in biomedical engineering. It also discusses key challenges and emerging opportunities for developing next-generation biodegradable biomaterials, emphasizing the need for continued research and interdisciplinary collaboration to realize the full potential of PHAs in future biomedical applications.

NLRP3 Inflammasome Drives SOD2 Acetylation and Oxidative Stress Independent of Sirtuin Signaling in Ischemic Stroke

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Neuroinflammation in response to ischemic insult is a defining feature of ischemic stroke. The inflammatory cascade in the brain involves cytokines, chemokines, and reactive oxygen species (ROS), which collectively contribute to neuronal injury. Immune cells such as microglia, macrophages, and neutrophils help clear necrotic debris but also sustain chronic neuroinflammation, thereby exacerbating neuronal death and tissue damage. Among the molecular mediators of this process, the NLRP3 inflammasome plays a central role in sensing cellular stress and promoting the maturation and release of pro-inflammatory cytokines. In this study, using complementary *in-vitro, in-ovo,* and *in-vivo* models, we investigated the role of NLRP3 inflammasome signaling in regulating oxidative stress during ischemic stroke. Particular attention was given to the interaction between sirtuin-mediated regulatory pathways and superoxide dismutase (SOD)-dependent antioxidant defense mechanisms. Our findings reveal that members of the sirtuin family (SIRT1–SIRT5) do not mediate acetylation of SOD2, suggesting that the canonical sirtuin-dependent regulation of SOD activity may not fully explain oxidative stress modulation in ischemic injury. Instead, our results indicate that NLRP3 activation promotes SOD2 acetylation, linking inflammasome signaling directly to mitochondrial oxidative stress. Furthermore, pharmacological inhibition of the NLRP3 inflammasome using MCC950 significantly reduced oxidative stress and inflammatory signaling while preserving neuronal viability. These findings highlight NLRP3 inflammasome signaling as a key regulator of oxidative and inflammatory stress pathways in ischemic stroke and support the therapeutic potential of NLRP3-targeted interventions for limiting neuroinflammation and neuronal damage.

Translational Research: Bridging Basic Science Discoveries to Clinical Applications

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Translational research represents a dynamic and integrative approach that converts fundamental scientific discoveries into practical clinical applications aimed at improving patient outcomes. It serves as a critical bridge between bench and bedside, accelerating the transformation of laboratory findings in molecular biology, genomics, proteomics, metabolomics, and bioinformatics into diagnostics, therapeutics, and preventive strategies. In the era following the Human Genome Project, rapid advances in high-throughput sequencing, biomarker discovery, and precision medicine have redefined disease understanding at the molecular level.

The translational research continuum encompasses multiple phases—from preclinical validation (T0–T1), early clinical trials (T2), evidence-based implementation (T3), to population-level health impact (T4). Innovations such as CRISPR-based gene editing, RNA therapeutics, and targeted biologics exemplify successful translation of molecular insights into transformative therapies. Institutions like the National Institutes of Health and initiatives such as the Clinical and Translational Science Awards have strengthened collaborative ecosystems that integrate clinicians, basic scientists, epidemiologists, and public health experts.

Despite remarkable progress, challenges remain, including reproducibility gaps, regulatory complexities, funding constraints, and disparities in implementation across diverse populations. Effective translational research requires interdisciplinary collaboration, robust biostatistical frameworks, ethical oversight, and community engagement

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to ensure equitable health benefits.

In conclusion, translational research is not merely a scientific process but a strategic paradigm that transforms biological knowledge into tangible health solutions. By fostering integration between laboratory innovation and clinical practice, it holds the promise of advancing precision medicine and achieving sustainable improvements in global health outcomes.

Future-Ready Healthcare: Artificial Intelligence, Ethics, Policy, and Sustainable Health Innovations

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Artificial Intelligence (AI) is transforming healthcare systems reshaping how decisions are to be made, and services are delivered. As AI systems increasingly influence critical aspects of human life, ethical considerations have become central to their development and deployment. The role of ethics in AI is to ensure that technological innovation aligns with fundamental human values such as fairness, accountability, transparency, privacy, and respect for human rights.

Ethical frameworks in AI address key challenges including algorithmic bias, data privacy violations, lack of explainability, autonomous decision-making risks, and potential misuse of AI technologies. Without proper ethical oversight, AI systems may reinforce social inequalities, compromise individual freedoms, or produce harmful and discriminatory outcomes. Therefore, integrating ethical principles into AI design — often referred to as "ethics by design" — is essential to promote responsible innovation.

Hence, there is the importance of interdisciplinary collaboration among technologists, policymakers, ethicists, and stakeholders to develop robust governance models and regulatory standards. It also emphasizes the need for transparency, continuous monitoring, and accountability mechanisms to build public trust in AI systems. Ultimately, embedding ethics at every stage of AI development ensures that artificial intelligence serves humanity in a safe, equitable, and socially beneficial manner.

Genetic Landscape in Origin of Down Syndrome-Associated Acute Lymphoblastic Leukemia

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Down syndrome-associated acute lymphoblastic leukemia (DS-ALL) is a high-risk hematologic malignancy uniquely arising in children with trisomy 21, marked by a distinct mutational landscape and clinical behavior. Given the elevated leukemia risk in individuals with Down syndrome, this study systematically analyzes and compares the mutational landscapes of DS-ALL and non-DS ALL to uncover shared and divergent pathogenic mechanisms. The analysis revealed 58 genes frequently mutated in DS-ALL, with *JAK2, IKZF1*, and *CDKN2A/B* identified as particularly significant. The prevalence of the *CRLF2* rearrangement, especially in association with *P2RY8*, was markedly higher in DS-ALL (29.55%) compared to non-DS ALL (1.5%). In contrast, non-DS ALL showed higher incidences of *IKZF1*, *PAX5*, and *CDKN2A/B* among the 596 genes identified. Gene Ontology (GO) revealed that DS-ALL mutations were enriched in chromatin organization, STAT signaling, and B-cell differentiation, while non-DS ALL mutations predominantly affected lymphocyte activation, transcription regulation, and potassium channel complexes. KEGG pathway analysis highlighted enrichment in JAK-STAT and leukemogenesis pathways in DS-ALL, whereas transcriptional misregulation dominated in non-DS ALL. Notably, Chromosome 9 emerged as a critical genomic hotspot, harboring multiple mutated genes, thereby challenging the conventionally held view that chromosome 21 alone mediates DS-related leukemogenesis. Drug gene interaction analysis identified therapeutic targets such as *JAK2, KRAS*, and *EZH2*, which are already being explored in hematologic malignancies, and novel targets such as *DNMT3A* and *IKZF1*. Ruxolitinib (JAK inhibitor) and dabrafenib (BRAF inhibitor) emerged as promising candidates for DS-ALL and non-DS ALL. The study advocates for developing Down syndrome-specific ALL models and encourages the validation of novel therapeutic targets.References:
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Forensic Medicine: Resolving unsolved mysteries through Biomedical Sciences

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Forensic Medicine has traditionally served as the interface between medical science and law, yet many questions surrounding death continue to challenge investigators, courts, and society. The present discourse addresses four fundamental mysteries: When did death occur? Why does forensic evidence sometimes fail to reveal the truth? Can the dead still speak through scientific identification? Does science offer answers to the concept of life after death?

The determination of time since death remains central to medicolegal investigation. Through the application of thanatochemistry—biochemical analysis of postmortem changes—objective and reliable estimation of postmortem interval can be achieved, reducing dependence on subjective indicators. Equally critical is understanding why forensic laboratory results occasionally fail in courts of law. Contrary to common belief, errors often arise not from analytical incompetence but from improper handling, preservation, and transport of biological samples. The application of thanatophysics—the study of physical changes affecting biological evidence after death—has demonstrated how environmental factors such as air exposure and desiccation maintain sample integrity. Under an ICMR-funded research initiative at All India Institute of Medical Sciences Bhopal, innovation of a controlled sample-drying device and the formulation of standardized handling SOPs significantly improved laboratory reliability and evidentiary value.

India reports nearly 50,000 unidentified bodies annually, underscoring the magnitude of the identification crisis. Thanatoidentification, through integration of forensic anthropology, DNA profiling, odontology, and allied biomedical sciences, restores identity not merely as a name but as scientific certainty for law, closure for families, and dignity for human remains. The ICMR-supported UMID project has demonstrated practical success in establishing identities of unknown deceased individuals.

Beyond identification lies the emerging science of thanatobiology—the study of biological processes persisting after death. In a landmark ICMR-funded study conducted at AIIMS Bhopal, the largest human study of its kind worldwide (263 postmortem retrievals over three years), viable spermatozoa were successfully recovered up to 21 hours after death under Indian climatic conditions. This breakthrough highlights the potential of postmortem gamete retrieval for assisted reproductive technologies, challenging traditional boundaries between death and the continuity of life.

Thus, the integration of biomedical sciences with forensic medicine transforms death investigation from a descriptive discipline into an evidence-based, innovation-driven science. At AIIMS Bhopal, collaborative research continues to expand the frontiers of forensic discovery, demonstrating that through scientific rigor, even the most profound mysteries of death can be approached with objectivity, humanity, and hope.

Biomarker-Guided Precision Therapy in Diabetic Macular Edema: Predicting Anti-VEGF Therapeutic Response and Non-Response

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Background: Diabetic macular edema (DME) results from retinal vascular leakage and endothelial barrier dysfunction. Although anti-VEGF therapy is the clinical standard, nearly one-third of patients show suboptimal anatomical and functional improvement despite repeated intravitreal injections. This highlights the need for reliable prognostic biomarkers to enable early identification of patients who are unlikely to respond to therapy.

Methods: In this prospective translational study, DME patients receiving at least three intravitreal anti-VEGF injections were followed for six months. Patients were stratified into responders and non-responders based on central retinal thickness (CRT) outcomes (<300 µm vs. >300 µm). Serum biomarkers spanning angiogenic, inflammatory, endothelial junctional, and immunomodulatory pathways were quantified using multiplex bead-based flow cytometry. Associations with clinical outcomes were assessed through correlation, network analyses, and ROC-based predictive evaluation.

Results: Responders demonstrated a vascular-stabilizing molecular profile marked by higher Ang-1 levels and an increased Ang-1 to Ang-2 ratio, correlating with greater retinal thickness reduction and visual improvement. Protective mediators, including sFLT-1 and sST2, were enriched among responders, suggesting enhanced VEGF sequestration and suppression of IL-33–driven inflammation. Non-responders exhibited elevated IL-18 and increased circulating CD31, consistent with persistent

endothelial disruption. VEGF levels alone did not reliably distinguish treatment responses. Network analysis revealed coordinated angiopoietin and immunoregulatory signaling in responders, contrasted by sustained inflammatory and angiogenic coupling in non-responders.

Conclusion: Integrated serum biomarker profiling identifies clinically relevant signatures predictive of anti-VEGF responsiveness in DME. These findings support a precision medicine approach to identify patients who may benefit from adjunctive or alternative pathway-targeted therapies.

Decoding Metabolic Rewiring in Retinoblastoma using NMR-based Serum Metabolomics

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Keywords: Retinoblastoma, metabolic rewiring, NMR, serum metabolomics, diagnostic markers.

