NATIONAL CONFERENCE ON OMICS IN REDEFINING HEALTHCARE

ABSTRACTS & SOUVENIR

23 & 24 AUGUST 2024

ORAH

OMICS-REVOLUTIONIZING APPROACHES IN HEALTHCARE

Editors
Dr Dileep K.V., Dr Remya C., Dr Saji K.G.,
Ms Mridula V., Ms Vanditha M. and Ms Hafiza P.

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Dear Delegates,

I am extremely happy to have the opportunity to organize this prestigious national conference on OMICS in redefining healthcare.

As the Organizing Secretary of this event, I hope this proposed conference will provide an excellent platform to exchange knowledge as well as gain an insight into the current techniques and applications in the evolving field of OMICS. These two days will be a combination of interesting deliberations and engaging discussions that will enrich our current knowledge and skills.

The **OMICS sciences** aim to identify, describe, and quantify the biomolecules and molecular processes that contribute to the form and function of cells and tissues. Over time, various branches have evolved, including genomics, proteomics, transcriptomics, lipidomics, metabolomics, and bioinformatics. The impact of OMICS is most apparent in medicine. The sequencing of the human genome has significantly advanced personalized medicine. Similar connections between OMICS and personalized medicine have emerged from metabolomics, which has led to the discovery of new disease biomarkers with the potential to improve early diagnosis. However, managing and integrating data from OMICS studies with other sources, such as clinical data collected during routine physician visits, remains a challenging task for scientists. Bioinformatics and computational biology are working to address this gap and facilitate the interpretation of experimental data, often on a very large scale.

On behalf of the organising committee, I extend a warm welcome to all our speakers, participants and colleagues to the National Conference on OMICS in Redefining Healthcare scheduled for August 23rd and 24th, 2024, at the Jubilee Centre for Medical Research in Thrissur, Kerala, India.

We also extend our gratitude to our co-sponsors—DBT, SERB, KSCSTE, CSIR and DSIR—and other esteemed benefactors for wholeheartedly supporting this initiative and going a long way in bringing it to fruition.

We hope that this interaction between clinicians and scientists will help bridge the gap between current medical practices and the latest knowledge in OMICS. We also hope that scientists and the medical community will converge on a common understanding to redefine healthcare in the OMICS era.

Welcome to the National Conference on OMICS in Redefining Healthcare, ORAH 24

Dr P R Varghese
Organising Secretary

Day 1 –Friday 23rd August 2024

8.00 AM	**Registration**
8.00 AM to 9.00 AM	**Breakfast**
9.15 AM to 10.55 AM	**Genomics in Clinical Medicine I** **Dr. K Thangaraj, PhD** Centre for Cellular and Molecular Biology, Hyderabad *Topic: Population Genomics and Public Health* **Dr. Vinod Scaria, MBBS, PhD** Vishwanath Cancer Care Foundation, Bangalore *Topic: Personal Genomes for Precision Medicine* **Dr. Kausik Mandal, MD, DM** Sanjay Gandhi Post-Graduate Institute of Medical Sciences, Lucknow *Topic: Sequencing and MLPA in clinical practice* **Dr. Moinak Banerjee, PhD** Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram *Topic: Deriving hopes in autism spectrum disorders: Challenges and opportunities*
10.55 AM to 11.15AM	**Industry Presentations** ***Cytiva***
11.15 AM to 11.30 AM	Tea Break
11.30 AM	**Inauguration**
12.30 PM to 2.00 PM	**Lunch & Poster Session I Genomics and Proteomics**
2.00 PM to 3.15 PM	**Bioinformatics in Health & Disease I** **Dr. R Sowdhamini, PhD** National Centre for Biological Sciences, TIFR, Bangalore *Topic: Structural studies on disease-associated mutants of a lipid phosphatase* **Dr. Rahul Kaushik, PhD** Technology Innovation Institute, Abu Dhabi UAE *Topic: Harnessing Computational Protein Folding, Design, and Engineering: A Case Study on Screening Neutralizing Antibodies Against SARS-CoV-2* **Dr. Dileep K Vijayan, PhD** Jubilee Centre for Medical Research, Thrissur *Topic: One random molecule to a high precision drug: The transformation through computational and structural biology*
3.15 PM to 4.05 PM	**Proteomics in Healthcare I** **Dr. P S Suresh, PhD** National Institute of Technology, Calicut *Topic: A study on the interplay between phosphatase-estradiol receptor and non-coding RNA in breast cancer*

Dr. Arkasubhra Ghosh, PhD
Narayana Nethralaya, Bangalore
Topic: Distinct proteomic profiles associated with human diseases and consequent clinical applications

4.05 PM to 4.30 PM Tea Break

4.30 PM to 7.00 PM **Young Scientist and Best Paper Award Competitions**
Venue @ Mother Theresa Hall – Bioinformatics
New CCM Hall – Genomics
Old CCM Hall – Proteomics

7.00 PM to 7.30PM Cultural Program

7.30 PM Dinner

Day 2 – Saturday 24th August 2024

7.30 AM to 8.30 AM **Breakfast**

8.40 AM to 9.30 AM **Bioinformatics in Health & Disease II**

Dr. Dileep Vasudevan, PhD
Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram
Topic: Characterization of a Plasmodium falciparum protein as a nucleoplasmin: A structure function approach

Dr. Aditya K Padhi, PhD
Indian Institute of Technology (BHU), Varanasi
Topic: A Multifaceted Approach Integrating Protein Design, Machine Learning, QM/MM, and Clinical Insights to Unveil Resistance Mutations in SARS-CoV-2

9.40 AM to 11.20 AM **Genomics in Clinical Medicine II**

Dr. Ashwin Dalal, MD, DM
Centre for DNA Fingerprinting and Diagnostics, Hyderabad
Topic: Mission Program in Paediatric Rare Genetic Disorders (PRaGeD)

Dr. Sreelata B Nair, PhD
Lifeline Super Specialty Hospital, Adoor, Kerala
Topic: Genetics and Genomics in Reproductive Medicine- Expectations & Realities

Dr. Sumita Danda, MD, DM
Christian Medical College & Hospital, Vellore
Topic: *Genetic basis and its utility in "Inborn errors of metabolism"*

Dr. Ravindran Ankathil, PhD
Jubilee Centre for Medical Research, Thrissur
Topic: Cancer genomics in the era of precision oncology with emphasis on myeloproliferative neoplasms

11.20 AM to 11.40 AM	**Tea Break, Poster II Bioinformatics** & **Multi OMICS**
11.40 AM to 11.55 AM	***Industry Presentations DDRC Agilus***
12.00 AM to 12.15 PM	**Special Session on Multi OMICS**
	Dr. Sheela Nampoothiri, DNB, M.Sc Amrita Institute of Medical Sciences, Kochi *Topic: Lethal aortopathy due to Fibulin 4*
12.15 PM to 12.45 PM	**Contributing Speakers**
	Dr. Shubhra Ghosh Dastidar, **PhD** Bose Institute, Kolkata *Topic: Allosteric Changes in Drug Targets: Insights from Jiggling Ball-and-Stick Models*
	Dr. Yasmin Ahmad, PhD DRDO, Timarpur, Delhi *Topic: Decoding Hypobaric Hypoxia: Advances in Proteomics, Prophylaxis, and Modelling Approach*
	Dr. Abhishak Chandra Gupta, PhD Artemis Hospital, Haryana *Topic: Expression of Arginase-1 specific to the liver in the diagnosis of non-alcoholic fatty liver disease progression.*
12.45 PM to 1.45 PM	**Lunch Poster II Bioinformatics & Multi OMICS**
1.45 PM to 2.45 PM	**Contributed papers** Venue **I** Mother Theresa Hall – Proteomics: Venue **II** New CCM Hall - Genomics & Bioinformatics
2.50 PM to 4.05PM	**Proteomics in Healthcare II**
	Dr. B K Binukumar, PhD CSIR-Institute of Genomics and Integrative Biology, New Delhi *Topic: Cyclin-Dependent Kinase 5 to Neuronal Health: Deciphering Signaling Pathways in Neurodegeneration*
	Dr. K G Raghu, PhD Jubilee Centre for Medical Research, Thrissur *Topic: Identification of a lead for NAFLD acting via AMPK pathway and PPAR alpha modulation*
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Abstracts
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POPULATION GENOMICS AND PUBLIC HEALTH

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Modern India is a region of remarkable cultural, linguistic, and genetic diversity with over 4,500 anthropologically well-defined groups. We have been studying various Indian/South Asian populations to understand their origin, affinities, and impact of endogamy. Our genetic study provided evidence that the enigmatic tribal populations of Andaman Islands are the first modern humans, who migrated out of Africa (*Science*, 2005). Subsequently, we demonstrated that the contemporary Indian populations have descend from two divergent groups: (1) Ancestral South Indians, & (2) Ancestral North Indians (*Nature*, 2009), and these two founding groups have admixed during the past 2000 – 4000 years (*Am. J. Hum. Genet*., 2013). Since then, almost all the populations in Indian subcontinent have been practicing endogamy. To assess the impact of endogamy, we have analysed 275 distinct South Asian groups and found that 81 out of 275 groups have strong founder event than the one that occurred in both Finns and Ashkenazi Jews (*Nat. Genet*., 2017). We are now analysing populations with strong founder event to understand the genetic basis of diseases, which would help us to provide prenatal and premarital counseling to avoid disease burden.

PERSONAL GENOMES TO PRECISION MEDICINE

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Over the past two decades, the field of genomics has undergone transformative advancements, fundamentally changing the landscape of medical science and leading to the era of precision medicine. The sequencing of the human genome, completed in 2003, marked a pivotal milestone, setting the stage for a deeper understanding of the genetic underpinnings of health and disease. Since then, technological innovations have dramatically reduced the cost and time required for sequencing, making personal genomics increasingly accessible. This evolution has paved the way for its application in diagnosing rare genetic diseases, assessing carrier status, and evaluating cancer risk, thereby tailoring healthcare to individual genetic profiles.

The application of personal genomes in diagnosing rare genetic diseases represents one of the most significant advancements in clinical genomics. Traditionally, these conditions were challenging to diagnose due to their rarity and phenotypic variability. However, the integration of whole-genome and whole-exome sequencing has revolutionized this field. By allowing comprehensive analysis of an individual's genetic makeup, clinicians can now identify pathogenic variants that contribute to rare diseases, enabling precise diagnosis and facilitating early intervention and targeted therapy. This precision is especially crucial for conditions where early detection can significantly alter disease progression and improve patient outcomes.

Carrier screening has also benefited substantially from personal genomics. Couples planning to conceive can now undergo genetic testing to determine their risk of passing on genetic disorders to their offspring. This application of genomics helps identify carriers of autosomal recessive and X-linked conditions, enabling informed reproductive decisions and the consideration of alternative options such as *in vitro* fertilization with pre-implantation genetic diagnosis. The proactive identification of carrier status is a crucial step in reducing the incidence of hereditary diseases and advancing public health.

In cancer risk assessment, personal genomics plays an instrumental role in identifying individuals with genetic predispositions to various cancers. By analyzing specific mutations, healthcare providers can assess an individual's risk and recommend personalized surveillance strategies or preventive measures. This approach not only enhances early detection but also empowers patients with knowledge about their genetic risks, fostering proactive health management and

potentially reducing cancer incidence.

Pharmacogenomics, another cornerstone of precision medicine, leverages genetic information to optimize drug therapy. Understanding how genetic variations influence drug metabolism, efficacy, and toxicity allows clinicians to tailor medications to each patient's genetic profile. This approach minimizes adverse drug reactions and enhances therapeutic outcomes, representing a paradigm shift from the traditional "one-size-fits-all" model to a more individualized treatment strategy.

Beyond individual applications, the aggregation of genomic data from diverse populations offers invaluable insights into disease prevalence and genetic variation on a broader scale. Large-scale genomic databases enable researchers to identify patterns, correlations, and novel genetic markers associated with diseases. This aggregated data not only enhances our understanding of disease mechanisms but also informs public health strategies and the development of targeted interventions for at-risk populations.

In conclusion, the progression from personal genomes to precision medicine over the past two decades underscores the profound impact of genomics on healthcare. From diagnosing rare genetic diseases and assessing cancer risk to informing pharmacogenomic decisions and public health initiatives, genomics has become an indispensable tool in modern medicine. As the field continues to evolve, the integration of genomic data into clinical practice promises to enhance patient care, improve outcomes, and usher in a new era of personalized healthcare.

SEQUENCING AND MLPA IN CLINICAL PRACTICE

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Introduction: Genetic testing has become necessary for inherited (germline) and somatic variations giving rise to various constitutional genetic disorders and cancers in humans. Sequencing and Multiplex Ligation Probe Amplification (MLPA) are techniques which help to detect various single nucleotide changes, deletions and duplications (small and large) in the genome. Here we will be discussing the above two techniques and their utilities in inherited genetic disorders.

DNA sequencing: Sequencing essentially targets to find out the sequence of nucleotides in a given segment of the genome. We assume that a change of a nucleotide/ base (A, T, G or C) by another (substitution) or omission (deletion) or introduction (insertion/ duplication) of one or few nucleotides in an exon of a gene or in nearby areas is likely to affect the protein encoded by the gene. There can be a change in amino acid (missense mutation) in the sequence or introduction of a stop codon (Nonsense mutation), shift in the coding sequence (frameshift mutation) or aberrant splicing defect (splice-site mutation). The technique has evolved with time and can be divided into generations as below:

The Generations of DNA Sequencing

- **1st Generation**
  - **Sanger Sequencing**
  - Capillary based (96 capillaries * 4 hours) = 512 Seq / day
  - Di-deoxy sequencing reaction (prior to machine run)
  - Variable length reads; typically 700-1000 nucleotides long
- **2nd Generation**
  - **Illumina / Ion Torrent Sequencing (NGS)**
  - Chip or slide based sequencing of 'clusters' – 10s of millions of reads
  - Sequencing-by-synthesis – sequence is generated with cycles of incorporation
  - Typically fixed length short reads; 100nt – 250nt (depends on application / platform)

- **3rd Generation**
  - **"Long read sequencing" or SMRT-sequencing**
  - Continuous native process (ZMW + phospholinked nucleotides)
  - Variable length reads; 100 nt to 75,000 nt in length

Applications of Sanger sequencing

- Targeted analysis for known sequence variations
  - Achondroplasia
  - Apert
- Small genes with fewer than 15 to 20 exons
  - Beta- thalassemia (3 exons)
  - VHL (3 exons)
- Few small genes/ certain mutation causing the same phenotype
- Along with NGS
  - Validation of NGS result
  - Sequencing gaps
  - Targeted testing in family members for segregation
  - Targeted testing for prenatal

Applications of NGS:

NGS is done for

- Large gene where sequence variations are cause of disease
- Multiple causative genes for a phenotype
- Difficult clinical diagnosis
- Novel disease gene discovery

Panels: Exons and known mutations of selected genes responsible for similar phenotypes e.g. Nephrology panel, Hereditary cancer panel
Exome sequencing: Exons (comprises of 1% of genome) harbouring more than 80% of mutations
Whole genome sequencing: produces huge amount of data

Multiplex Ligation Probe Amplification (MLPA):

In various single gene disorders, the variation might be deletions or duplications which are fairly large, involving whole or large part of an exon (many nucleotides). Sequencing techniques, as described above are unable to pick them up, since, in heterozygous condition, the normal allele will amplify and show normal peaks in Sanger and in homozygous condition, the area of deletion would be uncovered in NGS. In such situations, the technique used is MLPA, which has the capability of dosage analysis.

Usefulness and limitations of MLPA

- Detect small deletions (less than around 4 Mb)
- Can also detect duplications
- Does not require living cells
- Shorter reporting time
- Limitations
    - Does not detect balanced translocations
    - Does not detect polyploidy
    - Prior knowledge of target

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DERIVING HOPES IN AUTISM SPECTRUM DISORDER: CHALLENGES AND OPPORTUNITIES

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Autism Spectrum Disorder is highly complex and there are multitude of factors that are associated with Autism, but still the real initiating factor remains an enigma. There is no clarity on its etiology and besides the etiology has to be understood from Indian perspective. In addition, ASD is often debated on grounds of gain and deficits in brain function. It implies tremendous genetic and phenotypic heterogeneity. ASD is also associated with large number of De novo mutations (DNM). What causes these DNMs? Besides the issue of ASD is somewhere determined at prenatal stage. It seems to have induced during maternal fetal interaction through stress, diet, circadian rhythmicity, medication, microbiome and comorbid history which in turn may regulate or define the etiology, pathology or phenotype. The threshold of all these influencing factors can be determined through their genetic and epigenetic predisposition. The influencing environmental and societal factors and their corresponding genetic and epigenetic factors are likely to be different from western literature. Besides the conflicting reports on the biochemical and neurochemical indicators of Autism, further complicate the issue. Therefore, it becomes all the more important to understand its influence based on underlying genetics and epigenetics. Some of these conflicts and ways to resolve will be discussed.

STRUCTURAL STUDIES ON DISEASE-ASSOCIATED MUTANTS OF A LIPID PHOSPHATASE

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Our laboratory is generally interested in protein sequence-structure-function relationships and recently we analysed genetic mutations on a gene, MTM1. Mutaions in this gene are implicated in X-linked myotubular myopathy which affects 1 in 50,000 male babies and children. MTM1 encodes for a protein that contains lipid phosphatase as the catalytic domain, accompanied by lipid-binding domain and a coiled-coil domain. The coiled-coil domain enables dimerization of the protein. We focussed on mutations in the lipid-binding domain and catalytic domain. Three-dimensional modelling, ligand docking and molecular dynamics of the wild type and select mutants revealed less stable interactions of the mutants with the substrate. Finally, in collaboration with Prof Raghu Padinjit's laboratory in NCBS, we employed appropriate in vitro assays to show that most of the deleterious mutants indeed bind less efficiently to the lipid or retain reduced catalytic activity. The learnings from this study provide additional impetus to examine other disease-causing mutations as well.

HARNESSING COMPUTATIONAL PROTEIN FOLDING, DESIGN, AND ENGINEERING: A CASE STUDY ON SCREENING NEUTRALIZING ANTIBODIES AGAINST SARS-COV-2

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Computational techniques are critical for understanding, diagnosing, treating, and managing diseases in a variety of medical and biological disciplines. Implementing computational protein folding, design, and engineering methodologies to better understand and target infectious diseases may prove a game-changing strategy at the crossroads of biology, computer science, and medicine. This multidisciplinary field seeks to decipher the complicated three-dimensional structures of proteins implicated in disease processes, predict their behavior under various conditions, and design new proteins with tailored functionalities to combat certain diseases. Computational protein folding begins with modeling the intricate folding pathways that proteins undergo to achieve their functional forms. In the realm of protein design, computational methods facilitate the creation of novel proteins or protein variants optimized for therapeutic purposes. This includes designing proteins that can bind to and inhibit crucial viral or bacterial targets, impairing their potency to infect host cells. Additionally, computational approaches aid in vaccine design by predicting antigen structures that can elicit robust immune responses. Optimizing the properties of therapeutic proteins, such as enhancing their stability, solubility, and specificity can be achieved through protein engineering for target specific strains of pathogens or to circumvent drug resistance mechanisms, thereby extending the effectiveness of treatments. The integration of computational protein folding, design, and engineering with experimental approaches has a huge potential to accelerate the drug discovery and development process through identification of promising drug candidates more efficiently and precisely. This synergy not only reduces the time and resources required for drug discovery but also expands the range of therapeutic options available for combating infectious diseases. Here, a computational framework to screen effective neutralizing antibody therapeutics against SARS-CoV-2 will be discussed as a case study to demonstrate an efficient integration of state-of-the-art computational approaches.

ONE RANDOM MOLECULE TO A HIGH PRECISION DRUG: THE TRANSFORMATION THROUGH COMPUTATIONAL AND STRUCTURAL BIOLOGY

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The journey from a random molecule to a high precision drug represents a remarkable transformation enabled by advancements in computational and structural biology. This process begins with the identification of a potential therapeutic molecule among countless candidates, often starting from a large chemical library or even a natural source.

Computational biology employs sophisticated algorithms and models to simulate the interactions between molecules and biological targets. Techniques such as molecular docking and molecular dynamics simulations allow researchers to visualize and optimize the binding of molecules to their targets with high precision. This significantly accelerates the initial stages of drug discovery, saving both time and resources.

Structural biology complements these efforts by providing detailed three-dimensional structures of biological molecules. Techniques like X-ray crystallography, cryo-electron microscopy, and nuclear magnetic resonance spectroscopy reveal the intricate architecture of proteins, nucleic acids, and other biomolecules. Understanding the exact structure of these targets enables scientists to design drugs that fit perfectly into the active sites, enhancing their specificity and effectiveness.

The integration of computational and structural biology not only streamlines the drug discovery process but also enhances the precision of the resulting therapeutics. By leveraging these advanced techniques, researchers can transform a random molecule into a high-precision drug with greater accuracy, predictability, and efficiency. This synergy holds immense promise for developing targeted therapies for a wide range of diseases, ultimately improving patient outcomes and advancing the field of medicine.

A STUDY ON THE INTERPLAY BETWEEN PHOSPHATASE-ESTRADIOL RECEPTOR AND NON-CODING RNA IN BREAST CANCER

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Breast cancer remains one of the leading causes of death among women worldwide. Antiestrogen treatment for breast cancer targets ER α. About 50% of ER-expressing breast cancer is fundamentally resistive to antihormone therapy, therefore increasing responsiveness is crucial. Dynamic ER phosphorylation and dephosphorylation impact antihormone response and activity. We studied whether *PTPH1* modulates ER tyrosine phosphorylation and breast cancer antihormone sensitivity. *In vitro* and in breast cancer cells, *PTPH1* dephosphorylates ER at Tyr537. Cell culture and xenograft models showed that *PTPH1* increases ER nuclear accumulation and breast cancer sensitivity to TAM and/or fulvestrant. Research indicated that *PTPH1*'s catalytic activity increased ER nuclear accumulation and breast cancer antihormone sensitivity. These studies identified *PTPH1* as a novel ER phosphatase and showed that dephosphorylating ER by *PTPH1* improves breast cancer susceptibility to antiestrogens. Suresh et al., 2014 Mol Cancer Ther). Immunohistochemistry and methylation-specific polymerase chain reaction were used to evaluate *PTPH1* protein expression, clinical characteristics, ER/PR/HER2/neu statuses, and promoter methylation in Indian breast cancer tissues. *PTPH1* was elevated in 58.21% (39/67) of tumors and downregulated in the remainder. It was linked to ER, PR, and HER2/neu statuses (p values <0.0001, 0.0113, and 0.0448). Breast cancer had significantly methylated CpG sites in the 2 kb region upstream of *PTPH1*. *PTPH1* status and the ER were strongly correlated with ubiquitous promoter methylation at specific CpG sites regardless of cancer type or protein expression (Venkatesh et al., J Cell Physiol, 2019). Long noncoding RNA-miRNA and mRNA axis studies in breast cancer will also be discussed in my talk.

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DISTINCT PROTEOMIC PROFILES ASSOCIATED WITH HUMAN DISEASES AND CONSEQUENT CLINICAL APPLICATIONS

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Disease pathology in the human body encompasses a variety of processes, signalling and interactions between various tissue specific cell types as well as immune cell types. The study of human disease mechanisms and potential treatments has traditionally relied on *in vitro* cell based models and animal models. However, with the advent of large scale techniques such as proteomics, and multiplex assays, immunophenotyping, etc, it became possible for deep phenotyping of human patients. We have meticulously established a biorepository of annotated clinical samples that now serve as an important tool to understand disease processes better. We can now analyse a large number of proteins from a patient tear samples and establish underlying disease biology. Using ocular surface conditions as an example, our proteomics data demonstrate unique new understanding about disease biology. We discovered that in the ocular surface dystrophy Keratoconus, that has a higher prevalence in south Asians and west Asians, there exist unique new mechanisms such as autophagy dysregulation, skewed inflammation apart from inflammation and extracellular matrix remodelling. These pathways correlated with multiplex protein assays and ocular surface immunophenotyping data that demonstrate a unique dysregulation in the Natural Killer (NK) cell and Neutrophil population. Using this knowledge, we have now developed a point of care diagnostic kit that informs the treating ophthalmologist about which procedure or treatment to be used for Keratoconus patients in the clinic. Further, the knowledge allowed for the unique application of autophagy modulators in Keratoconus for treatment. Since topical treatment methods are not available for Keratoconus treatments, our studies illustrate an evolving pathway for application of the knowledge generated from proteomics for clinical applications in both diagnostics and therapy.

CHARACTERIZATION OF A *PLASMODIUM FALCIPARUM* PROTEIN AS A NUCLEOPLASMIN: A STRUCTURE-FUNCTION APPROACH

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Plasmodium falciparum is a protozoan parasite that causes human malaria. The life cycle of *P. falciparum* is complex and involves multiple hosts and various developmental stages. An organized regulation of gene expression and DNA replication in the various developmental stages is critical for the parasite. A precise gene regulation event is dependent on the dynamic architecture of chromatin, which in turn is governed by several factors, such as histone chaperones, epigenetic factors, and chromatin remodelers. Nucleoplasmins, a class of histone chaperones, perform histone chaperoning activity and are involved in various developmental processes in eukaryotes. However, the presence of a nucleoplasmin isoform has not been reported in the malarial parasite. A search in the PlasmoDB database revealed a possible single isoform of nucleoplasmin in *P. falciparum* and we went ahead characterizing the same. Our crystallographic studies confirmed that the N-terminal core domain of the protein adopts the characteristic pentameric doughnut conformation. Each monomer features eight beta strands antiparallel to one another, yielding a beta-sandwich fold arranged in two sheets. Furthermore, our studies revealed that PfNPM exists as a pentamer in solution, and the nucleoplasmin core domain exhibits high thermal and chemical stability. Further, our interest was to check whether the protein shows histone interaction properties, like other characterized histone chaperones. PfNPM pentamer was found to interact individually with the H2A/H2B dimer and the H3/H4 tetramer with an equimolar stoichiometry, wherein the acidic tracts of PfNPM, C-terminal to its core nucleoplasmin domain, were found necessary for these interactions. Further studies revealed that the H3/H4 tetramer displays a higher binding affinity for PfNPM than the H2A/H2B dimer, potentially due to stronger electrostatic interactions. The interaction studies also revealed that the two histone oligomers might share the same binding site on the PfNPM distal face, wherein the H3/H4 tetramer could substitute the H2A/H2B dimer due to a higher binding affinity. Intriguingly, PfNPM neither displayed nucleosome assembly function nor demonstrated direct interaction with the nucleosome core particles, suggesting it may not be directly associated with histone deposition on the parasite genomic DNA. Furthermore, our immunofluorescence results revealed that PfNPM predominantly localizes in the nucleus and exhibits expression only in the early blood stages, such as ring and trophozoite. Altogether, we provide the first report on the structural and functional characterization of a nucleoplasmin from *P. falciparum*.

A MULTIFACETED FRAMEWORK INTEGRATING PROTEIN DESIGN, MACHINE LEARNING, HYBRID QM/MM, AND CLINICAL INSIGHTS TO UNVEIL RESISTANCE MUTATIONS IN SARS-COV-2

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The emergence of novel mutations in the SARS-CoV-2 spike (S) protein has significantly challenged the efficacy of various therapeutics, including monoclonal antibodies (mAbs). Understanding resistance mutations and pinpointing vulnerable S-protein residues is crucial for designing next-generation therapeutic antibodies. For instance, the appearance of resistance mutations in the S-protein targeted by the therapeutic mAb sotrovimab underscores the need to comprehend the structural and molecular characteristics of these mutations for therapeutic advancements. However, the complex landscape of potential mutations and key residues conferring resistance to mAbs like sotrovimab remains unclear.

This study introduces an integrated computational framework that combines interface protein design, machine learning, hybrid quantum mechanics/molecular mechanics (QM/MM) methodologies, and correlation analysis with clinical and experimental reports. Starting with interface-based design and analysis, this framework elucidates the interaction between sotrovimab and the S-protein, identifying critical residues and plausible resistance mutations. Machine learning algorithms then identify potential resistance mutations using structural-sequence-binding affinity-energetics features. The hybrid QM/MM approach assesses the impact of mutational residues as quantum regions on stabilizing the macromolecular complex.

The predictions are validated by correlating identified resistance mutations with clinical sequencing data and empirical evidence from sotrovimab-treated patients. Notably, two residues, E340 at the S-protein-sotrovimab interface and Y508 distal from it, align with clinically observed resistance mutations. Furthermore, machine learning approaches predict novel S-protein sequences with altered affinity for sotrovimab, structurally validated using AlphaFold. This integrated framework effectively identifies potential resistance mutations, offering a multidimensional strategy for decoding resistance mechanisms in SARS-CoV-2. Its translational relevance extends to understanding resistance mechanisms and designing novel antibody therapeutics in other systems.

MISSION PROGRAM ON PEDIATRIC RARE GENETIC DISORDERS (PRaGeD)

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India owns rich genetic diversity with wealth of information on rare single gene diseases, owing to the large population and practice of consanguineous marriages. Identification of novel variants or genes for various unexplained inherited phenotypes has been challenging using conventional diagnostic methods. NGS-based analysis including Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS) led to the discovery of novel monoallelic disorders. Such a revolutionary state of the art sequencing platform has provided unique opportunity for identification of novel genes or novel variants in known genes which can help in better prenatal diagnosis and management of rare diseases. Mission program on Pediatric Rare Genetic Disorders (PRaGeD) is a PAN-India initiative involving 16 centres funded by the Department of Biotechnology (DBT), Ministry of Science and Technology, Government of India. We aim to develop an expanded program spanning diagnostics, research and counseling for "Pediatric rare genetic disorders". Patients with undiagnosed genetic diseases are recruited through telemedicine with a network of medical colleges (Pediatric Departments), DBT-UMMID centres, and collaborating centres across the country. WES and WGS based analysis of patients and/or parent-offspring trios is performed using bioinformatics pipeline. Database for PRaGeD is developed comprising of variant details identified from the genome analysis. Web resource for clinicians and researchers is created and is being updated by the collaborating centres. Novel variants identified from the genome analysis are further being characterised for their functional roles using cell lines or model organisms such as mice, drosophila or zebrafish. Awareness programs in the form of workshops, community awareness programs, visit to primary health centres, colleges, schools are being conducted by each centre infographics and videos are developed and circulated to create awareness among the people. Hence, Mission project PRaGeD funded by DBT embarks to discover & characterize new genes/mutations, achieve genetic diagnosis, and to develop new therapies for pediatric rare genetic diseases in India.

GENETICS AND GENOMICS IN REPRODUCTIVE MEDICINE: EXPECTATIONS AND REALITIES

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The innovations and technological advances have led to better understanding of genetics and genomics in the practice of human reproduction, male and female infertility. Genome sequencing technologies have become interestingly important in reproductive medicine. It not only includes prenatal screening and diagnosis but also encompasses preconceptional and preimplantation genetic testing/diagnosis (PGT/PGD). The division of reproductive genomics offers cutting edge, high throughput, quick reliable genetic/genomic (Chromosomal micro arrays, next generation sequencing, targeted panel, non invasive) testing and result interpretation using bio informatics tools. Changes in standard of care in pregnancy offers screening (Double/Quadruple markers) and diagnostic testing [Chroinic villus sampling(CVS), Amniocentesis] available to all women, regardless of age, race and socio economic status. The advent of non invasive prenatal testing (NIPT) where-in cell free fetal DNA (c-ff DNA) is extracted from maternal blood has gained popularity in clinic and with women who want to avoid prenatal diagnosis, but wants to make sure the fetus they are carrying is free from specific genetic conditions.

Cytogenetic testing and array comparative genomic hybridization (aCGH) is commonly utilized for prenatal diagnosis to identify small gains and losses as well as large cytogenetic abnormalities. Families at risk of a genetic condition due to a history of a previously affected child or family member can avail targeted gene testing/ clinical exome/ whole exome or even couple carrier screening testing (in case of a deceased affected child) using multiple Omic technologies. The classification of these variants as pathogenic, likely pathogenic and VUS as per the standard and national guidelines is possible with latest computational tools and correct correlation between the phenotype and genotype. It's not surprising that India has got many rare diseases and rare mutations due to heterogenous and consanguineous population and also is under represented in many databases due to lack of published studies.

The high throughput sequencing technologies and ultra low input (or even single cell) omics have paved a way for novel discoveries where *In vitro* fertilization and genetic testing have joined hands. Preimplantation Genetic Testing (PGT) is a test performed to analyse the DNA from Oocytes (polar body biopsy) or embryos (cleavage stage or blastocyst biopsy) for determining

genetic abnormalities. This includes

1. PGT-A for aneuploidies
2. PGT-M for monogenic disorders
3. PGT-SR for structural rearrangements
4. PGT-HLA for HLA typing

Infertility is a complex disorder and genetics now play an essential role in all stages of reproductive path. The rapid progress of technologies provides several diagnostic, screening options for the identification of chromosomal and monogenic disorders related to Infertility, Sub fertility, recurrent pregnancy loss. Genetics of premature ovarian failure, Amenorrhea and reproductive incompetence can be now studied extensively by various techniques that will make possible healthy reproduction.

Integration of genetics and genomic technologies in reproductive genetics aid the birth of healthy offsprings by prevention of inheritable conditions/genetic/genomic disorders and possible therapeutic paths to improve reproductive outcome.

GENETIC BASIS AND ITS UTILITY IN "INBORN ERRORS OF METABOLISM"

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Inborn errors of metabolism (IEMs) are heterogeneous and rare genetic diseases with a variety of overlapping or non-specific clinical phenotypes. IEM are a result of block in chemical pathways due to enzyme deficiency, sometimes due to cofactor or transporter deficiency. Though IEM diseases are individually rare, collectively they are quite common. They pose a challenge to diagnosis because of the fact that it would present with non-specific signs and symptoms. The manifestations of IEM are protean. Mostly they present in neonates or early childhood but adult onset IEM are also being recognised due to molecular testing and biochemical confirmation. Among the storage disorders, Lysosomal storage disorders (LSD) are a group of conditions where new therapy in the form of ERT and BMT are emerging and providing significant improvement to patient when diagnosis and intervention happen early. The establishment of an LSD diagnosis is mainly by clinical suspicion and biochemical investigations. However the specificity and sensitivity of biomarkers is not always high. The accurate identification of the molecular basis of these diseases is important for appropriate patient treatment and genetic counselling. Towards this we established & analysed the utility of targeted panel sequencing (NGS) for the diagnosis of IEMs The ampliseq panels are made to order set of genes that are pre-validated and selected using ion ampliseq designer. A total of 143 genes are in this IEM panel including Lysosomal and organic acid disorders.

