CRIST

Collaborative Research Initiatives on Science and Technology

THE COLLECTION OF ABSTRACTS

Editors: Dr.Dileep Vijayan, Dr. Remya Chandran,
Dr. Saritha Francis, Dr. Ajeena George

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Collaborative Research Initiatives on Science and Technology

LCSB
LABORATORY FOR COMPUTATIONAL AND STRUCTURAL BIOLOGY

Jubilee Centre for Medical Research
JMMC & RI, THRISSUR, KERALA, INDIA

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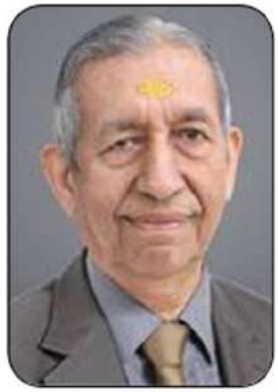

FOREWORD

The Laboratory for Computational and Structural Biology (LCSB) is an important component part of the Jubilee Centre for Medical Research (JCMR). It was established on on July 1, 2021, with support from the JMMC & RI, the Department of Health Research (DHR)-Govt. of India and the Spices Board-Govt. of India. To celebrate the second anniversary of the LCSB and in conjunction with JCMR's decennial celebrations, the LCSB team is hosting a program called "Collaborative Research Initiatives on Science and Technology" (CRIST).

CRIST aims to bring together researchers, professionals, and enthusiasts from different fields on a single platform. It seeks to encourage meaningful discussions, idea exchange, and potential collaborations among researchers, industry professionals, and policymakers. The main goal of CRIST is to promote collaboration and the sharing of knowledge beyond traditional academic boundaries. By gathering experts in various fields, CRIST creates an active and diverse community.

The initiatives taken by the LCSB of the JCMR in Thrissur to unite these young scientists are highly commendable. As the research director of JCMR, I warmly welcome all the enthusiastic individuals joining us at JCMR, and I sincerely wish the program great success.

Dr. D. M. Vasudevan
Research Director, JCMR

Government of Kerala

MESSAGE

I extend my warm greetings to all the esteemed scientists who have gathered as part of the 'Collaborative Research Initiatives on Science and Technology (CRIST)' and commend their efforts in strengthening the scientific and technological capabilities of our nation through collaborative research endeavours. As the Higher Education Minister, Government of Kerala, I am keenly aware of the pivotal role that science and technology play in shaping the future of our society.

The exceptional initiatives taken by the Laboratory for Computational and Structural Biology of Jubilee Centre for Medical Research, JMMC & RI, Thrissur in bringing together these young scientists is truly commendable. The objectives of this CRIST event align perfectly with the state's vision of fostering a culture of scientific excellence and technological innovation.

As the Minister responsible for the Higher Education, I strongly urge scientists from diverse fields to join their hands and participate in the events like CRIST that aims to unlock new frontiers of knowledge, ignite innovation, and tackle the challenges that lie ahead. By working together, pooling expertise, and leveraging collective resources, it is possible to create a vibrant ecosystem that nurtures ground breaking research and technological advancements.

Once again, I express my heartiest greetings and best wishes to the organizers of CRIST and wish all the success.

Dr. R. Bindu
Minister for Higher Education & Social Justice
Government of Kerala

MESSAGE

As the Director of Jubilee Mission Medical College and Research Institute, I consider it as a great privilege to be a part of this esteemed Collaborative Research Initiatives on Science and Technology (CRIST).

Throughout our journey, Jubilee Mission Medical College has consistently strived to lead the way in healthcare advancements and innovative research. It brings me immense joy to witness scientists from various institutions acknowledging the transformative power of research collaborations and their willingness to engage in fruitful discussions on the pressing challenges in the realm of science and technology. I extend my heartfelt appreciation to the entire team of Laboratory for Computational and Structural Biology (LCSB) at Jubilee Centre for Medical Research for their enthusiastic efforts in successfully hosting the CRIST event.

I firmly believe that by joining with distinguished individuals like yourself, it is possible to foster an environment of interdisciplinary cooperation that sparks new ideas and drives breakthrough discoveries. I am sure that these collaborative endeavours hold the potential to not only to expedite the progress of scientific knowledge but also contribute to the development of innovative technologies and solutions that will have a profound impact on patient care and societal well-being.

Together, let us seize this opportunity to embark on a remarkable journey of research excellence and forge a path towards a brighter future.

Wish you all the very best for the CRIST.

Fr. Renny Mundenkurian
Director, JMMC & RI

MESSAGE

As the Principal of Jubilee Mission Medical College and Research Institute (JMMC & RI), it is my great pleasure to extend warm regards to all the Scientist who are gathered as part of this Collaborative Research Initiatives on Science and Technology (CRIST).

At JMMC&RI, we have always been committed to fostering excellence in scientific research and promoting interdisciplinary collaborations. We understand the vital role of research collaboration in advancing the knowledge and innovation. The initiatives by Laboratory for Computational and Structural Biology, Jubilee Centre for Medical Research is truly commendable.

I strongly believe that the CRIST will be a unique platform for networking, idea exchange, and collaborative research projects. By joining forces with individuals of diverse backgrounds and expertise, it is possible to tackle pressing challenges and explore new frontiers in the domains of science and technology. Together, we can unravel the mysteries of our natural world, contribute to sustainable development, and address critical issues that impact our planet.

I extend my heartfelt wishes for success and fulfillment to all the esteemed scientists and faculties who are actively participating in the CRIST. May your endeavors be marked by remarkable achievements and groundbreaking contributions to the realm of scientific knowledge and technological advancements.

Dr Praveenlal Kuttichira
Principal, JMMC & RI

JUBILEE CENTRE FOR MEDICAL RESEARCH

Jubilee Centre for Medical Research (JCMR) is the central research facility of all the institutions under the Jubilee Mission Hospital Trust. This is a DSIR recognized and KUHS approved research center. It is a recognized center by Ministry of finance u/s 351(ii) to receive donations and Ministry of Corporate Affairs for carrying out CSR activities.

JCMR is established by the Jubilee Mission Hospital Trust. The other Institutions under the Trust are the following.

1. The Jubilee Mission Medical College Hospital established in 1951 and now one of the largest hospitals in Kerala with a 1500 beds inpatient capacity and 1750 out patients per day with 32 specialty departments. Also offers DNB programme of Central Board.
2. Jubilee Mission Medical College affiliated to Kerala University of Health Sciences (KUHS) Medical College offers MBBS course, 18 MD/MS courses and 2 DM programmes.
3. Jubilee Mission College of Nursing, B.Sc & M.Sc nursing courses
4. Jubilee Mission School of Nursing
5. Jubilee Ayurveda Mission Hospital & Research Institute
6. Jubilee Mission College of Allied Health Sciences

To involve in research activities, along with clinical practice, is a commitment of faculty and students of these institutions. The faculty and students are actively participating in various research programs funded by government and private sectors and the parent institution. JCMR has completed several research projects funded by ICMR, DRDO, DST, DHR, KSCSTE etc. Currently there are 13 external funded research projects. JCMR has central minister recognized Human and Animal Ethical Committee. Ph.D programs in the faculty of Medicine, Nursing, Paramedical & Allied Health Sciences are undertaken.