Retinoblastoma (RB) is a rare and aggressive form of ocular malignancy that mostly affects children under 5 years of age. Delayed diagnosis of RB results in vision loss and metastasis, underscoring the need to develop diagnostic and prognostic markers for RB. Although metabolic rewiring is a well-recognized hallmark of all cancer cells, it has yet to be explored in RB. This study aims to develop a non-invasive screening strategy for early detection of RB using NMR-based serum metabolomics. A total of 70 metabolites belonging to classes of amino acids, organic acids, carbohydrates, and others were qualitatively and quantitatively profiled in serum samples from 24 RB patients and 26 controls. PLS-DA model depicted distinct clustering of RB patients and controls, highlighting key discriminatory metabolites. Metabolic fingerprints unique to unilateral and bilateral RB patients were observed, which might be an outcome of their distinct mutational backgrounds. 11 metabolites displayed consistent alterations in both groups, with the effect being heightened in bilateral RB, indicating greater disease severity. Metabolic discrepancies among non-invasive and invasive unilateral patients were also observed, with the more pronounced alterations in invasive RB. Additionally, assessment of patients with active RB and regressed tumors revealed the suppression of metabolites in the regressed group that were elevated in active disease and vice versa. Altogether, these findings reveal profound metabolic rewiring in RB, implying the potential of serum metabolites as non-invasive diagnostic and prognostic markers for RB.

N-acetylcysteine intervention in Fluoride-induced developmental Neurotoxicity: Experimental evidence for Translational application

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Keywords: Fluoride, N-Acetylcysteine, Developmental Neurotoxicity, Oxidative Stress, Neuroprotection.

Prenatal fluoride exposure is known to cause neurobehavioral deficits and neuronal damage through oxidative stress and neurotransmitter dysregulation in offspring[1]. The present study investigated the neuroprotective potential of *N*-acetylcysteine (NAC), a potent antioxidant and glutathione precursor, against fluoride-induced developmental neurotoxicity using *in-vitro* and *in-vivo* models. The *in vitro* approach, primary hippocampal neuronal cultures, neurons, and glial cells (80:20). Exposure to fluoride caused elevated intracellular calcium levels, increased ROS and lipid peroxidation (MDA), depletion of glutathione (GSH), and reduced cell viability, indicating pronounced oxidative stress and neuronal cytotoxicity. NAC treatment significantly reversed these alterations, stabilizing intracellular calcium, restoring antioxidant balance, and improving neuronal survival. In the *in vivo* study, pregnant mice received deionized water (control), fluoride (100 ppm), NAC (100 mg/kg body weight), and combined fluoride and NAC throughout the gestation period. Offspring were subjected to histological and neurochemical assessments in pups of day 0, 14 and 30 and evaluated for spatial learning and memory in 30 days pups (Morris water maze and classical maze). Fluoride exposure led to impaired cognitive performance, neuronal degeneration, and reduced acetylcholinesterase activity, accompanied by elevated NADPH-d and nNOS

expression, indicating disrupted cholinergic and nitrergic signaling. Interestingly, NAC co-administration markedly improved behavioral performance, preserved neuronal morphology, and normalized neurotransmitter enzyme activity across developmental stages. Collectively, these findings demonstrate that NAC effectively mitigates fluoride-induced developmental neurotoxicity through its antioxidant, anti-apoptotic, and neurotransmitter-modulatory activity. The study highlights the translational potential of NAC as a preventive and therapeutic strategy against fluoride-related neurodevelopmental disorders in both humans and animals.

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Two decades of cancer genomics: Chromatin Remodelers to Gene fusions to novel discoveries

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Cancer incidence and mortality are continuously rising in India. Previous studies have provided evidence for the occurrence of distinct clinicopathological features and tumor subtypes in Indian cancers. However, we continue to implement patient management and treatment regimens defined in the West. In my talk, I shall highlight our cardinal discoveries based on analysis of patient-derived samples from four important tumor types of namely squamous cell carcinoma of the tongue and esophagus and adenocarcinoma of the pancreas and colon/rectum. I shall describe the discovery of early-onset rectal cancer as a unique and poorly studied colorectal cancer (CRC) subtype in India besides highlighting discovery of novel driver genetic alterations. In addition, I shall discuss significant deviations from the central dogma driving both sporadic and familial forms of CRC. Further, I shall reveal identification of frequent genetic alterations targeting the SWI/SNF complex, the cardinal chromatin remodeler in human development and adult life, across cancer types. Finally, I shall highlight the discovery of a novel mode of gene activation, of PAN-cancer relevance, emanating from an interesting association between gene fusions and chromatin compartments.

Chagas disease Cardiomyopathy & Immunopathology: Therapeutic efficacy of a Drug combination

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Keywords: Chagas disease, *T. cruzi, invasion*, replication, benznidazole, therapeutic efficacy

Drug combinations and drug repurposing have emerged as promising strategies to develop novel treatments for infectious diseases, including Chagas disease. In this study, we aimed to investigate whether, the repurposed drugs chloroquine (CQ) and colchicine (COL), known to inhibit *Trypanosoma cruzi* infection in host cells, could boost the anti-*T. cruzi* effect of the trypanocidal drug benznidazole (BZN), increasing its therapeutic efficacy while reducing the dose needed to eradicate the parasite. The combination of BZN and COL exhibited cytotoxicity to infected cells and low antiparasitic activity. Conversely, a combination of BZN and CQ significantly reduced *T. cruzi* infection *in-vitro*, with no apparent cytotoxicity. This effect seemed to be consistent across different cell lines and against both the partially BZN-resistant Y and the highly BZN-resistant Colombiana strains. *In-vivo* experiments in an acute murine model showed that the BZN+CQ combination was eight times more effective in reducing

T. cruzi infection in the acute phase than BZN monotherapy. In summary, our results demonstrate that the concomitant administration of CQ and BZN potentiates the trypanocidal activity of BZN, leading to a reduction in the dose needed to achieve an effective response. In a translational context, it could represent a higher efficacy of treatment while also mitigating the adverse effects of high doses of BZN. Our study also reinforces the relevance of drug combination and repurposing approaches in the field of Chagas disease drug discovery.

Journal of Academy of Biomedical Sciences
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Interleukin-10 Gene polymorphism in Schizophrenia and its relation with diseases severity and Cognitive Dysfunction

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Background: Inflammatory markers are known to alter in schizophrenia. The objective of the study was to investigate the genotype and allele frequency of IL-10 gene polymorphism (rs1800872 and rs1800871) and plasma IL-10 levels in schizophrenia and their relation with disease severity and cognitive status.

Materials and methods: The study was conducted in 216 Schizophrenia patients and 216 controls. Single nucleotide polymorphism of IL-10 and its plasma levels were assessed in both the groups. Cognitive status was evaluated using ACE-III scores.

Results: The Co-Dominant model of rs 1800872 polymorphism was found to be significantly associated with the risk of schizophrenia (p = 0.035). The rs1800871 variant was associated with the severity of schizophrenia (p=0.040). Plasma IL-10 was positively correlated with total ACE III score (p= 0.006), attention (p = 0.012), language (p = 0.036) and memory score (p = 0.008) in schizophrenia.

Conclusion: We conclude that single nucleotide polymorphisms of IL-10 was associated with severity of schizophrenia.

Study of Serum calcium, Vitamin D3 and Vitamin B12 in Backache patients

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Keywords: Serum calcium, vitamin D3, vitamin B12, musculoskeletal, bone health

Introduction: Backache is a common musculoskeletal problem and may be associated with deficiencies of calcium, vitamin D3 and vitamin B12. This study aims to evaluate serum levels of these micronutrients in patients with backache to understand their possible role in adult population with back ache and which will support appropriate management.

Objectives: The objectives of this study were to find the association between serum calcium, vitamin D3 and vitamin B12 backache patients.

Methods: The present cross-sectional study were included 30 patients (30-60 Years) diagnosed with backache attending orthopedic OPD, MGM Hospital, Kamothe, Navi Mumbai in 2025. Patients with H/O chronic kidney disease, endocrine disorders, or those actively taking calcium and vitamin supplementation were excluded.

The blood samples are collected under aseptic condition and processed for Serum calcium, and Vitamin D, and B12 by CLIA technique. Statistical analysis done by SPSS version 25.

Results: The mean age of the study population is 43.07 ± 10.96 years. The mean serum calcium level is 8.26 ± 0.60 mg/dL. The mean serum Vitamin D3 level is 25.47 ± 2.33 ng/ml. The mean serum Vitamin B12 level is 473.95 ± 264.39 pg/mL.

Conclusion: This study highlights the importance of assessing serum calcium, vitamin D3 and vitamin B12 in patients with backache. We found serum calcium and vitamin D3 levels were insufficient, indicates impaired bone-muscle metabolism leading to musculoskeletal pain. Identification of deficiencies of these micronutrients may aid in early intervention and contribute to improving clinical management and prevention of backache related complications.

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Ubiquitin specific Peptidase 37 facilitate Replication stress tolerance to promote Prostate cancer Oncogenesis.

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Several reports have suggested that the DUBs (deubiquitinating enzymes) are highly-elevated in various cancers, Reverses the process of ubiquitination and are responsible for stabilization of oncoproteins. Among DUBs, Ubiquitin-specific peptidase 37 (USP37) is one of the least studied member of the Ubiquitin specific protease family. USP37 controls numerous aspects of oncogenesis, including stabilizing many oncoproteins as reported in our recent studies. Prostate cancer (PC) is the most common cancer diagnosis made in men remains the leading cause of cancer death in men. However, the biological functions of USP37 in prostate cancer remain unclear. Analysis of TCGA data indicated that overexpression of USP37 correlated with reduced progression free survival (PFS) in prostate cancer patients. Mass spectrometry (MS) analysis of Prostate cancer cells (DU145) indicated that distinct set of genes were altered on knockdown of USP37. Survival Data indicate that USP37 overexpression confers survival advantage while its depletion enhances sensitivity for cell killing in PC cells. USP37 overexpressing cells were able to resolve DNA damage foci much more rapidly than the control cells or cells in which USP37 was depleted in response to genotoxic stress. USP37 depletion results in reduced resolution of γ H2AX and 53BP1 DNA damage foci which indicates the reduced ability of cells to carry out constitutive DNA replication. USP37 was found to interact with different replication factors as also seen in our MS analysis including many previously reported partners. We further correlated our data with archived tissue blocks of PC patients by analysing if USP37 overexpression correlated with disease progression. Present data suggests that USP37 is required for tolerance of replication stress in PC and is required to dock additional replication factors and stabilize DNA replication fork. The current data provides novel pathways regulated by USP37 in PC cells which reinforce development of targeting strategies against USP37 in context of Prostate Cancer.

Artificial Intelligence inspired Multi-epitope vaccine against *Streptococcus pneumoniae* for Broader Serotype coverage

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Streptococcus pneumonia is the leading cause of respiratory deaths globally. The available polysaccharide vaccines and glycoconjugate vaccine provide suboptimal protection and doesn't have similar response against all the targeted serotypes. Current work has focused on the design of multi-epitope protein-based vaccine against *Streptococcus pneumonia,* which can provide better immune response and can cover multiple serotypes through the conserved epitope targeting. The conserved as well as non-conserved B cell and T cell epitopes in the diverse proteome Streptococcus pneumonia were identified using artificial intelligence and bioinformatics tools. Epitopes were selected based on their strong IFN-g stimulation and limited allergenic response. β-defensin 1 was added as an adjuvant, and linkers were employed to link the epitopes and adjuvants in the final vaccine. The vaccine showed a high antigenicity score, was non-allergenic, non-toxic, and demonstrated stable physicochemical properties, including good solubility. Docking results indicated a ~14.5 kcal/mol binding affinity for the TLR4-vaccine interaction. MD simulations confirmed stability, with RMSD and hydrogen bond counts indicating consistent structure. Immune simulations showed robust responses, including memory formation in B and T cells, with a shift from IgM to IgG1/IgG2 dominance. Cytokine analysis revealed peak IFN-γ levels post-exposure, highlighting the vaccine's strong immune-stimulating potential. Further the vaccine construct was successfully expressed and purified using *E.* coli (BL21).