Proper history taking including family history, careful examination and correlating the phenotype with the genotype hallmarks the success of correct diagnosis and management. Dysmorphism can also help in giving clue to a diagnosis. With advancement of omics technology many complex disorders, dual and blended phenotype are emerging in the limelight, highlighting the challenges in diagnosing rare genetic disorders. This will lead to increased survival of these potential treatable conditions. Appropriate genetic counselling can help to better manage the patients and affected families. The talk will highlight the use of this NGS facility with selected case presentations.

CANCER GENOMICS IN THE ERA OF PRECISION ONCOLOGY WITH EMPHASIS ON MYELOPROLIFERATIVE NEOPLASMS

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Myeloproliferative neoplasms (MPN) such as CML, PV, ET, PMF etc are stem-cell derived hematological malignancies characterized by uncontrolled cellular proliferation. They are rapidly becoming a high priority field of research due to their increasing prevalence, potentially devastating clinical consequences and high symptom burden, as well as lack of disease-modifying therapeutics, and the growing focus on principles of precision medicine as their complex genetic landscape is progressively elucidated. Furthermore, MPN are age-dependent, and affect an ever-increasing proportion of the population with incidence rates expected to rise, making them an increasingly prevalent global healthcare problem. The discovery of the Philadelphia chromosome and its characterization in Chronic Myelogenous Leukemia (CML) marked the beginning of the modern genomic era of oncology. Later, unraveling of its molecular mechanisms paved the way to the development of first molecular targeted therapy: imatinib, which has revolutionized the management of CML patients. The first-generation Tyrosine kinase inhibitor (imatinib) followed by second generation (nilotinib, dasatinib and bosutinib), third generation Ponatinib and latest fourth generation asciminib has resulted in a near normal life expectancy in majority of the CML patients. However, some chronic phase CML patients with high-risk additional chromosomal abnormalities (ACA) and mutations in *ASXL1* gene are associated with inferior response to TKI treatment. Introduction of next generation sequencing in CML have identified mutations in cancer associated genes, which in future would help to identify potential targets for treatment in addition to BCR::ABL1, especially in drug resistant patients.

Advances in next-generation sequencing have uncovered critical driver mutations in genes such as *JAK2*, *CALR*, and *MPL*, which are integral to the pathogenesis of classical MPNs (PV, ET and PMF). Mutations in these genes result the activation of JAK/STAT pathway which in turn leads to an excessive production of mature blood cells of myeloid lineage. These genomic insights have not only enhanced diagnostic accuracy but also facilitated the development of targeted therapies, such as JAK inhibitors. Among the classic myeloproliferative neoplasm, PMF is considered as the more aggressive disease which needs more attention because of its fast progression towards acute myeloid leukemia. Ruxolitinib, fedratinib, and pacritinib are the currently

available drugs for MF patients. However, these inhibitors are only helpful for alleviating the symptoms, not capable for scratching its pathophysiology. Despite the genomics based precision medicine, the 10-year overall survival rates are 80%, 68%, 64% and 21% for CML, ET, PV and PMF respectively. While the genomic framework of MPN has been progressively delineated, there remain subgroups for whom comprehensive genetic characterization has lagged and who stand to benefit significantly from this. Whole genome and transcriptome analysis of MPNs is expected to significantly deepen our understanding of disease biology, identify novel drivers of disease, and reveal putative therapeutic targets. The identification of more genomic targets and development of more genomics-based precision medicine is warranted in myeloproliferative neoplasms. Cross-reference of genomics data with comprehensive clinical data will help to better predict clinical outcomes, inform patient management, and open the door to precision-based therapies.

LETHAL AORTOPATHY DUE TO FIBULIN 4

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We are presenting an extremely rare, inherited connective tissue disorder with lethal arteriopathy, associated with novel homozygous mutation (Asp203Ala) of Fibulin4 gene in 62 children from Malabar Mappila population of northern Kerala.

Our first description of novel homozygous (Kappanayil M et al, 2012) is the first and largest study of in humans. These babies expire before completing one year. Only seven patients amongst this cohort are alive. We are offering prenatal diagnosis for the couple who are heterozygous carriers for this disorder as this disorder cannot be identified by anomaly scan by 20 weeks of gestation. The aortic enlargement in fetal life is evident only in third trimester scan which is a main hindrance that the condition can not be picked before 24 weeks of gestation.

Currently our team received an ICMR project with Amrita institute as the nodal centre and Dr Mahesh K is the PI and Sheela Nampoothiri as co PI .This study is focused to identify the Functional significance of fibulin-4 and specifically the evolutionary and anthropological background of this syndrome. Zebrafish model of the mutation will be created and studied (RCB, Faridabad). Inheritance pattern will be studied, with special emphasis on migration history (NEHU, Shillong).

ALLOSTERIC CHANGES IN DRUG TARGETS: INSIGHTS FROM JIGGLING BALL-AND-STICK MODELS

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Allosteric communications in biological macromolecules are of tremendous importance in the context of drug design for several reasons. While state-of-art experiments can suggest the existence of allosteric transitions in a molecular system, the mechanism and atom-atom interaction network of allostery in a molecule is often non-trivial to understand just from the static models of molecular structures. To go beyond, computer simulations of molecular dynamics offer scopes to witness the jiggling atoms in action, mimicking a more realistic behaviour of the molecular structures and tell how exactly they are meaningfully choreographed. But how much it can really help to take the scientific understanding of allostery forward for possible applications? This presentation will address this issue with examples of various molecular systems like α,β-Tubulin [1-4], Bcl2 [5], TAK1 kinases [6-7], all of which are of tremendous importance in the field of drug design to combat cancer. Not only the structural and thermodynamic insights which will be presented, but also our latest initiatives to use machine learning [7] methods will be briefly discussed.

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DECODING HYPOBARIC HYPOXIA: ADVANCES IN PROTEOMICS, PROPHYLAXIS, AND MODELLING APPROACH

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Hypobaric hypoxia is a multifaceted condition with various molecular, pathophysiological, and biochemical dimensions. Understanding hypobaric hypoxia in its entirety requires considering these aspects collectively. Our research identified three critical gaps in the current literature: 1) A lack of high-throughput proteomics studies on hypobaric hypoxia. 2)The absence of a supplement with proven efficacy and safety that does not require medical supervision and is not contraindicated for hepatic, renal, and cardiac insufficiencies. 3)The need for a clinically validated rodent model of High-Altitude Pulmonary Edema (HAPE) without genetic or pharmacological manipulations. Our study aimed to address these gaps by proposing a model for rapid acclimatization based on molecular changes. We introduced a micronized aqueous suspension of silymarin, which is effective at low doses in providing antioxidant, anti- inflammatory, and hypoxia-adaptive vascular responses, alongside its role as a free radical quencher. Silymarin is known for its outstanding safety and effectiveness in humans. Furthermore, we developed a Sprague-Dawley (SD) rat model of HAPE, which we used to reverse-translate a known HAPE marker in humans *(SULT1A1)* and elucidate the synergistic occurrence of HAPE and inflammatory cascades. This represents the first radiologically validated rodent HAPE model. In conclusion, our research elucidated the molecular, biochemical, and pathophysiological aspects of hypobaric hypoxia, addressing the gaps left by previous studies.

EXPRESSION OF ARGINASE-1 SPECIFIC TO THE LIVER IN THE DIAGNOSIS OF NON ALCOHOLIC FATTY LIVER DISEASE PROGRESSION

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Background: A progressive form of non alcoholic fatty liver disease (NAFLD), known as non alcoholic steatohepatitis (NASH) can result in cirrhosis, hepatocellular carcinoma, and end stage liver disease. Till now, liver biopsy is still the most reliable way to diagnose NASH because there is no conclusive diagnostic marker for the condition. A binuclear manganese metalloenzyme called arginase-1 (Arg-1) catalyses the liver's conversion of arginine to ornithine and urea. Liver-specific Arginase-1 (ARG-1) has been introduced for pathologic differentiation of hepatocytes, as a sensitive and specific marker of benign to malignant. Our earlier data showed significant hepatic expression of Arg-1 on a high-fat fed diet rats. We hypothesized that expression of Arg-1 turns out to be a valuable diagnostic tool in routine surgical pathology practice in the liver disease patients. We aimed to evaluate and quantify the early Arg-1 expression in the development of non alcoholic fatty liver disease (NAFLD).

Methods: Using real-time polymerase chain reaction (RT-PCR) and immunohistochemistry, we investigated the quantitative expression of Arg-1 in the characterized NAFLD patient biopsies different from F0-F4 (N=3-5 in each stage).

Results: In comparison to F0, the relative gene expression of Arg-1 had considerably increased in the progressive stages of F2-F3 ($P<0.001$). Between F3 and F4, there was no discernible change ($p<0.08$). IHC revealed that Arg-1 expression was elevated and positively correlated with severity ($p<0.01$) in NASH patients. The percentage of stained cells (area) exhibiting Arg-1 positivity was found to be significantly higher between F0 and F4 ($p <0.001$). From stage F1 to F3, there was a significant positive trend ($p <0.01$). According to our findings, Arg-1 expression is elevated in liver disease patients and may have a role in the development of liver fibrosis and liver dysfunction.

Conclusions: Therefore, we conclude that hepatic Arg-1 expressions can be used as a pathological marker to monitor the progression of NAFLD. Our findings might open the door for cutting-edge treatment strategies that help NAFLD patients' liver disease progress more slowly.

CYCLIN-DEPENDENT KINASE 5 TO NEURONAL HEALTH: DECIPHERING SIGNALING PATHWAYS IN NEURODEGENERATION

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Type 2 diabetes (T2D) is a prevalent metabolic disorder associated with increased blood glucose levels and systemic complications, including cognitive decline and dementia. Recent studies have identified cyclin dependent kinase 5 (Cdk5) as a pivotal player linking T2D and neurodegeneration. Cdk5, known for its roles in neuronal development and synaptic plasticity, becomes dysregulated in conditions like Alzheimer's disease and Parkinson's disease, as well as in T2D. This dysregulation contributes to neuroinflammation, mitochondrial dysfunction, and neuronal damage. Our research has elucidated that in T2D, Cdk5 activation under glucotoxic conditions enhances cPLA2 activity and prostaglandin E2 (PGE2) synthesis, exacerbating neuroinflammation and myelin damage. Furthermore, hyperactive Cdk5 impairs mitochondrial function and mitophagy via KANSL1 phosphorylation, furthering neurodegeneration. We have identified novel Cdk5 inhibitors, BLINK11 and BLINK15, which show promise in penetrating the blood-brain barrier and offering dual benefits of reducing blood glucose levels and preserving cognitive function in T2D models. These findings underscore the therapeutic potential of targeting Cdk5 to mitigate neurodegeneration associated with T2D and related cognitive impairments.

IDENTIFICATION OF A LEAD FOR NAFLD ACTING VIA AMPK PATHWAY AND PPAR ALPHA MODULATION

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Liver associated diseases especially non alchoholic fatty liver disease (NAFLD) is now a very serious issue to public and clinicians due to lack of any effective drugs so far. Moreover, NAFLD cases are increasing day by day due to on-going socio-economic transformations and genetic predisposition. Based on literature available on traditional use of Garcinia species against liver complaints; we planned to explore the possible beneficial effects of fukugiside (FKS) a biflavonoid from *Garcinia travancorica* against NAFLD. To evaluate the potential of FKS against NAFLD using *in vitro* and *in vivo* models and to elucidate the molecular mechanisms responsible for its effects, if found effective. HepG2 cells treated with oleic acid (100 µM for 24 h) was the *in vitro* model used for PPAR α activation and anti-lipogenic activity by FKS. Western blot analysis and real time PCR of various proteins involved in lipid metabolism were also studied. C57BL/6J mice fed with methionine / choline deficient diet (MCD) was used to evaluate the potential of FKS against NAFLD *in vivo* system. FKS caused up-regulation of PPARα and AMPK, lipoprotein lipase (LPL) and the low-density lipoprotein receptor (LDLR). Besides, FKS caused decrease in the mRNA levels of lipogenesis genes (SREBP-1c, FAS and ACC), but up-regulated that govern lipid oxidation (PPARα and CPT-1). The lipid profile was refined with FKS (10 and 20 mg/Kg/day) after 4 weeks of treatments showing decreased total cholesterol (TC), triglycerides (TG) and low-density lipoprotein-cholesterol (LDL-C) and increased high-density lipoprotein-cholesterol (HDL-C). Liver malondialdehyde , alanine aminotransferase (ALT) and fat deposition in the liver of NAFLD mice were reduced with FKS. Over all data showed FKS is very effective against NAFLD both *in vitro* and *in vivo* studies. Upregulation of PPARα and AMPK are found to be major molecular mechanisms responsible for its beneficial effect. Since not even single drug is available for NAFLD now, FKS is expected to be a promising one for future drug development.

Abstracts

Genomics in Clinical Medicine

Total number of abstracts: 39

Oral presentations
Young Scientist Award: 7
Best Paper: 5
Contributed Paper: 2

Poster presentations
Young Scientist Award: 4
Best Paper: 9
Contributed Paper: 12

INSIGHTS INTO ANTIMICROBIAL RESISTANCE THROUGH GENOMIC ANALYSIS OF *ENTEROBACTER HORMAECHEI* AND *KLEBSIELLA PNEUMONIA*

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) and multi-drug resistant (MDR) pathogens like *Enterobacter hormaechei* and *Klebsiella pneumoniae* are major contributors to the global health crisis of antibiotic resistance.

Methodology: Whole genome sequencing (WGS) was performed on a clinical MDR strain of *E. hormaechei* (GC26) and *K. pneumoniae* (GC29) isolated from Thiruvananthapuram using Oxford Nanopore sequencing platform. Antibiotic resistance profiles were determined using Kirby-Bauer disc diffusion and minimum inhibitory concentration (MIC) assays. Multi-Locus Sequence *Typin* and phylogenetic analyses were conducted to understand the evolutionary relationships and sequence types.

Major Findings: For *E. hormaechei* GC26, WGS identified several drug-resistance genes (*bla, tet, armA, qnrB, and fos*) and virulence genes (*fimD, csgD, csgE, csgF, and csgG*). The strain demonstrated high-level resistance to multiple antibiotics, including meropenem, ampicillin, erythromycin, cefotaxime, cefixime, tetracycline, and streptomycin, as evidenced by MIC. Two IncFIB-type conjugative plasmids, sized 12,714 and 6,002 bp respectively, were detected. The latter carries the *blaOXA-10* gene, conferring resistance to extended cephalosporins. A novel sequence type (*ba28) was discovered, with GC26 occupying a distinct phylogenetic branch within the *Enterobacter* genus, closely related to an Indian strain. For *K. pneumoniae* GC29, resistance to 33 FDA-approved antibiotics was observed, with high MIC values for critical antibiotics. Genome analysis revealed multiple resistance genes (*CTX-M-15, OXA-1, OXA-232, sul1, dfrA12, aadA2, armA, tet(D), fosA5, mphE, and arnT*) and unique virulence genes (*allA, sciN, impF, and acpXL*). GC29 belonged to the novel sequence type *703b and contained two plasmids, IncHI1B and ColKP3, associated harbouring drug resistance and virulence genes.

Conclusion: The WGS of *E. hormaechei* and *K. pneumoniae* provides valuable insights into the genetic basis of MDR in these strains. These findings highlight the importance of continuous genomic surveillance and targeted interventions to monitor and control the spread of antibiotic resistance.

Keywords: *Enterobacter hormaechei, Klebsiella pneumoniae,* antimicrobial resistance, whole genome sequencing

CLINICAL UTILITY OF IVF BASED PREIMPLANTATION GENETIC TESTING FOR NEUROGENETIC DISEASE: RESULT-GUIDED ACTIONABILITY AND OUTCOME - A CASE REPORT

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Background: Neurogenetics aim to identify specific genes and genetic variations associated with neurological disorders. In this case study, Couple married type is non-consanguineous and the couple's previous two children are affected with *Spastic Paraplegia 47*. On genetic analysis, both the children were found to harbour a homozygous likely pathogenic variant, c.617G>A in *AP4B1* gene, associated with autosomal recessive *Spastic Paraplegia 47*. Therefore, the couple opted for IVF using self-gametes and their day 5 trophectoderm biopsies were referred for chromosomal aneuploidy screening by Preimplantation Genetic Testing Aneuploidy and mutation testing by Preimplantation Genetic Testing Monogenic disorders.

Methodology: The exome sequencing was performed on the Whole Exom Sequency and analysed using Anderson Variant Analysis Tool and suspected causative variant validate by Sanger sequencing. Preimplantation genetic testing for aneuploidy was performed using Ion ReproSeq™. Preimplantation genetic testing for monogenic disorders includes isolation of genomic DNA from the embryo biopsies and peripheral blood samples of the affected and unaffected family members were subjected to whole genome amplification using Ion ReproSeq™ kit.

Major findings: The couple underwent exome screening which revealed heterozygous variant, c.617G>A in *AP4B1* gene, associated with autosomal recessive Spastic Paraplegia 47 was detected carrier status both. The couple underwent In vitro fertilization using self-gametes and four embryos were generated. The Euploid embryo was screened for the suspected *AP4B1* variant by Sanger sequencing and was found to be heterozygous and carrier for the suspected disease condition.

Conclusion: Based on phenotype-genotype correlation, *AP4B1* was chosen as the risk variant. Spastic Paraplegia 47, autosomal recessive (OMIM# 614066) is caused by homozygous mutation in the *AP4B1* gene (OMIM* 607245) and its recurrence risk with each pregnancy. This impacted the couples' reproductive decision making and led them to opt for Preimplantation genetic testing for monogenic disorders. This Euploid embryo was transferred to the female partner and a successful pregnancy was achieved.

Keywords: Neurogenetics, spastic paraplegia, PGT-A, PGT-M

GENETIC VARIATIONS AND ADVERSE DRUG REACTIONS TO COMMONLY USED ANTIBACTERIAL AGENTS: A NARRATIVE REVIEW

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Background: Genetic variations can significantly impact the occurrence of adverse drug reactions (ADRs) to antibacterial agents. This review examines the role of genetic polymorphisms in ADRs to beta-lactams, tetracyclines, aminoglycosides, and macrolides.

Methodology: A comprehensive literature review was conducted using the MEDLINE/PubMed database, focusing on studies published from 2000 to November 2023.

Major findings: Beta-lactams: Amoxicillin-clavulanic acid: HLA alleles DRB115:01-DQB106:02, HLA-A02:01, and HLA-B15-18 are associated with a threefold increased risk of drug-induced liver injury. Aminoglycosides: MT-RNR1 gene mutations, particularly m1555A>G, are associated with an increased risk of ototoxicity. The m1555A>G mutation is present in 5-33% of patients with aminoglycoside toxicity. Macrolides: Genetic variations in CYP3A4 and ABCC2 genes may affect erythromycin and clarithromycin metabolism and transport.

Conclusion: Genetic variations play a significant role in ADRs to several antibacterial agents. However, systematic genetic screening before antibiotic administration is not currently recommended due to the complexity of genetic factors involved and the time required for testing. Further research is needed to establish clear associations between genetic polymorphisms and antibiotic-related ADRs, as well as to develop rapid and cost-effective screening methods.

Keywords: Pharmacogenomics, adverse drug reactions, genetic variations, pharmacovigilance

"DISEASE X AND MULTI-OMICS" IMPLICATIONS IN POSSIBLE H5N1 PANDEMIC

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Background: Disease X represents a hypothetical pathogen that can cause a global emergency health threat. It is a "placeholder" concept, meaning it may be replaced with the actual name when it occurs in reality. World Health Organization in February 2018 placed the concept of Disease X in the blueprint high priority diseases to represent a hitherto unknown pathogen that can cause a pandemic. This preponderance, the constant need and awareness for supreme vigilance, diligent research, and great preparedness in the face of uncertainty in global health threats. It should be noted that this concept was placed well before the last SARS-CoV-2 (COVID-19) pandemic. There has been a recent surge of highly pathogenic avian influenza HPAI, type A H5N1, across the globe. Spread from fowls to cattle is reported. Human infections have been reported with high mortality. So far, no human-to-human spread is noticed. However, Influenza H5N1 spillover can occur that may cause human to human spread. Need for caution here and review also how multi omics can help us in winning the battle should it occur.

Methodology: The recent data of H5N1 occurring across the globe is collected and analysed. Human infections of the avian influenza and the mortality is studied. Possibility of reassortment of the virus is looked into considering the influenza pandemics from the year 1918.

Major findings: The role played by muti-omics in the last SARS-CoV-2 pandemic highlighted by thorough literature study.

Conclusion: Analysing the influenza pandemics from the year 1918, the global threat of H5N1 spillover is real. Deploying high-throughput sequencing, related computer science and algorithms, various omics branches like genomics, epigenomics, transcriptomics, metabolomics and proteomics, the global preparedness for possible H5N1 pandemic is made more appropriate, driving developments in diagnostics, therapeutics and vaccine deployment.

Keywords: Disease X, H5N1, pandemic preparedness, multi-omics, genomics, reverse vaccinology

GENERATION OF STABLE IRF2BPL-KNOCK OUT SHSY5Y NEUROBLASTOMA CELL LINE AS A NOVEL TOOL TO UNDERSTAND THE MECHANISM OF NEURODEVELOPMENTAL DISORDERS

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Background: Neurodevelopmental disorders (NDD) are caused by impairments in brain development and function resulting from genetic and environmental insults. They are characterized by high levels of phenotypic and genetic heterogeneity, which limits genotype-phenotype correlations and poses a diagnostic challenge. Recently, loss-of-function (LoF) mutations in Interferon Regulatory Factor 2 Binding Protein-Like (IRF2BPL) have been reported to be causal for a rare NDD manifesting a characteristic phenotype of neurodevelopmental regression, abnormal movements, loss of speech, and epileptic seizures (NEDAMSS).

Methodology: We designed guide RNAs targeting the first and only exon of IRF2BPL using a bioinformatics tool named "CRISPick" from the Broad Institute. We chose the best two gRNAs based on specificity and minimal off-target effects and cloned these guide RNAs into the pLKO5.sgRNA.EFS.GFP plasmid (Addgene, 57822). Clones obtained were confirmed by PCR and Sanger sequencing. For transfection, we used guide RNA plasmids expressing GFP and a Cas9 plasmid (Addgene, 57819) expressing RFP. The SHSY5Y cell line was transfected with Cas9 and guide RNA plasmids using the Xfect transfection reagent according to the recommended protocol. Untransfected cells were used as a control. Cells were collected 72 hours post-transfection, and colonies showing green and red fluorescence signals were sorted by FACS and expanded.

Major findings: We generated an IRF2BPL knockout SHSY5Y neuroblastoma cell line, which can be further used to elucidate the potential mechanisms by which IRF2BPL regulates neurodevelopment and the disease-associated phenotypes upon its perturbation in vitro.

Conclusion: The stable IRF2BPL-KO SHSY5Y cell line will be used for studying the effect of IRF2BPL gene knockout in neuronal differentiation, and the data can provide insights into the potential mechanisms of neurodevelopmental disorders, which will lead to in-depth mechanistic studies.

Keywords: IRF2BPL, neurodevelopmental disorders, NEDAMSS, CRISPR-Cas9, SHSY5Y cell line

REVIEW OF SELECTED ORTHOPAEDIC IMPLANTS FOR THEIR GENOTOXICITY POTENTIAL

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Background: Orthopaedic implants are intended to be part of a biological system for a considerable amount of time; hence, it is essential to test for their genotoxicity. This review investigates the genotoxicity associated with various orthopaedic implant materials.

Methodology: We collected genotoxicity studies conducted on twenty different types of orthopaedic implant materials in our laboratory from 2015 to 2022, along with their accompanying reports. Based on these reports, the implants were categorized into groups according to their materials of construction. This paper includes a thorough evaluation of the findings from the genotoxicity tests obtained from the bacterial reverse mutation assay, chromosomal aberration assay, and micronucleus assay conducted on orthopaedic implant materials in our laboratory.

Major findings: A total of 20 different orthopaedic implants were tested in our laboratory for their genotoxic potential. These 20 implants were made of four different materials: titanium alloys, ultra-high molecular weight polyethylene, stainless steel, and cobalt chromium molybdenum alloys. All these implants were tested using the Ames test, chromosome aberration test, and/or *in vivo* micronucleus tests. None of the materials showed any evidence of mutogenicity.

Conclusion: This is the first open paper highlighting the results of genotoxicity testing of selected orthopaedic implant materials.

Keywords: Orthopaedic implants, genotoxicity, chromosomal aberration, Ames test, micronucleus assay

AN INDIAN STUDY ON GENETIC VARIATIONS OF *IL-18* GENE PROMOTER REGIONS -607 C>A (rs1946518) AND -137 G>C (rs187238) IN PCOS

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Background: Polycystic Ovary Syndrome (PCOS), categorized as a metabolic, reproductive, and familial disorder with an altered endocrinal profile, causes perpetual detrimental ramifications among women, hindering their quality of life. Metabolic manifestation of PCOS includes both insulin resistance and obesity, of which insulin resistance is the prominent manifestation leading to type 2 diabetes mellitus, whereas obesity exacerbates the pathophysiology of PCOS to cardiovascular diseases. Research suggests that women with PCOS have consistently elevated levels of IL-18. Promoter variations of the *IL-18* gene, -607(rs1946518) and -137(rs187238), can alter the *IL-18* expression with the change in binding of transcription factors. Three prior polymorphism studies were done among Chinese and Korean PCOS patients. Our study is the first from India genotyping the *IL-18* gene promoter region polymorphism -607(rs1946518) and -137(rs187238) in PCOS.

Methodology: We stratified 121 PCOS cases and 121 healthy controls based on BMI as lean, normal, overweight and obese. We used ARMS-PCR for genotyping and confirmed using Sanger sequencing.

Major findings: Lean, overweight, and obese study subjects show no significant variations in their genotype, allele and haplotype frequencies. However, normal BMI PCOS study subjects showed significantly higher C allele frequencies (p=0.0251) of *IL-18* gene -137 polymorphism, which has 1.94-fold higher risk for PCOS in contrast to G allele (OR 1.9496, 95% CI = 1.0818 - 3.5133 and p=0.0263). In the haplotype association analysis, normal BMI PCOS study subjects have significantly higher -607A/-137C haplotype frequency. Normal BMI subjects with -607A/ -137C haplotype have a 1.87-fold increased risk for PCOS (OR 1.8768, 95% CI = 1.1615 - 3.0326 and p = 0.0101).

Conclusion: C allele at the -137 position and the haplotype -607A/-137C at the promoter region of the *IL-18* gene is a potential risk for PCOS with normal BMI subjects.

Key words: *IL-18*, PCOS, BMI, rs1946518, rs187238

MICROBIAL DIVERSITY AND RESISTANCE IN PERIYAR RIVER SEDIMENTS: METAGENOMICS FOR EPIDEMIOLOGICAL INSIGHTS AND POLLUTION MONITORING

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Background: The research explores the microbial landscape in the sediments of the Periyar river in southern India. Metagenomic approach is employed to gain insights into microbial diversity, their resistance characteristics, and environmental interactions.

Methodology: We employed 16S rRNA gene sequencing, quantitative PCR (qPCR), and inductively coupled plasma optical emission spectrometry (ICP-OES) to analyze microbial communities and resistance genes across varying pollution levels. Additionally, environmental factors like total dissolved solids (TDS), salinity, electrical conductivity (EC), and temperature were measured.

Major findings: A rich microbial diversity was discovered, predominantly consisting of Proteobacteria, Firmicutes, and Bacteroidetes. Pollution levels notably influenced specific groups like methanogenic and sulfur-reducing bacteria. Key resistance genes, including *inti1*, *aadA*, *qnrS*, and *copA*, were identified, indicating the impact of pollution on the prevalence of resistance genes.

Conclusion: Microbial communities serve as early-warning systems for pollution. While different pollution levels resulted in similar overall structures, there were variations in their composition and resistance genes. The study provides valuable information for environmental monitoring and targeted pollution control.

Keywords: Metagenomics, antimicrobial resistance, pathogenic bacteria, epidemiology, water pollution

APPLICABILITY OF ILLUMINA *BRACAI* AND *BRACAII* PANELS IN PREDICTION OF BREAST CANCER IN INDIAN POPULATION

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Background: Early detection BRCA kit for breast cancer is based on the American population. All these studies genetically not related to the Indian population. Developing country has lack of awareness about cancer among the women. Indian continent has different environment, food habit, and culture that affect the gene regulations as well as gene metabolisms. Indian genotype is poorly studied. Targeting breast cancer genotype in Indian population may reveal new gene mutation pattern specific to Asian continent. As trend going for personalize medicine it is necessary to understand genome wise diversity among Indian women for better treatment and control of breast cancer.

Methodology: Sample will be collected after informed consent from tissue as well as blood. Then transported in 100% ethanol eppendorf tubes and blood in the EDTA voccutainer with safety care. DNA isolation will be on the QIA gene QIA cube system by blood and tissue kit protocol. Targeted gene like *BRACA* will be amplified by using PCR techniques. Region of interest will be sequenced by NGS Illumina or by Sanger Sequencing. Then statistical analysis will be performed. The data will be tabulated in microsoft excel software and standard deviation, E value, significant coefficient, t- test, chi –square test use in data analysis.

Major findings: Identification of variations in *BRCA* gene will be identified from the patients and will be compared with that of a large populations data to see whether the identified variations are only present in the Indian population or not. Further the genomic data bank for breast cancer patients will be prepared based on these variants.

Conclusion: This study will contribute towards the development of a comprehensive genomic data bank for breast cancer patients, enhancing our understanding of the genetic factors influencing the disease and potentially guiding personalized treatment approaches.

Keywords: *BRCA*, breast cancer, NGS, Sanger sequencing

GUT MICROBIOME-DERIVED METABOLOMICS IN NON-ALCOHOLIC LIVER DISEASES

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Background: Non-invasive microbiota-derived metabolites play a crucial role in the pathophysiology of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), especially in patients with decompensated cirrhosis. The gut microbiota and its metabolites represent a niche for the diagnosis of NAFLD. We aimed to identify gut microbiota-derived metabolomic signatures related to the progression of NAFLD.

Methodology: We analyzed the stool metabolomes and untargeted metabolomics based on clinical parameters of 80 patients [Fatty liver (FL: n=16); steatohepatitis (SH: n=26); cirrhosis (CH: n=19) and healthy control (HC: n=19)]. Metabolomics analysis was performed using GC-TOF-MS and LC-MS.

Major findings: A total of 103 untargeted metabolites were quantified. Metabolic discrimination of FL, SH, and CH was assessed in principal component analysis. Short-chain fatty acids (SCFAs) such as acetate (p=0.03), butyrate (p=0.0008), and propionate levels were significantly reduced among NAFLD patients. The stool cholic acid (p=0.001) level was significantly increased in NAFLD. Among SH and CH, palmitoylcarnitine and L-carnitine were significantly amplified. These metabolites' phenotypic risk was related to higher β oxidation levels. The correlation coefficient of significant metabolites was analyzed. The fold value of sitagliptin increased in FL and CH compared to SH. The stercobilin and kynurenic acid were relatively downregulated in stool NAFLD. 3-indole propionic acid (3-IPA, p=0.001) was significantly downregulated in SH and CH. Curiously, 3-IPA was increased in FL. Another indole-associated microbial metabolite was perplexed in NAFLD. Microbial metabolites in stool are produced as a result of host and microbe variability in NAFLD. In brief, microbiota-SCFA signaling reverses the reduction of acetic acid (p=0.01, SH, and p=0.03, CH) and propionic acid in NAFLD. Microbial metabolites were highly effective in the treatment and prevention of NAFLD/NASH.

Conclusion: The association of microbiome and its metabolites phenotype like amino acids, fatty acids, and several metabolites suggest a novel microbial metabolome in FL, SH, and CH metabolic pathway influencing in NAFLD/NASH.

Keywords: Liver diseases, microbiome, metabolomics, LC-MS, NAFLD, cirrhosis, metabolic pathways

PRECISION MEDICINE IN THE ERA OF NGS: ARE WE THERE YET?

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Background: Exome sequencing is a key tool for diagnosing genetic disorders, especially when clinical symptoms involve multiple organ systems. This case study details the diagnostic journey of a patient with chronic kidney disease, bilaterally small kidneys, glomerulonephritis, and sensorineural hearing loss who underwent exome sequencing. Despite its utility, exome sequencing without a control dataset can lead to diagnostic challenges and misinterpretations.

Methodology: Exome sequencing data were analysed bioinformatically and variants were interpreted using existing literature and databases. In this patient, a hemizygous variant in the *COL4A5* gene (c.64C>T; p.Gln22Ter) was identified, consistent with Alport syndrome. Additionally, two heterozygous variants in the *ADAMTS13* gene (c.1492C>T; p.Arg498Cys and c.1423C>T; p.Pro475Ser) were found. The patient's ADAMTS13 enzyme activity was repeatedly low, initially leading to a misdiagnosis of compound heterozygous thrombotic thrombocytopenic purpura (TTP), preventing a kidney transplant.

Major findings: The *COL4A5* variant confirmed Alport syndrome, but interpreting *ADAMTS13* variants was challenging without control data. Homozygous and compound heterozygous *ADAMTS13* variants cause TTP. The c.1492C>T (p.Arg498Cys) variant, reported in TTP patients, was also found in an unaffected sibling in a heterozygous state. The c.1423C>T (p.Pro475Ser) variant was a variant of uncertain significance (VOUS) and was present in the heterozygous state in the patient's father. A reanalysis nine years later reclassified this variant as benign, highlighting a significant delay in the patient's ability to receive a kidney transplant.

Conclusion: This case emphasizes the limitations of exome sequencing without control datasets and the potential for misdiagnosis when multiple variants are identified. While exome sequencing is a powerful diagnostic tool, its limitations, particularly the lack of control datasets, necessitate careful variant interpretation and thorough genetic counselling to avoid misdiagnoses and inappropriate management strategies.

Keywords: Exome sequencing, Alport syndrome, *COL4A5* gene, *ADAMTS13* gene, thrombotic thrombocytopenic purpura

EPIGENETIC ALTERATIONS IN *WNT* SIGNALLING GENES LINKED TO DEVELOPMENTAL LANGUAGE DISORDER

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Background: Approximately 7 % of school-age children are affected by the neurodevelopmental disorder, the Developmental language disorder (DLD). The normal speech and language skills of the affected children fail to develop and this is a major public health concern. There are adverse impacts on their communication, social and academic skills. For proper brain development, the regulation and expression of multiple genes are essential and to be accurate in the temporal and spatial aspects. The key regulators that modulate gene expression involved in neurodevelopment are considered to be the epigenetic factor, the DNA methylation, where the DNA sequence is not altered.