LABORATORY FOR COMPUTATIONAL AND STRUCTURAL BIOLOGY

The Laboratory for Computational and Structural Biology (LCSB) operates within the Jubilee Centre for Medical Research, Jubilee Mission Medical College and Research Institute, Thrissur, Kerala, India (www.lcsb.in). The LCSB was established as an official entity on 1st July 2021 with generous support from JMMC & RI, the Department of Health Research (DHR), the Government of India and the Spices Board operating under the Ministry of Commerce and industry, Government of India. Our team comprises a dynamic and enthusiastic group of researchers dedicated to tackling intricate biological challenges through a multidisciplinary approach encompassing computational analysis, *in vitro* and *in vivo* investigations. Two postdocs, two Ph.D students, one Ayurveda physician and three summer interns are the current members of LCSB. Our primary focus lies in the field of drug discovery, where we strive to identify and develop novel candidate molecules for the betterment of humanity. Furthermore, using structural bioinformatics approach, we explore the intricacies of disease-causing missense mutations. The lab is also focused on the understanding the phenotypic-genotypic correlation of prakriti through a multi-dimensional approach and such studies may provide insight into pharmacogenomics and helps designing personalized Ayurveda medicine. LCSB is equipped with a comprehensive range of state-of-the-art facilities for protein production and purification, crystallization and computational facilities for drug discover. LCSB is also equipped with high performance computational facility specifically designed for drug discovery, enabling us to facilitate the initial studies in this field. In the past two years, LCSB has been a part of 11 publications, demonstrating a steadfast commitment to promoting innovation, research excellence, and knowledge sharing in the field of science and technology. These publications reflect LCSB's unwavering dedication to fostering collaborations not only at an inter-institutional level but also within and beyond national borders.

In celebration of LCSB's first anniversary, we conducted a three-day lecture series featuring presentations by esteemed individuals. On July 1st 2022, Dr. Shabeesh Balan from IMHANS shared his groundbreaking research findings on epigenetic modifications in autism spectrum disorder. On July 7th 2022, Dr. NHV K Rao from Nagoya University enlightened us

with his valuable insights on the Cryo electron microscopy, and on July 14th 2022, Dr. Rakhi Rajan, Associate Professor, The University of Oklahoma captivated the audience with her research contributions on crisper CAS structural Biology.

LCSB is currently offering a comprehensive six-month training program in computational and structural biology. This course is specifically designed for biological researchers who are eager to expand their knowledge on macromolecular structures, including the overexpression, purification and crystallization of proteins, process of structure determination, as well as gain proficiency in utilizing essential bioinformatics resources for understanding the structure and function of biomacromolecules. Additionally, short term training on computer aided drug discovery is also providing at LCSB.

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Abstracts of invited talks

Multidisciplinary research on disorders affecting cognition and communication

Dr. Anitha Ayyappan Pillai
Institute for Communicative and Cognitive Neurosciences (ICCONS)
Kavalappara, Shoranur, Palakkad, Kerala

ICCONS is an autonomous institute under Ministry of Health, Women and Child Welfare, Government of Kerala. It was established at Thiruvananthapuram in 1998, and subsequently at Shoranur in 2000. The Department of Scientific and Industrial Research (DSIR) has recognised ICCONS Shoranur as a Scientific and Industrial Research Organization (SIRO). The primary objective of our research is to unravel the neurobiological mechanisms involved in basic cognitive functions by integrating current cutting-edge research across multiple disciplines. This is expected to reveal the etiological mechanisms underlying cognitive and communicative disorders.

Our ongoing and completed research projects belong to the basic pre-clinical category. The following cognitive neurological disorders, which includes monogenic-, polygenic-, and complex- disorders, are being studied- autism spectrum disorders, Rett syndrome, epilepsy, developmental language disorder, spinal muscular atrophy, polymicrogyria, stroke, and Alzheimer's disease. The research projects are managed by a multidisciplinary team comprising of Neurologist, Paediatrician, Geneticist, Biochemist, Speech Language Pathologist, Audiologist, Linguist, Psychologist and Physiotherapist. Multiple aspects of the disorders, such as genetics, genomics, epigenetics, biochemistry, neuroimaging, electrophysiology, speech-language pathology, and audiology manifestations are taken into consideration in our research projects. Our studies are expected to, **(1)** Identify biomarkers that can be used in diagnostic and prognostic predictions, **(2)** Reveal novel drug targets, paving way to novel therapeutic strategies.

ICCONS collaborates with the following institutes for basic pre-clinical research projects of mutual interest, **(1)** CSIR Institute for Genomics and Integrative Biology (CSIR-IGIB), New Delhi, **(2)** Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram, **(3)** National Ayurveda Research Institute for Panchakarma (NARIP), Thrissur, **(4)** Government Medical College, Thiruvananthapuram (GMCT), **(5)** P K Das Institute of Medical Sciences

(PKDIMS), Palakkad. We collaborate with the following engineering colleges for projects involving EEG signal processing, speech signal processing, and neuroimage signal processing, **(1)** Indian Institute of Technology (IIT), Palakkad, **(2)** Government Engineering College Sreekrishnapuram (GECSKP), Palakkad, **(3)** Government Engineering College (GEC), Thrissur, **(4)** MES College Marampally, Aluva.

The major source of our research funds is extramural projects. Our research projects are funded by the Science and Engineering Research Board (SERB; 2 projects), Department of Science and Technology-Cognitive Science Research Initiative (DST-CSRI; 5 projects), Indian Council of Medical Research (ICMR; 1 project), and the Kerala State Council for Science, Technology and Environment (KSCSTE; 2 projects). Apart from this, we also have projects funded by Centre of Excellence for Disability Studies and Kerala State Commissionerate for Persons with Disabilities. During the next five years, we are planning to focus on epigenetics and metabolomics of cognitive and communicative disorders. The state government has earmarked funds to set up an advanced centre for neurometabolomics and neurogenetics research and diagnostics at ICCONS. We are now looking forward for collaborations in *in vitro*, *in vivo* and *in silico* studies, and translational research. ICCONS has published more than 30 research papers in peer-reviewed indexed journals since 2015. The cumulative impact factor of our publications is 40.

Elucidating the molecular pathogenesis of neuropsychiatric disorders employing behavioural phenotyping and genetics

Dr. Shabeesh Balan
Neuroscience Research Laboratory,
The Center for Interdisciplinary Brain Sciences (CIBS),
Institute of Mental Health and Neurosciences (IMHANS),
Kozhikode, Kerala, India

Our team is interested in the discovery of novel genetic and epigenetic risk factors for neuropsychiatric diseases such as schizophrenia, obsessive-compulsive disorders, autism, and attention deficit hyperactivity disorder. We further aim to mechanistically evaluate the genetic risk factors by molecular, cellular, and behavioural phenotyping to characterise molecular pathogenesis of neuropsychiatric diseases for druggable targets and biomarkers. From the behavioural neuroscience aspect, we also work on characterizing electrophysiological correlates of cognition and evaluating sleep and circadian rhythm deficits in psychiatric disorders. Our work has been funded by **(i)** the Department of Health Research, Ministry of Health and Family Welfare, India, **(ii)** Science and Engineering Research Board (SERB), Department of Science & Technology, Government of India, **(iii)** Kerala State Council for Science, Technology & Environment (KSCSTE), Government of Kerala, India, and **(iv)** State University Research Excellence (SURE), Science and Engineering Research Board (SERB), Department of Science & Technology, Government of India.

Synergistic mitigation of *Staphylococcus aureus* biofilm by nanoparticle-antibiotic conjugates outperforms individual components

Dr. Dileep Francis
Department of Life Sciences, Kristu Jayanti College (Autonomous), Bengaluru, Karnataka, India.

According to WHO, in 2019, five million deaths were attributed to bacterial antimicrobial resistance (AMR), of which 1.29 million were directly related. UNEP estimates that by 2050, the numbers could touch 10 million. AMR has been included in the list of the top ten global public health threats facing humanity. Methicillin-resistant *Staphylococcus aureus*, the multi-drug resistant variant of the gram-positive human commensal *S. aureus,* is a significant contributor to the healthcare threat paused by AMR. A leading cause of nosocomial infections worldwide, this versatile bacterium quickly develops resistance. It is endowed with a diverse, sophisticated arsenal of virulence factors, making it an indomitable pathogen of the human host. According to the Global Antimicrobial Resistance Use and Surveillance System (GLASS) data, the average incidence of MRSA in blood-stream infections is 12.11% (IQR-6.4-26.4). To worsen the scenario, *S. aureus* is endowed with the ability to form biofilms on biotic and abiotic surfaces. The nosocomial infections caused by *S. aureus* are exacerbated in intensity and rendered challenging to treat due to biofilm formation on indwelling medical devices such as catheters. Our research group's primary focus has been finding solutions to combat infectious agents, particularly those with unique challenges such as AMR. In this line, a recent approach that we deployed involves the use of nanoparticles (NPs). There is growing evidence for the antibacterial activity of functionalised metal nanoparticles.