Cellular and Acellular Approaches in Cardiac Repair: Comparative Assessment of c-Kit$^+$ Amniotic Fluid Mesenchymal Stem Cells versus Their Secretome

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Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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c-Kit (CD117) positive amniotic fluid mesenchymal stem cells (AF-MSC) demonstrate promising cardiomyogenic potential in myocardial injury models. However, the administered cells exhibit limited differentiation and homing capacity at injury sites, suggesting cardio-protection could occur primarily through paracrine mechanisms rather than direct cellular integration. While cell-free therapies have emerged as promising alternatives, direct comparative studies evaluating c-Kit$^+$ AF-MSCs and their secretome remain absent. Here, we have compared the cardioprotective efficacy of c-Kit$^+$ AF-MSC versus their secretome using in-vitro ischemia-reperfusion injury models and in-vivo isoproterenol (ISO)-induced myocardial injury in rats. In-vitro assessments measured cell survival and apoptosis in injured cardiomyocytes at days one and three post-treatment. The in-vivo evaluation employed cardiac function analysis, including 2D-echocardiography and electrocardiography, alongside assessment of infarct size, fibrosis, apoptosis, oxidative stress, and inflammatory markers. Both c-Kit$^+$ AF-MSC and their secretome improved cardiomyocyte survival and reduced apoptosis, with the secretome showing significantly superior outcomes at both time points. In the ISO-induced rat model of myocardial injury, both therapeutic approaches exhibited cardioprotective efficacy; however, secretome therapy consistently outperformed cell-based treatment across all evaluated parameters. These findings establish that, while both modalities provide cardio protection, cell-free secretome therapy demonstrates superior efficacy compared to cell-based approaches in myocardial injury. Overall, this study highlights that the c-Kit$^+$ AF-MSC-derived secretome is a compelling candidate for advancing cardiac regenerative medicine, potentially overcoming limitations of conventional stem cell transplantation and offering improved therapeutic outcomes for myocardial injury.

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Mechanistic Exploration of Natural Bio-actives and Repurposed Drugs in Combating *Candida albicans* Infections

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Keywords: *Candida albicans*, Biofilm, drug combination, drug resistance, phytochemicals, virulence factors

Candida albicans is an opportunistic human fungal pathogen and it can cause infections in immunocompromised and hospitalized individuals. The antifungal drug resistance, side effects and limited availability of drugs of drugs are the main challenges for practitioners and drug developers. There is a need to find an alternative strategy to treat fungal infections. Identification of novel antifungal molecules, drug repurposing, and drcombinationsion can be alternative strategies for drug development. Antifungal activities of compounds capric acid, caprylic acid, phenazine methosulphate, glucosinolate derivatives, zingerone, berberine, bisabolol and caryophyllene have been identified with their molecular targets in *C. albicans*[1,2]. These molecules are able to inhibit the growth, morphogenesis, adhesion, and biofilm formation in *C. albicans*. The FDA approved antibiotics, antivirals, and antimalarial drugs were studied under the repurposing strategy[3]. Moreover, research on the mechanisms of action and molecular targets of these putative compounds showed that they could impact *C. albicans* virulence factors, gene expression, cell cycle progression, and cell membrane integrity. Since these compounds have several targets in *C. albicans*, there is a lower likelihood that these medications would cause resistance. The *in-vitro* prevention of *C. albicans* biofilm formation was achieved through the identification and use of synergistic combinations between allyl isothiocyante and fluconazole. Also, synergistic combination of vidarabine with fluconazole and caspofungin has shown activity against *C. albicans* growth and morphogenesis. Mice and silkworms are employed as animal models in '*in-vivo*' research to examine the efficiency of some successful medications. The

formulations based on these antifungal small molecules can be used as therapeutic aagentsfor candidiasis.

Acknowledgment: Authors are thankful to D.Y. Patil Education Society, Deemed to be University, Kolhapur, Maharashtra, India for providing infrastructure facility and funding support (DYPES/DU/R&D/2025/3035).

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Regulation of altered Synaptic transmission by Semaphorin in Temporal Lobe epilepsy

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Temporal lobe epilepsy (TLE) is associated with altered regulation of glutamatergic synaptic activity in the hippocampus and extra-hippocampal structures, which contributes to generation of distributed networks. Semaphorins are known to regulate neuronal excitability by influencing the surface expression of glutamate receptors. We investigated the role of semaphorin 3F in regulating glutamatergic activity in the animal model of TLE. mRNA and protein expression of semaphorin 3F and glutamate receptor subunits were measured in Li-pilocarpine rat model TLE after inhibiting semaphoring 3F using intra-hippocampal administration of siRNA. TLE rats demonstrated EEG patterns indicative of spontaneous epileptic seizures, conversely, TLE rats treated with semaphorin 3F siRNA exhibited EEG patterns similar to control group. Expression of semaphorin 3F, Plexin A3, and GLUR4 receptor subunits were significantly increased in the TLE rats. Golgi-Cox staining of brain samples showed a reduction in the length of apical dendrites and spine density in TLE rats, and not in TLE rats injected with Sema 3F siRNA. Whole-cell patch clamp recordings indicated increase in the frequency and amplitude of glutamatergic activity in the brain samples of TLE rats, but such changes were not observed in siRNA-treated TLE rats. Further, we observed that the magnitude of alteration post semaphorin 3F inhibition was different in the hippocampus as compared to extra-hippocampal samples in TLE rats. Our findings suggest that semaphorin 3F differentially regulates the AMPA receptor-mediated glutamatergic activity in the hippocampus & extra-hippocampal structure of TLE rats which may be responsible for the development of independent networks in these regions.

Targeting HDAC6 Restores Peroxiredoxin-1 Acetylation and Attenuates Oxidative Stress–Driven Seizures in Focal Cortical Dysplasia

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Background: Focal cortical dysplasia (FCD) is a major cause of drug-resistant epilepsy, characterized by abnormal cortical architecture and underlying molecular disturbances. Despite advances in diagnostic classification

and surgical management, the biological mechanisms driving epileptogenesis in FCD remain incompletely understood, and effective non-surgical treatments are limited. Oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant capacity, has been implicated in FCD pathology. This study explores the role of histone deacetylase 6 (HDAC6) in regulating oxidative stress and seizure activity through modulation of the antioxidant enzyme peroxiredoxin-1 (Prdx1).

Methods: Cortical tissues from patients with FCD Type II and from a BCNU-induced rat model were analyzed using qRT-PCR, immunoblotting, and co-immunoprecipitation to determine HDAC6 expression and Prdx1 acetylation status. Intracellular ROS levels were assessed using the dichlorofluorescin diacetate assay. The effects of selective HDAC6 inhibition were evaluated using Tubastatin A (TubA), with outcomes measured in terms of oxidative stress markers and pilocarpine-induced seizure parameters.

Results: HDAC6 expression was significantly elevated in both human FCD samples and the BCNU rat model. Increased HDAC6 activity was associated with reduced Prdx1 acetylation and heightened oxidative stress. Treatment with TubA restored Prdx1 acetylation, reduced ROS accumulation, delayed seizure onset, and significantly lowered seizure frequency.

Conclusion: These findings identify HDAC6 as a critical regulator of oxidative stress and seizure susceptibility in FCD. Pharmacological inhibition of HDAC6 may represent a promising therapeutic strategy for managing FCD-associated epilepsy.

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Injury-Specific Neuroinflammatory Trajectories Converge on Impaired Resolution: Implications for Brain Repair and Therapeutic Intervention

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Key words: Neuroinflammation, Brain injury, Viral infection, Repair, Therapeutic Intervention

Neuroinflammation occurs in many neurological disorders, but its effects depend on the type of injury, its timing, and the duration of the injury. Brain injury and viral infections both activate macrophages and microglia; however, the phase of activation, responses to intracellular stress, and long-term outcomes differ. Disease progression appears to relate less to inflammation and more to whether immune responses resolve appropriately. When resolution fails, ongoing cellular stress can contribute to neurodegeneration. This talk will discuss the importance of stage-specific treatment strategies that match therapy to the phase of injury and to the CNS during viral infection, supporting recovery and repair pathways.

From MTHFR Genotype to Taurine Deficiency: A Metabolic Axis in Neurodegeneration

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Neurodegenerative disorders are complex, multifactorial conditions in which genetic susceptibility intersects with metabolic dysregulation to drive disease onset and progression. Taurine, a sulfur-containing amino acid essential for neuroprotection, mitochondrial stability, and redox homeostasis, has emerged as a potential metabolic determinant of neurodegeneration. This explorative cross-sectional analytical study was conducted at the All India Institute of Medical Sciences (AIIMS), Patna, to evaluate the role of plasma taurine and its interaction with the MTHFR C677T polymorphism within the framework of one-carbon metabolism.

The study included 108 participants comprising 54 clinically diagnosed cases of age-associated neurodegenerative disorders (Parkinsonism, dementia, motor neuron disease, and Wilson's disease) and 54 age- and sex-matched healthy controls. Neurodegenerative patients exhibited marked plasma taurine depletion compared to controls (45.86 µmol/L vs. 84.92 µmol/L; $p < 0.001$), representing an approximately 45% reduction independent of aging. Plasma taurine demonstrated excellent diagnostic performance (AUC = 0.98; sensitivity 92.6%; specificity 94.4%) with a very high odds ratio (OR = 212.5), identifying it as a robust metabolic biomarker.

Genetic analysis revealed a strong association between the MTHFR C677T polymorphism and disease susceptibility, with a 4.96-fold increased risk among mutant allele carriers (CT + TT) and complete disease penetrance in TT homozygotes. A clear gene-dosage–dependent reduction in plasma taurine levels was observed across MTHFR genotypes, implicating impaired folate-dependent one-carbon metabolism and transsulfuration pathway dysfunction as mechanistic drivers of taurine deficiency. Together, these findings support a synergistic "dual-hit" metabolic model in which MTHFR genetic variation and taurine depletion act as interdependent risk factors for neurodegenerative disease. Combined assessment of MTHFR genotype and plasma taurine levels may enable metabolic risk stratification and inform targeted therapeutic strategies.

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Alteration in Molecular dynamics in Microglia signature genes leads to Neuroinflammation in Mice

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Keywords: Brain, Neuroinflammation, Microglia, Olfml3, Tmem119

Microglia are innate immune cells in the brain that play a vital role in regulating neuroinflammation-driven neurological disorders. Olfml3 and Tmem119 have been identified as microglia signature genes whose expression has been shown to alter during neurodegenerative diseases. However, the possible roles of Olfml3 and Tmem119, as well as their potential involvement in microglia-mediated neuroinflammation, remain unclear. Interacting partners of Olfml3 and Tmem119 were found to be microglia-specific proteins, including Iba1, Fcrls, P2RY12, Sall1, and Siglec-H. Molecular docking and MD simulation revealed stable physical interactions between Olfml3, Tmem119, and Iba1. Levels of Olfml3, Tmem119, and Iba1 increased during neuroinflammation. Silencing *Olfml3* and *Tmem119* with siRNA reduced *Iba1* expression. Inhibiting microglial activation significantly increased Tmem119 expression, downregulated Olfml3 and Iba1, and improved behavioural deficits in neuroinflammatory mice. Results highlight the crosstalk between microglia signature genes in regulating microglia functions in the management of neuroinflammation.

Acknowledgements: Financial support from the Indian Council of Medical Research (ICMR) and Institution of Eminence (IoE), University of Delhi, is gratefully acknowledged.

Hippocampal Neurodegeneration Triggers Transient Regeneration Followed by Long-Term Exhaustion of the Neurogenic Niche

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Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
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Hippocampal neurodegeneration is commonly associated with cognitive decline, yet the dynamic response of the endogenous neurogenic niche to injury remains insufficiently understood. In this study, we investigated the temporal regulation of adult hippocampal neurogenesis following experimentally induced neurodegeneration. Our findings reveal a biphasic response within the dentate gyrus: an early surge in proliferation of neural progenitor cells, followed by a progressive decline that culminates in long-term exhaustion of the neurogenic pool. This transient regenerative attempt is characterized by enhanced activation of $Sox2^+$ and DCX^+ progenitors; however, sustained inflammation, altered microglial states, and niche remodeling impair the long-term maintenance of stemness. Ultimately, the neurogenic niche becomes structurally and functionally compromised, limiting its capacity for regeneration during chronic stages of damage. These results highlight the inherent, but short-lived, compensatory potential of endogenous hippocampal progenitors and underscore the need for therapeutic strategies aimed at preserving niche integrity to support long-term neuronal replacement. Our study provides conceptual and mechanistic insights relevant to neurodegenerative disorders such as epilepsy, Alzheimer's disease, and age-associated cognitive decline.