Methodology: The genome-wide methylation differences between children with DLD and the control group were examined in this study and the findings were validated by real-time PCR (qPCR).

Major findings: Differential methylation of CpG sites in several WNT signalling regulator genes (*APCDD1*, *AMOTL1*, *LRP5*, *MARK2*, *TMEM64*, *TRABD2B*, *VEPH1*, *WNT2B*) were observed in DLD groups when compared with the control group.

Conclusion: WNT signalling associated with DLD is been reported for the first time in this study. The findings are significant in light of the crucial role of WNT in neuronal myelination and the altered myelination in DLD as revealed by magnetic resonance imaging.

Keywords: Epigenetics, methylation, WNT signalling, developmental language disorder

NOVEL GENETIC VARIANTS IN SENSORY PERCEPTION GENES IDENTIFIED IN WHOLE EXOME SEQUENCING OF MONOZYGOTIC TWINS WITH AUTISM SPECTRUM DISORDER

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Background: Autism spectrum disorder (ASD) is a neurodevelopmental condition that begins in childhood, marked by difficulties in communication and social interaction, as well as by repetitive and stereotyped behaviours. ASD affects about one in every 36 children. Despite its high heritability, the genetic basis of ASD is intricate. To identify potential candidate genes associated with ASD, we conducted an extensive genetic study involving monozygotic (MZ) twins who are either concordant or discordant for the disorder.

Methodology: Five monozygotic (MZ) twins and their parents were recruited for the study. Of these twins, four pairs were concordant for ASD, while one pair was discordant. Whole exome sequencing was performed on both the twins and their parents. The exome DNA was enriched using the Twist Human Customized Core Exome Kit, and paired-end sequencing was carried out on the HiSeq system.

Major findings: We discovered several rare and pathogenic variants (homozygous recessive, compound heterozygous, and de novo) in individuals with ASD.

Conclusion: We have identified new variants in individuals with ASD, many of which are linked to brain-related functions and have not been previously reported in ASD. Interestingly, some variants were found in genes associated with sensory perception, including auditory (*MYO15A, PLEC, CDH23, UBR3, GPSM2*), olfactory (*OR9K2*), gustatory (*TAS2R31*), and visual (*CDH23, UBR3*) functions. This study represents the first comprehensive genetic analysis of MZ twins within an Indian population. Further validation is necessary to determine if these variants are indeed linked to ASD.

Keywords: Monozygotic twins, autism spectrum disorder, whole exome sequencing, sensory perception genes, rare variants

IDENTIFICATION AND COMPUTATIONAL ANALYSIS OF RARE VARIANTS OF HEARING LOSS GENES PRESENT IN HEARING LOSS PATIENTS OF SOUTH INDIAN CONSANGUINEOUS OFFSPRINGS

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Background: Non syndromic hearing loss (NSHL) is both genetically and clinically related heterogeneous disorder characterized by hearing loss (HL) in the inner ear without any other clinical defects. Globally, of every 1,000 newborns, 2.7 newborns are affected by sensorineural hearing loss and the prevalence of hearing loss in India is about 6.3% (WHO). The phenotypic complexity and genetic heterogeneity of NSHL make its molecular diagnosis obscure.

Methodology: Whole exome sequencing and homozygosity mapping were performed to identify the genetic variants in seven unrelated offsprings affected with NSHL born to third degree of consanguinity. *In silico* tools were used to predict the effect of identified variants and its functional impact on the proteins. The causal variants associated with *HL* genes identified were validated by Sanger sequencing. To predict the phenotype – genotype relationship, functional enrichment analysis was also performed in the genes containing variants with unknown significance (*VUS*).

Major findings: We identified five missense mutations (*MYO5A*, *RDX*, *COL4A6*, *WFS1*, *CDH23)*, and compound heterozygous mutations (c.3815_3816del, c.4910C>G) in *TRIOBP* gene of NSHL patients of south Indian consanguineous population. Additionally, a novel candidate gene (*NMNAT1*) was identified in the patient affected with profound NSHL. The causal variants validated by Sanger sequencing and functional enrichment analysis revealed the genes with *VUS* are related to sensory perception of sound and inner ear morphogenesis.

Conclusion: Our findings highlight the novel and known genetic variants contributing to hearing loss by integrating computational approaches to understand the pathophysiology of hearing loss in the south Indian consanguineous population.

Keywords: Sensorineural hearing loss, 3°consanguineous marriage, mutations, NGS

IDENTIFICATION OF NOVEL AND COMMON GENETIC VARIANTS IN ATRIAL FIBRILLATION THROUGH WHOLE EXOME SEQUENCING

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Background: Atrial fibrillation (AF), is the most common cardiac arrhythmia, affecting 3.3 million individuals globally, which further leads to stroke and heart failure. Multiple risk factors are associated with AF including age, hypertension, obesity, diabetes, and other cardiovascular disorders. The lack of a comprehensive understanding of the aetiology of AF has led to the deficit of effective AF diagnostic methods, making the management of AF difficult. Our study focused on understanding AF's molecular mechanism and genetic predisposition to improve early diagnosis and its treatment strategies.

Methodology: Whole exome sequencing (WES) was performed to identify rare and common genetic variants in patients diagnosed with AF and compared with controls. Biocomputational tools were utilized to predict the impact of these variants on protein function. Additionally, integrated approaches such as gene set enrichment analysis and pathway analysis were done to understand the phenotype-genotype relationship in AF.

Major findings: In this study, a novel variant was identified in AF patient's *TNNT2* gene (c.691G>A). Pathogenic variants found in *CTNNA3, SYNPO2L, NEBL, CUX2*, and *DSP* genes, and likely pathogenic variants found in the genes (*AGT, SYNPO2L, SYNE2, CASR, TTN, TIAM2*), highlighting the potential contribution to AF. Additionally, in all the patients, common variants were also found in the genes (*SCN1B, AGT, CUX2, TTN2, CASR*) associated with AF.

Conclusion: The identification of rare and common genetic variants associated with AF underscores the importance of genetic screening in understanding and managing AF. The significant proportion of pathogenic and likely pathogenic variants indicates a strong genetic predisposition to AF, which would guide personalized treatment strategies and improve patient outcomes.

Keywords: Atrial fibrillation, whole exome sequencing, pathogenic variants, *TNNT2* gene, genetic screening

MOVING BEYOND THE 'EXOME-ONLY' APPROACH: LESSONS FROM A WGS COHORT OF SKELETAL DYSPLASIAS

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Background: Mendelian diseases are primarily caused by disease-causing variants in coding/exonic regions of genome. Almost 85% of these variants are found in the 2% of protein-coding regions. The disease-causing relationship of variants in the non-coding regions is underrepresented for many rare diseases including skeletal dysplasias. The average diagnostic yield of skeletal dysplasias has been in the range of 50-70%. However, with the utility of improved sequencing technologies especially whole genome sequencing, there has been a substantial increase in finding the aetiology of many unresolved /exome-negative cases of skeletal dysplasias.

Methodology: Twelve unrelated families with different skeletal dysplasias and non-diagnostic exome sequencing results were recruited for the study with ethical clearance. Detailed clinical features, family history, along with the radiological, and biochemical findings were recorded. Systemic investigations were performed. Whole genome sequencing was performed for the index patient in all the families. Data analysis, interpretation and variant prioritization were performed using standard procedures.

Major findings: Thirteen deep intronic/genomic variants were identified in eight (of twelve) families in the genes known to be causal according to the clinical diagnosis. The monogenic causes of skeletal dysplasias included: Atrial defects, polydactyly multiple congenital malformation syndrome, Mucopolysaccharidosis type 4, Grebe dysplasia, Odontochondrodysplasia, Osteogenesis imperfecta, Achondrogenesis, Osteopetrosis, neonatal/infantile form, and Bone fragility with calvarial lesions. Segregation analysis using the parental samples confirmed the molecular diagnosis.

Conclusion: The clinical and biochemical hallmarks of many of the skeletal dysplasias are well documented. In view of a definitive clinical diagnosis, and non-diagnostic results of exome sequencing, clinicians should opt for genome sequencing for identifying the molecular etiology and thus improve the diagnostic yield. This study highlights the importance of genome sequencing and its utility in prenatal and postnatal clinical settings especially for the unexplained rare genetic disorders.

Keywords: Genome sequencing, exome-negative cases, skeletal dysplasia

PHARMACOGENETIC PERSPECTIVES ON HYPERTENSION AND INTRACRANIAL ANEURYSM: THE RELEVANCE OF PRECISION MEDICINE

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Background: Intracranial aneurysms, which is often associated with hypertension, pose a serious health concern in India and antihypertensives are the preferred mode of medication. Pharmacogenetics, the study of how genetic factors influence an individual's response to drugs, holds promise in improving treatment outcomes and reducing adverse reactions. This study investigated the presence of any reported pharmacogenetic variants in a cohort of intracranial aneurysm patients with hypertension.

Methodology: Genotyping of 93 intracranial aneurysm patients with hypertension was done using AxiomTM Asia precision medicine research array. The presence of reported variants in pharmacogenes was assessed. The possible influence of the variants on drug responsiveness was evaluated based on PharmGKB data and previously published research.

Major findings: Twenty reported pharmacogenetic variants were identified in the patient samples, spanning drug target, drug metabolizing and drug transporter genes. Examination of these variants showed that, a significant percentage of patients had genetic profiles associated with decreased response or no response to specific medications. It was identified that, in the Indian population the haplotype frequency for non-responsiveness or poor responsiveness varied considerably from approximately 20% to 50% for the pharmacogenes.

Conclusion: In conclusion, the importance of considering genetic factors during the selection and dosage of medications to patients with intracranial aneurysms and hypertension is highlighted in the current pharmacogenetic study. The findings also suggest that the integration of pharmacogenetic testing into clinical practice has the potential to enhance drug efficacy, mitigate adverse drug reactions, and facilitate the implementation of precision medicine methodologies. The development of more personalized treatment strategies for patients with hypertension and intracranial aneurysm can help in preventing adverse outcomes as haemorrhage. Further research may be warranted to validate the above findings and explore their clinical implications.

Keywords: Intracranial aneurysm, hypertension, pharmacogenetics, precision medicine

DIFFERENTIAL EXPRESSION OF NEUROGENESIS-RELEVANT GENES IN THE PERIPHERAL BLOOD LYMPHOCYTES OF POLYMICROGYRIA PATIENTS

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Background: Polymicrogyria (PMG) is a cortical development malformation influenced by neuronal proliferation, differentiation, and migration. This study compared the peripheral blood gene expressions of 31 PMG-associated genes between 20 PMG patients and 20 age- and gender-matched healthy controls using the SYBR Green-based comparative, with *GAPDH* as the reference gene. Significant differences were found in the expression of *TUBB2B, GPSM2, GMPPB, IBA57, NDE1*, and *RAB3GAP2*, which are crucial for neurogenesis and cerebral cortex development. This is the first study to examine the expressions of PMG/cortical malformation-associated genes in peripheral blood samples of PMG patients.

Methodology: The study approved by the Institutional Ethics Committee of Government Medical College Thiruvananthapuram and the Institute for Communicative and Cognitive Neurosciences, involved 20 PMG patients and 20 healthy controls. PMG diagnosis was confirmed showing 14 bilateral and 6 unilateral PMG cases in various brain regions. RNA was extracted from peripheral blood samples and converted to cDNA. Gene expression was analysed using SYBR Green-based qPCR with *GAPDH* as the reference gene.

Major findings: There was no significant difference in age or gender distribution between the PMG and control groups. Significant differences were found in the expression of six genes: *TUBB2B, GPSM2, GMPPB, IBA57, NDE1*, and *RAB3GAP2*.

Conclusion: We observed differential expression of neurogenesis relevant genes (*TUBB2B, GPSM2, GMPPB, IBA57, NDE1, RAB3GAP2*) in the peripheral blood lymphocytes of PMG patients compared to healthy controls.

Keywords: Polymicrogyria, peripheral blood lymphocytes, mRNA, tubulins

UNLOCKING THE THERAPEUTIC POTENTIAL OF THE MICROBIOME: TRANSFORMING MODERN MEDICINE

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Background: The human microbiome, an intricate network of microorganisms residing on and within the human body, plays a crucial role in maintaining health and influencing disease outcomes. Advances in microbiome research highlighted its impact on various physiological processes, including digestion, metabolism, and immune regulation. This field opened new avenues for therapeutic innovation, with microbiome-based therapies such as probiotics, prebiotics, synbiotics, faecal microbiota transplantation (FMT), and microbiome-derived metabolites promise in treating conditions from gastrointestinal disorders, metabolic diseases, autoimmune conditions, and cancer. Understanding the complex interactions between the microbiome and host health revealed potential for personalized treatments tailored to individual microbiome profiles. Challenges such as unclear therapeutic mechanisms, and safety concerns must be addressed to realize the potential of microbiome-based therapies.

Methodology: Microbiome samples are collected from various body sites and processed for DNA extraction and sequencing. The data is analysed to determine microbial diversity and function. In vitro and in vivo studies validate microbial interactions and effects. Probiotics, prebiotics, synbiotics, FMT, and microbiome-derived metabolites are then formulated, followed by clinical trials to test their efficacy and safety.

Major findings: Microbiome-based therapies show promise in treating gastrointestinal disorders like IBS (irritable bowel syndrome) and IBD (Inflammatory bowel disorder), improving metabolic health for conditions such as obesity and diabetes, and influencing immune responses to manage autoimmune diseases, allergies, and infections. They can also enhance the effectiveness of cancer immunotherapies. Personalized approaches are necessary due to the individuality of the human microbiome.

Conclusion: Microbiome-based therapies have the potential to revolutionize modern medicine by treating a wide range of diseases. While promising, these therapies, their effectiveness underscores the need for personalized treatment strategies tailored to individual microbiome profiles to maximize therapeutic benefits.

Keywords: Microbiome, prebiotics, synbiotics, FMT

MUTATIONAL LANDSCAPE OF HOMOLOGOUS RECOMBINATION REPAIR GENES IN OVARIAN CANCER

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Background: Ovarian cancers harbouring HRR deficiency typically exhibit sensitivity to poly-ADP ribose polymerase inhibitors (PARPi). Current guidelines recommend a range of approaches for genetic testing to identify predictors of sensitivity to PARPi in ovarian cancer and to identify genetic predisposition. In this study, we retrospectively analyzed the mutations of *HRR* genes in tumour tissues and evaluated their values for predicting the survival of ovarian cancer patients.

Methodology: Library preparation was performed using the Ion AmpliSeq™ Library Kit Plus using Oncomine HRR Pathway DNA Panel and loaded onto Ion Torrent S5 NGS platform. Variant calling was done using Ion Reporter (v5.18). Variants were called using Torrent Variant Caller plugin and were annotated using Ion Reporter software. Variants were further classified as per AMP/ASCO/CAP guidelines.

Major findings: A total of 30% cases had deleterious mutations in 6*HRR* genes, namely, *BRCA1* (18%), *BRCA2* (8%), *ATM* (2.66%), *RAD51C* (1.33%), *CHEK2* (1.33%) &*RAD54L* (1.33%). There is a strong mutual exclusion between *HRR* genes. According to the mutation allele frequency, about 6.65% of the patients had potential somatic non *BRCA HRR* gene mutations, which might be underestimated. *BRCA1* mutations tend to be present in younger patients with family history or multiple primary foci.

Conclusion: This study revealed the distribution of *HRR* gene mutations in EOC tissues. *BRCA1/2* account for the majority of *HRR* gene mutations and predict long prognosis in HGSOC. Non-*BRCA HRR* mutations also account for a very important proportion and might be associated with poor prognosis in HGSOC. It is suggested germ line status be further clarified in clinical algorithm for potential targeted therapy, genetic screening, and prognosis prediction.

Keywords: Homologous recombination repair, *BRCA*, ovarian cancer

PHARMACOGENOMIC PREDICTORS OF SODIUM VALPROATE-INDUCED WEIGHT GAIN IN PERSONS WITH EPILEPSY: A NESTED CASE-CONTROL STUDY FROM SOUTH INDIA

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Background: Sodium valproate, a commonly used anticonvulsant for treating epilepsy, is associated with a variety of side effects, the most frequent being weight gain. The association between genetic factors and valproate induced-weight gain is not studied in South-Indian (SI) population. Hence the study aims to 1. To evaluate the association between nine single nucleotide polymorphisms (SNPs) in drug metabolizing enzymes, appetite stimulation, energy homeostasis genes and valproate-induced weight gain in Persons with Epilepsy (PWE) from SI. 2. To compare the dose-corrected plasma valproate level between genotypes of genetic polymorphism of *UGT1A6*.

Methodology: 216 PWE of SI origin, aged 12-65 years of both genders, within 1 month of initiating Valproate monotherapy were included. Body weight was measured at baseline and after 6 months of follow-up, succeeded by the classification of PWE as cases and controls. Genotyping of extracted DNA was done by qRT-PCR and Valproate levels were estimated by LC-MS/MS.

Major findings: Of the 216 PWE recruited and followed up, 97 people were classified as cases (weight ≥ 5% of the baseline weight), while 97 were controls. Two SNPs in genes such as α2 catalytic subunit of AMPK (PRKAA2) –rs10789038 and Resistin (RETN)-rs1862513 showed significant associations with valproate-induced weight gain (p=0.0019, p=0.0045 respectively). SNP-SNP and SNP-environment interactions were carried out and interaction between rs10789038 and rs1862513 was found to be significant(p=0.009). *UGT1A6* was found to have a significant effect on valproate plasma levels, but there was no statistically significant difference between genotypes of *UGT1A6* in cases and controls and on valproate plasma levels.

Conclusion: Our findings provide preliminary evidence that SNPs in *PRKAA2* rs10789038 *RETN* rs1862513 may have value in predicting valproate-induced weight gain.

Keywords: SNP, sodium valproate, epilepsy, weight-gain

INTERMEDIATE SWEAT CONDUCTIVITY VALUES IN SUSPECTED CYSTIC FIBROSIS: THE ROLE OF GENETIC AND PHENOTYPIC FACTORS

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Background: Sweat conductivity analysis using Nanoduct System is one of the widely used screening test for diagnosis of cystic fibrosis in suspected patients. Values ≥ 80 mmol/L is considered almost diagnostic of CF, while values <50 mmol/L are considered less likely to be CF. Not much literature is available on implications of intermediate values (50-79 mmol/L).

Methodology: Sweat conductivity was measured on 104 patients with suspected CF, by Nanoduct system. Among these, 38 had intermediate values and underwent targeted CFTR gene sequencing. No significant CFTR variants were found in 29 of 38. For 9 of 29 and one with a heterozygous variant, clinical exome sequencing was done. Nine among them had significant variants in other genes (23.6%). We analysed their functional pathways using KEGG database and interaction with CFTR using STRING database.

Major findings: We identified 2 significant CFTR variants in 4 patients (10.5%), one variant in 5 (13.1%) and none in 29 (76.3%) patients with intermediate sweat chloride values. Of the latter 10 for whom CES was done, 9 had variants in genes other than CFTR and none in one patient. These other genes were not found to have any role in electrolyte transport or homeostasis pathway or functional association with CFTR. Nearly half (5/9) patients with variants in other genes had malnutrition, shown to be associated with elevated sweat chloride values.

Conclusion: Nearly a tenth of our patients with intermediate sweat conductivity values were confirmed to have CF. Among 9 others investigated by NGS, almost all had significant mutations in other genes not involved in sodium or chloride pathways. Half had malnutrition that is associated with elevated sweat chloride. The test is not as specific as considered traditionally. We suggest further evaluation of patients with intermediate values.

Keywords: CFTR, variants, NGS, malnutrition, pilocarpine-iontophoresis, nanoduct

EVALUATING CYTOGENETIC MARKERS IN MULTIPLE MYELOMA: INSIGHTS FROM AN INDIAN PATIENT COHORT

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Background: Multiple myeloma (MM) is a complex and heterogeneous disease. Cytogenetics is crucial for defining and prognosticating MM. High-risk MM includes primary IGH translocations t(4;14), t(14;16), t(14;20), and secondary aberrations such as gain/amp(1q), 1p deletion, del(17p), and hypodiploidy. This study aimed to evaluate the incidence of cytogenetic abnormalities in our patient cohort.

Methodology: Interphase FISH was performed on purified plasma cells using standard protocols in 577 newly diagnosed myeloma cases, utilizing specific probes. Karyotyping was also done wherever possible.

Major findings: The median age at diagnosis was 62 years, ranging from 22 to 92 years. Differences were observed between FISH-positive and FISH-negative groups. Of the 577 patients, 64% were males and 36 %were females. Deletion of chromosome 13 (13q14) was the most common abnormality, present in 124 (21.4%) cases. Deletion of chromosome 17 (17p) was observed in 38 (6.5%) cases. The most common translocation involving the IGH locus was t(4;14), seen in 50 (8.6%) cases. t(11;14) was present in 36 (6.2%) cases. Two abnormalities, del (13q) with t(4;14), were present in 8 cases, and del(13q14) with del(17p) was present in 46 cases. Gain of 1q and loss of 1p was studied in 50 cases, with amplification of 1q seen in 7 patients. Three abnormalities, del (13q14), del(17p), and t(4;14), were present together in 5 cases.

Conclusion: The incidence of IGH translocation was 16%, compared to 26% in another Indian study. This study highlights the importance of studying the Indian population to understand the prevalence of cytogenetic changes in MM. FISH is an effective method for detecting cytogenetic abnormalities and providing information for risk stratification.

Keywords: Multiple myeloma, cytogenetics, IGH translocations, FISH, karyotyping

AMELIORATING EFFECT OF SHORT CHAIN FATTY ACIDS (SCFAS) ON HEPATOCELLULAR CARCINOMA VIA TARGETING RISC MACHINERY AND TELOMERASE hTERT

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Background: Hepatocellular carcinoma refers to the carcinoma of the parenchymatous liver tissue originating from the hepatocytes. While multiple factors are associated with the causation of HCC, telomerase (human telomerase reverse transcriptase-hTERT) aberration is one of the common genetic causes underlining this condition. Short-chain fatty acids (SCFAs) are well-known secondary metabolites derived from healthy-gut microflora that are long known in maintaining cellular homeostasis. Our current study aims to elucidate the novel molecular mechanism role of SCFAs in regulating RISC machinery meditated hTERT expression in HCC and evaluate its anti-tumour effects using in-vitro cellular models.

Methodology: HCC cell line, Huh7 was cultured in F12-Hams complete medium. Cells were seeded for SCFA (Sodium butyrate and Sodium propionate) treatment in three groups: Control, Sodium Butyrate (SB) and Sodium Propionate (SP) respectively. IC50 of SCFAs was determined from WST-1 cytotoxicity assay. Wound healing assay was performed to assess the effect of SCFAs on cellular migration. Whole cellular RNA was isolated from the control and treatment groups for cDNA conversion and subsequent RNA quantification of telomerase components through real-time quantitative PCR (qPCR).

Major findings: Our in-vitro cell-based assays validated the effects of SCFAs on HCC cell lines by inducing cytotoxicity. IC50 concentrations for SB (2.4mM) and SP (4.6mM) respectively. It was determined that SCFA treatments at these concentrations inhibited the cellular migration ability of HCC cells. Our qPCR results further demonstrated that SND1 expression and hTERT was downregulated upon SCFA (SB & SP) treatment as compared to the control cells.

Conclusion: Through these findings, we explored the novel role of dietary SCFAs like sodium butyrate and sodium propionate and their ameliorating effects on HCC by mitigating the RISC machinery induced telomerase hTERT expression, which are commonly upregulated in HCC.

Keywords: Hepatocellular carcinoma, hTERT, RISC, sodium butyrate, sodium propionate

GENOMICS OVERVIEW OF NEXT GENERATION SEQUENCING APPROACH IN CLINICAL VIROLOGY

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Background: Next-generation sequencing (NGS), have produced a true revolution and opened new perspectives for clinical virology, owing to the high speed and throughput of data generation. These applications are particularly suitable for identifying viruses in blood stream and upper respiratory infection causing pathogens.

Methodology: Next-generation sequencing methodology includes template preparation, sequencing and imaging, and data analysis. This article discusses conventions and ideologies of diagnostic application of NGS in virology.

Major findings: Viral sequencing for the detection of drug-resistant variants helps to management of highly active antiretroviral therapy (HAART) for HIV relies. Additionally, it plays a crucial role in predicting the receptor tropism of HIV based on genetic characteristics, which has significant implications for treatment decisions. Genetically related viral variants, referred to as quasi -species, these can cause pressure on immune system and efficiency of antiviral drug treatments. Detection and quantification of these variants in-fact have biological and clinical relevance. However, these quasi species cannot be easily detected using the conventional clinical approaches.

Conclusion: Next generation sequencing offers unparalleled insights into viral dynamics, enabling the exploration of previously uncharted territories, including: The role of various viral reservoirs in the natural history of infection, co-receptor usage in minor viral populations within different cell lineage, The emergence of drug resistance, the re-emergence of latent genomes after treatment interruptions.

Keywords: Clinical virology, genomics, next-generation sequencing, quasi species

BIALLELIC NOVEL VARIANT IN *(PGAP3)* RELATED HYPERPHOSPHATASIA WITH IMPAIRED INTELLECTUAL DEVELOPMENT SYNDROME 4

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Background: Hyperphosphatasia with Impaired Intellectual Development Syndrome 4 (HPMRS4) is a rare autosomal recessive disorder caused by variations in *PGAP3*. The characteristic feature of this disease includes severe psychomotor delays, intellectual disability, seizures, lack of speech acquisition, and facial dysmorphism, and elevated serum alkaline phosphatase levels.
Methodology: One affected individual of age 1 year, born of a non-consanguineous marriage was ascertained for this study. Detailed clinical features, family history, along with radiological, and biochemical findings were recorded. MRI, chromosomal microarray was performed along with regular biochemical profile including serum alkaline phosphate (ALP) levels. Solo whole exome sequencing (WES) was performed for the proband, followed by data analysis and interpretation using standard procedures.
Major findings: The proband initially presented with global developmental delay, and facial dysmorphism. Detailed examination at age 1 year 6 months revealed facial dysmorphism, repetitive lip movements, abnormal small, folded ear, large head, turricephaly and significant speech delay. MRI of the brain and chromosomal microarray analysis was unremarkable. Serum ALP level of the patient was highly elevated, 730 IU/L (normal range 20–140 IU/L). On re-analysis of the WES data, a likely pathogenic novel variant, c.214T>C p.Cys72Arg in exon 2 of *PGAP3* was identified in homozygous state. This variant was absent in gnomAD population database (v4.1). Segregation analysis revealed that the parents were the carriers of this particular variant.
Conclusion: Hitherto, 66 patients of different ethnicities have been reported in the literature. We present and report an Indian patient in literature with *PGAP3*-related HPMRS4. Exome sequencing along with biochemical investigation cues (increased ALP levels) together helped us to reach at the final molecular diagnosis, and thus validate the likely cause of the disease in the first Indian patient with HPMRS4.
Keywords: *PGAP3*, hyperphosphatasia, impaired intellectual development syndrome

CASE REPORT OF AN INDIAN PATIENT WITH HK1-RELATED NEURODEVELOPMENTAL DISORDER WITH VISUAL DEFECTS AND BRAIN ANOMALIES

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Background: Neurodevelopmental disorder with visual defects and brain anomalies (NEDVIBA, OMIM# 618547) is defined by impaired intellectual development, global developmental delay, visual and muscular tone abnormalities, and structural brain anomalies. This condition results from heterozygous mutations in the *HK1* gene and it follows an autosomal dominant mode of inheritance pattern.
Methodology: A 19-month-old female child, born to non-consanguineous parents, was ascertained for this study. Comprehensive clinical features, family history, and radiological and biochemical findings were documented. MRI, routine biochemical profile, and urine GCMS were performed. Solo whole exome sequencing (WES) was performed for the problem.
Major findings: The proband initially presented with knee swelling, acute kidney injury, microcephaly, dysconjugate gaze, retinitis pigmentosa, hypernatremia, and neonatal jaundice. She also had a history of severe developmental delay and seizures. Detailed clinical examination revealed nystagmus, tapering fingers, clinodactyly, facial dysmorphism, short neck, and Mongolian spots. MRI revealed bilateral cerebral atrophy. Biochemical investigations showed that the child had elevated glycine, ornithine, and alanine levels. The initial data analysis of WES did not identify a potential variant that corresponded with the patient's clinical phenotype. On re-analysis, a likely pathogenic variant, c.1370C>T p.(Thr457Met) in exon 10 of *HK1* was identified in a heterozygous state which was previously reported to cause NEDVIBA. This variant was absent in the gnomAD population database (v4.1). Segregation analysis confirmed the de-novo state of the variant.
Conclusion: Hitherto, 7 cases have been reported for NEDVIBA in the literature. This is the first report from India of a de-novo disease-causing variant in *HK1* causing NEDVIBA. Thus, we provide additional evidence of *HK1*-related associated diseases from India.
Keywords: *HK1*, neurodevelopmental disorder, whole exome sequencing, NEDVIBA

REPORT OF AN INDIAN PATIENT WITH A NOVEL VARIANT IN *AGTPBP1*-RELATED NEURODEGENERATION, CHILDHOOD-ONSET, WITH CEREBRAL ATROPHY

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Background: Neurodegeneration, childhood-onset, with cerebral atrophy (CONDCA, OMIM#618276) is a rare autosomal recessive disorder caused by disease-causing variations in *AGTPBP1*. The characteristic features of this disease include global developmental delay, impaired intellectual development, poor or absent speech, and motor abnormalities. Brain imaging shows cerebellar atrophy.

Methodology: The study involved two affected individuals, aged 26 and 30 years, and an unaffected female sibling (24 years) born from a consanguineous marriage. Clinical features, family history, radiological findings, and biochemical results were documented. MRI, karyotyping, biochemical profiles, and BAER were also performed. Solo whole exome sequencing (WES) was performed for the proband along with data analysis.

Major findings: The elder sibling presented with regression of myoclonic epilepsies, delayed developmental milestones, hyperactivity, progressive difficulty walking, gait abnormalities, truncal ataxia, and hyperkinesia. Similar features were noted in younger sibling who also had fever-induced seizures and loss of ability to speak. MRI of the younger sibling revealed atrophy of the corpus striatum. Other systematic investigations were unremarkable. Solo WES data analysis helped in identifying a disease-causing variant c.3251C>T p.Thr1084Ile, in exon 24 of the *AGTPBP1,* in homozygous state causing CONDCA. This variant was absent in the gnomAD population database (v.4.1). The deleterious state of the variant in AGTPBP1 protein was confirmed by in-silico prediction tools. On segregation analysis parents and unaffected siblings were carriers of this disease.

Conclusion: To date, 31 patients from 25 unrelated families with CONDCA, carrying homozygous or compound heterozygous mutations in the *AGTPBP*1 from different ethnicities have been reported in the literature. We report the first Indian patient with *AGTPBP1*-related CONDCA. As both the parents are carriers of this disease, segregation analysis helped us in counselling the family about the risk of inheritance to offspring.

Keywords: *AGTPBP1*, neurodegeneration, childhood-onset with cerebral atrophy

GENOMICS IN PREVENTIVE CARDIOLOGY - AN OVERVIEW

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Background: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality globally. Although CVD events do not typically manifest until older adulthood, CVD develops gradually across the life-course, beginning with the elevation of risk factors observed as early as childhood or adolescence and the emergence of subclinical disease that can occur in young adulthood or midlife. Genomic background, which is determined at zygote formation, is among the earliest risk factors for CVD. With major advances in molecular technology, including the emergence of gene-editing techniques, along with deep whole-genome sequencing and high-throughput array-based genotyping, scientists now have the opportunity to not only discover genomic mechanisms underlying CVD but use this knowledge for the life-course prevention and treatment of these conditions.

Methodology: The following techniques are widely used: - Whole genome sequencing, gene editing, high-throughput array-based genotyping.

Major findings: The current review focuses on innovations in the field of genomics and their applications to monogenic and polygenic CVD prevention and treatment. With respect to monogenic CVD, we discuss how the emergence of whole-genome sequencing technology has accelerated the discovery of disease-causing variants, allowing comprehensive screening and early, aggressive CVD mitigation strategies in patients and their families. We further describe advances in gene editing technology, which might soon make possible cures for CVD conditions once thought untreatable. In relation to polygenic CVD, we focus on recent innovations that leverage findings of genome-wide association studies to identify druggable gene targets and develop predictive genomic models of disease, which are already facilitating breakthroughs in the life-course treatment and prevention of CVD.

Conclusion: We hope to underline the value of leveraging genomics and broader multiomics information for characterizing CVD conditions, work which promises to expand precision approaches for the life-course prevention and treatment of CVD.

Keywords: Genomics, genotyping, monogenic CVD, polygenic CVD

NON-SYNDROMIC HEARING LOSS - VARIANTS IN CAUSATIVE GENES: A CASE SERIES

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Background: Non-syndromic sensorineural hearing loss (NSNHL) comprises of a wide range of hearing disorders affecting people of all age groups and most cases are autosomal recessive (AR). The objective of the study was to understand the genetic mutations that results in SNHL through screening of patients with symptomatic hearing loss.

Methodology: A total of 21 patients between the lifespan January2022- January2024 who were known case of hearing deficiency (non-syndromic) were taken up for mutation screening through audiology follow up and protest genetic counselling in the Department of Genetics at Lifeline hospital- Adoor, Kerala. An informed written consent was taken from patients/parents prior to blood collection. Genetic screening was done by using clinical exome sequencing.

Major findings: Two affected children showed pathogenic homozygous and compound heterozygous mutation in *GJB2* gene. Another affected child showed pathogenic compound heterozygous mutation in *MYO15A* gene related to deafness. An adult deaf and mute couple showed pathogenic homozygous mutation in *GJB2*gene. The husband of the couple and his twin brother(identical) had also *VUS* compound heterozygous mutation in *OTOF* gene related to deafness. In almost 50% of the cases, no mutation was detected in Gap junction beta-2protein-*GJB2* gene irrespective of consanguinity.

Conclusion: Genetic testing for non-syndromic hearing loss helps in identifying pathogenic/likely pathogenic mutations thereby helping the families the option of prevention by prenatal diagnosis and management possible by cochlear implants.