Further, NPs have been effectively used for biofilm dispersal. In a recent study, we assessed the efficacy of nanoparticle-antibiotic conjugates against *S. aureus* biofilms *in vitro.* Silver nanoparticles functionalised with polyvinylpyrrolidone (PVP) were conjugated to ampicillin, streptomycin, gentamycin and tetracycline and characterised using UV-Visible spectrophotometry, Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM) and Fourier Transform Infrared (FTIR) Spectroscopy. The NP-antibiotic conjugates were tested against *S. aureus* biofilms allowed to be formed on glass and polystyrene surfaces, along with the antibiotics and nanoparticles as controls. The impact of the conjugates on the

growth and biofilm formation of *S. aureus* was assayed using broth microdilution and crystal violet biofilm quantification assay, respectively. Microbial Adhesion to Hydrocarbon (MATH) assay and Blood Survival Assay were deployed to derive insights into the mechanism of biofilm inhibition. The results revealed that NP-antibiotic conjugates mitigate biofilm formation more efficiently than either component alone. Further, conjugates suppress the virulence of *S. aureus* by rendering it susceptible to opsonophagocytosis much better than the individual components, with better efficiency than the antibiotic and the nanoparticle alone, as revealed by blood survival assays. Interestingly, the MATH assay revealed that neither the antibiotics nor the conjugates modulate the cell surface hydrophobicity. Collectively, the study reveals the potential of NP-antibiotic conjugates in mitigating biofilm formation and provides evidence for their enhanced anti-biofilm activity compared to the individual components. Although the exact mechanism of the antibiofilm activity is still under investigation, it appears to be independent of cell-surface hydrophobicity.

Enabling entrepreneurship via proactive collaborations

Mr. Vineeth Vasu
C - SIX LABS Pvt. Ltd.
Ground Floor, 12/761, Building No. 42, Jayanagar
Chandranagar PO, Palakkad, Kerala, India.

C-six labs Pvt. Ltd., its subsidiary Agrowings and Microbolite Pvt. Ltd. are backed by 15 plus years of techno-commercial experience in the domain of applied Genomics and leverages on the strength of its founders in Start-up ecosystem, nutraceuticals and genomics.

My journey began in 2006 as a technician for molecular biology CRO, followed by an exciting journey in the world of NGS before moving to a core sales profile and currently exploring the world of entrepreneurship. The proactive collaborations and networking gave us the opportunity to serve the scientific community with products and services from leading brands like Metasystems, Theracues, Barcode Biosciences, MP Biomedicals, Bioxia and B Medical systems.

We offer cytogenetics-FISH probes, that are shipped at room temperature and promise a shelf life of 3 years, Metasystem also offers fully automated FISH and karyotyping microscopy solution including microscope, camera and AI based software, Theracues offers one of its kind spatial biology solutions (transcriptomics and proteomics) using the nanostring platform. Theracues is the only Nanostring commercial service /solution provider in India, their nCounter platform enables reliable and reproducible assessment of the expression of up to 800 genes in a single assay. We offer Sanger sequencing, microbial identification, fragment analysis, synthetic gene and primer-probe synthesis at competitive prices and fast turnaround time. Routine reagents and enzymes for molecular biology are supplied at competitive pricing without compromising on turnaround time. Bioxia offers unique products including chambers for anaerobic, microaerophilic cultures and hypoxia chambers, cytotoxic cabinets, while B medical systems offers minus 80 freezers with 5 year compressor warranty and sample transport boxes with lifetime warranty. MP Biomedicals has a unique Fast prep bead beating system which in combination with their patented lysing Matrix, enables homogenization of up to 24 samples in 40 seconds. Agrowings supplies agricultural drones for seed and fertilizer dispersal and pesticide spraying, the drone technology enables it to cover 1 acre in 15 minutes of flight time, and also is a revenue model for aspiring agri-entrepreneurs and FBOs.

Stem cells as a tool for disease modelling to unravel the mystery of neurological disease mechanism

Dr. Divya M S,
Scientist-C, Department of Pathology,
Sree Chitra Tirunal Institute for Medical Sciences and Technology,
Thiruvananthapuram, Kerala, India.

My lab is interested in **(a)** elucidating the role of regulatory elements in defining neuronal fate specification, and its dysregulation in neurodevelopmental disorders, **(b)** modelling late onset neurodegenerative disorders in vitro for elucidating the gene regulatory network involved in the disease onset **(c)** testing the utility of these regulatory factors as bio-markers for disease pathogenesis/progression, and **(d)** evaluating the targetability of these factors to modulate or reverse disease pathogenesis/progression. We use human induced pluripotent stem cells (hiPSC) for neuronal differentiation to model neural development and neurodegeneration *in vitro* and employ CRISPR based genomic perturbation to evaluate cellular and molecular phenotypes. Currently we have two extramural projects. In the first project, we are trying to model ±-synucleinopathy *in vitro* by overexpressing Synuclein Alpha (SNCA) gene in human iPSCs along with temporal induction of aging by a combinatorial approach. This work is funded by Accelerator program for Discovery in Brain disorders using Stem cells (ADBS) seed grant program a collaborative initiative by National Centre for Biological Sciences (NCBS), the Institute for Stem Cell Biology and Regenerative Medicine (InStem) and the National Institute for Mental Health and Neurosciences (NIMHANS). In our second project funded by SERB-POWER grant, we are trying to elucidate the neurodevelopmental phenotypes caused by rare loss-of-function (LoF) mutations in Interferon regulatory factor 2 binding protein-like (IRF2BPL) using human induced pluripotent stem cells. In order to knock out IRF2BPL, we have designed gRNAs targeting the first exon of the gene and cloned them into a gRNA cloning vector. These plasmid constructs will be used for transfection in hiPSCs and the downstream effect of knockout will be evaluated by cellular and molecular phenotyping.

Field to Clinic: Zebra fish in behavioural neuroscience

Dr.Binu Ramachandran
Assistant Professor, Neuronal Plasticity Group, Department of Zoology, University of Calicut, Thenhipalam, Malappuram, Kerala, India.

It was in the late 1960s, phage geneticist George Streisinger began to look for a model system to study the genetic underlying of vertebrate neural development. This hunt for an efficient experimental model paves the way to one of the most popular animal models in research history. His passion for tropical fish led him to the humble zebra fish. One of the great challenges in neuroscience is to unravel how brain activities give rise to behaviour. The zebra fish is regarded as an ideal vertebrate model to address this challenge, thanks to the capacity, at the larval stage, for precise measurements of behaviour, genetic and experimental manipulations, recording and manipulation of neural activity noninvasively and at single-neuron resolution throughout the whole brain. These techniques are being further developed for application in freely moving animals and juvenile stages to study more complex behaviours including learning, decision-making, and social interactions. Our neuronal plasticity group conducts intensive research for a better understanding of human behaviour from a neurobiological perspective. Using zebra fish animal model, the researchers in this lab are able to make comparative connections to humans on a wide variety of behavioural sets. Our main focus is exploring the neural basis of cognition, learning, memory, etc. It is a passion that drives one to take steps in a direction, where no one had ever dared to. Believing in the same path, four years before we initiated the behavioural research using zebra fish as a model organism. It was not at all a sparkling route for us. We successfully established the zebra fish maintenance unit and standardised the breeding conditions first and now we are rearing 2000 above lab-bred fish in our unit. Researchers in the lab mainly concentrating on shoaling, gut-brain axis, neurotoxicology and anxiety with special emphasis on behavioural phenomics. A combination of pharmacology, Next generation sequencing, Transcriptome analysis and behavioural assays will provide the molecular mechanism of different neurodevelopmental, neuro-degenerative and neuro-toxicological diseases. My lab is funded by DST-SERB & University of Calicut. We have 16 publications with a cumulative impact factor 151.64.