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Vitamin D from Deficiency to Toxicity: Changing Spectrum in Modern Pill-popping Era

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Background

Vitamin D deficiency is common. Besides improving musculoskeletal health, supplementation of vitamin D has pleiotropic benefits in conditions ranging from cardiac and neurological conditions to metabolic disorders like diabetes mellitus. Besides sunlight, good sources of vitamin D are fish, eggs, and vitamin D supplements. Vitamin D is thus being prescribed by physicians, orthopedics, gynecologists and other specialties, many times without checking 25(OH) D levels, sometimes as weekly megadoses. Self-medication is also becoming common along with vitamin D fortification in several supplements. In this scenario, Vitamin D toxicity is being increasingly seen.

Methods

This was a retrospective analysis of data collected over the past 1 year. All samples of vitamin D [25OHD] collected and reported over past 1 month were also included. Additionally, a search for hypervitaminosis D was done in all reports of vitamin D.

Results

Among the 1401 vitamin D samples, Deficiency (<20 ng/mL) was seen in 613 (43.75%), and Insufficiency (20–29 ng/mL) in 414 (29.55%). Vitamin D Sufficiency (30–100 ng/mL) was seen in 369 (26.34%), while Hypervitaminosis D (100–150 ng/mL) was present in 5 (0.36%).

When further scoping was done for hypervitaminosis D over past 1-year, a total of 95 samples were found to be in this category. 82 patients had vitamin D levels between 100-150 ng/ml while 2 had levels >500ng/mL. There were clinical manifestations in these patients of vitamin D toxicity. Manifestations are due to hypercalcemia and include anorexia, abdominal pain, constipation, recurrent vomiting, malaise, fatigue, muscle weakness, hyporeflexia, hypotonia, myalgia, arthralgia, bone pain, polyuria. Hypercalcemic crises were also seen presenting with dehydration, nephrocalcinosis, renal failure and neurological manifestations including confusion, apathy drowsiness, depression, ataxia, psychosis, stupor and coma.

Other known complications include joint effusion, chondrocalcinosis, dwarfism, mental retardation, memory loss, hypertension, arrythmias, bradycardia, heart blocks, cardiac arrest, and vascular calcification.

Conclusion

Vitamin D deficiency is very common. However, upto one-thirds of the individuals tested may have sufficient levels of vitamin D and do not require any external supplements. Vitamin D toxicity, although less common, is being increasingly seen. Vitamin D toxicity has significant morbidity ranging from mild symptoms to serious consequences including mortality. Thus, a rational prescription and intake of vitamin D can help reduce vitamin D toxicity and its deleterious effects.

Role and Regulation of Extracellular microRNAs in Neurodegeneration

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MicroRNAs (miRNAs) are small regulatory RNA molecules demonstrated to play role in different pathological and cellular development and differentiation situations. Parkinson's disease (PD) is a neurodegenerative disorder caused by the loss of dopaminergic neurons (DA-nergic) in the substantia nigra (SNpc). Currently, PD is diagnosed mostly based on motor impairments that develop when more than 80% of the DA-nergic neurons in the SNpc are destroyed. The development of new biomarkers is required for effective PD management. Our studies have shown significant deregulation of miRNAs and specific proteins in serum of PD patients. Exosomes are small extracellular vesicles (50–150 nm) that carry different kind of biomolecules in their lumen and facilitate intercellular communication. Serum contains large amount of exosomes (around 10^{12}/ mL of serum) and exosomes contain relatively more amount of small RNAs than large RNAs. Quantifying the absolute number of specific miRNA molecules in exosome is critical for understanding their functional relevance and developing them for diagnostic tool in diseases like PD. We have developed a new protocol for copy number assay of miRNAs in exosome that combines nanoparticle tracking analysis (NTA) to quantify vesicle concentration with absolute quantification of miRNA using a standard curve based q-PCR approach. Using same method, we have identified significant alterations in expression of miRNAs, which can be used as new biomarkers of PD.

Metabopsy of Inherited Metabolic Disorders (IMDs): Discard to Diagnosis ApproacheS

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Background: Inherited Metabolic Disorders (IMDs) are genetic disorders caused by deficient enzymes leading to defective metabolism. Recently, notable forms of IMDs, including organic acidurias and amino acidurias, have grown substantially, highlighting the need for timely diagnosis, as many IMDs are treatable. However, the approach to detecting IMDs using non-invasive, affordable methods in children is limited. Also, an *in-silico* approach that can alleviate clinical implications due to different IMDs is not emphasized.

Methods: We have developed a novel methodology for detecting IMDs using non-invasive biological samples by employing an in-house designed Vertical Tube Gel Electrophoresis (VTGE) system and 96-well plate colorimetric assays. LC-HRMS analysis was used for metabolic profiling and validation. Further, we extended our research to develop mimetics of metabolites computationally against the pathway-associated enzymes by using molecular docking and MD simulations.

Results: IMD suspected samples showed three folds elevated levels of methylmalonic acid in tears, 2-3 fold increased hydroxyglutaric acid in nail, urine and 4-5 folds increased hydroxyproline in milk teeth, compared to the healthy controls, after performing 96-well plate colorimetric assays. LCHRMS analysis validated these findings. Furthermore, we designed the mimetics of metabolites as potential inhibitors of respective enzymes and studied their interactions using docking and MD simulation.

Conclusion: This research provides the first and novel method to use non-invasive samples for early detection of IMDs such as organic aciduria and amino acidurias by employing VTGE and 96-well plate colorimetric assays. Also, the development of mimetics is a beneficial approach to overcome metabolic conditions in patients.

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Carvacrol Suppresses Benzo(a) pyrene-Induced Lung Tumorigenesis by Regulating Cell Proliferation and Apoptosis in Mice

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Keywords: Benzo(a)pyrene; lung cancer; Carvacrol; cell proliferation; apoptosis; cell cycle Objective:

Lung cancer accounts for the highest incidence and mortality among all cancers worldwide, representing a major global health burden despite advances in prevention and treatment strategies. Carvacrol, a naturally occurring monoterpenoid phenol found in essential oils of oregano and thyme, has attracted attention for its pharmacological potential. The present study aimed to evaluate the anticancer efficacy of carvacrol against benzo(a)pyrene (B(a)P)-induced lung carcinogenesis in Swiss albino mice.

Methods

Lung cancer was induced by administering B(a)P (50 mg/kg body weight) twice weekly for four consecutive weeks, followed by an experimental period of 20 weeks. Carvacrol was supplemented to assess its chemopreventive potential.

Results

Carvacrol supplementation significantly suppressed lung tumor development, as evidenced by reduced serum levels of carcinoembryonic antigen (CEA) and neuron-specific enolase (NSE). Carvacrol treatment normalized cytochrome P450 (CYP450) enzyme activity, attenuated abnormal cell proliferation, and induced apoptosis through modulation of Bax, Bcl-2, and caspase-3 expression. Histopathological evaluation demonstrated preservation of lung architecture, while TEM analysis confirmed reduced cellular and mitochondrial damage in treated mice.

Conclusion:

These findings demonstrate that carvacrol effectively inhibits B(a)P-induced lung carcinogenesis by regulating tumor burden, xenobiotic metabolism, cell proliferation, and apoptotic pathways, supported by histopathological and ultrastructural evidence, highlighting its potential as a chemopreventive agent.

In-silico identification of Pore-forming Toxin inhibitors to Mitigate *Escherichia coli*- associated Sepsis

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Sepsis is a life-threatening condition caused by a dysregulated host immune response to infection, resulting in systemic inflammation, immune dysfunction, and multi-organ failure. *Escherichia coli*, a major pathogen, is a leading cause of sepsis and is frequently associated with septicemia, urinary tract infections, and gastrointestinal diseases. A critical virulence determinant of *E. coli* is the secretion of pore-forming toxins that disrupt host cell membrane integrity and promote immune evasion. Hemolysin E (HlyE), also known as silent hemolysin A, is an α-pore-forming toxin that assembles into transmembrane pores, driving host cell lysis and contributing to toxin-mediated septic progression. Given the limitations of antibiotic therapy, including toxin amplification and resistance development, targeting bacterial virulence factors represents a promising therapeutic strategy. In this study, a structure-based in-silico screening approach was employed to identify inhibitors of HlyE (PDB ID: 1QOY). Molecular docking and drug-likeness analyses identified the plant-derived flavonoid Cianidanol as a high-affinity ligand (-5.760 kcal/mol). Virtual screening of natural phenolic compounds and ADMET profiling further supported its favorable pharmacokinetic properties. MM-GBSA binding energy calculations and 100 ns molecular dynamics simulations confirmed the stability of the HlyE-Cianidanol complex. These findings highlight Cianidanol as a promising non-bactericidal anti-virulence inhibitor with potential to mitigate toxin-driven sepsis while reducing selective pressure for antibiotic resistance.

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Total Laboratory Automation: Transforming Clinical Laboratories through Integrated, Intelligent, and Standardized Workflows

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Keywords: Total laboratory automation, Laboratory workflow, Artificial intelligence, ISO 15189, Sustainable diagnostics

Background

Modern clinical laboratories face increasing test volumes, demand for rapid turnaround time, and stringent quality and accreditation requirements. Total Laboratory Automation (TLA) has emerged as a comprehensive technological solution that integrates pre-analytical, analytical, and post-analytical processes into a single, continuous workflow, enabling reliable and efficient diagnostic services.

Description

Total Laboratory Automation encompasses automated sample reception, barcode-based identification, centrifugation, decapping, aliquoting, analytical processing, storage, and retrieval, all connected through conveyor-based systems and middleware. Integration with laboratory information systems enables real-time sample tracking, auto-verification, and intelligent rule-based result validation. Artificial intelligence and data-driven algorithms further enhance decision support, anomaly detection, workload balancing, and predictive maintenance of analyzers.

Quality and Compliance

TLA supports compliance with NABL and ISO 15189 standards by minimizing manual interventions, reducing pre-analytical errors, ensuring traceability, and standardizing processes. Automated documentation, quality indicator monitoring, and audit-ready data improve laboratory governance and accreditation preparedness.

Sustainability and Workforce Optimization:

Automation contributes to sustainable laboratory practices by optimizing reagent usage, reducing repeat testing, minimizing sample wastage, and improving energy-efficient operations. TLA also enables optimal utilization of skilled laboratory personnel by shifting focus from manual tasks to quality assurance, data interpretation, and clinical consultation.

Conclusion

Total Laboratory Automation represents a paradigm shift in laboratory medicine, offering an integrated, intelligent, and sustainable approach to diagnostics. Its adoption is essential for future-ready laboratories aiming to deliver high-quality, standardized, and patient-centric services in evolving healthcare systems.

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Engineering Controlled Destabilization: The "Magic Methyl" Effect in RNAi Enhancement

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SiRNAs silence genes via endogenous RNAi pathways and hold promise as therapeutics. We report the synthesis of 2′-alkoxy/fluoro-m^3C phosphoramidites and their incorporation into siRNAs to probe the role of thermodynamic destabilization in gene silencing. We showed that incorporation of N^3-methyl-uridine (m^3U) into siRNA duplexes selectively destabilizes Watson–Crick base pairing, leading to improved thermodynamic asymmetry and enhanced guide-strand selection. This results in significantly increased RNAi activity at the intracellular level when these modifications were incorporated at cleavage or 3′-overhang of passenger strand.