Keywords: Non-syndromic sensorineural hearing loss, autosomal recessive, gap junction beta-2 protein, otoferlin

MUTATIONAL LANDSCAPE IN CONSANGUINEOUS FAMILIES AND PREVALENCE OF AUTOSOMAL RECESSIVE DISORDERS IN TERTIARY CARE CENTRE – RETROSPECTIVE SHORT STUDY

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Background: Consanguineous marriages have been a longstanding practice in human history. There is an increased risk of autosomal recessive genetic disorders in consanguineous marriages as there is a higher probability that both the parents carry same genetic mutation. The present study was carried out to know the prevalence of pathogenic and likely pathogenic mutation in autosomal recessive disorders.

Methodology: A total of thirty couples consanguineously married (III degree) from central Kerala who had bad obstetric history, children with mental retardation and neonatal death were taken up for carrier screening to rule out single gene disorders. The study was carried out during the period of Jan 2020-Jan 2024. Approximately 500 panel genes by clinical exome/ carrier screening and specific targeted sequencing were screened. Variant of Uncertain Significance not relevant to the phenotype was ignored. The findings were tabulated and results are discussed.

Major findings: Thirty couples were analysed and the most common condition noted in our study was SMA. Congenital adrenal hyperplasia and cystic fibrosis was seen in one case each. However, we have come across rare other autosomal recessive conditions such as Raine syndrome, Cohen syndrome, restrictive dermopathy 1 etc.

Conclusion: Carrier screening is important in couples with bad obstetric history, children with mental retardation, neonatal death and consanguinity. Identifying single gene disorders have implications in future reproductive planning, prevention by prenatal diagnosis or preimplantation genetic testing.

Keywords: Autosomal recessive conditions, congenital adrenal hyperplasia, cystic fibrosis, Cohen syndrome, genetic disorders

GENETIC VARIATIONS IN ONE CARBON-METABOLIC GENES PREDICTS NOVEL ASSOCIATION WITH RHEUMATOID ARTHRITIS SUSCEPTIBILITY RATHER THAN METHOTREXATE DRUG RESPONSES

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Background: Rheumatoid arthritis (RA) is a disease of the immune system that affects the diarthrodial joints and is symbolized by decreased self-tolerance. Methotrexate (MTX) is the first baseline therapy used for the treatment of rheumatoid arthritis globally. Genetic variations in the drug transporters and metabolizing genes in the folate metabolic pathway may affect MTX medication in RA. Thus, our study focuses on genetic variation liable for pharmaco-genes of methotrexate drug responses and RA risk in rheumatoid arthritis individuals.

Methodology: A retrospective cohort study was conducted with 107 RA individuals from Malayalam-speaking ethnic groups in South India to address this issue. A case-control study was also performed to investigate the significant association of folate genes with RA outcomes.

Major findings: Our study suggests that *MTRR* rs1532268 C/T, a drug metabolizer gene, was substantially correlated with MTX treatment responses in RA individuals. The association with this SNP was actively involved in the regulation of the methionine cycle and vitamin B12 intake by stabilizing the OCM pathway. Besides, a case-control study reveals a strong correlation with variants of the folate genes *ABCB1* (rs1045642C/T), *MTHFR* (rs1801133C/T), *MTR* (rs1805087A/G), and *MTRR* (rs1532268C/T) for RA risk.

Conclusion: Interestingly, polymorphic variants of *MTRR* rs1532268 play a dual role in MTX drug responses and RA susceptibility in our population. None of the other folate genes show associations with drug responses but with RA susceptibility. Therefore, the present study concludes that the genetic variants of the metabolizing genes are real predictive markers for both methotrexate drug responses and RA susceptibility.

Keywords: Methotrexate, genomics, folate, methionine, methylation

EFFECTS OF NONCODING VARIATIONS IN THE CHROMATIN ORGANIZATION IN NONSYNDROMIC HEARING LOSS

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Background: Hearing loss (HL) is the most prevalent sensory deficit, affecting nearly 5% of the world population. Genetic factors contribute to HL in newborns, with 70% of cases being nonsyndromic (NSHL). Genetic variations in NSHL-associated genes are mainly in noncoding regions, which affect gene expression regulation. Regulatory elements interact with genes by forming loops in three-dimensional space, which aggregate into topologically associated domains (TADs) that maintain the local chromatin environment. The study aims to identify genetic variations in NSHL patients and evaluate the effect of noncoding variations on genome organization.

Methodology: Whole genome genotyping was performed in 127 patients and 143 controls, followed by a case-control association study. CNVs were computationally predicted from the genotyping data. The spatial organization of the chromatin in blood cells was evaluated by analyzing the publicly available Hi-C sequencing data. The Identified variations were mapped to the Hi-C chromatin interaction matrices to find the overlapping regions with chromatin loops, TADs and epigenetically active or inactive compartments.

Major findings: 10 markers were significantly associated with NSHL in our study population, among which the *GJB2* pathogenic variant causes protein truncation. 20 NSHL-associated genes were found to be harbouring CNVs in their vicinity, and these noncoding CNVs were overlapping with the reported regulatory elements. Several CNVs identified in the study overlap with chromatin loops and TAD boundaries, disrupting the three-dimensional chromatin organization. Additionally, regions with CNVs were observed to segregate into epigenetic compartments differently.

Conclusion: The genetic landscape of NSHL is highly variable among populations and ethnicities. Large genetic variations in the noncoding regions can affect gene expression directly by disrupting the regulatory interactions or indirectly by disrupting the TADs. The epigenetic status of different CNV regions reveals that the effect of the CNVs is determined by the epigenetic permissibility.

Keywords: Non-syndromic hearing loss, TADs, 3D chromatin organization

ENHANCING DIAGNOSTIC UTILITY AND OVERCOMING CHALLENGES: MLPA IN SUSPECTED DMD CASES

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Background: Pathogenic variations in the largest human gene dystrophin (DMD) is the most common cause of Duchenne/Becker muscular dystrophy (DMD/BMD), an X-linked neuromuscular disease. Genetic variations in the *DMD* gene can be deletions or point mutations. Around 70% of the genetic defects are predominantly large deletions. The remaining are small nucleotide variants including nonsense and missense mutations, small insertions, deletions or splicing alterations. Multiplex Ligation-dependent Probe Amplification (MLPA) technique has emerged as a standard approach for identifying frequent deletions or duplications in 79 exons of *DMD* gene.

Methodology: This study retrospectively reviewed 93 cases that underwent MLPA analysis, including 59 suspected DMD cases and 34 carrier screening cases. Among these, 59 cases were tested positive for DMD by MLPA (45 suspected DMD and 14 carrier screening), while 34 cases yielded negative results (16 suspected DMD and 18 carrier screening). To validate the negative MLPA results by correlating with clinical findings 14 MLPA negative samples (comprising 10 suspected DMD and 4 carrier screening) were re-analyzed using Next-Generation Sequencing (NGS).

Major findings: Of the 14 cases, NGS analysis identified both single and multiple pathogenic point mutations in 11 cases (9/10 suspected DMD and 2/4 carrier screening). Notably, two samples exhibited pathogenic point mutations in intron 5 and 53 of the *DMD* gene.

Conclusion: These findings demonstrate that while traditional MLPA assays exhibit an impressive analytical sensitivity (>99%) for detecting deletions/duplications, they fall short in identifying pathogenic point mutations. This study underscores the significance of intronic mutations, which are not uncommon. To address these limitations, future diagnostic strategies could benefit from integrating next-generation sequencing (NGS) alongside traditional MLPA assays. Such a combined approach would enhance sensitivity and enable comprehensive detection of both point mutations and indels.

Keywords: Duchenne muscular dystrophy, multiplex ligation-dependent probe amplification, next-generation sequencing

PHARMACOGENOMICS: A PATHWAY TO PERSONALIZED MEDICINE

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Background: Pharmacogenomics, the study of how genetic variations influence drug response, is a cornerstone of personalized medicine. By understanding the genetic factors that affect drug metabolism, efficacy, and toxicity, healthcare providers can tailor treatments to individual patients, improving outcomes and reducing adverse effects.

Methodology: This study involved a comprehensive review of existing literature and clinical trials focusing on pharmacogenomic applications in various therapeutic areas.

Major findings: Pharmacogenomics is concerned with the complex interactions between genetics, medication metabolism, and therapeutic outcomes. Individual pharmacological reactions vary depending on genetic variations in drug-metabolizing enzymes, drug transporters and drug targets. The rate at which medications are metabolized affects both efficacy and toxicity which can be considerably impacted by differences in the cytochrome P450 enzyme family (CYP450). In HIV patients with HLA-B*5701 allele Abacavir carries higher risk of hypersensitivity reactions. Tamoxifen, a breast cancer drug's effectiveness can be influenced by variations in the *CYP2D6* gene. Warfarin and Clopidogrel, the Blood thinners where genetic variations in *CYP2C9* and *VKORC1* (for Warfarin) and *CYP2C19* (for Clopidogrel) can affect dosing and risk of adverse effects. Pharmacogenomics also has significant role in reducing the risk of graft rejection and maximizing graft survival, pain management and tailoring cancer therapy.

Conclusion: Pharmacogenomics holds immense potential in advancing personalized medicine by enabling more precise and effective drug therapies. The integration of genetic information into clinical practice can lead to better patient outcomes, reduced adverse drug reactions, and overall healthcare cost savings. However, challenges such as the need for robust infrastructure, education of healthcare providers, and patient access to genetic testing must be addressed. Continued research and collaboration among scientists, clinicians, and policymakers are essential to fully realize the benefits of pharmacogenomics in clinical settings and paving a better path for personalized medicine.

Keywords: Pharmacogenomics, precision medicine, genetic variations, drug metabolism

EXPLORING THE ASSOCIATION OF *SRD5A2* GENE POLYMORPHISM (rs523349) WITH POLYCYSTIC OVARY SYNDROME

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Background: Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder that impacts 11.33% of women who are of reproductive age and exhibit hyperandrogenism, oligoovulation, and polycystic ovaries on ultrasound. Individuals with PCOS often experience associated conditions such as infertility, hyperlipidemia, insulin resistance, cardiovascular risks, obesity, and psychological challenges. Hirsutism is a common manifestation of hyperandrogenism, where it is associated with both androgen excess and individual unit response to androgens. In the context of PCOS, hirsutism displays considerable variability. Ethnicity contributes to this heterogeneity, implying a potential genetic influence on hirsutism severity within the PCOS population. One pivotal enzymatic process in androgen metabolism involves steroid 5α-reductase, which converts testosterone into the more potent dihydrotestosterone (DHT). Notably, both ovarian and peripheral 5α-reductase activity appear elevated in PCOS. There is no study regarding rs523349 polymorphism and PCOS from the Indian population. Our hypothesis proposes that genetic variations within the 5α-reductase genes may serve as risk factors for PCOS development and contribute to the varying expression of hirsutism among affected women.
Methodology: We recruited 134 controls and 137 PCOS patients based on Rotterdam criteria. Genomic DNA was extracted from the samples, followed by PCR-RFLP. Results were confirmed using Sanger sequencing. Statistical analysis was done using SPSS version 27.
Major findings: The PCOS and control groups did not differ significantly regarding genotype frequency and allele frequency ($p = 0.17541$). In our study, we observed no statistically significant association between the rs523349 polymorphism and various demographic parameters including age, weight, height, BMI, Ferriman Gallway score, lipid profile, and testosterone. We observed a significant difference in hirsutism (Ferriman-Gallway score) between the PCOS group and control group.
Conclusion: No association was found between *SRD5A2* rs523349 polymorphism and PCOS. This pioneering study from India should be replicated in more samples.
Keywords: Polycystic ovary syndrome, *SRD5A2*, rs523349, hirsutism, testosterone

PARENTAL TRANSMISSION EFFECTS OF THE *IRF6* POLYMORPHISMS AMONG NON-SYNDROMIC CLEFT LIP WITH OR WITHOUT CLEFT PALATE IN KERALA POPULATION

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Background: Orofacial cleft primarily cleft lip and cleft palate constitutes one of the most commonly occurring congenital abnormalities. The purpose of this study was to assess the Interferon Regulatory Factor-6 (*IRF6)* gene polymorphisms in the etiology of Non-syndromic Cleft Lip with or without Cleft Palate (NSCL/P) among the Kerala population using a case-parent trio design.

Methodology: The study comprised of hundred case-parent trios of NSCL/P from the Kerala Population. Genomic DNA was isolated from the trios. The polymorphisms rs2235371 and rs7552506 were genotyped using polymerase chain reaction (PCR) and Sanger sequencing method. PLINK software was used for the statistical analysis. Pairwise linkage disequilibrium (LD) was computed using the Haploview program.

Major findings: We found a significant association of the rs2235371 (p-value = 0.0094, OR = 2.2) with NSCL/P. The allelic TDT analysis 'A' allele of rs2235371 showed significant paternal transmission (p-value = 0.03), whereas the 'C' allele of rs7552506 (p-value = 0.0094) showed an excess maternal transmission. The pairwise linkage disequilibrium (LD) values (D'= 0.83 and r^2 =0.033) between rs2235371 and rs7552506 revealed that these two SNPs are not in strong LD. Haplotype G A showed a significantly reduced risk for oral clefts (p=0.035).

Conclusion: The current study revealed that polymorphism rs2235371 is associated with NSCL/P. The parent-of-origin effects were observed as the two polymorphisms demonstrated a significant parental transmission. The rs2235371 showed a significant paternal transmission, whereas the rs7552506 showed an excess maternal transmission suggesting that the *IRF6* gene may influence the risk of NSCL/P in the Kerala population.

Keywords: Orofacial clefts, *IRF6*, case-parent trios, parent-of-origin, haplotype, LD

POPULATION DYNAMICS AND MIGRATION EVENTS OF THE THREE POPULATIONS OF LAKSHADWEEP ARCHIPELAGO

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Background: Lakshadweep archipelago has ten human-inhabited islands among a total thirty-six. Human-inhabited islands are classified as Northern/Amini group islands and Southern/ Laccadive group islands. According to archaeological records, Amini is said to be the first inhabited island in the archipelago. There are three groups/tribes that maintain strict endogamy, namely Koya, Malmi, and Melacheri. All the three tribes showed distinct admixture pattern from main land Indian populations. The admixture time of these studied populations was 50± 8 generations (1260–1740 AD).

Methodology: Blood samples were randomly collected and DNA was extracted using the standard Phenol Chloroform method. Whole mitochondrial DNA was sequenced using Sanger Sequencing protocol. Data were analysed using different analysis tools. Statistical analyses were performed using PCA, Bayesian analysis, mismatch analysis, pairwise FST analysis and beast analysis.

Major findings: Based on 16226bp analysed and 137 sequences, the average number of pairwise differences between Koya and Malmi was 26.893, between Koya and Melacheri 29.991 and between Melacheri and Malmi 26.896. Nei's distance between Koya and Malmi was 1.883, between Koya and Melacheri 6.527 and between Melacheri and Malmi 3.423. Both these tests show that Koya may be relatively more divergent from Melacheri than Malmi. Through Bayesian skyline plot we also observed that the increase in the population size between 20-25kya in all the three Lakshadweep population. Tajima D value for Melacheri was more negative (D=-1.7) suggesting that Melacheri underwent a drastic demographic change due to founder effect.

Conclusion: All three tribes show distinct maternal lineages, which are well preserved in the islands because of the strict cultural endogamy and matrilineal kinship practices. As compared to three tribes, Koya tribe shows divergence from Melacheri and Malmi and an exponential growth around 20-25kya. Therefore we suggest that, as compared to Kya and Malmi, Melacheri shows least divergence and demographic change due to founder effect.

Keywords: Population dynamics, founder effect, Bayesian analysis

IN VITRO ANALYSIS OF *SORT1* EXPRESSING LUNG CANCER CELL LINES AND THEIR EXOSOMES ON IMMUNE CELLS AND CARCINOGENESIS

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Background: Lung cancer is the most diagnosed type of cancers with high mortality rate (1.2 million) and estimated data shows cancer will become the leading cause of deaths (18.9 million), a 2.18-fold increase, by 2030. Exosomes**,** a type of EV**,** are small membrane-bound microvesicles (40–150 nm) released from cells. In cancer, exosomes change in both number and content affecting the microenvironment and inducing immune suppression, angiogenesis and pre-metastatic niche formation. SORT1, a trafficking protein, are present on cancer and immune cell-derived exosomes, and has been reported to show dichotomous roles in carcinogenesis.

Methodology: A549 (lung adenocarcinoma, high *SORT1*), SKMES1 (lung squamous cell carcinoma, low *SORT1*) and Jurkat-E6.1 were cultured for exosome isolation using precipitation method. The exosomes were characterized for their size and shape using NTA and TEM, respectively. The isolated exosomes were quantified using BCA assay. The exosomes from A549 and SKEMS1 were treated on Jurkat-E6.1 and vice versa with a concentration of 50µg/mL, followed by resazurin assay, scratch assay, RNA isolation, quantification, cDNA preparation and RT-PCR.

Major findings: The T cell-derived exosomes on A549 and SKMES1 enhance the proliferation rate of cancer cells while keeping a negligible effect on T cell proliferation upon cancer cell line-derived exosome treatment. Also, high migratory potential was observed in exosome treated cancer cells relative to non-treated. The genomic expression of *SORT1* and associated genes responsible for cellular cargo trafficking (*TRKA, TRKB, P75NTR, NGF,* and *BDNF*) showed varying expression upon exosome cross treatment. Furthermore, alterations in the carcinogenesis pathways such as survival, proliferation, epithelial-mesenchymal transition, and angiogenesis was also observed.

Conclusion: *SORT1* and associated cargo molecules as such in the cells and on exosomes possess direct role in carcinogenesis. Focusing more into their molecular mechanism will potentially open up a novel therapeutic intervention.

Keywords: *SORT1,* lung cancer, exosome, cross-treatment, immune cell

Abstracts

Proteomics in Healthcare

Total number of abstracts: 23

Oral presentations
Young Scientist Award: 4
Best Paper: 5
Contributed Paper: 5

Poster presentations
Young Scientist Award: 0
Best Paper: 3
Contributed Paper: 6

A COMPARATIVE STUDY OF SERUM BETA TRACE PROTEIN AND ALBUMINURIA IN TYPE 2 DIABETES MELLITUS

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Background: Type 2 diabetes mellitus (T2DM) is a common metabolic disorder associated with multisystemic complications. Diabetic nephropathy (DN) is a major microvascular complication of diabetes mellitus, characterized by increasing albuminuria and progressive loss of kidney function. Although urinary albumin is recognized as an early marker of DN, significant glomerular damage has occurred in many diabetic cases without albuminuria. Therefore, a new biomarker, beta trace protein (BTP), which has more sensitive and specific prognostic ability, can potentially diagnose DN. BTP is also known as prostaglandin D2 synthase. To evaluate the serum concentration of BTP in nondiabetics, diabetics without nephropathy, and diabetics with nephropathy, and to correlate it with albuminuria.

Methodology: Using cross-sectional analysis, this study analyzes the effect of BTP, a low-molecular-weight protein which appears to be constantly produced. It is freely filtered by the glomerulus, reabsorbed, catabolized, and not secreted by the renal tubules, and is found to be increased in the serum of patients with renal diseases. As a result, reductions in GFR are associated with increased plasma concentrations of BTP.

Major findings: This study focuses on the analytic sensitivity, reference intervals, Pearson correlation, and ROC curve used to determine the accuracy of BTP and the diagnostic performance of BTP against albuminuria in the general population and in specific subpopulations of patients.

Conclusion: Serum BTP is a predictive marker useful in the detection and diagnosis of DN and has been proposed as an endogenous marker for the estimation of GFR. It detects renal injury earlier than albuminuria.

Keywords: Diabetes mellitus, diabetic nephropathy, beta-trace protein, albuminuria, prostaglandin D2 synthase

QUANTIFICATION OF E-CADHERIN AND NUCLEAR MORPHOMETRIC FEATURES AS A MEASURE OF INVASIVE POTENTIAL IN BREAST CANCER CELL LINES

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Background: Breast cancer is the most common cancer in women worldwide and is the second leading cause of cancer-related death in women. The incidence rate of breast cancer has increased alarmingly in the last 40 years, with a 0.5% annual increase. Breast cancer is often associated with invasiveness, leading to metastasis; therefore, it is necessary to quantify the invasive potential of breast tumors in affected individuals. This quantification is essential at the cellular level to better understand the invasive potential of cells. E-cadherin is a major epithelial protein that binds epithelial cells together, and its downregulation leads to cells attaining a migratory phenotype.

Methodology: MCF-7 and MDA-MB-231 cell lines were used for this study. A scratch assay was performed on these cell lines to assess their healing potential. Immunocytochemistry was performed for E-cadherin expression at various time points, and images were captured with the help of a fluorescence microscope. Membranous and cytoplasmic expression of E-cadherin was quantified for different cells, and the ratio was calculated for each cell. Additionally, nuclear morphometric features were studied.

Major findings: Cells with greater migratory potential were found to have higher cytoplasmic expression of E-cadherin than cells with inhibited migratory potential. Significant differences in nuclear morphometric features were observed between migratory and non-migratory cells.

Conclusion: Migratory cells had a higher cytoplasmic-to-membranous ratio, whereas cells with diminished ability to migrate had a lower cytoplasmic-to-membranous ratio. Additionally, migratory cells had altered morphometric features compared to non-migratory cells.

Keywords: Breast cancer, E-cadherin, nuclear morphometry

EFFECTS OF BRAHMI AND MANDUKAPARNI RASAYANA ON THE NEUROPATHOLOGY AND METABOLIC PROFILES OF ALZHEIMER'S DISEASE IN A MOUSE MODEL

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder that affects people over 65 years of age, leading to cognitive impairment and memory loss due to the deposition of extracellular amyloid plaque and the formation of intracellular neurofibrillary tangles. Currently, there is no complete cure for AD, and available medications only reduce the symptoms of the disease. The Ayurvedic medicinal plants *Bacopa monnieri* (brahmi) and *Centella asiatica* (mandukaparni) are medhya rasayana plants that have nootropic effects, enhancing cognitive ability, intelligence, memory and nerve functions. Early administration of these medhya rasayana plants at a young age can delay/prevent the progression of AD, offering hope for people with increased life expectancy.

Methodology: Early administration of these medhya rasayana plants and LC MS-based untargeted metabolite profiling of serum from rasayana-treated mice (administered for 1 month, 2 months, or 3 months). Alzheimer's disease was induced chemically by intrahippocampal injection of the amyloid β 1-42 oligomer into mice. Amyloid β 1-42 deposition in the hippocampus was investigated after 7, 14, and 21 days of AD induction in mice pre-treated with rasayanas for two months.

Major findings: LC MS-based untargeted metabolite profiling of serum from rasayana-treated mice revealed alterations in the levels of amino acids and their derivatives, carbohydrates, and lipids. The immunohistochemistry data showed a significant reduction in amyloid deposition in the hippocampal region in the rasayana-administered (2 months) + AD-induced groups of mice compared to that in the AD group.

Conclusion: Taken together, our study indicate the potential neuroprotective properties of rasayanas and their effectiveness as a therapeutic intervention for alleviating Alzheimer's disease.

Keywords: Alzheimer's disease, *Bacopa monnieri*, *Centella asiatica*, hippocampus

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IDENTIFICATION OF POTENTIAL TREATMENT STRATEGIES TO OVERCOME BORTEZOMIB-RESISTANCE IN MULTIPLE MYELOMA

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Background: Targeted therapy is the cornerstone of personalized cancer treatment. Several small molecule inhibitors and monoclonal antibodies have proven successful in the treatment of multiple cancers. The proteasome inhibitor bortezomib was approved for the treatment of multiple myeloma. Despite its success, clinical relapse due to the development of secondary drug resistance has proven to be a significant clinical challenge. Therefore, we aimed to develop pre-clinical bortezomib-resistant models of multiple myeloma that may serve to test alternative treatment strategies.

Methodology: Using the K562 cell line, two bortezomib-resistant cell lines (BR1 and BR2) were derived by clonal evolution, and the resistance mechanisms were studied using metabolite profiling and gene expression analysis.

Major findings: Both BR1 and BR2 cell lines displayed sensitivity similar to that of the parental wild-type cell line towards ABL kinase inhibitor imatinib, multikinase inhibitor sorafenib, and the HDAC inhibitor vorinostat, indicating that the developed resistance is specific to bortezomib. Notably, next-generation proteasome inhibitors displayed sensitivity towards BR1 and BR2, suggesting their potential to overcome bortezomib resistance. Interestingly, bortezomib-resistant cell lines showed enhanced sensitivity towards geldanamycin, thus offering HSP90 inhibitors as a potential alternative for the treatment of multiple myeloma following relapse upon bortezomib treatment.

Conclusion: The current study identified potential treatment strategies for bortezomib treatment-refractory multiple myeloma.

Keywords: Bortezomib resistance, multiple myeloma, HDAC, HSP90, BR1 and BR2 cell line

MELATONIN ASSOCIATED GENE RORα, A POTENTIAL NOVEL THERAPEUTIC TARGET FOR HEPATOCELLULAR CARCINOMA

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Background: Hepatocellular carcinoma (HCC) constitutes more than 90% of liver tumours and is characterized by hepatocyte transformation. The IKKβ-dependent NF- kB signalling pathway plays a crucial role in liver inflammation and regulating the expression of various growth factors and cytokines in HCC. Suppressing this pathway is critical for developing effective cancer treatments. Melatonin, hormone has a crucial role in sleep regulation. It is known for its potential to inhibit cancer growth but its mechanism is poorly understood.

Methodology: First, to study the effect of melatonin on HepG2 and Huh7 hepatocellular carcinoma (HCC) cell lines *in vitro*. Next, we used the Protein Atlas website to search for the gene of interest RORα. Navigated to sections displaying hepatic tissue data and the pathology site for normal and cancerous expression details. Captured the images showing expression levels in both conditions and note the differences. Finally, use GraphPad Prism to plot graphs comparing the expression levels between normal and cancerous conditions.

Major findings: We discovered that melatonin inhibits HCC by reducing proliferation, migration, and invasion while inducing apoptosis and nuclear fragmentation. Notably, tumour cells showed higher NF-kB expression, whereas normal cells had higher RORα expression. Melatonin activated RORα and induced BMAL1 and CLOCK gene expression and suppressed NF-kB activity and showed potent anti-tumour effects. These findings suggest that Melatonin shows strong potential in developing targeted therapies for HCC via RORα.

Conclusion: Based on these findings, melatonin, through its interaction with RORα, exhibits a potential tumor suppressive role on HCC by inhibiting NF-kB signalling. This study highlights that melatonin target gene RORα act as a promising target for developing novel therapeutic strategies against HCC.

Key words: Hepatocellular carcinoma, RORα, NF-kB, CLOCK, BMAL1

ACYL PROTEIN THIOESTERASE-2 INHIBITION SUPPRESSES COLONY FORMATION ABILITY AND SCRIB TRANSCRIPTION IN BREAST CANCER CELLS

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Background: Breast cancer (BC) is the most common malignancy among women. Radiation, chemotherapy, and surgical resection remain the primary therapeutic techniques for the treatment of BC. S-palmitoylation, a post-translational reversible modification of proteins required for membrane attachment, is present in several proteins linked to cancer. Depalmitoylation is catalyzed by enzymes belonging to the α/β hydrolase family of serine hydrolases called acyl protein thioesterases 1/2 (APT 1/2). SCRIB, STAT3, and TNFR1 are the known targets of APT-2.

Methodology: APT-2 specific inhibitor ML349 treatment decreased the number and size of colonies formed by both murine and human breast cancer cells in soft agar. ML349 treatment induced mRNA expression of p21 and inhibited cyclin D1, showing its antiproliferative effect. APT-2 has been reported to catalyze SCRIB depalmitoylation, thereby affecting palmitoylated or depalmitoylated SCRIB levels but not total protein or mRNA levels.

Major findings: In our experiments, for the first time, pharmacological inhibition of APT-2 by ML349 inhibited SCRIB protein levels. Further studies showed that ML349 inhibited SCRIB mRNA expression in breast cancer cells, indicating that the suppressive effect may be at the gene transcription level. Genetic knockdown of APT-2 inhibited mRNA expression of SCRIB. Palmitoylated SCRIB has been reported to play a role in activating the Hippo cascade (inhibiting YAP/TAZ activation), an important regulator of tumorigenicity. mRNA expression studies showed that ML349 can inhibit the YAP/TAZ target genes CTGF and CYR61 in both murine and human breast cancer cells. Similar results were obtained when APT-2 was knocked down by siRNA.

Conclusion: APT-2 suppression inhibits breast cancer cell colony formation and the pro-tumorigenic SCRIB/YAP/TAZ cascade in breast cancer cells. Further studies are required to understand the role of APT-2 in the regulation of SCRIB and the Hippo/YAP pathway in breast cancer cells.

Keywords: Breast cancer, palmitoylation, acyl protein thioesterase-2

AmpC AND ESBL PRODUCING CLINICAL ISOLATES OF *KLEBSIELLA PNEUMONIAE* - A CROSS SECTIONAL STUDY IN A TERTIARY CARE TEACHING HOSPITAL, SIKKIM

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Background: *Klebsiella pneumoniae* causes variety of nosocomial and community acquired infections. Multidrug resistance is seen in Klebsiella ssp., which serves as a common cause of increased morbidity and mortality. Emergence of extended spectrum beta-lactamases (ESBLs) and AmpC beta-lactamases pose newer diagnostic and therapeutic challenges. This study evaluates the antibiotic susceptibility profile of I and production of ESBL and ampC among these isolates.

Methodology: It is a cross-sectional study conducted in Department of Microbiology, Sikkim Manipal Institute of Medical Sciences from April 2023 to March 2024. All *Klebsiella pneumoniae* isolates identified by VITEK 2 Compact system (bioMérieux) from various clinical specimen is included. Antimicrobial susceptibility testing was performed by VITEK 2 Compact (bioMérieux) system and ESBL detection was done by disk diffusion method according to CLSI guidelines 2022. AmpC detection was done by disk diffusion method using cefoxitin and phenylboronic acid.

Major findings: Total 105 isolates identified as *Klebsiella pneumoniae* were included and majority of the isolates were obtained from urine (53.3%), followed by sputum (19%). AST profile showed high susceptibility to tigecycline (78.1%), amikacin (71.4%), and meropenem (67.6%), whereas, high resistance to cefuroxime(63.8%) and ceftriaxone (62.9%). Out of 105 strains, 69 strains showed resistance to 2nd and 3rd generation cephalosporins, which is used as indication for ESBL and AmpC production. Out of 69 isolates tested, ESBL production was seen in 40 isolates (57.9%) and AmpC production in 21 isolates (30.43%). Prevalence of MDR and XDR were 19% each and PDR was 8.6%.

Conclusion: Most of the *K. pneumoniae* isolates demonstrated resistance to wide range of antibiotics and high prevalence of beta-lactamases. The findings also highlight the necessity to identify MDR beta-lactamases strains for effective therapy in severe as well as in mild infections.

Keywords: AmpC, ESBL, *Klebsiella pneumoniae*, beta-lactamase

PEGYLATED IRON OXIDE- GOLD CORE-SHELL NANOPARTICLES AS TUMOR-TARGETED DRUG DELIVERY SYSTEM: A STUDY USING RAPAMYCIN

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Background: Gold-coated magnetic nanoparticles were prepared and loaded with Rapamycin as an anti-cancer drug delivery system. The compositional structure of the gold-coated Fe_3O_4 nanoparticles was recorded on an X-ray diffractometer (XRD). The XRD pattern of nanoparticles was shown to have unique Fe_3O_4 and gold peaks. Scanning electron microscopy (SEM) determined the surface morphologies of the nanoparticles. Conjugation of rapamycin onto nanoparticles was achieved using the physical adsorption method and was confirmed by FTIR analysis.

Methodology: In the in vitro drug release studies performed using UV visible spectroscopy; around 50% of the drug was released in the first 20-24 hours. Cytotoxicity of Rapamycin-loaded gold core-shell Fe_3O_4 nanoparticles was evaluated by MTT on normal and cancer cell lines. The safety of the formulation was tested using Hemolytic assay. Anti proliferative assays such as, trypan blue dye exclusion assay, bright field microscopy, Fluorescent staining, and clonogenic assays were performed in human breast adenocarcinoma cell line (MCF-7). Apoptosis induction was confirmed by nuclear hoescht staining, phospatidyl serine externalization assay using Annexin V –FITC, and assessed the mitochondrial membrane potential using Rhodamin 123 staining. The mechanism of rapamycin-loaded (PEGylated Fe_3O_4@Au) induced cell death was analyzed by flow cytometry and also, confirmed the effect of Rapamycin loaded (PEGylated Fe_3O_4@Au) on the induction of apoptosis by western immunoblot analysis.

Major findings: Our *in vitro* study of the effects of rapamycin loaded (PEGylated Fe_3O_4@Au)on cell viability in a MCF-7 confirmed the efficacy of drug delivery using the nanoparticle system. Further results implied the induction of apoptosis in MCF-7 cell line.

Conclusion: APT-2 suppression inhibits breast cancer cell colony formation and the pro-tumorigenic. This drug delivery system using Rapamycin could be a potential candidate in the treatment of breast cancer.

Keywords: Rapamycin, hemolytic assay, clonogenic assay, western immunoblot analysis

EVALUATION OF PERFORMANCE OF BIOCHEMICAL ANALYTES IN A NON NABL ACCREDITED TEACHING HOSPITAL BIOCHEMISTRY LABORATORY USING SIX SIGMA METRICS AND QUALITY GOAL INDEX IN SIKKIM

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Background: Six sigma is an assessment for laboratory performance, identification of defects in quality control and provides guideline for assay improvement and monitoring. Quality goal index (QGI) is used for a low sigma value to identify inaccuracy and imprecision. This study aimed to evaluate performance of most commonly done biochemical parameters in a non NABL accredited, teaching hospital clinical Biochemistry laboratory by using six sigma metrics and QGI in Sikkim.

Methodology: The study was conducted in clinical biochemistry laboratory of Sikkim Manipal Institute of Medical Sciences. Thirteen commonly assayed analytes were assessed where bias, TEa and CV% were calculated from January to June, 2023 to analyze sigma value. QGI ratio was calculated for values of sigma less than 4.

Major findings: Level 1 and 2 of protein, direct bilirubin, creatinine, and level 1 of albumin, total bilirubin had a sigma metrics ≤ 2 along with level 1of total bilirubin and level 2 of urea. The Level 1 control of urea had a sigma level between 2-3. Whereas sigma metrics for level 1 and 2 of alkaline phosphatase, and level 2 of cholesterol, total bilirubin were marginal between 3 to 4. Furthermore, the level 1 control of SGOT and cholesterol along with level 2 of albumin were good with score between 4 to 5. Only level 2 of SGOT had an excellent score of 5 to 6. The parameters that had world class sigma level of ≥ 6 were high density lipoprotein, triglyceride and uric acid for both level 1 and level 2 controls. For any score below 4 QGI analysis done and imprecision was noted for the parameters.