Post translational lipid modifications as a target against cancer stemness and inflammation

Dr. Manu Aryan
Dept. of Immunology,
Amala Cancer Research Centre,
Amala Nagar, Thrissur, Kerala, India

Cancer heterogeneity was identified about three decades before and found a small population of cells with key features like self-renewal, tumorigenicity and therapy resistance which later called cancer stem cells or tumor initiating cells. Resistance to therapy is the most important hall mark of cancer stem cells. Cancer stem cells were also believed to possess EMT features and increased metastatic potential. We are interested to study cancer 'stemness' and how tumor immune microenvironment and innate immune system can influence it. Post translational lipid modifications are important in regulating cellular functions of various proteins. Protein S-Palmitoylation is a post-translational lipid modification, which involves the attachment of Palmitic acid to the cysteine residue (most commonly) of proteins. Palmitoylation is essential for many proteins for it's functional regulation and localization and it is mostly associated with membrane proteins in which palmitoyl group helps for membrane attachment. My lab is interested to look the role of palmitoylation and depalmitoylation cycle of some of the key proteins involved in inflammation, stemness and therapy resistance. We are also interested to find suitable molecules that can interfere with tumor cancer stemness and therapy resistance in various cancers.

Genomics in the 21st century and its implication in Kerala

Dr. Amjesh R,
Kerala Genome Data Centre,
Kerala Development and Innovation Strategic Council (K-DISC),
Thiruvananthapuram, Kerala, India.

Genomic data has revolutionized emerging fields such as synthetic biology and bio-manufacturing. By unraveling the genetic foundations of biological processes, scientists can engineer cells to produce desired substances or optimize the production of existing products. Synthetic biology utilizes genomic data to design novel biological systems with unique functions, while bio-manufacturing employs it to streamline the production of biological goods. This revolution has had a profound impact on the global economy by opening up new avenues of research and fostering innovation in various domains, including healthcare, drug development, agriculture, and environmental science. Genomics has played a crucial role in personalized medicine by facilitating the identification of genetic variations linked to specific diseases. This knowledge allows for targeted and individualized approaches to diagnosis and treatment, leading to improved patient outcomes and reduced healthcare costs. Moreover, it has paved the way for the development of customized drugs and therapies that align with an individual's genetic makeup.

In the realm of agriculture, genomics has significantly contributed to the creation of crops that exhibit enhanced resistance to pests and diseases, as well as improved nutritional content. This development holds the potential to bolster food security while minimizing the environmental impact of agricultural practices, promoting sustainability. Furthermore, genomics has proven instrumental in comprehending and safeguarding the environment. Researchers can employ genomic data to identify endangered or threatened species and devise conservation and restoration strategies accordingly.

The vast amounts of genomic data generated by high-throughput sequencing technologies have also presented novel opportunities for data science and artificial intelligence. These disciplines aid in the analysis and interpretation of genomic data, leading to new discoveries and deeper insights into the genetic underpinnings of complex traits and diseases.

From lab bench to clinics; our era of translational research

Dr. Unnikrishnan S.
FFE, Kerala University of Fisheries and Ocean Studies,
Panangad, Kochi, Kerala, India.

Our lab works on model systems for identifying and evaluating the potential of various agents to alleviate inflammation, degeneration, and carcinogenesis and also to induce neurogenesis. We use different cell culture models and co-culture systems to screen promising candidates for their anti-oxidant, anti-inflammatory, and anti-cancer activities. The transgenic *Ceanoharbiditis elegans* model systems are utilized for studying the improvement in learning, memory, and cognition when treated with potential agents. We also use various mouse cancer models to validate the anti-cancer properties *in vivo*.

We are regularly doing rat and mice stereotaxic surgeries for implanting stem cells and injecting neuromodulatory agents. The mice and rat behavioral analysis setup is equipped with a Morris-Water maze, Radial Arm maze, Rotarod, marble burial test, etc to check different aspects of memory and cognition. We are doing extensive work on the microbiome-gut-brain axis. We have developed an antibiotic-induced gut dysbiosis model for studying the molecular and cellular pathways involved in the gut-brain axis. One of the aims of this project is to study the role of gut microbiome in neurogenesis and neurodegeneration.

Structure function of the nicotinic acetylcholine receptors

Dr. Kathiresan Natarajan,
Rajiv Gandhi Centre for Biotechnology,
Thiruvananthapuram, Kerala, India.

Neurotransmitter receptors serve as a link between cells in the central and peripheral nervous systems and are necessary for a variety of physiological functions. The chemical methods by which they communicate with one another are mainly unknown. Noncommunicable neurological disorders such as strokes, epilepsy, Parkinson's and Alzheimer's disease, schizophrenia, depression, and drug addiction are all prevalent issues. Our research group is interested in the biophysical and molecular processes that occur in neurotransmitter receptors under normal and pathological situations. To elucidate the functional processes of single receptor molecules, the group uses cutting-edge computational and biophysical approaches.

Our group is focused on nicotinic acetylcholine receptors, a large family of neurotransmitter receptors involved in rapid signalling throughout the body. Nicotinic receptors are found across the body, with some subtypes being especially prevalent in immune cells. They work as chemically triggered electrical switches through neurotransmitter binding sites and membrane-bound ion channels. They have been linked to a variety of neurological, mental, and inflammatory diseases due to their broad functions. When these receptors connect to acetylcholine, they activate an ion channel that is normally closed. Excessive electrical activity may come from too many or too long open channels in nerve cells. As a result, understanding the structure-function relationship of nicotinic acetylcholine receptors is crucial for understanding their role in health and disease.

Spectroscopy as a tool for cancer diagnosis

Dr. Shaiju S Nazeer,
Indian Institute of Space Sciences and Technology,
Thiruvananthapuram, Kerala, India.

Cancer is one of the leading causes of disease associated deaths worldwide. Early detection can improve the chances of survival in most patients. However, diagnosis at early stages can be challenging as precancerous conditions are usually asymptomatic. Excision/ punch biopsy followed by histopathology is gold standard for cancer diagnosis. It involves tissue staining and morphological pattern recognition. Even though it is an essential part of clinical diagnosis, histopathologic evaluation often remains time consuming and cumbersome. This technique is having limited statistical confidence due to inherent operator variability. Also, the dyes and chemicals used can be cytotoxic and may perturb small metabolites within the tissue. Therefore, a fast and robust method of detection based on molecular changes is needed for early and accurate diagnosis.

Optical spectroscopic techniques such as fluorescence spectroscopy, infrared spectroscopy, and Raman spectroscopy are the emerging diagnostic tool for cancer. These techniques have the capability to overcome problems associated with conventional diagnosis techniques. These spectroscopic techniques are promising tools for fast and real time identification of disease progression and underlying causes. Spectral diagnosis is acheived by analysing the variation in protein-protein, protein–lipid, protein-nucleic acid interactions and conformational changes among various stages/grades of cancers. I will be emphasizing regarding the application of fluorescence spectroscopy as spectral pathology tool for diagnosis. Recent works on the differentiation and classification of different grades of liver fibrosis using fluorescence spectroscopy will be specifically highlighted.

Converging mitochondrial and endolysosomal pathways in the pathogenesis of Parkinson's disease

Dr. Goutam Chandra
Center for Development and Aging Research,
Inter University Center for Biomedical Research,
Mahatma Gandhi University campus, Thalappady,
Kottayam, Kerala, India.