We further combine m^3U modification with 2′-O-hexadecyl (C16) conjugation. siRNA duplexes containing 2′-alkoxy/fluoro-*N*^{3}-methylpyrimidines displayed significant thermal destabilization due to disrupted Watson–Crick hydrogen bonding and reduced base stacking. RNAi assays showed that incorporating 2′-alkoxy-m^3U/m^3C at the sixth position of passenger-strand enhanced RNAi activity significantly.

Furthermore, using site-specific incorporation of 2′-fluoro-m^3U as a sensitive ^{19}F NMR probe, we directly map local loop environments within a parallel NG16 G-quadruplex. Importantly, loop modification suppresses complementary strand invasion, thereby stabilizing the G-quadruplex against duplex formation.

These findings demonstrate that deliberate destabilization through 2′-functionalized N^3-methyl pyrimidines can fine-tune siRNA structure, enabling enhanced and safer RNAi activity, and G4 folding dynamics.

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Papain, A Cysteine protease, Degrades Insulin-induced Amyloid aggregation: Insights from *in-vitro* and *in-vivo* studies

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Amyloidogenic proteins, under specific conditions, undergo alternative folding pathways that lead to the formation of protease-resistant amyloid fibrils with a characteristic cross-β structure. These amyloids are associated with several diseases including Alzheimer's disease, Parkinson's disease, Creutzfeldt-Jakob disease, and insulin-derived amyloidosis, making their clearance a promising therapeutic strategy. Insulin, a well-studied amyloidogenic protein, serves as a model for studying amyloid-related disorders. Insulin-derived amyloidosis is a rare but underestimated condition caused by repeated insulin injections in diabetic patients, leading to subcutaneous deposition of insulin amyloid fibrils and associated clinical challenges. The present study investigates the therapeutic potential of papain, a cysteine protease, in mitigating insulin amyloidosis through integrated in vitro, in vivo, and in silico approaches. Papain exhibited a significant amyloid-degrading potential showing considerable fibril degradation as evaluated by turbidity assay, 80% degradation in 1h incubation. The highest proteolytic activity was observed at 200 µg/mL of papain. In SDS-PAGE complete degradation was observed at a concentration of 200ug. The CD spectroscopy showed negative ellipticity at 210 nm confirming disruption of β-sheet-rich amyloid structures upon incubation with Papain, while FTIR revealed reduced 1645 cm−1 peak intensity indicating breakdown of insulin amyloid fibrils and loss of β-sheet conformation. Further, *in-vivo* study using male Wistar rats to examine the ability of papain to degrade insulin amyloid was done. The results showed that insulin fibrils generated amyloid masses in rats after subcutaneous injection of insulin for two weeks. There observed significant reduction in size of insulin amyloid for the groups injected with papain. The reduction was more than 87% with a Papain dose of 60 mg/kg body weight. The histopathological results were analysed using light microscopy, polarized microscopy, and fluorescence microscopy. In all the studies, there observed a significant reduction in the insulin amyloid. Further, in-silico study

evaluated the interaction between Papain and IA, there observed the strong binding affinity -8.1 kcal/mol. Overall, this study demonstrates the degradation potential of papain against insulin amyloid. These findings suggest that papain can be considered as a promising insulin amyloid-degradation agent and a potential therapeutic candidate for managing amyloid-related disorders.

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In-silico variant Analysis of *MTHFR* involved in Autism Spectrum Disorders

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MTHFR is recognized as a high-risk gene for autism spectrum disorders (ASD), and variations within this gene can alter enzyme activity, contributing to disease onset. Identifying variants that exert deleterious effects on protein structure and function is crucial for advancing our understanding of disease genetics and improving diagnostic and therapeutic strategies. In this study, we performed computational analyses of *MTHFR* variants associated with ASD to evaluate their structural and functional impact. *MTHFR* variants were collected from the SFARI database and text mining. The variants were predicted for pathogenicity scores using Varsome tools and protein domains were predicted using InterPro. The mapping of these variants was done manually. The *MTHFR* has 12 exons and the transcripts expressed in the brain encode 656 amino acids. Among the nine ASD-specific variants, four, c.199C>T, c.665C>T, c.776T>C, and c. 1090C>T, with residue changes of p.P67S, p.A222V p.I259T, and p.P364S, respectively had a pathogenicity score > 50%. The homology models and stability predictions for these variants indicate that they can disrupt the MTHFR protein. The network analysis revealed that the MTHFR protein is biologically connected. Therefore, these deleterious variants impair MTHFR function and result in ASD. Further, this study supports laboratory validation and facilitates the development of clinically useful markers for early ASD detection for therapeutic strategies.

Appetite modulator Quercetin Enhances Antioxidant Defence and Neuroprotection in induced Aging Rat model

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This study investigated the neuroprotective and antioxidant effects of a potent appetite modulator Quercetin in a d-galactose-induced accelerated aging model using male Wistar rats. Animals were assigned to four groups: control, Quercetin-treated, d-galactose-induced aging, and d-galactose and Quercetin treatment. Quercetin was administered orally (100 mg/kg) and d-galactose subcutaneously (300 mg/kg) for 28 days. Biochemical analyses included measurement of ferric reducing antioxidant power (FRAP), glutathione (GSH) content, malondialdehyde (MDA), protein carbonyl (PCO) formation, and activities of superoxide dismutase (SOD) and catalase in brain tissue homogenates. Levels of appetite regulatory hormones leptin, ghrelin and insulin were also measure in serum. Gene expression of Beclin-1, ULK-1, SIRT1, NSE, TNF-α, IL-6, GSHR, and GLP-1 was assessed by RT-PCR. Histopathological evaluation of hippocampal architecture was performed, and statistical significance was determined by ANOVA with Bonferroni post-hoc analysis. D-galactose significantly reduced FRAP, GSH, SOD, and catalase activities while increasing MDA and PCO levels, alongside downregulation of autophagy and neuroprotection-related genes and elevation of inflammatory cytokines. Quercetin treatment effectively restores antioxidant markers, reduced oxidative stress indices, improved enzymatic activity, upregulated neuroprotective and autophagy-associated genes, and attenuated inflammation. Histopathological

assessment confirmed preservation of neuronal structure in treated rats. Quercetin supplementation robustly enhances cerebral antioxidant defenses, mitigates oxidative damage, modulates gene expression related to neuron survival and inflammation, and confers histological neuroprotection in experimental aging.

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Dual Phyto-Enzyme Strategy: Combination of nano-encapsulated Eugenol and Alginate Lyase Combat *Pseudomonas aeruginosa* via Antibacterial Activity, Preventing Biofilm Formation, and Disrupting Mature Biofilms

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Biofilm formation is a central virulence strategy of multidrug-resistant *Pseudomonas aeruginosa*, driven by quorum sensing and production of a dense extracellular polymeric substance matrix rich in alginate, hindering antibiotics penetration and action. Effective control, therefore, requires simultaneous bactericidal and antibiofilm interventions. This study describes a dual approach combining eugenol, a phytocompound purified from *Piper betle* leaf essential oil, with alginate lyase, an enzyme that degrades alginate in mature biofilms. Eugenol demonstrated strong antibacterial activity through membrane disruption and significant antibiofilm efficacy by suppressing pyocyanin production, swarming motility, protease activity, mucoviscosity, and rhamnolipid and alginate synthesis, effectively downregulating quorum-sensing gene LasI and LasR. Alginate lyase effectively disrupted pre-formed biofilms, as confirmed by crystal violet and SEM analysis and showed stable activity in the presence of eugenol as detected through thin layer chromatography and UV spectroscopy. When used together, eugenol and alginate lyase exerted synergistic effects, inhibiting quorum-sensing mediated biofilm formation and degradation of established EPS matrix. Further, to improve stability, delivery, and therapeutic performance, both agents were nano-encapsulated using biopolymer-based carriers and characterised through zeta potential, FTIR, and SEM analysis. The nano-formulations exhibited sustained release profiles, while retaining bactericidal and antivirulence properties. In-vivo efficacy was validated using *Galleria mellonella* larvae and murine infected wound models, where treatment significantly reduced bacterial burden, disrupted biofilms, and accelerated wound healing. Overall, this phytocompound-enzyme combination, integrated with nanoparticle delivery, offers a sustainable, eco-friendly and effective strategy against multidrug-resistant *P. aeruginosa* by targeting bacterial viability, quorum sensing and biofilm EPS integrity. This integrated platform underscores the translational potential of bio-based nanotherapeutics for managing persistent infections and reducing reliance on conventional antibiotics worldwide in clinical and environmental settings, contributing to One Health.

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SH-SY5Y cell line

Neurotoxicity effect of 2.4 GHz Electromagnetic Radiation on inducing oxidative stress causing Parkinson Disease: An in vitro study using SH-SY5Y cell line

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Background: The ubiquity of wireless devices emitting 2.4 GHz electromagnetic radiation (EMR) has raised concerns regarding its biological impact. Oxidative stress is a known driver of Parkinson's disease (PD), yet the specific role of EMR in inducing PD-like neurodegeneration remains under active investigation. **Methods:** SH-SY5Y neuroblastoma cells were divided into control, Rotenone-treated (positive PD control), and EMR-exposed groups (8, 12, 24, and 48 hours). Neurotoxicity was measured via electrochemical detection of dopamine. Cellular health was evaluated through intracellular calcium (Ca2+), Reactive Oxygen Species (ROS), Mitochondrial Membrane Potential (MMP), and lipid peroxidation. Cell death mechanisms were analyzed using Annexin V/PI flow cytometry, while genotoxicity was assessed via COMET assay. **Results:** EMR exposure and mimicking the rotenone-induced phenotype resulted that reduced dopamine levels. Oxidative stress markers (ROS and lipid peroxidation) peaked at 8 hours before shifting toward irreversible cellular damage. Conversely, Ca2+ accumulation and mitochondrial dysfunction with prolonged exposure (12–48 hours). Flow cytometry results has showed that early apoptosis at 8 hours to late apoptosis and necrosis at later stages. Genotoxicity, evidenced by DNA fragmentation in the COMET assay, increased significantly with exposure duration. **Conclusion:** 2.4 GHz EMR exposure induce neuronal integrity by inducing oxidative stress, calcium overload, and mitochondrial failure. The observed progression to necrosis and loss of dopamine highlight the potential effect of EMR posing it as a risk factor for neurodegenerative conditions such as Parkinson's disease.

Polydopamine-Based Surface Modification of Hemoglobin Particles for Enhanced Antioxidant Properties and Reduced Heme Release in Oxygen Carriers

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The development of hemoglobin-based oxygen carriers (HBOCs) is limited by several challenges, including free heme release, auto-oxidation of hemoglobin to nonfunctional methemoglobin, oxidative side reactions, tetramer instability, nitric oxide scavenging, and a short circulatory half-life. To mitigate free heme release and reduce oxidative toxicity, we synthesized polydopamine (PDA) coated hemoglobin nanoparticles using a simple one-step method. Owing to the excellent adhesive and antioxidant properties of PDA, we investigated its effect on the structural stability and functional integrity of hemoglobin. UV–visible spectroscopy demonstrated that PDA coating does not compromise heme stability and preserves reversible oxygen binding. Furthermore, circular dichroism and fluorescence analyses revealed no significant alterations in the secondary or tertiary structure of hemoglobin upon PDA coating. Notably, PDA-coated β-F41K exhibited significantly enhanced $ABTS^{\bullet+}$ radical scavenging activity and ferric-reducing capability compared to the uncoated β-F41K. Importantly, PDA-coated recombinant hemoglobin showed a markedly reduced release of free heme into solution relative to uncoated hemoglobin. The nanoparticles also displayed good hemocompatibility and biocompatibility with blood and human embryonic kidney cells, respectively. Collectively, these results highlight PDA-coated recombinant hemoglobin as a promising platform for the development of artificial oxygen carriers with reduced toxic side effects.