Conclusion: Sigma metrics can act as a self-assessment tool for internal quality control and it is helpful in detecting errors.

Keywords: Six sigma matrices, quality goal index, coefficient of variance

NEXT GENERATION SEQUENCING AND PROTEOMICS ANALYSIS OF *MSH2/MSH6* GENE IN COLORECTAL CANCER

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Background: Colorectal cancer (CRC) is one of the most common types of cancer worldwide. It arises from the colon or rectum due to genetic and environmental factors. Understanding the molecular mechanisms underlying CRC is crucial for developing effective diagnostic, prognostic, and therapeutic strategies. NGS is a powerful technology that allows comprehensive analysis of genetic mutations, variations, and alterations. Integrating NGS and proteomics data provides a comprehensive view of the molecular alterations in CRC. Analyzing the expression levels of MSH2/MSH6 and related pathways helps to understand their role in CRC progression. The analysis of *MSH2/MSH6* genes through NGS and proteomics offers valuable insights into their role in CRC. Early detection and personalised medicine, supported by these advanced methods, promise to significantly improve patient outcomes and fight colon cancer more effectively. The study highlights the need for continued research and clinical trials to confirm the effectiveness of the identified mediators and explore their potential as a therapy for CRC.

Methodology: PyMol, Cytoscape, STRING, MMDB, RasMol, R-programming, Biopython, CBDOCK2, codon alignment.

Major findings: The 3D analysis of the active sites finding site and sequence similarity, drug has the potential to cure disease and visualising the gene expression data weighted co-gene expression of the genes of *MSH2- MSH6* and visualisation of the variants of these genes. The protein network analysis, finding the neighbourhood proteins. Computational analysis to generate schematic 2D representations of protein-ligand complexes from standard PDB file input.

Conclusion: The molecular analysis and docking studies conducted in this research contribute to our understanding of CRC at a molecular level and offer potential insights for the development of targeted therapies.

Keywords: Molecular analysis, colon cancer, 3D models, genetic analysis, computational methods, targeted therapies

EVALUATING THE STATUS OF OXIDIZED LDL (ox-LDL) AND MALONDIALDEHYDE (MDA) IN PATIENTS OF ISCHEMIC STROKE ATTENDING CENTRAL REFERRAL HOSPITAL, SIKKIM

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Background: Oxidized low density lipoprotein (ox-LDL) and malondialdehyde (MDA) are relevant markers in the context of ischemic stroke. This study aims to evaluate the status of these analytes in patients with ischemic stroke of varying severity.

Methodology: This is a hospital-based, cross-sectional study, which included 48 diagnosed patients with ischemic stroke who were further categorized into different groups based on their stroke severity scores according to the National Institutes of Health Stroke Scale (NIHSS). Serum MDA and ox-LDL were then measured for these subcategories.

Major findings: The mean age of patients enrolled in the study was 61.5±11.3 years, with a female preponderance. The mean values of MDA and ox-LDL in the ischemic stroke patients were 5.72±2 μmol/L and 215.1±96 ng/ml, respectively. The study demonstrated a significant difference in ox-LDL (p-value = 0.019) between minor stroke, moderate stroke, and moderate to severe stroke, with ox-LDL levels being highest in patients with moderate stroke (247.25 ng/ml). A similar trend for MDA was also observed in moderate stroke patients (5.84 μmol/L) but was statistically non-significant (p-value = 0.546).

Conclusion: Oxidative stress in ischemic stroke patients is more accurately reflected by ox-LDL compared to MDA, which is yet another oxidative stress marker.

Keywords: Ischemic stroke, oxidative stress, oxidized LDL, malondialdehyde

EXPRESSION OF ANTIOXIDANT AND ANTI-INFLAMMATORY MARKERS IN UVC-INDUCED OXIDATIVE STRESS IN HUMAN CORNEAL EPITHELIAL CELLS

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Background: Prolonged unprotected exposure to ultraviolet (UV) radiation from the sun and artificial sources (welder's arc, sun tanning beds, photographic flood lamps, lightning, electric sparks, and halogen desk lamps) cause corneal epithelial damage. This leads to ocular surface disorders like pinguecula, pterygium, climatic droplet keratopathy, OSSNs, carcinoma, UV keratitis and UV kerato conjunctivitis. The present study aimed to analyze the effect of *Vitex negundo* (VNE) extract and UVC radiation on the expression of corneal epithelial differentiation markers, antioxidant enzyme markers and the inflammatory cytokine levels in HCE cells.

Methodology: To analyze the protein expression in HCE cells, western blot analysis was performed. The proteins were extracted and the protein concentration was measured by Bradford method using spectrophotometer. The primary antibodies such as CK-3 and CK-12 for checking the expression of corneal epithelial differentiation, HO-1, SOD-2 and CAT for checking the expression of antioxidant enzymes and IL-1β, IL-6 and TNF-α for checking the expression of inflammatory cytokine levels in treated and non-treated HCE cells. Secondary antibody such as anti-mouse-HRP and anti-rabbit-HRP was used.

Major findings: The altered expression of corneal epithelial markers (cytokeratin-3 and cytokeratin-12) post UVC irradiation was improved after VNE extract treatment. The cytoprotective effect of VNE extract was due to the upregulation of antioxidant enzymes (heme oxygenase-1, superoxide dismutase-2 and catalase) and downregulation of inflammatory cytokines (IL-1β, IL-6 and IL-8) in UVC induced stress in HCE cells.

Conclusion: The result suggests that VNE extract can reverse the UVC-induced redox imbalance through, the inhibition of ROS, activation of antioxidant enzymes defence system, and reduction of inflammatory cytokines.

Keywords: *Vitex negundo*, oxidative stress, ultraviolet rays, corneal epithelium, antioxidant

EVALUATION OF APOLIPOPROTEIN B-100, AS AN INDICATOR OF ATHEROGENIC DYSLIPIDEMIA IN PATIENTS WITH TYPE II DIABETES MELLITUS ATTENDING CENTRAL REFERRAL HOSPITAL, SIKKIM

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Background: Dyslipidemia in type II diabetes mellitus (T2DM) is atherogenic and is a common risk factor for cardiovascular disease. Diabetic dyslipidemia has increased levels of triglyceride-rich lipoprotein and small dense LDL particles, which contain Apo B 100 as the major apolipoprotein. Thus, it may be suggested that the estimation of the Apo B 100 molecule is a direct estimation of the total number of atherogenic particles in the blood. To estimate the levels of apolipoprotein B 100 and lipid profile in patients with T2DM with and without comorbidities.

Methodology: This was a hospital-based cross-sectional study conducted among 90 participants diagnosed with T2DM with and without comorbidities (42 participants with hypertension as a comorbidity, 48 without any comorbidity) attending the OPD at CRH. Apo B 100 was estimated using the ELISA kit and lipid profile parameters (TC, TG, LDL, HDL), FBS, and PPBS were measured using an automated analyzer.

Major findings: Serum Apo B 100 levels among T2DM patients were found to be 130.74±35.46 mg/dL, with no significant difference even with the presence of comorbidities (130.92±34.10 mg/dL) compared to those without comorbidities (130.58±36.97 mg/dL) (p=0.964). T2DM patients with dyslipidemia demonstrated significantly higher levels of Apo B 100 (142.85±38.77 mg/dL) (p=0.013) than T2DM patients without dyslipidemia (123.74±31.69 mg/dL). Additionally, serum Apo B 100 exhibited a positive correlation with the lipid profile parameters: TC (r=0.219, p=0.038) and TG (r=0.285, p=0.006).

Conclusion: Apo B 100 may be considered an atherogenic dyslipidemic parameter in T2DM patients.

Keywords: Apolipoprotein B 100, dyslipidemia, type II diabetes mellitus, atherogenic, cardiovascular disease

DIFFERENTIALLY EXPRESSED GENES AND PROTEINS IN B3A2 AND B2A2 SUBTYPES OF CHRONIC MYELOID LEUKEMIA

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Background: Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm, which accounts for 15-20% of all leukemia affecting adults globally. Majority of CML patients harbor major BCR-ABL type (p210 BCR-ABL1), either B3A2 or B2A2 and rarely express both transcripts. It has been reported that patients with B3A2 and those with B2A2 subtypes shows difference in treatment response. The mechanisms underlying the differential molecular response of the transcripts B2A2 & B3A2 is still not clarified. In this study, we aimed at comparing B3A2 and B2A2 subtypes based on their transcriptome and proteome information and identify the alterations in pathways associated with different transcripts.

Methodology: K562 and KCL22 cell are the typical cell lines of CML transcript types. Transcriptome and proteome profiles of these cell lines are unclear. To gain more insight into the molecular mechanism, the mRNA and protein expression profiles were examined using NGS (next generation sequencing) and LCMS/MS. We also performed the microarray of 6 CML patient samples. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses were performed to identify the biological functions of differentially expressed RNAs and proteins.

Major findings: A total of 1513 differentially expressed genes (DEGs) and 436 differentially expressed proteins (DEPs) were identified in K562 versus KCL22 cell lines. Number of DEGs upregulated in B3A2 patient sample and B2A2 sample was 177 and 114, respectively. We found that these DEGs and DEPs participated in different biological process and pathways. DEGs are primarily involved in MAPK signaling pathway, HIF-1 signaling pathway and VEGF signaling pathway.

Conclusion: These results uncovered difference between B2A2 and B3A2 subtypes of cancer. Our results might guide the differential treatments of CML subtypes.

Keywords: CML, BCR-ABL, RNA sequencing

IDENTIFICATION OF A PREDICTIVE BIOMARKER FOR LYMPH NODE METASTASIS IN ORAL SQUAMOUS CELL CARCINOMA USING MASS SPECTROMETRY

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Background: Oral squamous cell carcinoma (OSCC) accounts for more than 90% of all malignant tumors of the oral cavity. Lymph node metastasis is an important prognostic factor in OSCC patients. There is a need for the discovery of molecular signatures that can predict lymph node metastasis and improve the overall survival of patients after the treatment. The present study aimed to identify the differential expression of significant upregulated and downregulated proteins of lymph node metastasis from archival formalin-fixed, paraffin-embedded (FFPE) blocks of OSCC using mass spectrometry.

Methodology: 15 FFPE tissue samples including 5 cases from each group were considered. The samples were divided into 3 groups based on lymph node metastasis and tumor staging. Group 1 was early T stage N0, group 2 was advanced T stage N0 and group 3 was advanced T stage N+. Data-independent acquisition (DIA) mass spectrometry-based proteomic analysis was done. The differentially expressed proteins obtained were analyzed by Reactome pathway enrichment analysis and were correlated with the survival of HNSCC patients from TCGA samples using the Gene Expression Profiling Interactive Analysis (GEPIA) database.

Major findings: Platelet degranulation pathways were the most common and highly enriched pathway when Advanced T stage N+ was compared to Early T stage N0 in Reactome analysis. THBS1, CCT3, CCT5, EIF3B, FAU, RPS25, RPL23, FAM3C, and SOD1 had poor prognosis in the survival analysis of HNSCC patients from TCGA database.

Conclusion: The proteomic study identified THBS1, CCT3, CCT5, EIF3B, FAU, FAM3C, RPS25, RPL23, and SOD1 as the most important hub genes associated with lymph node metastasis and poor prognosis. These candidate signatures will improve prognostic evaluations in OSCC patients and aid in the discovery of potentially novel targeted treatments to lower tumor recurrence or lymph node metastasis.

Keywords: Proteomics, lymph node metastasis, overall survival, prognosis, OSCC, FFPE

EXPLORING PROTEOMIC VARIATIONS IN KNEE ARTICULAR CARTILAGE BETWEEN OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS: INSIGHTS INTO EXTRACELLULAR MATRIX COMPOSITION, CHONDROCYTE METABOLISM, AND SIGNALLING PATHWAYS

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Background: Osteoarthritis (OA) and Rheumatoid arthritis (RA) are distinct joint disorders, characterized by different aetiologies. Profiling the proteome alterations among them could yield insights into disease biology, identification of biomarkers, and the leads for therapeutic targets.

Methodology: Proteomic analysis was performed on cartilage tissues isolated from RA and OA affected knees. There were 8 samples taken in each group. The proteomic analyses comprised extraction of soluble proteins from cartilage, separation of the protein mixtures followed by in-solution digestion, extracts were subjected to precipitation and subsequent tandem mass spectrometry analysis in conjunction with a database search for protein identification and semi-quantitation. Differential analysis was carried out using metaboanalyst software.

Major findings: Global proteome profile of OA and RA could identify a total of 741 and 1414 proteins, respectively. 108 (53.7%) proteins were common to each group, of which, 43 proteins were found significant with up and down-regulation. In RA, upregulation of proteins involved in extracellular matrix (ECM) organization, such as collagen, heat shock proteins, peroxiredoxins, and proteoglycans. Conversely, the downregulation of proteins was associated with biological pathways such as platelet degranulation, in which the participating proteins include apolipoproteins, clusterin, serpin C1, aggrecan, and cartilage oligomeric matrix protein.

Conclusion: Significant difference in the proteome between OA and RA was observed using proteomics analysis. The up regulated proteins of RA are involved in extracellular matrix (ECM) organization and down regulated proteins were associated with complement and coagulation cascade. Understanding these protein alterations could lead to tailored therapeutic interventions targeting inflammation in RA.

Keywords: Osteoarthritis, rheumatoid arthritis, proteomics, cartilage, proteins, serpin, clusterin

UNRAVELING THE ROLE OF COMPLEMENT AND COAGULATION FACTORS IN COPD PATHOPHYSIOLOGY: A COMBINED PROTEOMICS/BIOINFORMATICS APPROACH

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Background: Chronic Obstructive Pulmonary Disease (COPD) is a progressive, non-reversible lung disease projected to become the third leading cause of global mortality by 2030. Currently responsible for 3 million deaths annually, this figure is expected to rise to 5.4 million by 2060 due to factors such as population aging, smoking, and urbanization. Despite its prevalence, approximately 70 % of COPD remains underdiagnosed with high morbidity owing to an incomplete understanding of the disease pathophysiology. Prompted by previous studies implicating the role of complement and coagulation factors in chronic inflammation, this study attempts to investigate the role of these factors in stable and exacerbated COPD using a label-free proteomics/ bioinformatics approach.

Methodology: Mass spectrometry (LC-MS/MS) was utilized to identify differentially expressed complement and coagulation proteins in stable and exacerbated COPD. Bioinformatic tools were used to map these proteins to their biological processes, followed by protein network analysis and discriminant analysis.

Major findings: The study identified a consistent differential expression of complement and coagulation proteins, including coagulation factor XI and complement C2, distinguishing between stable and exacerbation states. These proteins demonstrated significant functional connectivity to inflammatory signaling within the lung microenvironment. Subsequent in-silico analysis revealed notable protein-protein interactions among complement and coagulation factors, leading to zymogen activation, positive regulation of hypoxia, and persistent inflammation in the pathophysiology of COPD.

Conclusion: The complex interactions between complement and coagulation systems highlight their combined impact on COPD progression. These findings emphasize the need for targeted therapeutic approaches addressing both complement and coagulation dysregulation for better clinical management of the disease.

Keywords: COPD, protein network analysis, hypoxia, inflammation, complement and coagulation factors

SYNTHESIS OF NANOPARTICLES OF VANADIUM AS POTENT ANTIOXIDANTS : AN *IN VITRO* APPROACH

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Background: Green-synthesized nanoparticles, mainly from plant sources are promising tool for the synthesis of nanoparticles, as this approach is biocompatible, non-toxic, low cost, environmentally compatible and easy to apply compared to classical chemicals.

Methodology: Vanadium nanoparticles were synthesized by green synthesis in an aqueous medium using *Cassia fistula* extract as stabilizing and reducing agents. The synthesized nanoparticles were characterized using different techniques including UV–Vis, Fourier transform infrared (FT-IR) spectroscopy, X-ray diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM) and energy dispersive X-ray spectrometry (EDS). To survey the antioxidant properties of vanadium nanoparticles synthesised at different temperatures, DPPH assay, metal chelating assay & total reducing power assay was used. To examine the cytotoxicity and nontoxic effects of green synthesised vanadium nanoparticles, morphology analysis, acridine orange/propidium iodide staining and MTT assay were done on RAW264.7 cell lines.

Major findings: The synthesized nanoparticles at different temperature 40^{o}C, 150^{o}C and 600^{o}C showed different size of particles i.e., 611nm, 379.5nm, 1nm and 178nm range. At 600^{o}C the nanoparticles of vanadium showed high crystalline nature. SEM images exhibited an irregular flake like crystals for the biosynthesized vanadium nanoparticles at 600^{o}C. The results of the antioxidant studies showed that nanoparticles synthesized at 600^{o}C has high antioxidant activity. Cell culture studies showed that vanadium nanoparticles synthesized at different temperatures were found to be nontoxic at a concentration up to 5µg/ml.

Conclusion: The present study is an essential step towards the use of these type of nanomaterials in any biomedical and clinical applications.

Keywords: Green synthesis, *Cassia fistula*, vanadium nanoparticles, antioxidant, RAW264.7 cell line, cytotoxicity

EXPLORING THE KEY INFLAMMATORY PATHWAYS IN RHEUMATOID ARTHRITIS THROUGH INTEGRATIVE PLASMA PROTEOMICS AND BIOINFORMATICS APPROACH

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Background: Rheumatoid arthritis (RA) stands as an autoimmune ailment marked by persistent synovial inflammation, characterized by cell hyperplasia, autoantibody production, systemic manifestations, and joint deformity. Despite extensive research, the underlying molecular mechanisms of rheumatoid arthritis pathophysiology remain incompletely understood. This study presents a comprehensive investigation into the pathophysiology of RA employing plasma proteomics using mass spectrometry and bioinformatics.

Methodology: Rheumatoid arthritis blood samples were obtained from a tertiary care hospital and were screened on basis of ACR guidelines and diagnosed by a rheumatologist. Plasma samples were subjected to immune depletion of highly abundant plasma proteins to unmask low-abundance proteins. Salt depletion was done to concentrate the proteins further and a high throughput mass spectrometric analysis was subsequently done. Samples were age and sex matched with healthy control group. Differentially expressed plasma proteins obtained from LC MS-MS analysis were functionally mapped to their biological processing using DAVID bioinformatics tool. The proteins were further assessed for their pathway over representation analysis in Metascape.

Major findings: Study has found out some plasma proteins namely Vitamin D binding protein, Afamin and Fibulin-1 which were differentially expressed in RA group. The DEPs obtained were found to be involved in molecular pathways such as PPAR signalling, DNA repair, and the complement and coagulation cascade and were linked to RA pathophysiology.

Conclusion: The study identified differentially expressed proteins namely Vitamin D binding protein, Afamin, and Fibulin-1 involved in key molecular pathways like PPAR signalling and DNA repair and highlighted the potential roles of these specific plasma proteins in RA pathophysiology. These proteins could offer new possibilities for understanding the disease and potentially guiding future therapeutic strategies.

Keywords: Rheumatoid arthritis, proteomics, complement, mass spectrometry, bioinformatics

UNREVEALING THE MULTI-OMICS ASPECTS IN ELEVATED ALTITUDE THROUGH THE MOLECULAR MECHANISM STUDY AND BIOMARKER DISCOVERY APPROACH

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Background: The rising rate of 0.9% in the population booming alerts us to think for the developments in the extreme geographical elevations, challenges for the ease of living at extreme stressful High-altitude environments need a quick attention in strengthening the defence system of our country in an alarming manner. During rapid ascend to high-altitude mountainous regions above 2,500 meters, High-Altitude Pulmonary Edema (HAPE) turns as a life-threatening condition that occur during activities such as trekking, mountaineering, high-altitude tourism and linked to the body's physiological responses due to reduced oxygen availability at high altitudes.

Methodology: In-depth investigations on high-altitude sojourners using the high throughput mass spectrometry explicate insights at the cellular level, shedding light on key regulatory pathways, cellular, molecular responses and opens door in exploring the possibilities of potential therapeutic targets. The multi-omics research includes the molecular profile of high-altitude exposed individuals, identifying the alteration in the molecular signatures involved in cellular respiration, metabolism, oxidative stress response and oxygen sensing.

Major findings: Investigating how the respiratory and cardiovascular systems maintain the cellular homeostasis during the hypoxic condition provides valuable insights in human physiology and the limits of tolerance to environmental stressors as well as comprehensive understanding on organ-specific adaptations during the progression of HAPE.

Conclusion: This research will also safeguard the health conditions of individuals exposed to high-altitude environments, advancing our understanding of human physiology in extreme environmental conditions informing medical practices and policies related to high-altitude activity.

Keywords: High-altitude hypoxia, HAPE, quantitative mass spectrometry, multi-omics technology, big data analysis

UNVEILING LUPEOL: METABOLOMIC INSIGHTS INTO THE ANTICANCER POTENTIAL OF *HEMIDESMUS INDICUS* AND *DECALEPIS HAMILTONII*

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Background: The exploration of natural products for therapeutic applications has garnered significant interest in recent years. Medicinal plants hold a variety of bioactive scaffolds for the treatment of multiple disorders. Among these, *Hemidesmus indicus* and its wild species *Decalepis hamiltonii* are two medicinal plants traditionally utilized for their diverse health benefits.

Methodology: This study focused on the metabolomic profiling of both *in vivo* and *in vitro* samples of these plants to identify various bioactive compounds using advanced metabolomic techniques such as gas chromatography-mass spectrometry (GC-MS) and high-performance liquid chromatography (HPLC). Lupeol, a triterpenoid known for its anticancer properties, was separated and analyzed from different samples of *Hemidesmus* and *Decalepis* using HPLC.

Major findings: A rich array of phytochemicals, including flavonoids, alkaloids, and terpenoids, were revealed in GC-MS analysis, with 2-Methoxy-4-Hydroxy Benzaldehyde being the major compound, showing a retention time of 11.16 minutes. The maximum amount of lupeol was present in *in vivo* roots of *Hemidesmus* (0.390 mg/g), followed by the *in vitro* suspension culture from root callus of *Hemidesmus* (0.380 mg/g). The root extract of *Decalepis* recorded higher lupeol content among different *Decalepis* samples (0.350 mg/g).

Conclusion: The significant presence of lupeol in both *Hemidesmus indicus* and *Decalepis hamiltonii* highlights their potential as natural sources of this potent anticancer compound. The findings from this study provide a strong foundation for further research into the therapeutic applications of these medicinal plants.

Keywords: *Hemidesmus indicus*, *Decalepis hamiltonii*, metabolomic profiling, GC-MS, HPLC, lupeol

TRANSCRIPTOMIC PROFILING REVEALS ESTRADIOL-MEDIATED GENE EXPRESSION DYNAMICS IN MCF-7 BREAST CANCER CELLS

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Background: Estradiol (E2), one of the three naturally occurring estrogens in females plays an important role in breast cancer by binding to its receptor and enhances the cell proliferation. Estrogens produce oxidant species for their metabolism (quinine metabolites) that can form adducts in DNA and generate reactive oxygen species (ROS) through a redox cycle. ROS suppress apoptosis and promote proliferation, invasiveness, and metastasis.

Methodology: In this study, the cell proliferative activity of E2 was studied in MCF-7 breast cancer cells. The effective concentration range of E2 on cell viability was analyzed using MTT assay. RNA was isolated from the E2 treated MCF-7 cells and Reverse Transcriptase PCR using estrogen receptor α (*ER*α) and estrogen receptor β (*ER* β) primers was done to find the gene expression. The protein expression of uncoupling protein-2 (*UCP-2)* gene in E2 treated cells was analysed by SDS PAGE followed by western blotting. The effect of estradiol mediated ROS production via mitochondrial *UCP2* in E2 treated cells was determined using flow cytometry.

Major findings: A dose dependent increase in cell viability was observed after treatment with different concentration of E2. The *ER* gene was upregulated and *UCP2* was downregulated by E2. ROS level also increased due to the downregulation of *UCP2*.

Conclusion: The result demonstrated that the E2 may act through *ER*α and exerts its effect on ROS and in turn *UCP2*.This pathway could contribute to the proliferative and metastatic properties of breast cancer cells and also helps in understanding the complex role of estrogen in breast cancer progression. This study has potential for identifying new therapeutic strategies or biomarkers for breast cancer diagnosis or treatment.

Keywords: Estradiol, *ER*α, MCF-7

UNVEILING THE MECHANISMS OF UTTROSIDE B IN PREVENTING NASH TO HCC TRANSITION: A TRANSCRIPTOMIC STUDY

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Background: Hepatocellular carcinoma (HCC), the most prevalent type of liver cancer, accounts for 85-90% of cases. Major risk factors include viral hepatitis infections (hepatitis B and C) and chronic liver conditions like cirrhosis, fibrosis, and non-alcoholic steatohepatitis (NASH) linked to metabolic syndrome. NASH-induced HCC has a poorer prognosis compared to other liver cancer etiologies. Our research team has previously demonstrated the exceptional efficacy of Uttroside B (Utt-B), a phytosaponin isolated from the methanolic extract of Solanum nigrum leaves, in combating HCC. Utt-B designated as 'Orphan Drug' against HCC by the US FDA. Our current study aims to evaluate whether Utt-B can inhibit the progression of NASH to HCC in a streptozotocin-induced steatohepatitis- derived HCC model (STAM mice model).

Methodology: To elucidate the mechanisms by which Utt-B impedes progression, we performed targeted transcriptome analysis of fibrosis-related genes using the NanoString nCounter fibrosis panel. These findings were subsequently validated through qPCR, Western blotting, and immunohistochemistry analyses

Major findings: The study revealed significant down-regulation of genes involved in collagen and ECM biosynthesis in the Utt-B-treated group, along with marked down-regulation of fibrosis-associated pathways. Conversely, there was an up-regulation of PPAR signaling and autophagy, and a down-regulation of TGF-β and PDGF signaling pathways. Notably, elevated PPARγ expression was observed, aligning with its known role in reversing hepatic fibrosis. Collectively, these findings have provided critical insights into the anti-fibrotic mechanisms of Utt-B.

Conclusion: These findings indicate that Utt-B effectively mitigates fibrosis and ECM remodeling, underscoring its potential as a therapeutic agent to prevent the progression of NASH to HCC.

Key words: NASH, hepatocellular carcinoma, uttroside B

Abstracts

Bioinformatics in health and diseases

Total number of abstracts: 36

Oral presentations
Young Scientist Award: 5
Best Paper: 5
Contributed Paper: 3

Poster presentations
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Best Paper: 11
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AUTISM SPECTRUM DISORDER PREDICTION USING DEEP LEARNING

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Background: Autism spectrum disorder **(**ASD) is a neurodevelopmental disorder characterized by a range of difficulties with behavior, speech, and social interaction. ASD is a multifaceted psychological disorder marked by enduring challenges with speech, nonverbal communication, restricted behaviours, and social interaction. Each person experiences this condition differently, and so do the symptoms' levels of intensity. The majority of the time, ASD symptoms start to show up between the ages of two and five and last throughout puberty and adulthood. Studies have demonstrated that early identification of this syndrome can help preserve children's behavioural and psychological development, even though there is no known cure for this illness.

Methodology: A prediction system based on conventional machine learning methods like random forest, naive Bayes, and deep neural network covers the majority of the material currently available on autism spectrum disorder. Accuracy, precision, and recall—three performance measurement metrics—are used to validate the suggested models.

Major findings: This study has examined and compared the prediction of autism spectrum disorders utilizing standard characteristics such as input data, simulation method, application type, and comparison methodology. Providing a consolidated platform for scholars working on autism spectrum disorder prediction is the main goal of this project. This study acknowledges the importance of early diagnosis for successful intervention and focuses on the application of machine learning algorithms to predict ASD. Although ASD is often diagnosed in childhood, reliable identification becomes more difficult as the disorder becomes more complex to identify in adolescence and maturity.

Conclusion: In this paper, we create predictive models by analyzing a large dataset that includes behavioural variables and using random forest, logistic regression, and support vector machine. Key performance measures are used to evaluate the models after they have undergone extensive training and validation on the dataset.

Keywords: Autism spectrum disorder, random forest, support vector machine, neurodevelopmental condition, logistic regression

EVALUATION OF THE CLINICAL SIGNIFICANCE OF DLK1-DIO3 IMPRINTED REGION IN HEPATOCELLULAR CARCINOMA: EVIDENCES FROM A NOVEL DATA-DRIVEN APPROACH

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Background: Hepatocellular carcinoma (HCC) is the sixth most common malignancy reported globally. This highlights the need for the identification of novel biomarkers that can be employed to study the molecular mechanisms, prognostic and diagnostic applications, and for the overall clinical management of HCC. Our study has devised a novel data-driven approach to identify the clinical significance of the DLK1-DIO3 imprinted region on Chromosome 14 and its genes in HCC.

Methodology: We mined the genomics and transcriptomics data from the TCGA-LIHC cohort to perform differential expression analysis of *DLK1-DIO3* genes. The putative promoter of the miRNA cluster (miRC) associated with the imprinted region was mapped with histone methylation and DNA methylation marks to understand the epigenetic regulation. Further, we constructed regression models to identify prognostic outcomes such as overall survival, ability to distinguish HCC stages, and TNM staging. Additionally, we identified the gene regulatory network, prominent hub genes, and their correlation with different immune signatures and their associations with HCC prognosis.

Major findings: We report a large imprinted region on human Chromosome 14 as a possible novel HCC biomarker. At least 30 clustered miRNA species, 1 long non-coding RNA, and 2 coding genes of the region were found to be differentially expressed in HCC. We also report a panel of 11 microRNAs (miRNAs) from this cluster that can differentiate normal and primary HCC and the entire miRC-related signature in overall survival. Our immune infiltration analyses showed that the hub gene targets were positively correlated with $CD8^+$/$CD4^+$ T cell populations but negatively correlated with tissue-resident macrophages.

Conclusion: Our study suggests that the imprinted region and its targets could be the markers for HCC management.

Keywords: Genomic imprinting, *DLK1-DIO3*, miR-379/656 cluster, hepatocellular carcinoma

A COMPREHENSIVE REVIEW ON WHOLE GENOME SEQUENCING OF *TERMINALIA ELLIPTICA*

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Background: *Terminalia elliptica* is a species of Terminalia also known as Indian laurel or Asna; saaj; matti (Kannada) etc. It is native to southern and southeast Asia found in India, Srilanka, Nepal, Bangladesh, Myanmar, Thailand, Cambodia, and Vietnam. It is a deciduous tree known for its characteristic bark appearance that resembles crocodile skin and is also commonly called as crocodile bark.

Methodology: It is a significant medicinal plant primarily valued for its timber, which is durable and resistant to termites. It is also known to have some medicinal properties and therefore can be extensively used in medicine for its pharmacological benefits.

Major findings: The medicinal attributes of this species can be fully understood at the genetic level based on the whole genome sequencing data. Whole genome sequencing of this species can provide comprehensive and detailed information about its genetic makeup that primarily aids in pharmacological research.

Conclusion: This review aims to provide the foundation for genetic makeup, methodologies, and applications for future genomic studies. This bioinformatics study enables scope for further extensive research on *Terminalia elliptica* and its applications in medicine against various health conditions.

Keywords: *Terminalia elliptica*, medicinal plant, bioinformatics, pharmacology, whole genome, sequencing

NETWORK PHARMACOLOGY-BASED MOLECULAR IDENTIFICATION OF NOVEL TARGETS OF CURCUMENOL AGAINST PARKINSON'S DISEASE

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Background: Repurposing, naturally occurring bioactive compounds has emerged as an effective drug development approach. Among many naturally derived molecules, curcumenol is a prospective therapeutic solution against numerous diseases. In this work, curcumenol's neuroprotective activity against Parkinson's disease (PD), which is a prominent neurodegenerative disease indicated by dopaminergic neuronal degeneration, has been explored by employing the "network pharmacology approach", which is an emerging drug research and development technique, under the broader field of OMICS technology.

Methodology: The work commences with network pharmacology predictions and screening to comprehend the intricate relationships between drug compounds and biological systems, to elucidate the significant targets of curcumenol in PD pathology. The findings were eventually evaluated via molecular docking studies. Ultimately, to authenticate, the predictions, the neuroprotective ability of curcumenol were studied in 6OHDA-induced SH-SYSY neuroblastoma cell lines using MTT viability assay and flow cytometric analysis.

Major findings: 27 core targets of curcumenol critical to the pathophysiology of PD were found and screened into 5 key proteins by analyzing the interactions of the targets via protein-protein interaction (PPI) network construction. The final molecular docking studies unveiled a strong inhibition of curcumenol to the caspase-3/7/9 proteins, the key activators in the apoptotic pathway. The *in vitro* studies consequently validated the neuroprotective ability of curcumenol with maximum activity shown at 50 µg/mL. The apoptotic mechanism studies employing flow cytometry finally substantiated the bioinformatic predictions.

Conclusion: In the current study, curcumenol is observed to have a considerable neuroprotective effect. Because caspase-3/7/9 proteins are linked to the apoptotic mechanism in PD disease, this impact could be explained by their inhibition by curcumenol. Further investigations can explore curcumenol's potential therapeutic effects against Parkinson's disease.

Keywords: OMICS, network pharmacology, curcumenol, molecular docking, apoptosis, cell viability assay

CRYSTAL STRUCTURE OF 1-(E)- [(5BROMO-2-HYDROXYBENZYLIDENE AMINO) PYRROLIDIN-2-ONE]: DESIGN, SYNTHESIS AND COMPUTATIONAL EVALUATION OF A NOVEL RACETAM CONGENER FOR EPILEPSY

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Background: The present investigation illustrates the conceptualization, synthesis, crystallographic analysis, and computational assessment of a new racetam derivative with a pyrrolidone ring as the pharmacophore. The compound demonstrates drug-like characteristics similar to LEV, an approved anti-epileptic drug, indicating its potential for developing novel epilepsy drugs.

Methodology: Molecular docking and molecular dynamics simulations were used to evaluate the binding affinity between the compound and SV2A, a protein-ligand complex.

Major findings: The protein-ligand complex attained structural equilibrium in the final 50 nanoseconds of the 200 nanosecond molecular dynamics simulation. The analysis reveals that regions with higher flexibility are primarily located in the extramembrane regions of the protein. Intermolecular contact analysis reveals hydrogen bonding and hydrophobic interactions as the primary types of interactions. The molecular mechanics poisson-boltzmann surface area (MMPBSA) calculation highlights the energetic aspects of ligand binding and the participation of important residues in the binding pocket. Unique interactions like those involving bifurcated hydrogen bonding, and novel pi-anion interaction makes the study significant. Quantum chemical calculations for the compound (LIG) done using DFT corroborates the protein-ligand interactions based on molecular electrostatic potential (MEP) maps.