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the selective loss of dopaminergic neurons in the substantia nigra region of the brain. Despite extensive research efforts, the underlying molecular mechanisms contributing to the pathogenesis of PD remain incompletely understood. Accumulating evidence suggests that mitochondrial dysfunction, including impaired electron transport chain complex I, defective mitochondrial dynamics, and compromised quality control mechanisms, contributes to neuronal vulnerability in PD. Moreover, there is recent evidence on the disturbances in the endolysosomal system as another key pathological feature of PD. Using cellular and animal models of PD, we aim to investigate the crosstalk and reciprocal interactions between mitochondrial dysfunction and endolysosomal pathway impairment in PD. We found that long-term mitochondrial dysfunction impaired lysosomal function, altered autophagy-lysosomal pathway, and caused abnormal protein degradation. These defective lysosomal clearance mechanisms result in the accumulation of toxic protein aggregates, including ∝-synuclein, a hallmark protein of PD pathology. These aggregates further impair mitochondrial function and enhance neuroinflammatory responses, leading to neuronal dysfunction and cell death. Taken together, our data on the convergence of mitochondrial dysfunction and endolysosomal pathway impairment highlights a critical mechanism driving neurodegeneration in PD. Elucidating the intricate interplay between these pathways might provide valuable insights into the development of innovative therapeutic strategies to halt or slow down disease progression in PD.

Research in our laboratory is funded by the Department of Biotechnology, The Department of Health Research and Indian Council of Medical Research (Government of India), Department of Health and family Welfare and the Department of Higher Education, (Government of Kerala).

Cellular and molecular basis of disease development

Dr. Alex George
Cellular and Molecular Biology Facility,
Jubilee Centre for Medical Research, JMMC & RI,
Thrissur, Kerala, India.

Cell and Molecular Biology Facility (CMBF) established on 2016, widely focuses on teaching and research providing facilities for students and fellow scientists to establish themselves. CMBF specifically concentrate on the methods including cell cultures, genotoxicity and genomic instability assays, nanopore based nucleic acid sequencing, SNP and haplotype analysis, telomere length analysis, extracellular vesicles isolation and characterization, western blot, and Geographic Information System to track the environmental based genetic risk factors and evidence based computational science. The CMBF has basic research facilities such as cell culture facility with BSL-2 (ESCO), MinION nanopore Sequencer (Oxford nanopore Technology), multimode reader (TECAN), G:BOX Chemi XRQ (Syngene), and CO_2 Incubator (ESCO).

CMBF persue with a fascinating search for genetic and environmental risk factors of orofacial clefts, in collaboration with H. S. Adenwala Institute of Cleft Lip and palate, the project is funded by Smile Train India. CMBF was a part of two completed ICMR projects in the past - **1.** Genetics of alcohol dependancy- where the study concluded that specific haplotype combination is a genetic risk factor for alcohol addiction and relapse and **2.** SARS-CoV-2 variation analysis in people living with HIV - variant analysis and SNPs in the genic portion of the variants are being analysed from this study. CMBF has an international collaboration on extracellular vesicles and cancers with Dr. Cornellia M. Wilson, Canterbury Christ Church University, United Kingdom.

Currently four CSIR-JRF qualified full-time Ph.D scholars from MG university uses the facilities for their doctoral degree in collaboration with Jubilee Centre for Medical Research. Their works comprises of genetics of orofacial clefts and small extra vesicle research in lung and breast cancers. Seven part-time Ph.D scholars from various institutions in and outside Kerala are working on orofacial clefts, cancers and scientometrics. Two post doctoral researchers are associated with the Smile Train India funded project on epidemiological and genetic background of orofacial clefts. Seven part time Doctoral researchers have completed

their projects on genotoxicity, occupational health, telomere genetics and SNP analysis from CMBF.

The future prospects of CMBF focuses on establishing facilities for vescicle biology Research and Human Occupational Health Biomonitoring.

Genomics and epigenetics of cancer and genetic disorders

Dr. Suresh Kumar R
Cytogenetics and Genomics Laboratory,
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Cytogenetics and Genomics Laboratory (CGL) is well equipped with conventional and molecular cytogenetic facilities for detecting both constitutional and acquired chromosome abnormalities . We have facilities and experts for handling chromosome analysis from peripheral blood and bone marrow, Fluorescence In Situ Hybridization (FISH) assays for haematological malignancies, solid tumours and various genetic disorders.

Our research focuses are on reproductive biology as well as haematological malignancies. Our team focus on identifying gene variants involved in disorders of sexual development. Understanding the genetics and epigenetic background of polycystic ovary syndrome is another area of our interest. In addition, we are interested in identifying diagnostic and prognostic markers in myeloproliferative neoplasms. Apart from this, our lab focuses in the characterization of novel chromosomal rearrangements in human genetic disorders and has published 15 research articles in International journals.

Dr. Ravindran Ankathil, an experienced Cytogeneticist is also belongs to our lab. His main area of research is on genetics, genomics and epigenetics of human cancer and is focused on three major areas. **(1)** studying the genomic alterations in cancerous and adjacent non-cancerous tissues of cancer patients, **(2)** studying genetic association of genetic variations such as single nucleotide polymorphisms with the predisposition (susceptibility) risk to cancers, **(3)** elucidating the genetic and epigenetic determinants that modulate good response and / or resistance to anticancer treatments namely chemotherapy and targeted therapy. He has authored 268 research publications in reputed national and international journals. Dr. Anakthil has mentored 24 PhD students as main supervisor. He has supervised 51 research projects funded by various organizations. Currently he has a breast cancer project funded by ICMR and another project has been technically approved by Department of Health Research, Govt. of India.

Proteomics of chronic inflammatory diseases; phytochemistry of bioactive ingredients and its biological applications

Dr Mathew John,
Biochemistry and Phytochemistry Research Division,
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The focus of our lab is to understand the biology of different proteins and phytochemistry. We majorly focusing on the blood proteomic and functional analysis of biomolecules in pursuit of biomarkers for chronic inflammatory diseases; phytochemical analysis of bioactive compounds such as flavonoids and alkaloids from *Carica papaya* L. red lady leaf and their biological applications *in- vitro* and *in- vivo*.

The major research highlights of our lab are **(1)** Identified differentially expressed proteins (DEPs) in blood of patients with Neuromyelitis optica spectrum disorders (NMOSD) connected with cholesterol transport, myelination and free radicals, blood coagulation and complement cascades, **(2)** Major DEPs in NMOSD: Smaug homolog protein, Plasma protease C1 inhibitor, Calcium binding protein 2, Truncated breast and ovarian cancer susceptibility protein, **(3)** Identified DEPs in erythrocytes of Chronic obstructive pulmonary disease (COPD) involved in inflammation, acute phase reactants, hypoxia, and calcium signaling, **(4)** Major DEPs in COPD: Protein S-100 A-9, S100 A-8, alpha-1 acid glycoprotein, flavin reductase, peroxiredoxin and thioredoxin, **(5)** Reported 4 novel flavonoids from *C papaya* red lady leaf viz. luteolin, astragalin, quercetin dimer and 2-(3,4-Dihydroxy-5-methoxyphenyl)-3,5,7-trihydroxy-6-metoxy-2,3 dihydro-4H-chromen-4-one and **(6)** The extracted flavonoids were found to have antioxidant and antihemolytic property.

The following works are progressing in our lab, **(1)** Plasma and erythrocyte proteomic analysis of COPD, Juvenile idiopathic arthritis and rheumatoid arthritis and ischemic stroke, **(2)** *In- vivo* study of platelet rich plasma proteins in reversing thrombocytopenia upon alkaloid treatment extracted from *C papaya* red lady leaf and **(3)** Calcium signaling events in human peripheral blood mononuclear cells upon flavonoid treatment using *in vitro* modeling. The future prospectives of our lab are **(1)** Identification of novel prognostic and diagnostic biomarkers in chronic inflammatory and autoimmune diseases in the form of proteins and

lipids- a multi omics approach, **(2)** Phyto-pharmacological evaluation of bioactive ingredients from *Carica papaya* L. leaf using *in- vitro*, *in- vivo* and *in- silico* approach.