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From Selection to Sensing: One-Step Aptamer Selection and Continuous Stress Monitoring

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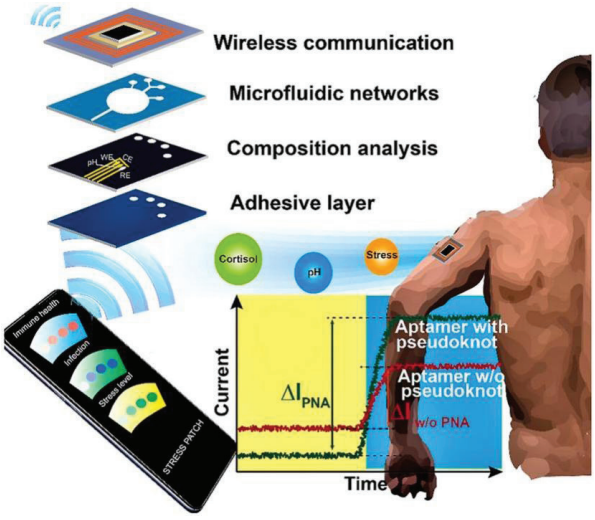
Aptamers are gaining attention for their versatility and cost-effectiveness in theranostics, offering a competitive alternative to antibodies. However, their selection process is complex. To streamline this, we developed the Hydrogel-based Aptamer Selection (HAS) method, which utilizes a diffusion-binding process in a non-fouling porous hydrogel with immobilized targets. HAS simplifies the process by reducing PCR rounds, skipping negative selection, and preserving the target's native 3D conformation. This method allows for easy synthesis and customization of aptamers, advancing medical research, personalized medicine, and biotechnological innovations.



Additionally, we address the need for precise stress monitoring with a non-invasive, wearable sensor that measures cortisol levels in sweat using conformation switching pseudoknot aptamer. Using a pseudoknot-assisted aptamer and a flexible microfluidic system, this sensor provides real-time, continuous monitoring of cortisol, offering a more specific alternative to traditional methods like heart rate variability. These advancements highlight the critical role of molecular recognition agents in modern healthcare and analytical sciences.

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Ketoconazole and Zingerone Synergistically Inhibit *Candida albicans* Growth and Virulence Factors

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Keywords: Anti-biofilm, *Candida albicans*, combination, drug resistance, phytochemical, virulence,

Topical fungal infections caused by *Candida albicans* remain a significant clinical concern, particularly due to increasing resistance and adverse effects associated with prolonged antifungal therapy. Ketoconazole, a widely used azole antifungal agent, exhibits broad-spectrum activity against *C. albicans* but is limited by reduced efficacy and potential toxicity when used alone. Zingerone, a bioactive phenolic compound derived from Zingiber officinale (ginger), has demonstrated notable antifungal, anti-inflammatory, and antioxidant properties. The present study explores the synergistic antifungal potential of a ketoconazole–zingerone combination against *Candida albicans* in the context of topical fungal infections.[1]

The study intended to evaluate the *anti-Candida* activity of Zingerone alone and with Ketoconazole (KTZ),

particularly against the biofilms. Results revealed the concentration-dependent activity of Zingerone against the planktonic growth and virulence factors of *C. albicans*. Significant ($p < 0.05$) inhibition of the biofilms was evident at ≤1 mg/ml concentrations of Zingerone. Notably, a combination of 0.125 µg/ml of KTZ and 0.062 mg/ml of zingerone prevented the biofilm formation. Similarly, the preformed biofilms were significantly ($p<0.05$) inhibited by the Zingerone - Ketoconazole combination. The fractional inhibitory concentration indices ranging from 0.132 to 0.375 indicated the synergistic activity of Zingerone and KTZ against the biofilm formation and the preformed biofilms. Zingerone was found to potentiate ketoconazole activity, by disrupting fungal cell membrane integrity, increasing drug permeability, and inhibiting virulence factors such as biofilm formation.[2]

The synergistic combination also suggests potential benefits in reducing ketoconazole dosage, thereby minimizing adverse effects, while maintaining therapeutic effectiveness. These findings support the development of a novel topical antifungal formulation incorporating ketoconazole and zingerone as a promising strategy for the management of *C. albicans*–associated skin infections. Further *in-vivo* and clinical studies are warranted to confirm safety, efficacy, and formulation stability for clinical application.[3]

Acknowledgement: Authors are thankful to DY Patil Education Society, Deemed to be University, Kolhapur, Maharashtra, India for providing infrastructure facility and funding support (DYPES/DU/R&D/2025/3035).

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Enhancing CSF Leak Detection: A Computational Pipeline for Epitope Mapping Towards Translational Diagnostics

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Background: CSF leaks arise form dural tare caused by trauma, iatrogenic or congenital factors. When diagnosed early, it may prevent fatal complications like meningitis. Current diagnosis using CSF biomarkers and imaging shows limited specificity, accessibility, and high cost. Developing POCT with improved specificity requires sensitive antibodies targeting CSF biomarkers. To address this, we integrated an in-silico pipeline for epitope prediction and antibody design and was benchmarked against antigen–antibody crystal structures. These findings hypothesise that the incorporated tools can support translational diagnostics and POCT development.

Methodology: Epitopes for three CSF biomarkers were predicted using Bepipred 3.0 and Discotope 3.0, with high-confidence regions filtered to identify consensus epitopes. Antibody modelled using AbodyBuilder was used for docking via HawkDock and top poses were ranked by MM/GBSA. Recurring contact residues (>3 models) were compared with predicted epitopes and benchmarked against solved antigen–antibody complexes.

Results: Benchmarking against five solved complexes (3W5D, 7OH0, 7K8S, 6ML8 and 2NY7) demonstrated that the consensus epitope prediction outperformed with contact and literature-defined epitopes (82%) than individual tools (Bepipred ~70%; Discotope ~73%). Applying the pipeline to CSF biomarkers identified distinct surface-exposed epitope clusters with favourable accessibility and stability. Domain-level structural fitting revealed several local surface motifs with low RMSD (0.02–0.05), highlighting candidate binding sites that may enhance assay specificity may improve diagnostic specificity.

Conclusion: This computational pipeline reliably identifies

surface-accessible, structurally consistent epitope clusters across clinically relevant CSF biomarkers. Consensus predictions outperform individual tools, generating testable hypotheses for antibody design and translational diagnostics.

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Nanoceria Capped Triazine-Based Brominated COFs: ^{13}C NMR-Validated Architectures with Enhanced Antibacterial Performance Against *S. aureus*

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This study presents the successful synthesis and characterization of triazine-based brominated covalent organic frameworks (TbBr-COFs) and their cerium-modified hierarchical derivatives Ce-(TbBr-COF)-C and Ce-(TbBr-COF)-L. This was accomplished through a solvothermal reaction utilizing 2,4,6-tris(4-bromophenyl)-1,3,5-triazine (TBPT) and 1,4-dibromobenzene (DBB) in mesitylene/dioxane with acetic acid as a catalyst at 120 °C for 80 hours, followed by probe sonication and homogenization processes. Comprehensive spectroscopic and microscopic analyses confirmed their structural integrity, enhanced crystallinity, porosity, and chemical stability, with SEM and HRTEM revealing distinct morphological features: rod-like structures for TbBr-COF and flower-like hierarchical assemblies for the cerium-modified derivatives. UV-Vis spectroscopy demonstrated efficient cerium loading (91.11% after 64 hours), whereas FTIR and XRD validated framework synthesis and π-π stacking interactions. ^{13}C solid-state NMR demonstrated great purity (>90%) with no residual precursors, and a downfield shift of triazine carbons (171.7 ppm) showing the electron-withdrawing influence of bromine. The cerium-modified COFs exhibited enhanced antibacterial effectiveness against Staphylococcus aureus, with inhibition zones measuring 3.5 cm (control), 2.2 ± 1.5 cm (TbBr-COF), 3.1 ± 0.5 cm (CeO2-NP), 3.5 ± 0.6 cm [Ce-(TbBr-COF)-C], and 2.9 ± 0.4 cm [Ce-(TbBr-COF)-L]. The TbBr-COFs, distinguished by tunable porosity, high surface area, and metal incorporation capability, offer a versatile platform for drug delivery, antibacterial applications, and hybrid material synthesis.

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Functional importance of Camptothecin and Sotorasib , DPPIV inhibitors in PDAC Cancer apoptosis

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Keywords: Pancreatic ductal adenocarcinoma (PDAC); KRAS mutation (G12C/G12D); Sotorasib; Sitagliptin; Linagliptin; Camptothecin; Drug repurposing; Combination therapy; Apoptosis; Autophagy; Reactive oxygen species; Chemoresistance; Network pharmacology.

Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive malignancy with poor prognosis, mainly driven by oncogenic KRAS mutations, especially KRAS G12C and G12D. Although, targeted therapies such as Sotorasib have shown clinical benefit, rapid acquired resistance limits their long-term efficacy. Drug repurposing and rational combination strategies offer cost-effective and promising ways to overcome therapeutic resistance in KRAS-driven cancers. In this study, we investigated the anticancer potential of the Dipeptidyl Peptidase-4 (DPP-4) inhibitors Sitagliptin and Linagliptin, and the synergistic efficacy of Camptothecin combined with sotorasib in KRAS-mutated PDAC cell lines (MIA PaCa-2 and PANC-1). We performed functional assays including MTT, wound healing, colony formation, ROS detection, DNA fragmentation, apoptosis, autophagy flux, cell cycle analysis, and qRT-PCR, followed by network pharmacology, Gene Ontology, and KEGG pathway enrichment analyses. Our findings showed that sitagliptin and linagliptin significantly suppressed proliferation, migration, and clonogenicity, while enhancing ROS-mediated apoptotic cell death. The combination of camptothecin and sotorasib produced strong synergistic effects, inducing G1/S cell cycle arrest, upregulating pro-apoptotic genes, downregulating KRAS pathway-associated genes, and modulating autophagy-related markers compared to monotherapies. Network analysis further supported the involvement of apoptosis- and autophagy-related hub genes. These findings provide strong preclinical evidence supporting DPP-4 inhibitor repurposing and combination strategies to improve therapeutic outcomes in KRAS-mutated PDAC.

Prevalence of DPYD Alleles and their Association with Fluoropyrimidines Toxicity: A Pilot Pharmacogenetic Study in Gastrointestinal Cancer Patients in Central India

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Aim and Objectives:

To evaluate the comparative prevalence of selected DPYD gene polymorphisms (*9A, *5, *6, and rs2297595) in central Indian gastrointestinal cancer patients versus observed allele frequencies in IndiGenomes and global population data, and to determine their association with fluoropyrimidine-induced toxicity.

Methodology:

This pilot, an observational ambispective study included 50 adult gastrointestinal cancer patients receiving fluoropyrimidine-based chemotherapy. Demographic, clinical, treatment, and toxicity data were recorded using structured case records. Peripheral blood samples were collected for DNA extraction and genotyping of DPYD polymorphisms done using real-time PCR–based TaqMan predesigned SNP assays. Toxicity was graded using standard criteria. Minor allele frequencies were calculated and compared with IndiGenomes and global datasets, and genotype–toxicity associations were analysed using relative risk estimation.

Results:

Minor allele frequencies (MAF) observed in the 50 study participants were 0.25 for DPYD*9A, 0.06 for DPYD*5, 0.09 for DPYD*6, and 0.13 for rs2297595, which were broadly comparable with IndiGenomes and global population datasets, with relatively higher frequencies noted for DPYD*6 and rs2297595 in this Central Indian population.