Conclusion: The study establishes the structure-activity relationship (SAR) of the newly developed pyrrolidone-based compound, identifying it as a promising lead molecule for epilepsy treatment.

Keywords: Anti-epileptic drug (AED), levetiracetam (LEV), SV2A protein, pyrrolidone derivative under study (LIG), racetams docking and simulation

SYNERGISTIC ANTIBACTERIAL ACTION: *IN SILICO* DOCKING ANALYSIS OF ANTIBIO-LYSINS DERIVED FROM PLYC, PLYG AND PLYPY WITH AMOXICILLIN AND OTHER ANTI-MICROBIAL AGAINST BACTERIAL MEMBRANE COMPONENTS

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Background: The escalating threat of antibiotic resistance necessitates innovative solutions. This study investigates the repurposing of antibiotics via the fusion with bacteriophage endolysins, termed "antibio-lysins." By integrating active groups from PlyC, PlyG and PlyPy endolysins with amoxicillin, we create novel antibacterial agents.

Methodology: The *in-silico* docking analysis was done by AutoDock software and evaluated the binding affinities of antibio-lysins to bacterial membrane components, particularly peptidoglycans. Visualization of molecular structures were done by PyMoL; All programming tasks were done by C language. Galaxy Project used for the integrated data analysis.

Major findings: Our research proposes repurposing antibiotics via bacteriophage endolysin integration to combat antibiotic resistance, leveraging bioinformatics tools such as NCBI databases for sequence analysis. We elucidate the rationale, emphasizing antibiotic-endolysin synergy in combating infections. Docking analysis focuses on antibio-lysin binding affinities to bacterial membrane components, specifically PlyC, PlyG and PlyPy derivatives. The introduction of PlyC, PlyG and PlyPy provides a comprehensive overview of antibiotic resistance, emphasizing its global impact and the urgent need for novel strategies. It explores the historical context of antibiotics, their mechanisms, and resistance emergence, addressing challenges associated with antimicrobial resistance, including excessive antibiotic use. In response to the antibiotic crisis, this study explores bacteriophages as therapeutic alternatives. It discusses bacteriophage characteristics, replicative cycles, and phage therapy concepts, while acknowledging challenges such as horizontal gene transfer and resistance spread.

Conclusion: Our findings offer a bioinformatically-driven solution to antibiotic resistance. Antibio-lysins present a promising avenue for developing novel antibacterial agents, potentially mitigating dire consequences of antibiotic resistance.

Keywords: Antibiotic resistance, bacteriophage endolysins, antibio-lysins, PlyC endolysins, PlyG endolysins, PlyPy endolysins

IDENTIFICATION AND PREDICTION OF NOVEL CANCER BIOMARKERS IN GLIOBLASTOMA THROUGH *IN SILICO* ANALYSIS

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Background: Glioblastoma multiforme (GBM) is the most aggressive primary brain tumor, with an inexorably lethal course, a median survival of only 12-15 months and comprising nearly 15% of intracranial neoplasms; hence much need to find reliable biomarkers for early detection and diagnosis as well as selecting personalized therapeutic strategies. Advanced technologies provide massive data collection, which allows profiling all molecular content of cancer cells and simultaneously searching for large numbers of putative biomarkers. Nevertheless, these data are of higher-dimensional nature and require advanced bioinformatics pipelines to transform them into biologically relevant insights along with promising biomarkers.

Methodology: In this work, three gene expression microarray datasets (GSE50161, GSE7696, GSE4290) from Gene Expression Omnibus database were assessed by GEO2R analysis. In total, 228 common DEGs were obtained after plotting the Venn diagram and subjected to Gene Ontology and KEGG for function enrichment analysis. Protein-protein Interaction network among DEGs utilizing Search Tool for the Retrieval of Interacting Genes (STRING) online tool and Cytoscape software. The MCODE application in Cytoscape software was employed to identify the key HUB Genes.

Major findings: Survival analysis via gene expression profiling and interactive analyses 2 assessed their prognostic value. The gene expression profiling and interactive analyses online tool is used to further confirm three genes involved in poor prognosis of GBM patients. Among them, according to the survival curve analysis, the gene that appears to be the most promising candidate for becoming a biomarker is FN1. These findings are based solely on the survival curve data, and further validation in larger cohorts and functional studies would be necessary to confirm FN1 as a clinically relevant biomarker.

Conclusion: FN1 appears to be the most promising candidate among the genes analyzed.

Keywords: Glioblastoma multiform, biomarker, bioinformatics analysis, survival analysis, gene ontology.

VALIDATING NOVEL VACCINE CANDIDATES FOR HPV INDIAN STRAINS USING AN ANTIGEN-ANTIBODY COMPLEMENTARITY ANALYSIS

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Background: Human Papillomavirus (HPV) is a sexually transmitted pathogen causing genital warts in both men and women. Long-term infection with some strains of HPV initiates malignant changes and considered to be the major cause of cervical cancer in women. Vaccination against specific strains of HPV has been demonstrated to be quite effective in reducing cervical cancer burden. Recently, we have identified T-cell and B-cell epitopes from four proteins: the major capsid protein (L1), oncogene-E7, fusion protein-E4, and oncogene-E6; of oncogenic HPV strains prevalent in India.

Methodology: T-cell epitopes along with linear and conformational B-cell epitopes of Indian HPV strains were predicted employing a consensus approach. Selected B-cell epitopes from our dataset were subjected to protein-protein interaction analysis using ClusPro2.0 webserver; against IgG, one of the most common antibodies elicited during viral infections. Binding affinities and antigen-antibody interface residues are documented and compared with that of known HPV epitopes.

Major findings: A number of predicted epitopes from our dataset found to have structural complementarity and favorable binding affinity with IgG, further validating their potential to elicit immune response. Moreover, they form atomic interactions with interface residues comparable to antigen-antibody complexes in Protein Data Bank.

Conclusions: Our work is expected to augment vaccine design endeavors against HPV Indian strains and the fight against the second major cancer found in Indian women.

Keywords*:* Human papilloma virus, oncogenic, cervical cancer, NCBI, PDB, epitope

A COMPUTATIONAL APPROACH TO STUDY THE ANTIHYPERTENSIVE ACTIVITY FROM THE MEDICINAL PLANTS OF MUTRAVIRECHANEEYA DASHEMANI (DIURETICS)

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Background: Hypertension accounts for about 7.5 million deaths worldwide. The renin-angiotensin-aldosterone system (RAAS) is the principal regulator of blood pressure in the human body, and many therapeutic strategies target RAAS for the regulation of hypertension. Despite the availability of antihypertensive drugs, the occurrence and prevalence of hypertension and its complications are increasing at an alarming rate. The present work introduces a novel system-based approach, focusing on multiple targets in the RAAS axis as a system with multiple ligands rather than monotargeted therapy. In Ayurveda, different combinations of drugs have been used for therapeutic purposes. Leveraging traditional Ayurvedic knowledge, the present study aims to target the entire RAAS axis with phyto-compounds from the medicinal plants used in Ayurveda. The medicinal plants of Mutravirechaneeya Dashemani (diuretics in Ayurveda), described in classical Ayurvedic texts, were considered for the study.

Methodology: Molecular docking, molecular dynamics, library generation of secondary metabolism, drug likeliness screening.

Major findings: Potential phytocompounds that can interact with multiple targets in the RAAS have been identified based on computational studies, and they need to be experimentally validated further. This work contributes to bridging the gap between traditional Ayurvedic knowledge and modern pharmacology, providing a scientific basis for the medicinal use of Mutravirechaneeya Dashemani in treating hypertension.

Conclusion: The present study could be a scientific validation of the system-based concepts in Ayurveda, which could be helpful for clinicians in prescribing drugs for people suffering from hypertension.

Keywords: Mutravirechaneeya Dasemani, renin-angiotensin-aldosterone-system, ayurinformatics, hypertension

AN *IN-SILICO* STUDY TO IDENTIFY THE POTENTIAL INHIBITORS FROM THE FRUIT OF VIDANGA (*EMBELIA RIBES* BURM.F.) AGAINST *HELICOBACTER PYLORI* THROUGH ADME SCREENING AND MOLECULAR DOCKING

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Background: *Helicobactor pylori* (*H.pylori*) persists as a major health concern causing significantly to the morbidity and mortality due to peptic ulcer and stomach cancer. It is the most common bacterial infection occurring in approximately 4.4 billion people representing over 50% of the world population. The World Health Organization consider it as class 1 carcinogen leading to peptic ulcer disease and gastric cancer. It is commonly spread through contaminated food and water and unhygienic living conditions. Currently, the most frequently adopted first line medication is triple therapy, which combines a proton-pump inhibitor (PPI) with amoxicillin and clarithromycin (PPI-AC). The other choice for medication bismuth-based quadruple therapy, which involves a PPI, bismuth, tetracycline and metronidazole (PPI-BTM). But increased resistance to these antibiotics reduced the global eradication of *H.pylori* infection. Therefore, it is necessary to develop novel treatment strategy against *H.pylori* and to boost eradication rate.

Methodology: The purpose of this study is to apply the molecular docking techniques to identify possible bio active phytocompound inhibitors from the plant drug *Embelia ribes* Burm.f. against the selected targets implicated in the pathophysiology of *H.pylori* infection.

Major findings: Seven protein targets confirmed to be involved in the pathogenic pathway of *H.pylori* infection were selected as the targets for the docking analysis and 88 phytocompounds of *Embelia ribes* were docked with each of these proteins. Among them, most effective interaction was observed with the target hydroxy acyl- acyl carrier proteins dehydratase with the ligand, dihydroartemisinin.

Conclusion: On molecular docking of phytocompounds of *Embelia ribes* Burm.f. with the chosen protein targets of *H.pylori*, most effective interaction was observed with the target hydroxy acyl-acyl carrier protein dehydratase with the ligand dihydroartemisinin showing a better score than the commercial drugs and also shown same amino acid residue interactions.

Keywords: *H.Pylori, Embelia ribes* Burm.f, proton pump inhibit, peptic ulcer

ELUCIDATING THE IMPACT OF MISSENSE MUTATIONS IN THE PROGESTERONE RECEPTOR'S LIGAND BINDING DOMAIN: IMPLICATIONS FOR MYOMA AND PROGESTERONE INTOLERANCE

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Background: Progesterone (P4) is a female reproductive hormone acting through progesterone receptor (PR), a member of the ligand-dependent transcription regulator nuclear receptor family. Variations in the PR gene (*PGR*) can disrupt cellular signalling.

Methodology: This investigation examined the missense variations in the protein-coding regions of the human *PGR* gene using databases such as dbSNP, HGMD, Clinvar, OMIM, PharmaGKB, Ensemble, gnomAD, and LOVD. The pathogenic nature of these missense mutations was predicted by Polyphen2, MutPred, SNPs&GO, PON-P2, SIFT, MAPP, PhD-SNP, SNAP, and PANTHER. The stability of the structure was assessed by Dynamut, CSM, SDM, DUET, CUPSAT, MuPro, Mastero web, PopMuSic, and FoldX. Ensemble docking studies assessed P4 binding, and protein-protein docking studies using HEX8.0.0 examined steroid receptor co-activators (SRCs) binding. MMGBSA calculations after MD simulation evaluated co-activator binding affinity, supported by allosteric prediction tools OHM and AlloSigMA.

Major findings: Out of 285,217 variants, 66 missense variants within the LBD were scrutinized. The study identified 11 missense mutations that are potentially deleterious and structurally destabilising. These mutations, despite their LBD location, had limited impact on P4 binding but significantly disrupted co-activator binding crucial for PR signalling. Notably, mutations R869H and C798Y were implicated in myoma and progesterone intolerance, respectively, supported by MMGBSA calculations and allosteric prediction tools.

Conclusion: This study provides an *in silico* insights into myoma and progesterone intolerance conditions associated with missense mutations in the PR.

Keywords: Progesterone receptor, missense mutation, MD simulation, co-activators, myoma, progesterone intolerance

CHEMICAL SIMILARITY-GUIDED IDENTIFICATION OF COIXOL AS A POTENT MAO-B INHIBITOR

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Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, amyloid-beta plaque accumulation, neurofibrillary tangles, oxidative stress, and neuroinflammation. Among the protein molecules involved in AD progression, monoamine oxidase (MAO) is a key target. MAO, particularly MAO-B, is responsible for the metabolism of neurotransmitters like dopamine, serotonin, and norepinephrine. Inhibiting MAO-B has shown promise in alleviating symptoms and potentially slowing AD progression. This study focuses on coixol, a natural molecule from the medicinal plant *Coix lacryma-jobi*, which exhibits potential MAO-B inhibitory activity. Coixol shares structural similarity with isatin, a known MAO-B inhibitor.

Methodology: Molecular docking studies were conducted to compare the binding affinity and interactions of coixol with MAO-B against the reference ligand, Isatin. MD simulations were also performed to assess the stability of the coixol-MAO-B complex. Cytotoxicity profile of coixol on different cell lines was assessed by MTT method. Finally, *in vitro* enzyme inhibition assays were performed to assess the inhibitory effect of coixol on AD drug targets.

Major findings: Molecular docking studies revealed that coixol exhibits similar binding modes and molecular interactions to those of isatin. MD simulations showed a stable coixol-MAO-B complex with a root-mean-square deviation (RMSD) around 1Å. Cytotoxicity assays indicated coixol's nontoxic nature up to 400µM. In vitro enzyme inhibition studies demonstrated that coixol has a superior inhibitory effect on MAO-B activity compared to AChE activity.

Conclusion: The findings suggest that coixol is a promising candidate for further testing in AD animal models. Ongoing investigations aim to explore coixol's neuroprotective properties, potentially offering a new therapeutic approach for AD.

Keywords: Coixol, Alzheimer's disease, monoamine oxidase B, molecular docking, MD simulation, neurodegenerative disorder

EXPLORING THE ANTI-AGGREGATION PROPERTIES OF *ELETTARIA CARDAMOMUM'S* SECONDARY METABOLITES ON LYSOZYME

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Background: Lysozyme aggregation is implicated in diseases like systemic amyloidosis, familial amyloidosis, and age-related macular degeneration. Understanding and mitigating this aggregation is critical for developing therapeutic strategies. Present study investigates the inhibitory potential of secondary metabolites (from *Elettaria cardamomum*-namely bornyl acetate, β-caryophyllene, and α-caryophyllene) on lysozyme aggregation.

Methodology: To explore the inhibition of human lysozyme aggregation, a comprehensive methodology was employed. Initially, a thioflavin T (ThT) assay monitored the effects of varying concentrations of bornyl acetate, β-caryophyllene, and α-caryophyllene on lysozyme aggregation, measuring ThT fluorescence intensity over time. Subsequently, scanning electron microscopy (SEM) visualized changes in fibril morphology caused by the metabolites. Following this, cytotoxicity assays were conducted to assess the safety of the metabolites on HEK cells. Finally, molecular docking simulations were performed to elucidate the potential binding mechanisms between lysozyme and the three metabolites.

Major findings: Results showed that β-caryophyllene, α-caryophyllene and bornyl acetate significantly inhibited lysozyme aggregation, as indicated by the ThT fluorescence assay which was confirmed by SEM analysis. Molecular docking analysis has unveiled promising binding sites for the selected molecules on the lysozyme.

Conclusion: These results imply that secondary metabolites found in cardamom, notably β-caryophyllene, α-caryophyllene, and bornyl acetate, hold significant potential as therapeutic agents for diseases linked with lysozyme aggregation. However, comprehensive investigations are warranted to elucidate their mechanisms of action and broaden their therapeutic scope.

Keywords: Lysozyme aggregation, cardamom secondary metabolite, thioflavin T assay, systemic hereditary amyloidosis, molecular docking

COMBINING *IN VITRO* AND *IN SILICO* METHODS TO STUDY SPECIFIC AYURVEDIC FORMULATIONS AGAINST AD PATHOLOGIES

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Background: Alzheimer's disease (AD) is the most prevalent form of dementia, causing irreversible neuronal damage and death. Current treatments for AD offer only modest benefits, and the WHO predicts that AD will become a global epidemic by 2050. Given the complexity of AD, polypharmacological agents are more promising than single-targeted therapies. Most Ayurvedic formulations operate on the principle of polypharmacology. A specific type of Ayurvedic preparation, known as 'Medhya Rasayanas' (MR), is well-known for improving memory, intelligence, youthfulness, immunity, health, and longevity. Due to their nootropic effects, we hypothesize that MR could potentially be used for the treatment of AD. We expect that the plant components in MR will act on multiple pathologies contributing to AD, potentially offering a more comprehensive therapeutic approach.

Methodology: The selected MR formulations were first subjected to enzyme inhibition studies targeting various proteins associated with AD. The bioactive compounds responsible for enzyme inhibition were investigated through molecular docking studies. Additionally, their cytotoxicity was assessed in neuroblastoma cell lines, including SH-SY5Y and Neura2A. The neuroprotective properties of these formulations were further evaluated against various toxic insults, such as amyloid-beta (Aβ) and lipopolysaccharides (LPS), using the MTT assay.

Major findings: We selected five MR formulations for this study. Enzyme inhibition studies against various target proteins in AD revealed that these formulations can inhibit specific AD target proteins with varying degrees of potency. Neuroprotective assays against Aβ and LPS demonstrated that these formulations can mitigate the pathologies induced by Aβ and LPS.

Conclusion: The formulations exhibit neuroprotective properties against Aβ-induced toxicity and neuroinflammation, along with enzyme inhibitory profiles against AD drug targets, indicating their therapeutic potential for AD.

Keywords: Medhya rasayana, AD, neuroprotection, MTT assay

INTEGRATIVE *IN SILICO* STRUCTURE AND *IN VITRO* CELL CULTURE ANALYSES REVEALS *CHRYSEOMICROBIUM AMYLOLYTICUM* TYPE II ASPARAGINASE AS A PROSPECTIVE BIOBETTER FOR BLOOD CANCER THERAPY

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Background: L-asparaginase is a vital antineoplastic drug approved by the FDA and WHO for treating hematological malignancies. The side effects of currently used commercial formulations prompted us to explore novel candidates with efficient pharmacological features. Preliminary screening of the hemolymph-associated bacteria of the marine crab *Scylla serrata* identified *C. amylolyticum* as an extracellular type-II L-asparaginase producer without concurrent L-glutaminase and urease activities, which are the most desirable properties for clinical application.

Methodology: The complete functional gene of *C. amylolyticum* type-II L-asparaginase (ansB) was generated. Detailed *in silico* analysis, 3D protein structure modeling, and docking studies were performed. Additionally, cytotoxic studies (MTT assay) using leukemia cell lines (THP-1) and normal human fibroblast (HDF) cells were conducted using the purified enzyme.

Major findings: The study generated the 3D structure of *C. amylolyticum* type-II asparaginase for the first time. Detailed *in silico* analyses predicted its physicochemical parameters. Furthermore, the evaluated enzyme was predicted to be nonallergenic. The binding affinity of the studied enzyme was highest with L-asparagine, followed by L-glutamine and urea. Additionally, the purified enzyme exhibited excellent enzymatic activity (Km = 9.9 µM) and stability at pH 7.4 and 37°C, suggesting proper functioning inside the human body. Native PAGE revealed the molecular weight to be 142 kDa. The purified protein displayed 100% cytotoxicity against THP-1 cells at 7.1 UI/mL, whereas cytotoxicity against HDF cells was only 7.5%.

Conclusion: The results indicate that *C. amylolyticum* type-II asparaginase is an optimal candidate for blood cancer therapy.

Keywords: *Scylla serrata*, haemolymph, glutaminase, urease, *ansB*

IN SILICO CHARACTERIZATION OF PATHOGENIC MISSENSE MUTATIONS IN THE *TEX13B* GENE ASSOCIATED WITH MALE INFERTILITY

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Background: The *TEX13B* gene is crucial for testis development due to its specific expression in male germ cells and spermatogonia, which are foundational for sperm formation and overall testicular function. Proper functioning of *TEX13B* ensures the development of healthy sperm, essential for male fertility. Mutations in *TEX13B* have been linked to azoospermia, a significant cause of male infertility characterized by the absence of sperm in semen. This study explores the relationship between *TEX13B* mutations and azoospermia.

Methodology: In this study, we analyzed *TEX13B* missense variants from the NCBI-dbSNP and Ensembl databases. The pathogenicity of these variants was evaluated using SIFT, PolyPhen2, Mutation Assessor, REVEL, CADD, and GERP. Further, the functional characterization was carried out using I-Mutant 2.0, MutPred, MUpro, iStable, and Consurf tools to analyze protein stability and evolutionary conservation. 'Project Hope' modeling tool was used to assess their impact on structure and function.

Major findings: A total of 196 missense variants from both databases were analyzed. Twenty-four highly pathogenic mutations were identified: L150R, E142G, E142A, E142Q, N123H, E121G, E121K, E119Q, E119K, I21N, A108G, A103V, A79V, A73T, L72P, C67F, C67S, A66V, E65G, E47K, N38H, E37A, F34L, and V18G. Functional analysis indicated a significant decrease in protein stability for most pathogenic mutations, many of which occurred at evolutionarily conserved sites. MutPred predicted structural changes and functional alterations in *TEX13B*, while structural analysis through Project Hope suggested these mutations likely cause significant conformational changes, disrupting interactions essential for spermatogenesis.

Conclusion: Identification and characterization of highly pathogenic missense mutations in *TEX13B* highlight its critical function in sperm maturation and the genetic basis of azoospermia. These findings pave the way for future research on targeted therapies and diagnostics for male infertility linked to *TEX13B* mutations, offering hope for improved treatment and management of the condition.

Keywords: *TEX13B*, missense variants, MutPred, male infertility, MUpro

IDENTIFYING BIOMARKERS AND THERAPEUTIC TARGETS BY MULTIOMIC ANALYSIS FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA-AN INDEPTH *IN SILICO* ANALYSIS

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Background: Head and neck squamous cell carcinoma (HNSCC) is one of the major types of cancer, with 900,000 cases and over 400,000 deaths annually. It constitutes 36.9% of all cancers in India. As early diagnosis is the key to treating the disease, reliable biomarkers play an important role in the precision medicine of HNSCC. Despite treatments, the survival rate of cancer patients remains unchanged, and this is mainly due to the failure to detect the disease early. Thus, the objective of this study is to identify reliable biomarkers for head and neck cancers for better healthcare management.

Methodology: In this study, all available, curated human genes were screened for their expression against HNSCC TCGA patient samples using genomic and proteomic data by various bioinformatic approaches and datamining. Docking studies were performed using AutoDock or online virtual screening tools for identifying potential ligands.

Major findings: Sixty genes were short-listed, and most of them show a consistently higher expression in head and neck patient samples at both the mRNA and the protein level. Irrespective of human papillomavirus (HPV) status, all of them show a higher expression in cancer samples. The higher expression of 30 genes shows adverse effects on patient survival. Out of the 60 genes, 12 genes have crystal structures and druggable potential. We show that genes such as *GTF2H4*, *HAUS7*, *MSN*, and *MNDA* could be targets of Pembrolizumab and Nivolumab, which are approved monoclonal antibodies for HNSCC.

Conclusion: Sixty genes are identified as potential biomarkers for head and neck cancers based on their consistent and statistically significantly higher expression in patient samples. Four proteins have been identified as potential drug targets based on their crystal structure. However, the utility of these candidate genes has to be further tested using patient samples.

Keywords: HNSCC, biomarkers, gene expression, drug target

IN SILICO ANALYSIS OF *CYP17A1* IN THE PATHOGENESIS OF POLYCYSTIC OVARIAN SYNDROME (PCOS): MOLECULAR DYNAMICS AND GENOTYPIC CHARACTERIZATION

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Background: Polycystic ovarian syndrome (PCOS) is a complex reproductive as well as endocrinological disorder characterized by anovulatory dysfunction, androgen excess, and polycystic ovarian morphology. The *CYP17A1* gene, which encodes the enzyme cytochrome P450 17A1, plays a vital role in steroidogenesis and hormone synthesis. Missense mutations in *CYP17A1* have been implicated in PCOS pathogenesis due to their potential to disrupt normal enzyme function and subsequently alter sex hormone production.

Methodology: In this study *CYP17A1* missense variant was retrieved from the Ensembl database and highly pathogenic genetic variant was identified by *in silico* tools such as (sift, Polyphenv2, I-mutant, Mutpred, GERP, Consurf, and Project Hope modeling. The genotyping study was carried out by PCR-RFLP method and validated by Sanger sequencing for the variant rs743572. Statistical analysis was performed to find out the genotypic characters in the etiopathology of PCOS. Further, molecular dynamics study was carried out to unravel the impact of mutation at the structural level.

Major findings: A total of 1,636 variants were found in the database among which 96 variants were identified as highly deleterious. Of these, 6 variants were highly pathogenic and were present in the enzyme active site. Finally, based on Minor Allele Frequency (MAF) the rs743574 variant was selected for genotyping study. Statistical analysis shows the allele frequency distribution of AA (46%), AG (43%), and GG (9%) revealing significant differences between PCOS patients and controls with (OR 0.933, 95% CI 0.55-1.56, p-value of 0.069). The molecular dynamics simulations study revealed that the rs743574 mutation leads to significant conformational changes in the CYP17A1 enzyme, affecting its stability and function.

Conclusion: This study provides insights into the molecular mechanisms by which *CYP17A1* mutations contribute to the disorder, potentially offering new avenues for targeted therapeutic interventions.

Keywords: PCOS, *CYP17A1*, RFLP, Sanger sequencing, molecular dynamics

SCREENING OF ALLOSTERIC INHIBITORS OF RDRP OF SARS-COV-2 BASED ON DRUG REPURPOSING STRATEGY USING WELL TEMPERED METADYNAMIC SIMULATIONS

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Background: The COVID-19 outbreak became a pandemic because the SARS-CoV2 virus was more transmissible than MERS-CoV or SARS-CoV. Eventhough the vaccines were developed to combat the pandemic, vaccines have not yet proven their efficacy and long-term effects. Drug development against SARS-CoV-2 is challenging and time-consuming due to continuous mutations. The catalytic and allosteric regions of RNA dependent RNA polymerases (RdRp) of all RNA viruses especially Hepatitis C-Virus (HCV) and SARS-CoV-2 are conserved, making them a promising target for drug development. Therefore, allosteric inhibitors of HCV under clinical trials could be effective against SARS-CoV-2 also. A drug repurposing strategy was adopted to identify potential RdRp inhibitors of SARS-CoV-2 using molecular docking and well-tempered metadynamic simulations.

Methodology: Initial docking studies were performed using 12 allosteric non-nucleoside inhibitors of RdRp of HCV on to RdRp of SARS-CoV-2. The complexes were subjected to equilibration in water and ions uisng molecular dynamic simulations to asses the stability of docked complexes. Further the findings were validated using well tempered metadynamics simulations by generating free energy profile of dissociation of the ligand from the allosteric sites. This study utilized Collective Variables (Cvs): Number of Contacts (Nc) and Distvec (X) to find the best allosteric inhibitor.

Major findings: The study found that Setrobuvir and ABT-450 are potent allosteric inhibitors of RdRp of SARS-CoV2. Among different allosteric inhibitors of RdRp of HCV studied, Setrobuvir forms most stable complex with RdRp of SARS-CoV2 and it interacts with the loop esponsible for the opening and closing of the cavity of the enzyme during RNA sysnthesis.

Conclusion: This study suggest that Setrobuvir could be a lead molecule for drug development against COVID-19 and also suggesting the design and validation of novel analaogs of Setrobuvir which could be useful in combating SARS-CoV2 effectively.

Keywords: COVID-19, RdRp, drug repurposing, metadynamics

IMPACT OF TUBB4B-D161H TUBULIN ISOTYPE MUTATION ON MICROTUBULE DYNAMICS

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Background: Microtubules have an exceptionally high degree of structural homology across all eukaryotic organisms, making them an important cytoskeleton component. They perform essential roles in critical cellular functions and thereby control cell dynamics and trafficking. During cell division, they play a pivotal role in separating DNA into daughter cells. These vital roles made microtubules a potential anti-cancer target. Several TUBB4B tubulin isotype mutations have been identified among lung cancer patients. The consequences of these mutations in lung cancer progression remain unclear. Thus TUBB4B isotype mutations may play a significant role in lung cancer progression and potentially modify microtubule dynamics, potentially impacting cancer.

Methodology: The study examined the effect of lung cancer-related TUBB4B-D161H tubulin isotype mutation on microtubule dynamics using molecular dynamic simulations, site-directed mutagenesis, FACS, and microscopy studies.

Major findings: The study reveals a surprising role of the TUBB4B isotype in lung cancer. TUBB4B-D161H mutation alters tubulin structure and dynamics of β tubulin and allosterically amplifying the mutational effects in the tubulin dimer simulations. Experimental studies confirm this mutation alter the polymerization dynamics of microtubules.

Conclusion: Subtle changes in TUBB4B tubulin isotype can affect microtubule dynamics and lead to pathological conditions.

Keywords: Microtubules, cytoskeleton, tubulin isotypes, TUBB4B, cancer, molecular dynamics

IMPROVED PROGNOSIS PREDICTION AND IDENTIFICATION OF NOVEL PROGNOSTIC BIOMARKER CANDIDATES FOR GASTRIC CANCER USING MULTI-OMICS AND DEEP LEARNING

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Background: Gastric cancer (GC) is the fifth leading cause of cancer-related mortality worldwide, and the accurate prediction of its prognosis remains a significant challenge. In recent decades, the rapid advancement of deep learning techniques and high-throughput sequencing (HTS) technologies has significantly improved cancer prognosis prediction and identification of specific biomarkers. However, developing robust models capable of handling the high dimensionality and heterogeneous nature of multi-omics data integration in GC remains critical. To address this challenge, we propose a novel deep learning-based framework that utilises a variational autoencoder to identify survival subtypes effectively.

Methodology: The proposed semi-supervised learning method utilised a multi-omics dataset comprising RNA-seq, miRNA-seq, and methylation data from the TCGA database. The integrated omics data was employed to extract potential features using a variational autoencoder-based deep learning model, which was subsequently used to train a classifier for predicting cancer survival subtypes. The proposed method was validated using publicly available datasets, and its performance was evaluated using various metrics. Additionally, bioinformatics analysis was conducted to identify candidate genes and pathways associated with molecular subtypes.

Major findings: The deep learning framework achieved superior performance in predicting GC prognosis compared to existing methods, and its effectiveness in handling HTS data and incorporating the inherent heterogeneity of GC has been proven. Furthermore, the framework identified 13 significant molecular features that influence GC prognosis, including proteoglycans associated with the cancer pathway.

Conclusion: The study proposes *SYNM*, *HIF3A*, *DES*, *CHRNA3* and *SYNPO2* genes as potential biomarker candidates and therapeutic targets because of their significant influence on GC progression and survival.

Keywords: Gastric cancer, deep learning, multi-omics, dimensionality reduction, prognosis

MACHINE LEARNING AND INTEGRATED BIOINFORMATICS ANALYSIS FOR IDENTIFICATION OF NOVEL BLOOD BIOMARKERS IN LIVER CANCER

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Background: Liver cancer (LC) is the sixth most prevalent and the third leading cause of cancer-related death worldwide. Identifying non-invasive blood-based biomarkers is crucial for early detection and monitoring of LC, thereby improving patient outcomes. Recent advancements in bioinformatics analysis and machine learning (ML) offer promising avenues for identifying novel blood-based biomarkers for LC.

Methodology: The blood-secretory proteins were retrieved from the curated databases. Various ML models were developed and evaluated using selected features, resulting in the optimal model selection. To identify differentially expressed eenes (DEGs), the LC tissue transcriptome data from 7 cohorts were analysed. Protein-encoding DEGs were compared with curated blood-secretory datasets, and the remaining protein-coding genes were analysed using the ML model. Predicted and overlapping blood-secretory proteins were considered for the pathway enrichment analysis and the protein-protein interaction (PPI) network to identify hub genes. These hub genes were further validated as blood biomarkers using ROC curve analysis and tools like DeepSec, DeepHBSP, and SecProCT.

Major findings: 58 potential blood-secretory proteins associated with LC were identified from the analysis. PPI network identified 13 hub genes using bottleneck, closeness, and radiality methods. Among 13 genes, *MDK*, *GPC3*, *ESM1*, *FCN2*, and *COL6A6* emerged as promising biomarkers, each with an AUC value over 0.8 across all 7 cohorts. Out of which, *COL6A6* was found to be a novel potential blood-based biomarker for LC.

Conclusion: This study identified five non-invasive blood-based biomarkers for early detection and monitoring of LC. These biomarkers demonstrate high diagnostic accuracy and consistent dysregulation across various LC cohorts. The findings suggest the potential of integrating bioinformatics analysis and ML in discovering novel biomarkers for early detection and monitoring of LC, paving the way for improved patient management strategies.

Keywords: Liver cancer, differentially expressed genes, PPI networks, biomarker, machine learning

SYSTEMS BIOLOGY APPROACH TO IDENTIFY POTENTIAL TARGET CANDIDATES IN *LEISHMANIA* SPECIES

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Background: *Leishmania* is a protozoan parasite that is known to cause leishmaniasis, a neglected tropical disease affecting millions of people globally. Current treatments for leishmaniasis are inadequate due to toxicity, cost, and emerging drug resistance, highlighting the urgent need to identify novel drug targets for the development of novel/improved anti-leishmanial drugs. The present study employs systems biology approach to identify new therapeutic targets by analyzing protein-protein interaction (PPI) networks in five old world *Leishmania* species (viz., *Leishmania donovani, Leishmania infantum, Leishmania major, Leishmaniatropica* and *Leishmania turanica*).

Methodology: The protein sequences of the *Leishmania* species were collected from TriTrypDB database. PPI networks for each *Leishmania* species were constructed and analyzed using STRINGdb and Cytoscape. Different network centrality measures, namely degree, betweenness, closeness and eigenvector, were calculated for each network, and the top 200 proteins from each centrality measure were shortlisted. Proteins that were common to at least two centrality measures were referred to as hub proteins. These hub proteins were considered for the non-homology analysis, followed by pathway analysis through BlastKOALA and subcellular localization using PSORTb.