Different research projects that are undergoing in our lab are **(1)** Lipid protein multi-omics integrative approaches for differential diagnosis of autoimmune neuromyelitis optica disease spectrum – a comparative cross sectional study Funding agency: Indian Council of Medical Research - Co-investigators: Dr. P R Varghese (JCMR) and Dr. Harisuthan T (Neurology), **(2)** Non-invasive treatment of uterine fibroids through rationally designed Selective progesterone receptor modulators – DHR funded - PI: Dr. Dileep Vijayan and Co-PI: Dr. Mathew John and **(3)** Elucidating the role of spices as preventive and therapeutic agents for Alzheimer's disease – Spices board funded - PI: Dr. Dileep Vijayan and Co-PI: Dr. Mathew John. So far, there has been 24 publications has made with cumulative impact factor: 45.

Computational and structural biology of diseases

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The Laboratory for Computational and Structural Biology (LCSB), situated in Kerala, India, operates within the Jubilee Centre for Medical Research, Jubilee Mission Medical College and Research Institute. The LCSB team is a dynamic and enthusiastic group of researchers dedicated to tackling intricate biological challenges through a multidisciplinary approach encompassing computational analysis, *in vitro* and *in vivo* investigations. The present LCSB team comprises of two post doctoral fellows, two Ph.D students, three summer interns and one Ayurveda physician. Our primary focus lies in the field of drug discovery, where we strive to identify and develop novel candidate molecules for the betterment of humanity. Furthermore, using structural bioinformatics approach, we explore the intricacies of disease-causing missense mutations. By doing so, we aim to unravel the underlying structural, functional and molecular mechanisms associated with these mutations. While our laboratory is involved in general drug discovery efforts, our primary focus is directed towards the development of **(1)** polypharmacological agents targeting Alzheimer's disease and **(2)** selective progesterone receptor modulators (SPRMs) for the treatment of uterine fibroids (UF). We employ machine learning, computational and structural biology techniques for the drug discovery studies.

LCSB is also involved in the multi disciplinary researches like Ayurbiology, Nanotechnology. In the Ayurbiology programme we are trying to provide genetic basis for Ayurveda prakriti. Aditionaly the effect of medhyarasayana on Alzheimer's diseases is also investigating. In the Nanotechnology research, we are trying to provide a structural basis for the self assembly molecules that are used for the drug delivery.

LCSB is equipped with a comprehensive range of state-of-the-art facilities for protein production and purification as well as crystallization. LCSB is also equipped with high performance computational facility specifically designed for drug discovery, enabling us to facilitate the initial studies in this field.

Abstracts of Posters

Mutation screening of *WNT4* and *RSPO1* genes in 46,XX females with mullerian agenesis and/or gonadal dysgenesis

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The ovaries and mullerian duct-derived organs- the uterus, fallopian tubes, and vagina- comprise the female reproductive system. Wingless-related integration site family members 4 (*WNT4*) and R-Spondin 1 (*RSPO1*) are considered as the key genes involved in the differentiation of these structures. The molecular basis of the absence or agenesis of Mullerian-derived structures and gonads remains unclear, underscoring the current need for research. In the present study, we analysed the role of *WNT4* and *RSPO1* mutations in 46,XX females with these anomalies. We selected seventy-three adolescent girls with primary amenorrhea. Based on the cytogenetic and sex-determining regions of the Y gene investigation, 25 cases were included for mutation screening. PCR sequencing was performed for all coding exons of *WNT4* and *RSPO1*. The promoter region of the *RSPO1* gene was also analysed. Bioinformatic tools like Mutation Taster, Human Splicing Finder, and the MicroRNA Data Base (miRDB) were used. In sequence analysis, *WNT4* showed variations in three patients. Among these, one carried a known synonymous polymorphism (rs544988174). According to miRDB, this area lacks a microRNA regulatory site. The remaining cases showed an intronic nucleotide substitution, which does not affect the splicing mechanism. The coding regions of the *RSPO1* gene showed missense (rs36043533; N = 8) and synonymous (rs1372506524; N = 1) single nucleotide variations. Regarding the *RSPO1* non-coding regions, we observed 7 different single nucleotide variations (rs10908365, rs59740072, and rs11585920 (promoter region); rs187926864 and rs530760760 (5'UTR regions); rs386630409 and rs45577433 (intronic regions)). To conclude, we observed an absence of *WNT4* and *RSPO1* mutations in 46,XX patients with Mullerian agenesis and/or Gonadal dysgenesis.

Kyphoscoliosis peptidase and calpastatin as potential erythrocyte biomarkers for COPD exacerbations: An integrated mass spectrometry/bioinformatics approach

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Chronic Obstructive Pulmonary Disease (COPD), a progressive lung disorder projected to be the third leading cause of global mortality by 2030, is an increasingly important cause of disability and morbidity worldwide. Further, COPD is life-threatening in the present context of COVID. The aim of this study was to investigate the pathophysiology of COPD exacerbation by integrating erythrocyte proteomics with bioinformatics.

The specific objectives of the study were i) To identify proteins that are differentially expressed in exacerbated COPD compared to healthy controls using mass spectrometry analysis. ii) To analyze the differentially expressed proteins in terms of their functional annotation and pathway enrichment using bioinformatics tools, with the goal of understanding the role of these proteins in the pathophysiology of COPD exacerbations.

We obtained the COPD blood samples from a tertiary care hospital in accordance with GOLD guidelines with the help of a pulmonologist. By adopting a high throughput mass spectrometric analysis of the samples following hemoglobin depletion, we were able to identify some differentially expressed erythrocyte proteins associated with COPD. The differentially expressed proteins were then subjected to bioinformatic analysis such as PLS-DA, functional annotation and MCODE clustering to obtain highly enriched protein clusters in exacerbated COPD samples. The biomarker potential of screened proteins that were previously unreported in COPD exacerbation were carried out using ROC curve analysis.

The study identified differential expression of multiple proteins involved in inflammatory signaling pathways. Through bioinformatics analysis, it was found that the key proteins were enriched in molecular events, including MAPK signaling, hypoxia, apoptosis, neutrophil migration, and ciliogenesis. The DEPs were also enriched in pathways related to neutrophil granulation, antimicrobial resistance, and FGF signaling, which have been commonly found enriched in proteomic studies related to COVID as well. Notably, the study observed differential expression of proteins such as kyphoscoliosis peptidase, sperm-associated antigen-1, calpastatin, and LINE in COPD exacerbations. Among these proteins, kyphoscoliosis peptidase and calpastatin demonstrated biomarker potential based on ROC analysis. In relation to COPD, we have identified a set of erythrocyte proteins differentially regulated contributing to COPD pathophysiology. The study could open-up the relevance of erythrocyte proteomics in prognosis and diagnosis of COPD. Validation studies of some of the first-time reported proteins in our study could help in better understanding their biomarker potential leading to improved therapeutic management of COPD.

Targeting depalmitoylation enzyme acyl protein thioesterase-2 against therapy resistance in breast cancer

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Therapy resistance breast cancer (BC) is the most commonly occurring cancer in women and second most common cancer worldwide, after lung cancer. The main therapeutic modalities still used are surgical resection, chemotherapy and radiation. The past ten years have seen a rise in the effectiveness of targeted medicines. But Multidrug Resistance (MDR) to targeted and chemotherapy is still a significant issue in the treatment of breast cancer. Resistance to therapy is the key trait of cancer stem cells. More than 100 proteins that are linked to cancer rely on the post-translational reversible modification of protein s-palmitoylation for membrane attachment. Palmitoylation is reversed by deacylation and it is catalyzed by enzymes belonging to α/β hydrolase family of serine hydrolases called acyl protein thioesterases 1/2 (APT 1/2). Known targets of APT2 are SCRIB, STAT3, TNFR1, ZDHHC6 and MC1R. mRNA expression studies of cell cycle genes showed that APT-2 specific inhibitor ML349 can inhibit the cell cycle progression in human breast cancer cell line (MCF-7) cells. ML349 treatment decreased the number and size of colonies formed by murine breast cancer cells 4T1 in soft agar. MTT and 2D clonogenic assays showed that ML349 sensitized breast cancer cells towards first-line chemotherapeutics doxorubicin. The treatment with ML349 downregulated the mRNA expression of multidrug resistant gene ABCB1 both in the presence and absence of doxorubicin. Hippo-YAP pathway has been reported to regulate cancer stemness and therapy resistance and studies using YAP/TAZ target genes CTGF and CYR61, showed that APT-2 suppression induced effects may be through YAP/TAZ pathway.