Of which, 24% experienced at least one severe toxicity (Grade ≥3) and 74% developed multiple adverse drug reactions (>2 ADRs). The mean number of ADRs per patient was 4.7, and the mean ADRs per cycle was 1.51. Gastrointestinal toxicities were most common (78%), followed by general disorders (72%), vascular toxicities (30%), and neurological toxicities (16%).

Allele-specific analysis showed variable risks across DPYD polymorphisms. For severe toxicity, the relative risk (RR) was highest among DPYD*6 carriers (RR 2.28) and DPYD*9A carriers (RR 1.78). For multiple toxicities, the RR was 1.06 for *6, 0.97 for *9A, 0.89 for *5, and 0.95 for rs2297595. Neurotoxicity risk was elevated among *9A (RR 2.12) and *6 carriers (RR 1.52), while vascular and general toxicities showed minimal or lower associations across alleles.

Conclusion: DPYD polymorphisms, particularly DPYD*6 and DPYD*9A, showed a trend toward increased severe and neurological toxicity in fluoropyrimidine-treated patients. Though associations were modest, warranting validation in larger cohorts. Such findings can further inform pharmacogenetic clinical implementation.

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Diagnostic Potential of FOXO3a in Alzheimer's Disease: Evidence from Serum-Based Analysis

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Keywords: Alzheimer's Disease, Mild Cognitive impairment, Oxidative stress, FOXO3a, Blood based biomarker

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline and memory impairment. Oxidative stress is a major contributor to AD pathogenesis. Forkhead box O3a (FOXO3a) is a key transcription factor involved in cellular stress responses, mitochondrial homeostasis, and aging-related pathways. Dysregulation of FOXO3a may compromise oxidative stress resistance and metabolic balance, thereby accelerating neurodegeneration in AD.

Methods: Serum FOXO3a, Tau and pTau levels were quantified in individuals with AD (n=63), mild cognitive impairment (MCI, n=59), and age-matched geriatric controls (GC, n=58) using surface plasmon resonance (SPR) and compared with TauPET. Serum levels were further validated by Western blotting. Receiver operating characteristic (ROC) analysis and Pearson's correlation were performed to assess diagnostic accuracy and association with cognitive function.

Results: Serum FOXO3a levels were significantly reduced in AD (1.43 ± 0.04) and MCI (1.59 ± 0.13) groups compared to GC (1.89 ± 0.22). Tau was higher in AD (49.69 ± 2.38) and MCI (43.12 ± 1.19) as compared to GC (38.83 ± 3.6), both in serum and in PET scan. Serum pTau was higher in AD (0.18 ± 0.01) and MCI (0.15 ± 0.002) as compared to GC (0.15 ± 0.007). FOXO3a, Tau and pTau, demonstrated strong discriminatory power between AD vs. GC, MCI vs. GC as well as between AD vs MCI, with high sensitivity and specificity. Moreover, FOXO3a levels showed a significant positive correlation, while Tau and pTau showed a significant negative correlation, with cognitive scores, indicating an association with disease severity.

Conclusion: The findings suggest that reduced serum FOXO3a is associated with cognitive decline. Serum FOXO3a holds promise as a potential non-invasive blood-based biomarker for the early diagnosis and monitoring of AD.

Development of a Novel inhibitor of Rac1, for the Prevention of Breast Cancer Progression and Metastasis

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Key words Breast cancer; Inhibitor, Apoptosis; Rac1; Metastasis; Tumor

Introduction; Metastatic breast cancer is one of the leading causes of death, due to the dormancy of cancerous cells between the normal and metastatic stage. Thus, making it essential to target the molecular pathways which initiate the cell migration. During the early stages of cancer, the expression of Rac1 has been reported to higher and it remains the same throughout the metastatic pathway to regulate the formation of lamellipodia and filopodia. This study introduces a small peptide FGDWS based on the structure of Tiam1 binding site on Rac1.

Methods: The binding of peptide with Rac1 was verified by Surface plasmon resonance. The inhibition of Rac1 by the peptide and in combination with Doxorubicin (Dox) was assessed by MTT, anti-proliferative, cell migration, and apoptotic assay on breast cancer cells. Tumor regression experiment was done on swiss albino mice model.

Result: The peptide FDGWS showed strong interaction with Rac1 at Tiam1 binding sites with high binding energy by hydrogen bonds and hydrophobic interaction. The binding assay demonstrated dissociation constant KD 8.07 x 10^{-7} M. Substantial reduction of cell viability was observed with IC50 200 µm and 325 µm, in MCF-7 and MDA-MB-231, respectively. The cancer cell migration was highly reduced, and higher regression in migration was obtained in synergy groups with FGDWS and Dox. Peptide alone and with Dox induced apoptosis by activating caspase3/7 and annexin V. Treatment of FGDWS on breast cancer cell lines reduced the expression of Rac1 protein and other downstream proteins (p38MAPK, phospho-p38MAPK LIMK1, phospho-LIMK1, Cofilin1, phospho-Cofilin1) compared to untreated cells. The tumor size reduced by the treatment of peptide and more reduced in combinatorial effect with Dox. Further, the level of above-mentioned proteins down regulated in blood and tumor tissues after the treatment compared to untreated mice.

Conclusion: FGDWS can be a potent and specific therapeutic agent against Rac1 for breast cancer without developing toxicity on normal cells. The combinatorial effect of FGDWS and Dox may lead to therapeutic benefits both by enhancing treatment efficacy and by avoiding undesirable side effects.

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Association of Islet Amyloid Polypeptide and Inflammatory Biomarkers in Diabetic Coronary Artery Disease

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Keywords: cardiac myocytes, hyperamylinemia, insulin resistance, inflammatory mechanism, proteotoxicity.

Introduction: Type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) poses major threat worldwide contributing to excessive morbidity and mortality, these co-morbidities synergistically interact with inflammatory mechanisms. Amylin is fraternal twin of insulin, it has a great potential to fibrillation, aggregate formation, and deposition causes proteotoxicity to vital organs.

Aim: To find the association of amylin with inflammatory markers in T2DM with CAD subjects.

Methodology: Present cross-sectional study conducted on 262 subjects (30–60 years) T2DM with angiographically proven CAD cases (n = 131) and healthy controls (n = 131). The diabetic and lipid profile were estimated, and Serum Amylin, Insulin, hsCRP, TNF-α, and IL-6 levels were assessed by ELISA. Ethical approval and written informed consent were obtained. Subjects with other inflammatory diseases were excluded. Data were analyzed on SPSS-25 and descriptive statistics were performed for $p \leq 0.05$ (95% CI). Association between variables and area under the receiver operating characteristic curve (AUC of ROC) were performed to find the discrimination power.

Results: Blood Sugar Level-Fasting, Blood Sugar Level-Post Prandial, Glycosylated Haemoglobin (HbA1c), Insulin resistance (HOMA-IR), serum Total Cholesterol (TC), Triglyceride (TG), Low Density Lipoprotein- Cholesterol (LDL-C), very low density lipoprotein-Cholesterol (VLDL-C) and Non-HDL-C were significantly raised, whereas Insulin sensitivity check index (QUICKI) and high Density Lipoprotein-Cholesterol (HDL-C) decreased ($p \leq 0.001$) in T2DM-CAD compared with that of the control. The elevated level of amylin shows strong positive cor relation with TG and also with raised level of hsCRP, IL-6, and TNF-α in T2DM-CAD ($p \leq 0.001$), which may due to cytokines released by monocytes/macrophages. Hyperamylinemia could promote amylin deposition in pancreas causing apoptosis of pancreatic β-cells and causes structural and functional changes of cardiac myocytes in heart.

Conclusion: Assessment of amylin with inflammatory cytokines may predict pancreatic as well as cardiac dysfunction and it is helpful in stratification of severity risk; may provide a novel therapeutic target for DM-CAD patients.

Evaluation of Lipid Profile, High Sensitivity C-Reactive Protein (Hs-CRP), and Homocysteine in Premature Acute Myocardial Infarction: A Cross-Sectional Study

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Background: The incidence of acute myocardial infarction (AMI)in young adults is rising, presenting a significant public health challenge in developing nations like India.[1] While traditional risk factors are well-documented, the specific roles of novel inflammatory and thrombotic biomarkers in premature AMI remain under-evaluated in rural Indian populations.[3]

Materials and Methods: A cross-sectional study was conducted at a tertiary care center in Maharashtra, India, involving 105 participants. Subjects were divided into three groups: Young AMI (20–40 years, n=20), Old AMI (≥40-years, n=32), and age-matched healthy controls (n=53). Fasting venous blood samples were analyzed for lipid profile, hs-CRP, and homocysteine. Statistical analysis was performed using ANOVA for group comparisons and Receiver Operating Characteristic (ROC) curves to evaluate diagnostic accuracy.

Results: Young AMI patients were predominantly male (85%) and exhibited high rates of physical inactivity (90%) and non-vegetarian dietary habits (85%). The Young AMI group demonstrated significant atherogenic dyslipidemia, characterized by elevated triglycerides (238.00 ± 136.05 mg/

dL), total cholesterol, and LDL, with significantly reduced HDL (32.06 ± 9.96 mg/dL) compared to healthy controls (p<0.01). Inflammatory and thrombotic markers were markedly elevated; the mean hs-CRP was 4.33 ± 5.25 mg/L and homocysteine was 17.54 ± 11.10 µmol/L in Young AMI patients. ROC analysis revealed excellent predictive validity for both homocysteine (AUC 0.970) and hs-CRP (AUC 0.957) in identifying myocardial infarction.

Conclusions: Premature AMI in this population is strongly associated with modifiable lifestyle factors, atherogenic dyslipidemia, and elevated markers of inflammation and thrombosis. Both homocysteine and hs-CRP serve as robust independent predictors of AMI in young adults. Routine screening of these biomarkers may aid in early risk stratification and preventive intervention.

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Study Of Metabolic Risk Factors Contributing to Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) With and Without Diabetes.

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Key Words: MASLD, Diabetes mellitus, Insulin resistance, Dyslipidaemia, Liver enzymes

Introduction: Metabolic dysfunction associated steatotic liver disease (MASLD) is closely associated with insulin resistance, dyslipidaemia, and type 2 diabetes mellitus. Diabetes may further aggravate metabolic abnormalities and hepatic injury in MASLD patients.

Aim: To study metabolic risk factors in MASLD patients with and without diabetes.

Objectives: To compare the Biochemical and Metabolic risk factors in patients of MASLD who have Diabetes compared to non-diabetic patients with MASLD.

Methods: In this cross-sectional study, 30 MASLD patients were divided into MASLD with diabetes (Group 1, n=15) and MASLD without diabetes (Group 2, n=15). Glycaemic parameters, insulin resistance markers, lipid profile, and liver function tests were assessed. Data were expressed as mean ± SD.

Results: Group 1 showed significantly elevated fasting glucose (156.0 ± 10.4 vs 95.87 ± 5.05 mg/dL; p < 0.001), post-prandial glucose (259.0 ± 20.4 vs 132.47 ± 7.39 mg/dL; p < 0.001), and HbA1c (8.47 ± 0.60 vs 5.53 ± 0.22%; p < 0.001). Serum insulin (21.5 ± 3.1 vs 11.99 ± 1.94 µIU/mL; p < 0.001) and HOMA-IR (8.57 ± 1.63 vs 2.86 ± 0.61; p < 0.001) indicated significantly more insulin resistance in diabetic MASLD patients. AST (57.1 ± 8.7 vs 44.33 ± 6.61 U/L; p <0.001) and ALT (84.9 ± 8.9 vs 63.53 ± 4.76 U/L; p < 0.001) were significantly higher in Group 1 compared to Group 2.

Conclusion: MASLD patients with diabetes exhibit greater metabolic derangements and hepatic enzyme elevation, highlighting diabetes as an important metabolic risk factor.

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Study of Pancreatic Biomarkers in patients of Prediabetes and Type 2 Diabetes Mellitus

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Keywords: Diabetes mellitus, Prediabetes, Type 2 diabetes, Pancreatic biomarkers, Serum amylase, Serum lipase, HOMA-IR.