Major findings: Comparisons of top proteins, selected through centrality measures for each *Leishmania* species, led to the identification of 224, 225, 233, 226 and 229 proteins in *L. donovani*, *L. infantum*, *L. major*,*L. tropica* and *L. turanica*, respectively. A total of 109 proteins were found to be non-homologous to humans. Pathway analysis of these non-homologous proteins revealed their involvement in vital pathways/biological processes, such as terpenoid backbone biosynthesis, cytosolic DNA-sensing pathway, nucleotide excision repair, transcription and protein synthesis.

Conclusion: The identified hub and non-homologous proteins were considered as potential targets in *Leishmania*. These proteins and their pathways can be further targeted to unravel novel anti-leishmanial agents using structure-based drug design approaches.

Keywords: *Leishmania*, systems biology, drug targets, protein-protein interaction

IN SILICO ANALYSIS OF PHARMACOTHERAPEUTICS USED IN ORAL LICHEN PLANUS

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Background: Oral lichen planus (OLP) is a chronic inflammatory condition most commonly affecting females aged 30–60 years. It can arise or be exacerbated by certain drugs, stress, and some viruses. OLP is also associated with numerous systemic conditions such as diabetes mellitus, hypertension, and thyroid diseases. Malignant transformation to oral squamous cell carcinoma is its most feared complication. Although it has periods of exacerbation and remissions, it eventually requires treatment. The most frequently described therapy for OLP is the administration of topical corticosteroids. However, sometimes the lesion may respond poorly to topical treatment, and systemic immunomodulatory agents are needed. Understanding the pathogenesis of the disease is an essential requisite for targeted treatment. *In silico* analysis helps in understanding the intermolecular recognition and conformation of small-molecule ligands within the appropriate target binding site. Thus, the aim of this study is to evaluate the action of the commonly used drugs (synthetic and plant-based) in the treatment of OLP on various proteins, using molecular docking, and also to understand the interaction of drugs at the target site, eventually exploring the clinical utility and future possibilities of such studies.

Methodology: Ligand list preparation; Target prediction; Molecular docking; ADMET analysis and Network Analysis

Major findings: Triamcinolone acetonide has a higher binding affinity than other drugs. Among the phytochemicals, honey and licorice have similar binding affinities to that of triamcinolone acetonide. Among the target proteins, CDK6, CD38, and CCR1 have higher binding affinities to most of the ligands.

Conclusion: The results of this study explored the mode of action of commonly used drugs in the management of symptomatic OLP through their *in silico* behaviour, thereby prompting individualized treatment therapy with less morbidity and fewer side effects, especially in recalcitrant cases.

Keywords: Oral lichen planus, *in silico* analysis, CDK6, CDK13, molecular docking

A STRATEGIC APPROACH FOR MITIGATING PATHOGENESIS THREATS IN *ORYZA SATIVA* SUBSP. *INDICA* BY HOMOLOGY MODELLING OF PR1-PROTEIN IN RESPONSE TO *XOO* AND *RHIZOCTONIA SOLANI*

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Background: Kerala's agriculture systems are renowned for stress-resistant rice varieties, with pesticides controlling disease spread. By effectively targeting the Pathogenesis Related proteins (PR proteins) helps to control the spread of diseases in rice fields. By predicting the three-dimensional structure of PR1 protein based on their homologous, we gain insights into their interactions and functions.

Methodology: For the study, nine local rice varieties from North Kerala were used for finding out the resistance of *Xanthomonas oryzae* pv. oryzae (Xoo) and *Rhizoctonia solani* (*R. solani*), most common biotic constraints of rice which causes yield loss due to bacterial blight and sheath blight respectively. Identify the most resistant cultivars against *Xoo* and *R. solani*. Total RNA of these two resistant rice cultivars were isolated and one step RT-PCR was performed by designed PR1 primers. Sequence and submit obtained PR1 genes in NCBI and Homology modelling of these PR1 proteins were done by MODELER program from Discovery studio 4.0 with 1CFE as template.

Major findings: Chennellu and Kayma are the most prominent resistant rice cultivars against *Xoo* and *R. solani* respectively. It was observed that Chennellu and Kayma rice cultivars expressed PR1 protein in their defence mechanism. The importance of PR1 in conferring resistance to fungal pathogen is well known, present study investigated that the PR1 gene was also expressed during resistance against bacteria. The partial PR1 cDNA isolated by RT-PCR was sequenced and submitted to NCBI (ID: KP826795.1 & KP257093.1) which was determined to encode a PR protein. These PR1 proteins were modelled and submitted to PMDB.

Conclusion: Identified PR1 proteins serve as invaluable compounds for guiding researchers in the rational design of pesticides for mitigating the impact of pathogenic threats in agriculture.

Keywords: PR1 protein, homology modelling, pesticides, rice diseases, agriculture, defence mechanism

CHARACTERIZATION OF MISSENSE VARIANTS IN PWWP2A AND PWWP2B: IMPLICATIONS FOR PROTEIN STABILITY AND FUNCTION USING *IN SILICO* APPROACH

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Background: PWWP2A is a chromatin-binding protein that acts as an adapter between distinct nucleosome components and chromatin-modifying complexes, thus regulating histone acetylation. While the role of PWWP2B is largely unknown, it interacts with PWWP2A. PWWP motif is present in many chromatin-modifying complexes and are involved intragenic DNA methylation, DNA repair, alternative splicing, and repression of spurious transcription initiation. Genetic variations on PWWP2A & 2B protein reduces the interaction between them that results in the alteration of the protein structure and its function.

Methodology: In this study, we retrieved PWWP2A and PWWP2B domain missense variants from the NCBI-dbSNP, Ensembl databases. The pathogenicity of these variants was evaluated using by in silico tool SIFT, PolyPhen2, Mutation Assessor, REVEL, CADD, GERP. Furthermore, functional characterization was conducted using in silico tools such as I-Mutant 2.0, MutPred, MUpro, iStable, Consurf to assess protein stability and evolutionary conservation. Additionally, the Project Hope modeling tool was used to evaluate their impact on structure and function.

Major findings: In both databases, the PWWP2A has 355 and PWWP2B has 352 deleterious missense variants. A Thirteen highly pathogenic mutations were identified: Y728C, R719C, P711A, S710F, T701I, R680W, L674V, R672C, V655A, G650D, K515M, R564W and E569G. Functional analysis indicated a significant decrease in protein stability for most of these pathogenic mutations, many of which occurred at evolutionarily conserved sites. MutPred predicted structural changes and functional alterations in PWWP2A and PWWP2B, structural analysis through Project Hope suggested that these mutations likely cause significant conformational changes.

Conclusion: Our study provides significant insights into the missense variants of *PWWP2A* and *PWWP2B*. The mutations primarily lead to decreased protein stability and are found at evolutionarily conserved sites, indicating their critical role in protein function. This underscores the importance of these genes in chromatin-related biological processes and emphasizes the potential impact of their mutations on cellular function and disease mechanisms.

Keywords: PWWP2A, chromatin-binding protein, PWWP2B, missense variants, MutPred

MOLECULAR-LEVEL COMPARATIVE ANALYSIS ON HUB-PROTEINS OF PARKINSON'S DISEASE WITH SELECTED SYNTHETIC DRUGS USING *IN SILICO* APPROACH

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Background: Physical interactions between proteins are cardinal to biological processes. In order to restore their function, proteins must interact with one another. Hub proteins are densely interconnected proteins that have a wide range of biological significance and are also to blame for a number of illnesses, including cancer, autoimmune disorders, and neurodegenerative diseases. The most prevalent of these is Parkinson's disease. SNCA, alpha-synuclein, is a hub protein that is the main cause of this disease. Additionally, DJ-1 and Parkin are also responsible for Parkinson's disease.

Methodology: Through this study, we performed a molecular-level comparative analysis of hub proteins of Parkinson's disease with selected synthetic drugs using the *in silico* approach. In addition, a phytochemical investigation was conducted to determine the most effective natural source for Parkinson's disease. To determine the presence of safinamide, *Amaranthus spinosus*, *Centella asiatica*, and *Solanum tuberosum* were used as samples.

Major findings: The binding energy and complex energy identified the better efficacy of the drug. The Lipinski rule of filtering and the ADMET pharmacological parameters were satisfied by seven out of the twelve medicines. Levodopa among these medications had superior effectiveness with 4RKW and 5C32 in both approaches. Better LibDock scores, binding energies, and complex energies with 4RKW were displayed by safinamide. The binding stability of the 4RKW-safinamide complex was further validated by molecular dynamic simulation. The amount of GC content was also analyzed with the aid of a Python program to establish the stability of DJ-1.

Conclusion: From the phytochemical analysis, we conclude that *S. tuberosum* was a good source of monoamine beta-oxidase inhibitor, and it is better to include it in our diet to prevent Parkinson's disease.

Keywords: Hub proteins, Parkinson's disease, alpha-synuclein, safinamide

INTERFACE DESIGN OF SARS-COV-2 SYMMETRICAL NSP7 DIMER AND MACHINE LEARNING-GUIDED NSP7 SEQUENCE PREDICTION REVEALS PHYSICOCHEMICAL PROPERTIES AND HOTSPOTS FOR NSP7 STABILITY, ADAPTATION, AND THERAPEUTIC DESIGN

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Background: The COVID-19 pandemic, driven by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), underscores the need for a deep understanding of its lifecycle and genetic variability. As an RNA virus with high mutation rates, SARS-CoV-2 generates variants that pose significant implications. Key proteins like RNA-dependent RNA polymerase (RdRp), crucial for viral replication, form dimers through nsp subunits, particularly nsp7, essential for efficient RNA copying. Similar to SARS-CoV-2 main protease (Mpro), there is a possibility that nsp7 could undergo mutational events shaping more stable dimeric forms during virus evolution, yet comprehensive information on this remains lacking.

Methodology: We leveraged computational protein design (CPD), machine learning (ML), AlphaFold v2.0-based structural analysis, and related computational techniques to identify critical residues and mutations influencing nsp7 dimer stability and adaptation. Our methodology involved identifying potential hotspot residues within the dimeric nsp7 interface using an interface-based CPD approach.

Major findings: Using Rosetta-based symmetrical protein design, we modulated nsp7 dimerization, focusing on selected interface residues. Physicochemical features analysis revealed acceptable structural changes and detailed insights into protein-protein interactions. Our ML models, particularly the random forest regressor (RFR), accurately predicted binding affinities, and ML-guided sequence predictions corroborated CPD findings, highlighting potential nsp7 mutations and their impact on binding affinity. Validation against clinical sequencing data demonstrated our approach's predictive accuracy. Additionally, AlphaFold v2.0 structural analyses validated optimal dimeric configurations of affinity-enhancing designs, confirming methodological precision. These designs exhibited favourable energetics and higher binding affinity compared to their counterparts.

Conclusion: The obtained physicochemical properties, molecular interactions, and sequence predictions advance our understanding of SARS-CoV-2 evolution and inform potential avenues for therapeutic intervention against COVID-19.

Keywords: AlphaFold, Computational protein design, COVID-19, machine learning, nsp7, RNA-dependent RNA polymerase

TARGETING EIF4A3 IN GLIOBLASTOMA MULTIFORME: INTEGRATING PHYTOCHEMICALS FROM INDIAN MEDICINAL PLANTS INTO PRECISION ONCOLOGY

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Background: Glioblastoma Multiforme (GBM) is an aggressive grade-IV astrocytoma with a poor prognosis due to rapid growth. EIF4A3 regulates non-coding RNAs, including the oncogenes, viz., circMMP9, affecting cell proliferation, migration, and invasion in GBM. *EIF4A3* knockdown inhibits glioblastoma progression and increases apoptosis.

Methodology: *EIF4A3* expression was analyzed using UALCAN, OncoDB, and GEPIA, revealing overexpression in GBM samples. Overall survival analyses via cBioPortal, PrognoScan, UALCAN, and GEPIA linked elevated *EIF4A3* levels to poor prognosis. A PPI network was constructed using the STRING database. Phytochemicals from *Withania somnifera* (WS) and *Castanea sativa* (CS) were screened for ADMET studies, followed by docking studies with GOLD, AutoDock4.2, and LeDock, MD-simulation using GROMACs, and MM-PBSA for binding free energy analysis. EIF4A3 mutations were analyzed, with subsequent molecular docking and MD simulations to evaluate compounds like withaferin A (WA), withanolide, and thiamine.

Major findings: Elevated *EIF4A3* levels were associated with poor patient prognosis, suggesting *EIF4A3* as a potential prognostic marker. Network analysis using Cytoscape identified hub genes intricately linked to EIF4A3. Among the studied phytochemicals, WS-specific phytocompounds and Thiamine from CS exhibited good blood-brain barrier permeability, strong binding affinity to EIF4A3, and favorable ADMET properties. MD simulations confirmed the stability of these molecules with EIF4A3. EIF4A3 mutation analysis revealed recurrent alterations, A113S/Vfs*21, in the DEAD domain. Computational screening and docking studies indicated that WA and withanolide effectively inhibit both wild-type and mutated EIF4A3 proteins.

Conclusion: This study presents an opportunity to develop drug candidates targeting glioblastoma driven by EIF4A3 overexpression, integrating phytotherapy into precision oncology for tailored and precise natural cancer treatment strategies. Our findings illuminate the complex molecular landscape of glioblastoma and underscore EIF4A3's pivotal role, warranting further investigation into its therapeutic potential and molecular pathways in glioblastoma development.

Keywords: EIF4A3, glioblastoma, precision medicine, virtual screening, mutation analysis

BEBTELOVIMAB-BOUND SARS-COV-2 RBD MUTANTS: RESISTANCE PROFILING AND VALIDATION WITH ESCAPE MUTATIONS, CLINICAL RESULTS AND VIRAL GENOME SEQUENCES

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Background: The dynamic evolution of SARS-CoV-2 variants during the COVID-19 pandemic highlights the necessity for continual advancements in therapeutic strategies to combat such pathogens. While monoclonal antibody (mAb) therapies like bebtelovimab have shown promise, concerns regarding the emergence of resistance mutations persist. Certain single-point mutations in the receptor-binding domain (RBD) have been reported to resist bebtelovimab. Moreover, there are possibilities of the emergence of multipoint resistance mutations during the evolution of the virus. This study aimed to address this gap since comprehensive profiling of single-to-multipoint RBD mutants that may exert bebtelovimab resistance is missing.

Methodology: To predict potential resistance mutations to bebtelovimab, our study employed an interface-guided computational protein design approach. We extensively analyzed physicochemical properties, mutational preferences, and energetics to elucidate the intricate dynamics of the bebtelovimab-RBD interaction. Additionally, we integrated all-atom molecular dynamics (MD) simulations and coarse-grained MD simulations to elucidate the structural-dynamic-binding characteristics of the bebtelovimab-RBD complexes. Furthermore, we identified susceptible residues in the RBD prone to positive selection pressure.

Major findings: The study revealed the detailed intermolecular interactions between the RBD and bebtelovimab, highlighting potential resistance mutations. Through our integrated approach, we were able to profile both single-point and multipoint mutations that could confer resistance to bebtelovimab. The MD simulations provided insights into the stability and binding dynamics of the bebtelovimab-RBD complexes. Additionally, we identified specific residues in the RBD that are prone to positive selection pressure, which may be critical for the emergence of resistance.

Conclusion: Validation against clinically reported resistance mutations and viral genomic sequences enhances the translational significance of our findings. This study offers critical insights into the development of next-generation therapeutics capable of overcoming resistance, thereby bolstering the efficacy of antibody drugs amidst the evolving landscape of COVID-19 therapeutics.

Keywords: Bebtelovimab, molecular dynamics, protein design, protein-protein interactions, resistance mutations

DATABASE FOR MASS ANALYSIS OF CONUS PEPTIDES: DB-MASCOP, CREATED BY DC-MAPP

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Background: Marine cone snails belonging to the genus Conus are venomous. They use venom to paralyze and capture prey. Several investigations have established that their venom is concoction of cysteine-rich peptides called conus peptides or conopeptides or also conotoxins. These peptides can modulate certain specific ion channels and various other receptors. Ion channels play a vital role in numerous physiological functions and hence are attractive drug targets. Therefore, conus peptides can be neuroactive drug leads. Tandem mass spectrometry (MS/MS) involving MALDI and/or ESI is inevitable for elucidation of primary structure (viz., sequencing) of peptides and proteins. Suitable database(s) is/are needed for simplifying interpretation of MS/MS data. Currently available databases that contain conopeptides' sequences cannot be customized for interpreting MS/MS data. Using our recently published computational standalone tool, DC-MAPP, our aim is to build custom database that can facilitate interpretation of MS/MS data, particularly for deducing conopeptides' sequences.

Methodology: Sequences of fifty conopeptides from UniProtKB were uploaded in the Module 1 of DC- MAPP (http://vit.ac.in/DC-MAPP). Along with the sequences, appropriate options, e.g., post- translational modifications and different fragment ions (b, y, etc.) also were chosen. Using these details, the module 1 creates a database.

Major findings: DB-MASCOP is created in the form of an excel file. The details of each peptide are saved in one worksheet and hence, DB-MASCOP contains details of all the uploaded peptides in fifty different worksheets.

Conclusion: DB-MASCOP is successfully created, which can be useful to interpret experimental m/z values in the MS/MS spectra for sequence elucidation. By varying peptide sequences and other parameters DB-MASCOP can be customized, which can be useful to identify novel sequences also.

Keywords: Peptides, marine cone snails, ion channel, mass spectrometry, database, peptidomics

IN SILICO ANALYSIS FOR THE DIFFERENTIALLY EXPRESSED GENES IN DIFFERENT DEGREES OF NEURODENERATIVE DISEASES AND THEIR ROLE IN PROGRESS OF THE DISEASE

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Background: Neurodegenerative diseases (NDD) are defined by the progressive loss of neurons in the central (CNS) or peripheral nervous systems (PNS). Alzheimer's disease (AD), the most common form of dementia, is characterized by synaptic dysfunction, neuronal death, and cognitive decline. The complex pathophysiology of NDDs, especially AD, presents significant challenges in modern medicine. Virgin coconut oil (VCO), rich in antioxidants, has been proposed as a potential therapeutic agent to manage AD symptoms. This study investigates the potential relevance of differentially expressed genes (DEGs) in AD pathophysiology and explores the therapeutic effects of VCO.

Methodology: Gene expression data were obtained from the Gene Expression Omnibus (GEO) database, focusing on AD and control groups. GEO2R, a browser-based tool, was used to analyze gene expression values and generate a table of DEGs between the AD and control groups. The Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database was used to examine the interaction networks of the identified DEGs, visualizing protein-protein interactions and understanding potential functional relationships.

Major findings: GEO2R analysis identified significant DEGs between AD and control groups, highlighting genes potentially involved in AD pathophysiology. Protein-Protein Interaction Networks by STRING analysis revealed intricate networks of interactions among the DEGs, suggesting their involvement in key AD-related biological processes such as synaptic function and oxidative stress response. Potential therapeutic effects of VCO is that VCO contains antioxidants that may mitigate oxidative stress, a hallmark of AD, potentially protecting neurons from oxidative damage and managing AD progression.

Conclusion: The study identified DEGs in AD patients that may play crucial roles in the disease's pathophysiology.Future research should validate these findings and explore VCO's therapeutic potential in clinical settings.

Keywords: Neurodegenerative disease, virgin coconut oil, gene expression

EXPLORING THE MOLECULAR PATHOGENESIS OF *AXIN1* AND *AXIN2* AS HUB GENES IN COLON CANCER AND PARKINSON'S DISEASE USING BIOINFORMATICS TOOLS

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Background: AXIN1 and AXIN2 are key regulators of the WNT signaling pathway, which is crucial for cell proliferation, differentiation, and apoptosis and have been implicated in various diseases, including colon cancer and Parkinson's disease, suggesting that they play significant roles in the pathogenesis of both conditions.

Methodology: Publicly available datasets from The Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) were utilized to assess the expression levels of *AXIN1* and *AXIN2* in colon cancer and PD tissues compared to normal tissues. Differential expression analysis was conducted using GEO2R and GEPIA2 to identify significant changes in gene expression. PPI networks were constructed using STRING database and visualized with Cytoscape to identify key interacting partners and hub proteins. Pathway enrichment analysis was performed using KEGG to determine the biological pathways in which AXIN1 and AXIN2 are involved.

Major findings: Differential expression analysis revealed that *AXIN1* and *AXIN2* are significantly upregulated in colon cancer tissues compared to normal tissues, correlating with disease progression and poor prognosis. In PD, expression patterns of AXIN1 and AXIN2 were more variable, indicating a complex role in neurodegeneration. PPI network analysis identified several key interacting proteins, in colon cancer and PD.

Conclusion: These findings provide a deeper understanding of the molecular underpinnings of both diseases and highlight AXIN1 and AXIN2 as potential therapeutic targets. This approach will help in understanding the dual role of these genes in cancer and neurodegeneration, potentially leading to new avenues for treatment and diagnosis. Further experimental validation is warranted to confirm these findings and explore their clinical implications.

Keywords: AXIN1, AXIN2, colon cancer, Parkinson's disease, WNT pathway, TCGA, GEO, DAVID, KEGG

QUANTITATIVE N-LINKED GLYCOPROTEIN PROFILING IN ALPHA-L-FUCOSIDASE DEFICIENT PATIENT-DERIVED CELLS

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Background: Fucosidosis is categorized as a lysosomal storage disorder (LSD), which occurs due to a deficiency in alpha-L-fucosidase inherited in an autosomal recessive manner. It is among the rare LSDs with an occurrence of approximately 1 in every 2,00,000 live births worldwide. Fucosidosis is a heterogeneous disease that presents with a varied spectrum of clinical features in different individuals. The varied and overlapping symptoms with other diseases pose a major challenge for early diagnosis, thus delaying therapeutic intervention.

Methodology: To gain insight into the molecular alterations underlying the pathophysiology of fucosidosis, we performed quantitative proteomics and glycoproteomic analyses. We performed TMT-labeled proteomics and glyco proteomics on lymphoblastoid cell lines (LCL) derived from fucosidosis patients and apparently healthy individuals.

Major findings: We identified 52,972 peptides corresponding to 6,456 proteins in the global proteomics dataset. We also identified 2,116 intact glycopeptides, corresponding to 316 glycoproteins. HLA-DRB3, CD53, ITGAV, PTPRC, HLA-DRB1, CTSC, HLA-DPA1 are a few of the significantly dysregulated proteins in both global proteomics and glyco proteomics datasets.

Conclusion: Integrating proteomics and glycol proteomics data will provide insights into the downstream molecular pathways affecting cellular homeostasis in fucosidosis. This study aimed to improve our knowledge of the impact of alterations in protein expression and glycosylation patterns on fucosidosis pathogenesis.

Keywords: Fucosidosis, lysosomal storage disorder, glyco proteomics

COMPUTATIONAL ANALYSIS OF RNA SEQUENCING DATASET REVEALS NOVEL ASSOCIATIONS INRESPONSE TO ARTEMISININ-RESISTANT MALARIA: IMPLICATIONS IN DRUG DISCOVERY AND DESIGN

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Background: Artemisinin Combination Therapy (ACT) serve to be the most effective and influential class of drugs in malaria treatment. However, numerous challenges have emerged over their continued usage for decades. ACT has recently been found to be losing efficacy in Southeast Asia (SEA). The current understanding of the Mechanism of Action (MOA) of artemisinin remains controversial. Several reports suggest that the MOA involves multiple targets and it's unlikely that the mutations in these drug targets are the cause of high-level resistance. Among the reviewed drug targets, PI3K and their pathway members are strongly implicated in resistance.

Methodology: We reassessed an earlier experimental study representing an RNA sequencing dataset of a transcriptome from the trophozoite stage of the parasite in response to the artemisinin drug. We used differential gene expression analysis followed by enrichment analysis tools like GSEA and pathway analysis using Pathview.

Major findings: Our analysis involves the usage of the most recent computational tools with updated annotation records. Results indicate the fatty acid biosynthesis pathway representing alpha-linolenic acid enzymes associated with artemisinin resistance.

Conclusion: Hence, this study adds on to state that the FA biosynthesis pathway is to be targeted to overcome artemisinin resistance. Further experimental studies will have implications for drug discovery and the design of second generation anti-malarials.

Keywords: Di-Hydro Artemisinin (DHA), malaria, resistance, PI3K, RNA-sequence analysis, differential gene expression

INTEGRATED MULTI-OMICS AND META-ANALYSIS REVEAL MOLECULAR SIGNATURES AND THERAPEUTIC TARGETS ASSOCIATED WITH MITOCHONDRIAL DYNAMICS AND PEROXIN IN ALZHEIMER'S AND HUNTINGTON'S DISEASE

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Background: Mitochondrial dysfunction is hallmark of Alzheimer's disease (AD) and Huntington's disease (HD), driving neurodegeneration. Our multi-omics analysis revealed significant deregulation in mitochondrial energy production and neuronal signalling pathways, notably the downregulation of essential vitamins B2, B5, and B6, crucial for mitochondrial respiration and neurotransmitter synthesis. Altered expression of key OXPHOS genes (*NDUFS1, SDHB, UQCRC1*) and disrupted organellar fission, particularly involving PEX11β, further exacerbate mitochondrial and peroxisomal dysfunction, contributing to disease progression in AD and HD**.**

Methodology: To explore these findings, we conducted a commonality analysis focused on the dysregulation of mitochondria-related genes and organellar fission processes in both AD and HD, emphasizing OXPHOS genes and peroxisomal dynamics. Our *insilico* analysis was complemented by in vitro experiments using HD cell lines. Transcriptomics data from the Gene Expression Omnibus (GEO) database were analysed to identify differentially expressed genes, followed by pathway enrichment and transcription factor analysis, correlating these findings with proteomics and metabolomics data.

Major Findings: The study confirmed decreased expression of major OXPHOS genes in both AD and HD. The downregulation of PEX11β was linked to impaired peroxisomal function, which affects mitochondrial dynamics. Restoration of PEX11β expression in HD cell lines improved cell viability, highlighting its role in disease pathology. Additionally, our analysis underscored the critical role of B-vitamins in maintaining mitochondrial function and neuronal health.

Conclusion: The downregulation of PEX11β, along with deficiencies in essential vitamins like B2, B5, and B6, exacerbates mitochondrial dysfunction and contributes to disease progression. Targeting mitochondrial and peroxisomal pathways, including vitamin supplementation, could offer promising therapeutic strategies for managing neurodegenerative diseases.

Keywords: Alzheimer's disease, Huntington's disease, mitochondrial dysfunction, peroxisome, OXPHOS, PEX11β, Miro1, organellar fission, vitamin supplementation

Abstracts

Multi-omics in modern medicine

Total number of abstracts: 6

Poster presentations

Young Scientist Award: 0

Best Paper: 6

Contributed Paper: 0

PHYTOCHEMICAL PROFILING OF COCONUT HAUSTORIUM AND ANALYSIS ON ITS EFFECT ON FRUCTOSE INDUCED HEPATOSTEATOSIS IN CULTURED HEPG2 CELLS

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Background: Non-Alcoholic Fatty Liver Disease (NAFLD) has emerged as a significant health concern, particularly in the context of the escalating prevalence of metabolic disorders worldwide. One promising avenue is the exploration of functional foods as adjunctive therapies for NAFLD management. Among these, coconut and its derivatives have garnered attention for their potential health benefits. The haustorium of coconut, a nutrient-rich component, represents a promising candidate for investigation due to its diverse nutritional composition and potential bioactive properties.

Methodology: Methanolic extract was prepared from dried coconut haustorium and GCMS was carried out for analyzing chemical composition. Hepatosteatosis model in HepG2 cells was carried out to assess the effect of coconut haustorium extract on fructose-induced hepatosteatosis in cells. For the lipid content estimation cells will be collected in chloroform: methanol and the supernatant will be used for further analysis. The genes will be analyzed against internal control gene using standard methods.

Major findings: Using GC-MS techniques, the extract was found to contain various bioactive components. Treatment with coconut haustorium extract significantly reduced total cholesterol and triglyceride levels while suppressing inflammatory cytokines. Additionally, the extract exhibited antioxidant properties by increasing glutathione levels and enhancing antioxidant enzyme activities in HepG2 cells. It also influenced the expression of genes associated with lipid metabolism, suggesting its potential role in regulating hepatic steatosis.

Conclusion: These findings underscore the therapeutic potential of coconut haustorium extract in managing NAFLD and support its further exploration as a dietary intervention.

Keywords: NAFLD, coconut haustorium, hepatosteatosis, GCMS, antioxidant, anti-inflammatory

PHYTOCHEMICAL CHARACTERISATION AND BIOLOGICAL ACTIVITIES OF *THOTTEA SIVARAJANII* LEAF EXTRACT

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Background: *Thottea sivarajanii*, an underexplored plant within the *Thottea* genus, holds significant potential in ethnomedicine, with related species exhibiting notable pharmacological activities. Oxidative stress and inflammation are the major causes of various chronic diseases including, cancer. This study aims to characterize the phytochemical composition and assess the biological activities of *T. sivarajanii* leaf extract, with a particular focus on its antioxidant and anti-inflammatory properties

Methodology: The extract was prepared using Soxhlet extraction, methanol as solvent. Its phytochemical composition was analysed by GC-MS analysis. To assess the extract's antioxidant activity, it was tested against DPPH, ABTS, and FRAP. Its anti-inflammatory potential was studied in lipopolysaccharide induced RAW 264.7 macrophage cells.

Major findings: LC-MS analysis revealed the presence of bioactive compounds in methanolic extract of *T. sivarajanii* leaves. The extract exhibits significant efficacy against the DDPH, ABTS, and FRAP assays. The extract indicated its anti-inflammatory activity by reducing TNF-α, IL-1β, and IL-6 levels in Raw264.7 cells stimulated by Lipopolysaccharide.

Conclusion: This study confirms the *in vitro* antioxidant and anti-inflammatory effects of methanol-based leaf extract of *T. sivarajanii*. The phytochemicals revealed by GC-MS analysis are novel molecules as antioxidant and anti-inflammatory properties.

Keywords: Ethnomedicine, antioxidant, anti-inflammatory, oxidative stress

CHEMICAL COMPOSITION OF *CITRUS PARADISI* ESSENTIAL OIL EXTRACTED BY STEAM DISTILLATION AND EVALUATION OF ITS ANTI-OXIDANT AND ANTI-INFLAMMATORY ACTIVITIES

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Background: *Citrus paradisi*, an evergreen tree from the *Rutaceae* family, is widely found in tropical and subtropical regions. Valuable compounds found in biowastes from fruits and vegetables have the potential to be reused in different industries, providing additional value to the industrial and therapeutic sectors. This study investigates the chemical composition and biological properties of *Citrus paradisi* essential oil, there by proposing a value-added waste management strategy.

Methodology: The extraction of *Citrus paradisi* essential oil was performed using a modified Clevenger-type apparatus for hydro-distillation. The chemical composition of the EO was analyzed through gas chromatography-mass spectrometry (GC-MS), identifying the primary constituents. The biological activities of the EO were evaluated using various *in vitro* assays. Antioxidant activity was assessed through DPPH and ABTS assays, while anti-inflammatory activity was evaluated using the nitric oxide radical scavenging assay and hydrogen peroxide scavenging activity. To further understand the interaction mechanisms at the molecular level, molecular docking studies were conducted using the Mcule platform.

Major findings: Essential oils are known for their diverse therapeutic properties, including cancer prevention, detoxification, and anti-inflammatory effects. The results indicated that *Citrus paradisi* essential oil exhibits significant antioxidant and anti-inflammatory properties. The docking analysis provided insights into the potential bioactive compounds and their affinities toward target enzymes.

Conclusion: The findings suggest that *Citrus paradisi* essential oil could be a promising natural product for developing nutraceuticals, pharmaceuticals, and other bioactive applications. Further studies, including *in vitro* and *in vivo* experiments, are recommended to validate these findings and explore practical applications.

Keywords: Anti-oxidant, anti-inflammatory, GC-MS, pharmaceuticals, nutraceuticals

SERIAL EXTRACTION OF *AZIMA TETRACANTHA* LEAVES AND COMPARATIVE ANALYSIS OF ITS ANTIOXIDANT, ANTI-INFLAMMATORY AND ANTICANCER EFFICACY

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Background: *Azima tetracantha*, is a spinous shrub under the family salvadoraceae. It is used as a component of food and in preparation of herbal medicines in India, Madagascar and Africa. It is an underexplored plant with significant ethnomedicinal importance, was investigated for its chemical composition and biological activities for its therapeutic potential through serial extraction of its leaves.

Methodology: Soxhlet extraction methods were employed to obtain fractions enriched with bioactive compounds. LC-MS analysis of methanol fraction was conducted utilizing the 1290 infinity UHPLC system and GC-MS analysis of the sample was performed using Agilent 5977MSD Gas Chromatograph-mass Spectrometer. Soxhlet extracts were evaluated for their antioxidant activity using DPPH, ABTS and FRAP assays, while anti-inflammatory activity was evaluated using the hydrogen peroxide scavenging activity properties through inhibition of inflammatory markers, and anticancer efficacy against selected cancer cell lines.

Major findings: *Azima tetracantha* leaf Fraction exhibited substantial antioxidant activity, as evidenced by significant scavenging of free radicals in DPPH, ABTS, and high reducing power in the FRAP assay. LC-MS analysis supported these results by identifying specific bioactive compounds, including Retronecine, Quercetin3,7-dimethyl ether, Vanillic acid. GC-MS-analysis of acetone of the plant resulted in the identification of chemicals such as phytol, glutinol, and neophytadiene. Additionally, the methanol and acetone fraction exhibited significant anti-inflammatory activity, particularly in hydrogen peroxide scavenging.

Conclusion: *Azima tetracantha* could be valuable natural source for developing therapies targeting oxidative stress and inflammation, prompting further research in *in vivo* and clinical settings to validate its medicinal applications. Furthermore, the anticancer screening indicated potent cytotoxicity of the extracts against cancer cell lines, highlighting their potential as therapeutic agents.

Keywords: Anti-oxidant, anti-inflammatory, ethnomedicine, bioactive compounds, anticancer, cell line

UNVEILING THE ALCHEMY OF PUNARNAVAYOLEPAM CHOORNAM: A COMPREHENSIVE STUDY ON ITS IRON-ABSORPTION AND ANTIOXIDANT EFFICACY FOR TREATING IRON DEFICIENCY ANAEMIA

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Background: Punarnavayolepam choornam, rooted in the Ashtavaidya (Keraleeya Ayurveda) tradition, exemplifies the alchemy of ancient ayurvedic wisdom and modern scientific inquiry. This formulation involves smearing *Boerhavia diffusa* root (Punarnava) on cast iron trays, followed by drying and powdering and this process is called Ayolepam. It is traditionally utilised for conditions like edema, Pandu Roga (Anaemia), and Glani (fatigue). The formulation leverages the iron-absorbing properties of *Boerhavia diffusa* root, enhancing its therapeutic efficacy for iron deficiency anaemia.