Conclusion: APT-2 inhibitor ML349 inhibited the colony formation ability and therapy resistance in breast cancer cells and inhibited YAP/TAZ target genes and MDR1. More studies required to delineate the exact mechanism.

Impact of TUBB4B tubulin isotype mutations on microtubule dynamics

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Microtubules have an exceptionally high degree of structural homology across all eukaryotic organisms, making them an important component of the cytoskeleton. They achieve their functional specialisation via their interactions with microtubule associated proteins (MAPs). The isotypes of α and β-tubulin have been evolutionarily conserved. In recent years, the identification of tubulin isotypic mutations in human brain malformations, which are collectively known as tubilinopathies, has increased interest in the functional role of tubulin. Additionally, a spectrum of neurological malformations that can be attributed to mutations in several different tubulin isotypes has been identified. In patients with leber congenital amaurosis, mutations in a single copy of TUBB4B have been shown to be selectively expressed. The other neurological consequence of the TUBB4B mutations, on the other hand, has not been found yet. Therefore, it is plausible that the TUBB4B isotype plays a crucial part in the development of the nervous system. Furthermore, any mutation of it might modify the dynamics of the microtubules, which could potentially have ramifications for several neurological disorders. In this research project, we investigated the *in-silico* analysis of the TUBB4B tubulin isotype mutations and found that there is an alteration in the dynamics of tubulin. Our findings provide an unsuspected role of the TUBB4B isotype in neurodevelopmental disorders. For further understanding, detailed *in vivo* and *in vitro* analysis of TUBB4B mutant has to be performed.

Antioxidant and anti-hemolytic activity of flavonoids from *Carica papaya* L. Cultivar 'Red Lady' leaf

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Carica papaya L., one of the most popular fruit crops, belongs to the family Caricaceae. It is cultivated in the tropical and subtropical regions of the world. Leaves are traditionally used for the treatment of various diseases. It is rich in antioxidants such as flavonoids, which have health-oriented biological benefits such as anti-inflammatory, immunomodulatory, antiviral, antioxidant, and anti-carcinogenic properties. The aim of the present study is the isolation and characterization of flavonoids from *Carica papaya* L. cultivar 'Red Lady' leaf and the evaluation of their antioxidant and anti-hemolytic activity. In the present study, young leaves of *Carica papaya* L. cultivar Red Lady were collected from the premises of Jubilee Mission Medical College and Research Institute, Thrissur, Kerala, India. Young leaves from the plant were shade-dried and powdered using a rotary grinder. The powdered plant material was extracted in methanol, concentrated and dissolved in water, and further fractionated in chloroform and butanol. The flavonoids in the isolated butanolic fraction of *C. papaya* (FBC) were detected using UPLC-ESI-Q-ToF-MS/MS analysis. Antioxidant activity was evaluated by the DPPH free radical scavenging assay and the FRAP assay. The anti-hemolytic activity of the flavonoid fraction was evaluated by the erythrocyte membrane protection efficacy against H_2O_2-induced hemolysis, the OFT (Osmotic fragility test), and SEM analysis. UPLC-Q-ToF-MS/MS analysis detected 11 flavonoids in the isolated butanolic fraction, viz., quercetin, quercetin dimer, kaempferol, luteolin, 2-(3,4-Dihydroxy-5-methoxyphenyl)- 3,5,7-trihydroxy-6-metoxy-2,3 dihydro-4H-chromen-4-one, rutin, isoquercetin, manghaslin, nictoflorin, astragalin, and mauritianin. Among the detected flavonoids, luteolin, astragalin, 2-(3,4-Dihydroxy-5-methoxyphenyl)-3,5,7-trihydroxy-6-metoxy-2,3 dihydro-4H-chromen-4-one, and quercetin dimer are new reports in papaya leaves. The DPPH assay and the FRAP assay showed that FBC has significant antioxidant activity; it scavenges free radicals and reduces metal ions in a dose-dependent manner. FBC significantly inhibited H_2O_2-induced hemolysis

and lipid peroxidation in a concentration-dependent manner (0.2mg/ml, 0.4 mg/ml, and 0.8 mg/ml). FBC at concentrations of 0.2 mg/mL, 0.4 mg/mL, and 0.8 mg/mL inhibited hemolysis by 76%, 85%, and 87%, respectively. Lipid peroxidation caused by H_2O_2 was reduced to 35%, 45%, and 65% of FBC treatment in a dose-dependent manner. The osmotic fragility test of erythrocytes in hypotonic solutions showed that, as compared to negative and positive controls, FBC-pretreated (0.4 mg/mL) erythrocytes shifted the OFT curve towards the left, indicating the protection of erythrocytes from osmotic fragility. The membrane protection role of FBC in erythrocytes was further confirmed by scanning electron microscopy (SEM), which was marked by a reduction in erythrocyte membrane blebbing and echinocyte formation.

Mapping of orofacial clefts using Geographic Information System - A hospital based study from central Kerala

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Orofacial cleft (OFC) describes a range of abnormalities which manifest in the new born infant. OFC involves structures around the oral cavity which can extend on to the facial structures resulting in oral, facial and craniofacial deformity. These clefts occur when the lip or palate fail to fuse during their prenatal development (first trimester). As per World Health Organization (WHO) reports (2022), it has a global prevalence of between 1 in 1000-1500 births, with wide variation in different studies and population. In India alone the number of infants born every year with cleft lip and palate (CLP) is 28,600, which means 78 affected infants are born every day, or 3 infants with clefts born every hour. This study is aimed to obtain Geographic Information System as technology and its various application to find out distribution, pattern and environmental risk factor for OFC in Kerala, southern India. By using questionnaire data were collected for a period 1.5 years. GIS study was conducted for identifying the distribution pattern of OFC cases by QGIS software. The study included 740 patients where 77 patients had an associated syndrome with Pierre Robin sequence occurring in fifty patients. Among 740 patients, high incidence of CLP (56.9%), followed by cleft palate (26.9%) and cleft lip (16.2%) were observed. Out of 740 cases, 555 (75.03%) cases were from neighbouring districts viz. Ernakulam 66 (8.9%), Thrissur 120 (16.2%), Palakkad 105 (14.2%) and Malappram 260 (35.1%). The Geographic Information system was helpful for more background investigation and planning of cleft care management. Our study enables future studies of etiological factors and future birth registries.

Extracellular vesicle based sortilin, EGFR and CD9 protein expression as a diagnostic method in COPD and NSCLC subtypes

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As less invasive tests for the medical diagnosis of non-small cell lung carcinoma (NSCLC) and chronic obstructive pulmonary disease (COPD), blood-based biopsies would be considerably simpler to adopt. The investigation of blood biomarkers linked to NSCLC and COPD was aided by several inspective technologies. However, these investigated blood-based biomarkers did not get any additional screening or confirmation. To investigate their plasma levels, particularly in extracellular vesicles (EVs), and to forecast their molecular importance in disease, we chose three prospective biomarkers. The global plasma concentrations of sortilin were measured using ELISA. The EVs were isolated using differential ultracentrifugation and characterized by nanoparticle tracking analysis (NTA) and transmission electron microscope (TEM). EV proteins such as sortilin and EGFR as well as EV biomarkers like CD9, CD63 and Flot2 were quantified using western blot. The data analysis was performed in GraphPad prism software. Our findings provide the first-time description of CD9's impact on lung cancer and show how it affects EGFR and sortilin in terms of biomarkers. Sortilin may link with EVs because of the correlation between its global and EV-based forms. In lung adenocarcinoma (ADC) and squamous cell carcinoma (SQCC), there was an increased expression of EGFR and a considerable expression of CD9. Additionally, sortilin was downregulated whereas SQCC expressed considerably more than ADC. Sortilin was strongly expressed and CD9 levels were decreased in COPD, although EGFR showed no variation. In both COPD and NSCLC, there was an inverse relationship between CD9 and sortilin. In NSCLC subtypes, CD9 and EGFR were found to be inversely correlated. Additionally, a clear link between EGFR and CD9 was found in NSCLC subtypes. These data collectively show that sortilin, EGFR, and CD9 levels in EVs altered as NSCLC and COPD advanced. Additionally, their combination might be utilised to create a panel for accurately categorising NSCLC and COPD, offering a different strategy for creating a blood-based test for NSCLC and COPD screening.