Introduction: Diabetes mellitus is a metabolic disorder characterized by high blood sugar levels. Prediabetes is an early stage of blood sugar abnormality, with values higher than normal but below the diabetic range. People with prediabetes have an increased risk of progressing to type 2 diabetes mellitus (T2DM). Changes in glucose levels may affect exocrine enzyme secretion, such as amylase and lipase, which reflect pancreatic function.

Aim: To study pancreatic biomarkers in patients of Prediabetes and Type 2 Diabetes mellitus

Objectives: To measure serum pancreatic amylase and lipase in prediabetic and T2DM patients and assess their relationship with blood sugar, insulin, insulin resistance (HOMA-IR), lipid profile, and body mass index.

Methods: This cross-sectional study included 30 participants, divided into prediabetes (Group 1, n=15) and T2DM (Group 2, n=15). Blood tests included glycaemic parameters, serum insulin, HOMA-IR, lipid profile, serum amylase, and serum lipase.

Results: Prediabetic subjects showed elevated FBS (107.07 ± 4.59 mg/dL), PPBS (163.40 ± 12.41 mg/dL), HbA1c (6.11 ± 0.19%), insulin (11.41 ± 1.50 µIU/mL), and HOMA-IR (3.03 ± 0.53), which were significantly higher in T2DM (171.53 ± 11.22 mg/dL, 282.33 ± 23.96 mg/dL, 8.57 ± 0.54%, 18.55 ± 2.08 µIU/mL, and 7.90 ± 1.40; $p < 0.001$). Serum amylase and lipase were reduced in prediabetes (70.13 ± 3.23 U/L; 48.67 ± 3.22 U/L) and showed a further significant decline in T2DM (54.93 ± 3.20 U/L; 36.00 ± 2.59 U/L; $p < 0.001$).

Conclusion: Serum amylase and lipase progressively decline from prediabetes to T2DM, suggesting worsening exocrine pancreatic function with increasing glycaemic derangement.

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To study comparison of accuracy of spot Urine Protein/creatinine ration with 24-hour urine protein estimation in assessing degree of proteinuria in Chronic Kidney disease patient

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Corresponding Email: sultanshabana50@gmail.com), (badadezg@gmail.com)**Introduction:** Proteinuria is an important marker of disease severity and progression in chronic kidney disease (CKD). Although 24-hour urine protein estimation is considered the gold standard for quantifying proteinuria, it is time-consuming and prone to collection errors. The spot urine protein/creatinine ratio (UPCR) offers a convenient alternative.

Objectives: To study comparison of accuracy of spot urine protein creatinine ratio with 24-hour urine protein estimation in assessing degree of proteinuria in chronic kidney disease.

Methods: The study includes 55 participants diagnosed with chronic kidney disease attending the nephrology OPD and also patients admitted in medicine ward of MGM Hospital Kamothe during January to December 2025. Urine samples are collected and processed for UPCR and 24-hrs urine protein.

Results: A total of 55 chronic kidney disease patients aged 18–85 years were studied. The mean age is 54.6 ± 15.8 years. The mean 24-hour urine protein excretion is 3.01 ± 1.76 g/day, while the mean spot urine protein/creatinine ratio (UPCR) is 2.84 ± 1.78 g/g.

A strong positive correlation was observed between UPCR and 24-hour urine protein excretion ($r = 0.97$, $p < 0.001$). UPCR accurately reflected the severity of proteinuria across mild, moderate, and nephrotic range, showing good agreement with 24-hour urine protein estimation

Conclusion: Spot urine protein-to-creatinine ratio is a reliable, convenient, and accurate alternative to 24-hour urine protein estimation for assessing proteinuria in chronic kidney disease patients. Its use can reduce patient burden and improve clinical compliance in routine practice.

Key Words: Chronic kidney disease, Proteinuria, Spot urine protein/creatinine ratio, 24-hour urine protein, Renal function.

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Comparative Genomics Signatures of Venous Thromboembolism Across Altitudinal Extremes

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Background

Venous thromboembolism (VTE) is shaped by both genetic and environmental factors. High altitude causes hypoxic stress, affecting endothelial function and coagulation, and raising thrombosis risk. Molecular evidence distinguishing high-altitude from sea-level VTE remains limited. In this pilot study, we investigated differential gene expression patterns between high-altitude VTE patients (HAP) and sea-level VTE patients (SLP), focusing on coagulation and endothelial regulation genes.

Methods

A targeted panel of 10 genes associated with VTE were chosen due to their involvement in coagulation processes and endothelial activation. Total RNA was isolated from whole blood, and cDNA was synthesized using Qiagen First Strand cDNA Synthesis kit, followed by qRT-PCR for gene expression. Differential gene expression was analyzed using fold change, and statistical significance was determined using p-values.

Results

Patients with high-altitude VTE experienced significant upregulation of *FGF2, F10, and F2,* indicating enhanced endothelial activation and amplification of the common coagulation pathway under hypoxic conditions. In contrast, *PROCR*, an anticoagulant gene, was downregulated, suggesting impaired anticoagulant regulation. The molecular findings correspond with the recognized clinical biomarkers that signify coagulation activation and endothelial dysfunction.

Conclusion

In conclusion, this pilot study identifies a distinct hypoxia-associated transcriptional signature in high-altitude VTE, characterized by upregulation of *FGF2, F10, and F2*, and downregulation of *PROCR*. This comprehensive transcriptional modification distinguishes high-altitude venous thromboembolism (VTE) from cases at sea level, clarifying the mechanisms responsible for the heightened thrombotic risk at high altitudes and require validation in larger cohorts.

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An In Silico Quest: Validating the Cardioprotective Efficacy of CQA Against the Hypoxia and Hyperglycemia stressors.

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Keywords: Cardiovascular disease, CQA, ADMET analysis, molecular docking, molecular dynamic simulation

The natural rhythm of the heart has become a global call for concern due to the alarming rise in cardiovascular disease (CVD) mortality, which has increased from 13.1 million deaths in 1990 to 19.2 million in 2023. Hypoxia and hyperglycaemia are major contributors to CVD pathogenesis, creating an urgent need for novel cardioprotective agents. This study explores the potential of a natural compound, **CQA** to mitigate these stressors through comprehensive in-silico analyses. Molecular docking was employed to evaluate its inhibitory potential against the prolyl hydroxylase domain 2 (PHD2) protein (PDB ID: 5L9B) using Discovery Studio and Auto Dock Vina. Pharmacokinetic, toxicity, and drug-likeness profiles were assessed via SwissADME, ProTox 3.0, and pkCSM, while PASS analysis predicted its biological activity spectrum. To assess structural stability and interaction dynamics, molecular dynamics (MD) simulations were performed using GROMACS. The docking results revealed that **CQA** exhibited a binding energy of –6.8 kcal/mol, showing better interactions compared to standard drugs. ADMET and PASS predictions indicated favourable pharmacokinetics and safety, while MD simulations demonstrated enhanced stability of the ligand–protein complex relative to the native protein. Overall, the computational findings suggest that Caffeoylquinic acid possesses significant cardioprotective potential, warranting further, *in-vitro* and *in-vivo* validation to advance its development as a promising therapeutic shield for preserving heart function.

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Review - Nature's Pharmacy: Aloe Vera for the fight against Tuberculosis

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We have already come a long way, but a long way is still to be covered. The world has come forward in all terms, but diseases like Tuberculosis still hold the potential to take us back, especially when it comes to middle and low-income countries. TB's contribution to the world's mortality rate remains significantly high, compounded by the rise of multidrug-resistant (MDR) TB and the adverse side effects of commonly administered first-line drugs for the disease.

Medicinal plants have been a cure for most diseases since time immemorial, and half of our population still relies on them. Regarded as the backbone of traditional medicine, they are now central to efforts to combat diseases. According to WHO estimates, about 80% of the population in developing and underdeveloped countries depend on traditional herbal or botanical medicines for their primary health care needs. India has a rich diversity of medicinal plants with over 3,500 discovered species. There has been an accelerating interest in phytotherapy, integrating natural products as complements to boost the treatment efficacy and to scale down the side effects.

This review explores the possibility of Aloe vera as an adjunct in the TB treatment. It also assesses its potential synergy with first and second-line anti-TB drugs, examines its activity against multidrug-resistant TB, and evaluates its safety and pharmacokinetics. The aim is to critically study Aloe vera's contribution to anti-TB drug discovery and propose a roadmap for its integration into global TB control programs.

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Journal of Academy of Biomedical Sciences
An official Journal of Indian Academy of Biomedical Sciences (IABS)
www.iabsjournal.com

Artificial Intelligence in Transformative Mental Healthcare Research

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Mental health is an essential component required for one's overall development that helps us to make decisions and maintain interpersonal relationships. Recent developments in Artificial Intelligence (AI) have a significant potential in analyzing neurodegenerative disorders and thereby leading to the improvement in mental healthcare research. Parkinson Disease (PD) is a complex neurological disorder attributed by loss of neurons generating dopamine in the Substantia Nigra per compacta. Electroencephalogram (EEG) plays an important role in diagnosing PD as it offers a non-invasive continuous assessment of disease progression and reflects the complex patterns. The experimental study on an open EEG dataset consisting of 14 PD and 14 healthy individuals are subjected to Recurrence quantification analysis specific to gender, brain regions and EEG bands. The extracted recurrence features served as inputs to the Machine learning (ML) models, which achieved high classification performance across all the scenarios. The interpretability of the ML model decisions is investigated using explainability technique. In addition to this, Fuzzy recurrence plots and Deep learning algorithms are applied to examine the effects of eyes open and eyes closed conditions during ON and OFF medication states in PD patients. The progression of the neurodegenerative diseases, the effect of treatment, and its responses continuously change with time. This leads to the need for longitudinal data acquisition using multiple modalities. Hence, the performance of AI algorithms can be enhanced through the analysis of multimodal and longitudinal data. This paves the way to "Personalized AI" which is the recent trend in healthcare research.

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Circulating microRNAs as Predictive Biomarkers for Methotrexate Efficacy in Psoriasis: A Translational Discovery-Validation Study

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Background: Psoriasis is a chronic immune-mediated inflammatory disease with inter-individual variability in response to methotrexate (MTX), the most commonly used first-line systemic therapy in India. The absence of validated predictive biomarkers often delays therapeutic optimization. Circulating microRNAs (miRNAs), as stable post-transcriptional regulators of immune and inflammatory pathways, represent biologically plausible and minimally invasive biomarkers. This study aimed to identify and validate circulating miRNA signatures associated with MTX response in psoriasis.

Methods: A translational two-phase discovery–validation study design was employed. In discovery phase, global miRNA profiling using NGS was performed in 30 psoriasis patients and 30 age- and sex-matched healthy controls to identify disease- and MTX response–associated miRNAs. Candidate miRNAs were shortlisted based on fold change,

false discovery rate, biological relevance, and novelty. Validation was carried out using q-PCR in an independent cohort of 216 psoriasis patients receiving MTX. Clinical response was assessed at baseline and at 24 weeks using PASI and DLQI.

Results: Eleven candidate miRNAs were selected for validation. In validation cohort, 153 patients achieved treatment response, while 63 were non-responders. MTX therapy resulted in significant reductions in PASI and DLQI scores ($p<0.001$). Differential expression of miR-204-5p, miR-7-5p, miR-211-5p, miR-34c-5p, and miR-9-5p showed strong associations with treatment response and inflammatory pathways, representing one of the largest independent Indian cohorts validating circulating miRNAs in psoriasis.

Conclusion: This study provides robust translational evidence supporting circulating miRNAs as predictive biomarkers of methotrexate responsiveness and represents a rigorously validated translational biochemistry study enabling biomarker-guided methotrexate therapy in psoriasis.