Methodology: We at Vaidyaratnam Ayurveda Research Institute investigates the Ayolepa science (smearing raw materials on iron tray) and pharmacodynamics of Punarnavayolepam choornam. We focused on medicine preparation methods, iron estimation, *in vitro* digestion, and antioxidant evaluation. Iron estimation was performed using Atomic Absorption Spectroscopy - Flame. Gallic acid estimation, Ferrozine-based assay, and the antioxidant DPPH assay, were conducted to assess antioxidant activity and iron presence after digestion. Phytochemical studies and nutritional profiling were done to provide insights into its bioactives.

Major findings: Iron estimation using AAS revealed a significant increase in iron content post-Ayolepa procedure, with the Punarnava root absorbing 500 times more iron. The Gallic acid equivalence test and the DPPH assay indicated substantial scavenging activity. The Ferrozine-based assay indicated that significant iron had been absorbed after *in vitro* digestion revealed the importance of Punarnava in Punarnavaayolepa choornam. Phytochemical studies reveal that Punarnava contains antioxidants that neutralise free radicals, potentially promoting Fe^{2+} oxidation to Fe^{3+} (transferable form of iron). Certain phytochemicals may regulate oxidative enzymes like ceruloplasmin for smooth iron absorption.

Conclusion: This study bridges traditional Ayurvedic knowledge with contemporary scientific methods, offering insights that suggest that *Boerhavia diffusa* in Punarnavayolepam choornam has significant iron-binding and antioxidant properties.

Keywords: Punarnavayolepam choornam, iron absorption, antioxidant activity, *Boerhavia diffusa*

BIOASSAY-GUIDED FRACTIONATION AND PHARMACOLOGICAL EVALUATION OF *HUMBOLDTIA SANJAPPAE*

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Background: Ethnomedicinal plants serve as crucial sources for potential drugs, yet many, especially those in the Western Ghats, have not been thoroughly explored. *Humboldtia*, a genus in the Fabaceae family, flourishes in the rich biodiversity of the Western Ghats in Kerala, India, and holds significant ethnobotanical value. Despite this, numerous species of *Humboldtia* have not been extensively studied for their biological effectiveness, and some lack scientific evidence to support their traditional uses.

Methodology: Medicinally underexplored plant, *Humboldtia sanjappae*, was investigated for its phytochemical composition, as well as its antioxidant and anti-inflammatory properties using DPPH and ABTS assay. LC-MS analysis was conducted to understand the phytochemical constituents in the crude extract. The crude extract was targeted against various inflammatory proteins *in vitro* culture using RAW 264.7 cells. Bioassay-guided fractionation of the *H. sanjappae* extract further identified the most pharmacologically promising fraction.

Major findings: The ethanol extract of *H. sanjappae* demonstrated notable *in vitro* antioxidant activity in DPPH and ABTS assays. Additionally, significant results were observed in studies of cyclooxygenase (COX), lipoxygenase (LOX), inducible nitric oxide synthase, myeloperoxidase (MPO) activity, and cellular nitrite levels in RAW 264.7 cells. Bioassay-guided fractionation of the *H. sanjappae* extract further identified the most pharmacologically promising fraction.

Conclusion: Through meticulous investigation and experimentation, we have demonstrated unequivocally that ethanol-based *H. sanjappae* bark extract is highly effective at lowering inflammation.

Keywords: Lipoxygenase, cyclooxygenase, antioxidant, LC-MS, ethnomedicinal, anti-inflammatory

Souvenir

A LEGACY OF COMPASSION AND EXCELLENCE: THE MISSION OF JUBILEE MISSION MEDICAL COLLEGE HOSPITAL AND RESEARCH INSTITUTE

Dr. Benny Joseph Neelankavil, CEO, JMMC & RI, Thrissur

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Nestled in a sprawling 25-acre campus in the heart of Thrissur, apart from city Jubilee Mission serves patients from neighboring districts of Palakkad and Malappuram, offering quality treatment at affordable prices. Affectionately known as the "Poor Man's Hospital," Every year we provide substantial amount as charity for poor patients. Our dedication to modern medical facilities and super-specialty treatment ensures that everyone can access world-class healthcare.

From a modest 20-bed hospital, Jubilee has expanded into a 1500- bed multispecialty institution over 73 golden years. In 2003, we established a medical college, further complemented by a world class research center, a nursing college, a nursing school, an Ayurveda hospital, and an allied health science college. Today, our hospital handles a daily outpatient flow of about 2,000 patients across 42 departments.

Accredited with NABH, Jubilee Mission's commitment to quality care is reflected in our core values: Compassion, Integrity, Teamwork, and Excellence (CITE). Upholding our mission of "Transforming lives with love," we prioritize patient care over profit, ensuring special consideration and concessions for the underprivileged.

Our specialized services include an intensive care unit for burns treatment, anti-venom treatment for snake bites, the Charles Pinto Centre for cleft palate/cleft lip treatment, and geriatric home care. Often, we are the last resort for many in dire need.

Beyond healthcare, we are deeply committed to community service, supporting patients in myriad ways.

Jubilee Mission Medical College (JMMC)

Established in 2003, JMMC is a Christian Minority Institution with MCI recognition for 100 MBBS seats, 52 postgraduate seats, and 9 super-specialty (DM) seats. Our patron and chairman, H.G. Mar Andrews Thazhath, Archbishop of Thrissur, oversees the institution.

Jubilee Mission College of Nursing (JMCON)

Affiliated with Kerala University of Health Sciences, JMCON offers graduate and postgraduate programs in nursing. Our graduates are prepared to become exemplary nurses, adhering to ethical and professional conduct while meeting national healthcare aspirations.

Jubilee Mission School of Nursing (JMSON)

Since its inception in 1963, JMSON has educated thousands of nurses, providing a general nursing management program recognized by the Indian Nursing Council and the Kerala Nursing Council.

Jubilee Mission College of Allied Health Science (JMCAHS)

JMCAHS offers a range of allied health courses, distinct from nursing, medicine, and pharmacy, including diplomas in medical records technology, optometry, medical imaging technology, anesthesia technology, medical laboratory technology, critical care medicine, general nursing, Ayurveda Panchakarma and nursing, and various paramedical courses.

Jubilee Ayurveda Mission Hospital and Research Institute (JAMH)

Founded on December 7, 2015, Jubilee Ayurveda focuses on major life-threatening disorders such as cancer, kidney, liver, and cardiac issues. Our research projects encompass thyroid disorders, autism, infertility, chronic renal failure, and pediatric disorders. We also offer specialized Ayurveda Panchakarma treatments.

Jubilee Centre for Medical Research (JCMR)

A DSIR-recognized research center, JCMR coordinates research activities across Jubilee institutions, promoting projects funded by governmental agencies, NGOs, and academic degrees such as MD, MS, DNB, DM, and Ph.D.

Jubilee Mission, we don't just provide healthcare; we transform lives with love, every single day. Our impact resonates through the communities we serve, fostering a healthier, more compassionate society. Together, we continue to uphold our mission, making a tangible difference in the lives of countless individuals.

RESEARCH @ JUBILEE

Dr D M Vasudevan
Director-Research

Jubilee Centre for Medical Research (JCMR) is the central research facility for all the institutions under the Jubilee Mission Hospital Trust. There are six other institutions under the Trust which are Jubilee Mission Medical College Hospital, Jubilee Mission Medical College & Research Institute, Jubilee Mission College of Nursing, Jubilee Mission School of Nursing, Jubilee Mission College of Allied Health Sciences and Jubilee Ayurveda Mission Hospital & Research Institute.

The Medical College was established and recognized in 2003. It is a well renowned Medical College in Kerala. The research Centre (JCMR) was established in 2010. The research activities came to a full swing by 2014. It is recognised by the Department of Scientific and Industrial Research (DSIR), Government of India. JCMR has also received the IT exemption under 35.1(ii) from CBDT, Ministry of Finance. This is a recognized research Centre of Kerala University of Health Sciences for Ph.D programme.

The activities of the Centre are governed by a body chaired by the Archbishop of Trichur. A 11 member national level scientific advisory board gives proper suggestions for research initiatives.

Facilities

A team of 12 scientists now leads our research activities and we have 3 Research Assistants, 12 Project Fellows, 16 PhD scholars and 6 supporting staff. The Lab is equipped with most of the modern equipments worth more than seven crores and has a furnished space of 7750 sq feet. A Small Animal Research Facility of 2000 sq ft is also available. This Centre has Human Ethics Committee registered with NABH, CDSCO & DHR, Govt. of India and Animal Ethics Committee approved by CCSEA, Govt. of India.

Laboratory facilities are summarized as below.

- Bioinformatics facilities for performing molecular modeling simulations especially for performing protein-ligand docking and protein-protein docking.
- GPU enabled high performance computer for molecular modelling and AI based studies.
- Dedicated facilities to perform bacterial cultures such as incubators, laminar airflow etc.
- Refrigerators and deep freezers (-80 and -20) to store the samples.
- Electrophoresis units with power pack to separate DNA, RNA and protein molecules.

- Western blot apparatus for antibody related studies and Chemidoc for imaging, analysis of gels.
- Various photometers such as microplate readers, spectrophotometer and fluorescence readers to detect the biological, chemical and physical events that occur in the samples.
- Zeiss Axio Scope A1 for bright field and fluorescence applications.
- Echo therm vibration Chilling incubator for macromolecular crystallography.
- AKTA start Protein purification system.
- Freeze dryer for concentrating biological samples.
- Other necessary equipment including centrifuges, hot air oven, micro pipettes, weighing balance and necessary chemicals to carry out various molecular biology experiments.
- Animal house facility to perform animal studies.
- Minion-portable sequencer.
- Dedicated cytogenetics workbench equipped with peripheral blood and bone marrow culture facility, Leica hybridization chamber, Axio Scope A1 bright field and Fluorescence microscope, Ikaros karyotyping software and Isis fluorescence in situ hybridization software.
- Rotary evaporator, TLC chamber, Soxhlet apparatus and solvent filtration unit to extract the secondary metabolites from natural sources.

Research Divisions

1. Cell and Molecular Biology Facility, headed by Dr Alex George, is working on orofacial clefts, extracellular vesicle research, microbiome, occupational health and genotoxicity.
2. Biochemistry Research Lab, administered by Dr Mathew John is working on Clinical proteomics – multi omics approach and Enzymology.
3. Laboratory for Computational and Structural Biology, directed by Dr. Dileep Vijayan is developing Protein structure determination, drug designing and Ayurbiology.
4. Cytogenetics and Genomic Lab, headed by Dr. Suresh Kumar and Dr Ravindran Ankathil, is focusing on Obesity and breast cancer, male infertility, PCOS, disorders of sexual development.
5. Phytochemistry Research Division, supervised by Dr. Mathew John and Dr K G Raghu is doing isolation and characterization of secondary metabolites.
6. Bioinformatics division is looked after by Dr. Dileep Vijayan.
7. Small Animal Research Facility is headed by Dr C B Devanand.

Research Projects

During the last 5 years, JCMR has completed 6 major external grants and 10 small research projects, altogether having a total budget of Rs 4.62 crores. At present, there are 18 major external grants and 5 minor projects, with a total budget of around Rs.10 crores. Funding agencies include ICMR, DHR, DRDO, DST, DBT, SERB, KSCSTE, Smile Train, Spices Board, etc. Many projects are in the pipeline. Apart from this, about 10 institutional funded research projects are also ongoing.

Some of the ongoing externally funded research projects are

1. Lipid protein multi-omics integrative approaches for differential diagnosis of autoimmune neuromyelitis optica disease spectrum – a comparative cross sectional study (ICMR).
2. Elucidating the association of serum protein levels and genetic polymorphisms of FABP4 with obesity and breast cancer risk in post-menopausal obese women (ICMR).
3. Elucidating the roles of spices as preventive and therapeutic agents for Alzheimer's disease (Spices Board, Govt of India).
4. Targeting Alzheimer's disease with rationally designed polypharmacological prototypes (Kerala Govt).
5. Development and validation of a novel tool to measure medication adherence for select NCDs in the Indian population, An Exploratory sequential mixed method multicentric study (ICMR Task force- leading Centre).
6. Defining a normal reference range for rotational thromboelastometry (ROTEM) in healthy obstetric population (ICMR).
7. Epidemiological and Genetic Research among the Orofacial cleft patients from Central Kerala: A hospital based Case Control Study (Smile Train US/ India).
8. Long term Single versus Dual Antiplatelet Therapy in Patients with Ischemic Stroke due to Intracranial Atherosclerotic Disease: A Randomized Trial (STENOSIS) (ICMR).
9. Team-based collaborative care model, facilitated by a mHealth enabled and trained nurse, for management of heart failure in India (TIME-HF) (Wellcome Trust).
10. Non-invasive treatment of uterine fibroids through rationally designed Selective progesterone receptor modulators (DHR).
11. Haemostatic variables in snakebite: a regional prospective cohort to identify the role of global coagulation assays and serial laboratory testing in the management of snakebite coagulopathy (ICMR).

12. Elucidating the contribution of aberrant mRNAs and differentially expressed microRNAs of sperm RNA transcriptome to the etiopathogenesis of idiopathic male infertility and evaluating their potential as novel diagnostic biomarkers (DHR).

Success stories

- One of the important research projects is on Phenotypic and Genotypic Variations in Cleft Lip and Palate (CLP) Population. This is one of the major centres in the world handling cleft lip/palate reconstruction surgery. A thorough analysis on epidemiological, phenotypical and genotypical studies in CLP population can help in the establishment of the birth prevalence of CLP, improving quality of care and determining genetic and environmental aetiology of clefts. There may be population subgroups which have a particularly high or low risk of clefts due to a combination of genetic susceptibility and exposure which may be revealed by these studies.
- Our scientists are also studying the spatial positioning of chromosomes as a diagnostic tool. The positioning of chromosomes and genes within the nuclear landscape relative to specific functional landmarks plays an important role in gene regulation and disease. This study is focusing on how sex chromosomes and its important genes relocate its nuclear position in sex chromosome involved abnormal conditions and is in search for using spatial positioning as a diagnostic tool. In 2019, our centre has identified and published a novel missense mutation within the HMG domain of the SRY gene in a female disorder of sexual development patient with 46, XY karyotype.
- The research work on treatment of burns is unique here. Research on the production of bioengineered skin supported by DRDO, for the use in burn wounds is a success story.
- Jubilee has actively involved in an ICMR project on pre-hospital care to road traffic victims. The study is on the current pre-hospital trauma care system and the impact of training the available pre-hospital personnel so as to establish a district model. There are no structured educational systems for pre-hospital personnel and the significance of such an intervention is also unknown. We would like to train the currently available pre-hospital personnel with standard protocols and assess the impact it has on the system.
- We have successfully completed one DBT project on the advantage of hyperbaric oxygen therapy in patients with alcohol withdrawal symptom.
- A study on Tuberculosis in patients with Diabetes mellitus supported by Kerala Government has contributed substantially to research output.
- Another research work on microbiological data from three different health centres for the formulation of national antibiotics policy is also an important one.
- Effect of antenatal administration of Magnesium Sulphate on the neurodevelopmental

outcome of preterm infants born at less than 34 weeks gestation is a major research project in Jubilee.

- We also completed a Kerala Govt sponsored project on umbilical cord milking equal to stem cell therapy in preterm babies.
- Coagulation profile and analysis of outcome of blood component therapy in snake bite victims is an important project. This study will give an analysis of the indications and benefits of component therapy in snake bite victims who present with coagulation abnormalities.
- We have isolated and identified eleven flavonoids from Carica papaya leaf with four new reports. (1. Luteolin, 2. Astragalin, 3. Quercetin dimer, 4. 2 (3,4-dihydroxy-5-methoxy phenyl)-3,5,7 trihydroxy 6 -methoxy 2, 3 dihydro 4 H Chromen-4-0ne). These have great pharmaceutical and nutraceutical value.
- Alzheimer's disease (AD), a prevalent neurodegenerative disorder among the elderly, is significantly influenced by the impairment of the cholinergic system, with acetylcholinesterase (AChE) inhibitors like tacrine offering promising therapeutic benefits by slowing acetylcholine breakdown. Our study presents the 2.85 Å resolution X-ray structure of the human AChE- tacrine complex, revealing the low-energy configuration of tacrine and highlighting the induced fit effects on active site residues, providing valuable insights for future drug design targeting AChE in AD treatment.
- Recently we have discovered two proteins Reticulocalbin -1 and Sideroflexin-4 as candidate biomarkers from blood plasma for COPD exacerbations
- Jubilee has also witnessed numerous of research on COVID (42 publications). A study on COVID Vaccine Effectiveness and SARS-CoV-2 Variants in PLHIV in Central Kerala was recently completed with the funding of ICMR.
- More than 50 medical students completed short term research projects with ICMR support within the last few years. More than 55 faculty members of the Medical College are now directly involved in various research programmes.
- Every year, we publish more than 100 research articles in standard journals.

Jubilee Centre for Medical Research is committed for advanced research in both Medical and Basic Sciences. We carry out medical research with ethical considerations and creative ideas. It is our vision to bring forward science and research to address societal needs, education and service. The effort is take the research problems from the clinics and find solutions in the lab.

We hope that this two-day Conference on OMICS will be an important step to strengthen our research ambitions.

THE CULTURAL CAPITAL

Dr. Kumudam M. Unni
Nodal Officer, Jubilee Centre for Medical Research, JMMC & RI, Thrissur

The term Thrissur is the abbreviated anglicized form of the Malayalam word "THRISSIVAPERUR" which means the town of the "SACRED SIVA". The town is built on an elevated ground, at the apex of which is the famous "VADAKKUMNATHAN" Temple; a place of great antiquity,

Thrissur Geography and Climate

Thrissur district is situated in South Western India 10.52º N 76.21º E and is at sea level. Thrissur District is the central part of Kerala State of India. It is bounded on the north by Malappuram district, on the east by Palakkad district and Coimbatore district of Tamil Nadu, on the south by Ernakulam district, and on the west by the Arabian Sea. The Periyar, the Chalakudy, the Karuvannur, the Kurumali River (main tributary of the Karuvannur River) and the Ponnani (Bharatha Puzha) are the main river systems in the district.

The district has a tropical humid climate with an oppressive hot season and plentiful and seasonal rainfall. Annual rainfall is about 3000 mm. The hot season from March to May is followed by the South West Monsoon season from June to September. The period from October to December is the North East Monsoon season. However the rain stops by the end of November and the rest of the period is generally dry.

Thrissur, the Cultural Capital of Kerala state, India is synonymous with the world for its famous and extravagant Pooram Festival. The city which is rich in its cultural heritage is also the house to several cultural centers including Kerala Kalamandalam, Sahitya Academy and Sangeetha Nataka Academy.

The place has played an important role in shaping the political and social perspectives of the region. Thrissur had witnessed the rise and fall of various dynasties that include the Chera and Kulasekaharas in the 12th century, Zamorins in the 14th and 15th century followed by the Mughals (Tippu Sultan), Portugese, Dutch and British. Kodungalloor, the old harbour of India, attracted European powers to Kerala for trading spices and other commodities.

In the consequent centuries the European powers dominated the scene. In the start of 15th century, the Portuguese came and by the beginning of the 17th century the Dutch and the English appeared on the panorama and challenged the Portuguese. Internal conflict helped the Dutch to establish their domination in Kerala coast.

In the medieval age, the region prospered in culture and became home to communities including Jews, Christians and Muslims. The world's second oldest mosque namely, Cheraman Juma Masjid which is believed to be built in 628AD, seven years after the Prophet's migration to Medina is located at Methala in Kodungalloor in Thrissur.

Moreover, Thrissur is also the house of India's oldest Church, St. Thomas Church Palayur. The Church is believed to be built in AD 52 by the renowned Christian missionary, St. Thomas who spread Christianity in India.

Thrissur is also the home town to the great Hindu Saint, Adi Shankara. It is believed that Adi Shanakara was born in answer to the prayer made by his mother in Vadakkumnathan Temple. His disciples have established four Madhoms (mutts) in the city, namely the Northern Madhom, the Middle Madhom, the In-Between Madhom and Southern Madhom. Adi Shanakara after travelling several places spreading his teachings came back to Thrissur and spent his last days here.

Thrissur also gave birth to the renowned mathematician and astronomist, Aryabhata. He is believed to have been born in Kodungallor of Thrissur district. With the decline of Jainism and Buddhism as a result of growing Brahminism, Thrissur became an important center of Sanskrit learning and house for several sacred shrines. The architect of modern Thrissur is Raja Rama Varma, the enlightened ruler of Cochin who ascended the throne in 1790. Shaktan Thampuran, as he is popularly known, revived the cultural heritage of the region and built it up as the main commercial center of Kerala.

In 1790 Raja Rama Varma (1790-1805) popularly known as Saktan Tampuran ascended the throne of Cochin. With the accession of this ruler the English or modern period in the history of Cochin and of the District began. It may be noted in this connection that Saktan Tampuram had been at the helm of affairs since 1769 when all administrative authority in the state was delegated to him by the then reigning sovereign on the initiative of the Travancore Raja and the Dutch Governor. As his very name suggests, this prince was a strong ruler and his reign was characterized by firm and vigorous administration.

The wave of nationalism and political consciousness which swept through the country since the early decades of 19th century had its repercussions in the District as well. Thrissur District can claim the honour of having been in the forefront of the country-wide movement for temple entry and abolition of untouchability. The famous Guruvayur Satyagraha is a memorable episode in the history of the national movement.

The first step towards the achievement of the goal of Aikyakerala (United Kerala) was taken with the integration of Travancore Cochin States in July 1949. With the linguistic reorganization of States in India, in November 1956 the Kerala State came into existence.

Landmarks and Places to visit in Thrissur

Thrissur is known as the cultural capital of Kerala, and the land of Poorams. The district is famous for its ancient temples, churches, and mosques. Thrissur Pooram is the most colorful and spectacular temple festival in Kerala, happening in the April-May period. Some of the famous places to visit in the district are given below.

IN THRISSUR CITY:

Vadakkumnathan Temple:

One of the oldest temples in the State, the Vadakkumnathan Temple is a classic example of the Kerala style of architecture and has many decorative murals and pieces of art. This is the venue of the world famous Pooram festival celebrated annually in April-May. The fireworks at the Pooram are a spectacular sight. Non Hindus are not allowed entry into the temple. (Open: 04:00 - 10:30 am & 05:00 - 08:30 pm). The Paramekkavu and Thiruvambady temples are the main participants, along with eight other temples in the precincts of Thrissur, with Lord Vadakkumnathan as the presiding diety, during Thrissur Pooram.

Archaeological Museum (Town Hall Road):

Open from 10.00 – 17.00 hrs on all days except Mondays and national holidays.

Nehru Park: Oldest Children's park, located in Town centre.

Vaidyaratnam Ayurveda Museum, Thaikkattussery:

Meant to enlighten the public about the rich heritage of Ayurveda.It provides an audio viaual tour of the history of this science through artifacts, sculptors, scriptures and pictures. It is attached to the Vaidyaratnam Ayurveda College.

Art Museum:

Located in the Zoo compound, the art museum displays collections of wood carvings, metal sculptures and ancient jewellery. (Open 10.00 – 17. 00 hrs on all days except Mondays). It takes one hour to complete the visit.

Town Hall:

Houses the Picture Gallery where mural paintings from all parts of Kerala are on display.

Bible Tower(Shrine Basilica of Our Lady of Dolours)

The Bible Tower is situated in Thrissur city of Kerala, India. It was inaugurated on January 7, 2007. The tower is the tallest church tower in India and Asia. It is also the tallest structure in whole of Kerala. The 79 metre tower stands behind two towers of 42.5 metres height. The building has been certified as earthquake-proof by officials of the Geology Department of India. The red cross on the top of the Bible Tower is lit to "show the presence of the Roman Catholic Church in Thrissur." It can be seen from anywhere in the Thrissur city. In the tower we can see childhood of Christ carved in wood, healing of Jesus depicted in stained glass, miracles of Jesus in brass, sufferings of Jesus Christ in oil paints, beautiful painting of apostles in terra cotta, mural paintings of the life history of St. Thomas, and glorious resurrection of Jesus depicted in canvas. Working Hours:

10 am to 6 pm (Tuesday to Friday)
10 am to 7.30 pm (Saturday and Sunday)
Monday Holiday
Lunch Break 1.00 to 2.00 pm

Sakthan Thampuran Palace

This palace named as Vadakkekara Palace, was reconstructed in Kerala-Dutch style in 1795 by Shri. Ramavarma Thampuran of the erstwhile Princely State of Cochin, well known as Sakthan Thampuran, and is preserved by Archaeological Department.. This Palace is situated right at the heart of the city. This palace exhibits a mixture of traditional Kerala and Dutch architectural style. The palace has landscape which is spread over six acres. The palace got its name after King Rama Varma Shakthan Thampuran, who was believed to be the architect of the Thrissur town. There are three tombs including the tomb of Shakthan Thampuran. A flagpole dating back to 1827, and a royal insignia of two elephants, a conch and a lamp in the porch herald a welcome. There is snake temple inside the complex. This museum has the largest collection of excavated megalithic material in Kerala. You will also find very good ancient coins. In addition, the galleries depict the treasury, royal bedroom, and the royal kitchen utensils, besides displays of bronzes, weapons, and stamps.

Shobha City Mall: A complex of stores,supermarket,international food court and 6-screen multiplex cinema at Puzhakkal, Thrissur.

Other tourist spots nearby:

Mangroves at Chettuva: There is a dense mangroves forest in and around the Chettuva lake. This place is known for the back water experience provided to the visitors along with the opportunity to enjoy scenic beauty of dense mangroves forest. The place is also a well-known hub for migratory birds. The kind of ambience you experience during your sightseeing here is extraordinary. This place is 25 kms away from Thrissur city. Chavakkad and Vadanappally are the nearby main towns of Chettuva. It is only 10 kms way from the famous Guruvayoor temple.

Snehatheeram Beach: If you want to enjoy the sunset at a calm and quiet place, this beach is a right choice. It is 30 kms away from Thrissur town. Surely, it is a wonderful place to spend an evening. This beach, maintained by Kerala Tourism Development Corporation (KTDC), is definitely one of the most beautiful beaches in Kerala. There is one restaurant named as 'Naalukettu' near the beach and they are serving famous Kerala sea food.

Athirapally-Vazhachal waterfalls:

"Vazhachal Falls is a rushing watercourse in the Chalakkudy River in the Thrissur district of Kerala, South India. It is located 36 km from Chalakkudy and 5 km from Athirapally Falls. Athirapally Falls is situated in Athirapally panchayath in Thrissur district of Kerala, on the southwest coast of India. Located on the west-flowing Chalakudy River near the Vazhachal Forest Division and the Sholayar ranges, this 24-metre (80 ft) waterfall and the nearby Vazhachal Falls are popular tourist destinations. It is at 30 km to the west and the nearest airport is Kochi International Airport about 55 Km from the waterfall.

The journey to the Athirapally falls passes through a landscape of winding roads, small villages and lush green trees. Athirapally is situated amidst thick forest, thus night riding should be avoided. To reach at top of the Athirapally waterfall we can reach via a paved path that leads through thick bamboo clusters. A steep narrow path also leads to the bottom of the falls. About 7 million tourists visit the falls and Vazhachal picnic spot every year.

Thumboormuzhy Butterfly park is growing to be one of the important eco-tourism attractions in Chalakudy- Athirapally Ecotourism. A visit to Athirapally will be completed only with a visit to Thumboormuzhy. Thumboormuzhy is natural habitat of various species of butterflies .Of course, butterfly sighting is seasonal. The lifespan of some varieties of butterfly is only four days and in some other case it is up to 40 days.It is the second butterfly park in Kerala after Thenmala, Thiruvananthapuram.

Kauthukka Park is a park in Potta, Chalakkudi, on the road to Athirappilly waterfalls. You can feel & interact with many birds, small animals, and fishes. It is a small piece of nature.

Dreamworld Water Park: On the Athirappilly Road, Chalakkudi, is a waterpark, with several rides,42 rides, of which 24 are water rides.

Arattupuzha:

This village is known for the annual Pooram festival at the temple in April/May. The uniqueness of this festival is the ceremonial processions carrying the images of the deities of 41 neighbouring temples to this village.

St. Mary's Forane Church, Koratty (15 km from Cochin International Airport):

Also known as the Church of Koratty Muthy, this was established in 1381. The annual feast falls on the Saturday and Sunday following the 10th of October, during which the statue of Koratty Muthy is taken out in a procession from the church. An important offering here is the poovankula (bunch of plantain).

Guruvayoor (29 km west of Thrissur):

Guruvayoor is one of the most sacred and important pilgrim centres of Kerala. Its main attraction is the Sree Krishna Temple. This historic temple is shrouded in mystery. According to belief, the temple is the creation of Guru, the preceptor of the Gods, and Vayu, the God of winds. The eastern nada is the main entrance to the shrine. In the Chuttambalam (outer enclosure) is the tall 33.5 m high gold plated Dwajasthambam (flag-post). There is also a 7 m high Dipastambham (pillar of lamps), whose thirteen circular receptacles provide a truly gorgeous spectacle when lit. The square Sreekovil is the sacred sanctum sanctorum of the temple, housing the main deity. Within the temple there are also the images of Ganapathy, Lord Ayyappa and Edathedattu Kavil Bhagavathy. Only Hindus are allowed inside the temple.

Irinjalakuda Koodalmanickyam Temple:

Situated 10 km away from Irinjalakuda railway station, this ancient temple is dedicated to Lord Bharatha, the brother of Sri Rama. It is perhaps the only temple in India with Bharatha as the deity. The colourful eleven day annual festival with a pageant of thirteen caparisoned elephants is held in April/May. The festival in this temple marks the end of the Hindu temple festival season in Kerala. (Open: 03:30 - 11:30 am & 05:00 - 08:30 pm). This temple is one of the four in Kerala, that form a set called **Nalambalam**, each temple dedicated to one of the four brothers in the epic, Ramayana. The other temples are: Thriprayar Sree Rama Swami Temple, Thirumoozhikkulam

Sree Lakshmana Perumal temple, and Payammal Sree Shathrughna Swami Temple. In the first week of Karkidaka Malayalam month (July- August) , it is customary to visit all the 4 temples in a single day, in the order of Sree Rama, Bharata, Lakshmana And Shathrughna temples.

Kerala Kalamandalam, Cheruthuruthy (32 km north of Thrissur):

Cheruthuruthy is the seat of the Kerala Kalamandalam, renowned the world over for its Kathakali training centre. The music and dance academy was founded by the famous poet, Vallathol Narayana Menon. Training in Kathakali, Mohiniyattom, Thullal and other art forms of Kerala is imparted here. Cultural programmes are also arranged.

Cheraman Juma Masjid

The Cheraman Juma Masjid is a mosque in Methala, Kodungallur Taluk, Thrissur District. Built in 628 AD, it is the first mosque in India. It was built by Malik Deenar, an Arab propagator of Islam. It is believed that this mosque was first renovated and reconstructed in the 11th century AD.

St. Thomas Church, Palayur

St. Thomas Syro-Malabar Catholic Church, Palayur is located at Palayur, in Thrissur district in Kerala on the west coast of India. According to tradition, it was established in 52 AD by St Thomas, one of the twelve apostles of Jesus Christ. It is one of the oldest churches in India and is called an Apostolic Church credited to the Apostolate of St. Thomas who preached Christianity here. It was part of the seven churches that he established in India; the other six churches were established at Cranganore, Kokkamangalam, Kottakkavu, Kollam, Niranam, and Chayal. The original small Church structure has been retained at the oldest site. But substantial improvements around it were carried out during the 17th century by Reverend Fenichi, as necessary, without sacrificing the main sanctity of the place.

Punnathoorkota

Punnathurkotta is a fort and former palace located in Kottapadi, about 2 km from the Guruvayoor Sree Krishna Temple. Punnathurkotta was once the palace of a local ruler, but the palace grounds are now used to house the elephants belonging to the Guruvayoor temple, and has been renamed Anakkotta. There were 86 elephants housed there, but currently there are about 59 elephants. The elephants are ritual offerings made by the devotees of Lord Guruvayurappa. This facility is also used to train the elephants to serve Lord Krishna as well as participate in many festivals that occur throughout the year. Here one can see elephants of all ages including very small ones to old ones. The visiting hours are 9.30 am to 5.30 pm.

Shopping

There are a number of uniquely Keralite items available in Thrissur. The Thrissur Round has numerous shops selling everything from clothes to electronics. A memorable visit will be to the Khadi Gramodyog shop at Naduvilal, Round West. Items at the Khadi shop include Khadi clothing, printed silk sarees, hand -painted wooden crafts, coconut shell crafts, cane furniture, Kerala's traditional kasavu sarees, Hand-made soaps & candles, natural skin care products and organic spices. Khadi shops often support local artisans and promote sustainable practices so you will be contributing to a good cause while shopping. Remember to explore the shop and ask about the uniqueness of various items.

Aranmula Kannadi is a traditional Kerala metal mirror made from a special alloy of copper & tin, polished to perfection, known for its intricate designs. It is considered to be a symbol of good luck & prosperity , often used as during the traditional festival of Vishu as part of "kani" or as a gift item.

When shopping for Aranmula Kannadi, buy only from a reputed shop. Check the autrhenticity of the product, Look for the Aranmula Kannadi certification. Ask about any special care instructions.

All roads lead to Thrissur Round, making it a true nerve centre of the city. In and around the Round or the Swaraj Round are numerous textile shops interspersed with jewellery shops, restaurants , theatres and small businesses.

Events

Pooram Festival (April/May)
Thaipooya Mahotsavam at Sree Maheswara Temple:
Highlights: Kavadiyattam, Elephant procession, Karakattam, Mayilattam (January)
Utsavam at Sreekrishna Temple, Guruvayoor:
Highlights: Rituals, Elephant race, Cultural programmes, Krishnanattam (March)
Machattu Mamangam at Machattu Thiruvanikavu Temple:
Highlights: Kuthirakolams (motifs of horses) given as offering, Chendamelam, Pageantries, Cultural programmes (December)
Uthralikavu Pooram at Sree Ruthira Mahakalikavu:
Highlights: Elephant processions, Temple and folk arts, Panchavadyam, Pandimelam, All night Pooram on the concluding day (February)
Pulikali (Tiger dance) at the Swaraj Round is part of the Onam celebrations (September)
Arattupuzha Festival (April/May))
Kandassamkadavu Boat Races (August/September)
The official portal of district tourism promotion council is dtpcthrissur@gmail.com.
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