Genetic susceptibility of IRF6 gene in non- syndromic cleft lip and palate in Kerala population

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Orofacial cleft primarily cleft lip and cleft palate constitute one of the most commonly occurring congenital abnormalities and represent a global health care challenge (World Health Organization, Human Genetics Program 2002). Cleft lip with or without cleft palate is the most common craniofacial birth defect 1/700 live births. The *IRF6* gene plays an important role in the development of the lip and palate by directing epithelial motility, epithelial-mesenchymal transition, apoptosis, and epithelial adhesion. There are 36 SNPs in *IRF6* that have been linked to orofacial clefts and have been found in Asian, European, and American populations. Additional research in diverse populations revealed that SNPs in the *IRF6* gene are linked to NSCLP. *IRF6* is thought to have a significant role in NSCLP based on previous research. This study investigated the associations of *IRF6* SNPs with Non syndromic orofacial clefts. The study population consisted of 60 patients and the same number of non-cases. Non syndromic orofacial clefts were recruited from the Charles pinto Centre for Cleft Lip, Palate and Craniofacial Anomalies, Jubilee Mission Medical College Thrissur. Patients and controls each had 4 mL of peripheral blood drawn in an EDTA Vacutainer followed by extraction of genomic DNA. After Polymerase Chain Reaction (PCR), the PCR products were sequenced for analysis of the *IRF6* gene variants. The result of this study showed there is a significant difference in genotype and allele frequencies of *IRF6* gene polymorphism rs2235371 were observed between cases and non-cases. The frequency of A allele of rs2235371 has a statistically significant association with NSCLP (OR (95%CI) = 4.78 (1.56- 14.68), P=0.0029. A subgroup analysis by NSCLP types indicated that the variant A allele was significantly associated with NSCL. Genetic models showed negative association [dominant model - OR (95%CI) = 0.23 (0.072- 0.762), recessive model - OR (95%CI) = 7.36 (0.037- 145.75), and over dominant - OR (95%CI) = 0.32 (0.09- 1.06)] in our study. This study concluded that there is a significant difference in genotype and

allele frequencies of *IRF6* polymorphism rs2235371 G>A in NSCLP cases and non-cases in our study. Additionally, we observed that A allele has a significant association with NSCLP subtype. However, our results concluded that rs2235371 in *IRF6* gene are associated with decreased risk of NSCLP. Further comprehensive, and detailed studies with larger sample sizes are warranted to determine the clinical relevance of the association of *IRF6* SNPs with NSCLP.

Exploring the binding potential of natural monoamine oxidase B inhibitors for Alzheimer's diseaes: An *in-silico* approach

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline and memory loss. The pathological hallmarks of AD include the accumulation of amyloid-beta plaques and neurofibrillary tangles, accompanied by oxidative stress and inflammation. One promising therapeutic approach involves targeting monoamine oxidase (MAO), an enzyme responsible for the metabolism of neurotransmitters such as dopamine, serotonin and norepinephrine. MAO inhibitors have proven their clinical efficacy as potential drug leads for several neurological and neurodegenerative diseases. MAO-A inhibitors show efficacy for treating anxiety and depression, while MAO-B inhibitors appears to be effective for the prevention and treatment of neurodegenerative disorders. Spices, one of the most popular plant-based food additives, contain several secondary metabolites that act as antioxidants and have potential role against the neurological disorders like AD. In this study, we employed computational approaches to identify natural inhibitors of MAO-B. Initially, secondary metabolites from *Elettaria cardamomum* (EC) has been collected and computationally screened against MAO-B to identify compounds with high potential binding affinity towards MAO-B. Molecular docking in both open and closed conformation of MAO-B was employed to evaluate the binding affinities and interactions of these compounds. The compounds with the highest binding affinities were further subjected to molecular dynamics simulations to assess their stability within the binding site. Nerolidol shares structural similarities with farnesol, a known MAO-B inhibitor, were scored highest and exhibited a comparable binding mode and interactions as that of farnesol. However *in vitro* binding studies are warranted to further confirm the binding potential of the identified hits.

Deciphering the molecular underpinnings for elevated carbonyl stress in schizophrenia

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Elevated carbonyl stress was identified as a biomarker for identifying a subset of individuals with schizophrenia; characterised by specific clinical phenotypes (treatment resistance, inpatient status, low educational status, long duration of hospitalization, high dose of antipsychotics, and poor prognosis), and are clinically benefited from add-on therapy with antioxidants such as Vitamin B6 and Betaine. Carbonyl stress stems from the generation of increased levels of reactive carbonyl compounds (RCC), derived mainly from carbohydrate metabolism. These RCCs modify the proteins (Maillard reaction) and generate advanced glycation endproducts (AGEs). But, the underlying mechanism of elevated carbonyl stress observed in schizophrenia is elusive. Since the clearance of AGEs by scavenging RCC largely depends on the zinc metalloenzyme glyoxalase I (GLO1), it was suspected that genetic predisposition to enhanced carbonyl stress in schizophrenia might be due to the loss-of-function (LoF) mutations in GLO1. Though rare LoF genetic variants in GLO1 were observed in some patients, no statistically significant enrichment was observed in individuals with schizophrenia manifesting elevated carbonyl stress. We posit that schizophrenia-associated risk factors and their interaction with RCC scavenging mechanisms contribute to the elevated carbonyl stress in schizophrenia. We will present our findings on the relationship of schizophrenia-associated risk factors with elevated carbonyl stress.

Investigating the Inhibitory effects of secondary metabolites of cardamom on lysozyme aggregation

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Lysozyme aggregation has been implicated in several diseases, including systemic amyloidosis, familial amyloidosis, and age-related macular degeneration. Understanding the mechanisms and factors that contribute to lysozyme aggregation is important for developing therapeutic strategies to prevent or treat diseases associated with lysozyme aggregation. In this study, we investigated the inhibitory effects of secondary metabolites of cardamom on lysozyme aggregation. Cardamom contains various secondary metabolites such as terpenoids, phenolic compounds, and flavonoids, which have been reported to possess antioxidant and anti-inflammatory properties. We tested four secondary metabolites of cardamom, namely delta cadinene, alpha caryophyllene, beta caryophyllene, and bornyl acetate, for their inhibitory effect on lysozyme aggregation using Thioflavin T (ThT) assay. We also performed molecular docking to understand the binding mechanism of lysozyme and the inhibitor. The results showed that two compounds, alpha caryophyllene and bornyl acetate, have inhibitory effect on lysozyme aggregation. The other compounds delta cadinene and beta caryophyllene, did not show significant inhibitory effects. The findings provide new insights into the potential therapeutic effects of secondary metabolites of cardamom in the treatment of this disease.

Association of the *MCP-1* and *PAI-1* polymorphisms with polycystic ovary syndrome in the Indian population

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Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder that significantly impacts the quality of life for reproductively aged women. The prevalence of PCOS in the Indian population ranges from 3.7% to 22.5%, influenced by ethnicity and diagnostic criteria. Chronic inflammation plays a crucial role in the development of PCOS. The genes Monocyte Chemoattractant Protein-1 (*MCP-1*) and Plasminogen Activator Inhibitor-1 (*PAI-1*) are key components of the inflammatory pathway, functioning as chemotactic factors and serine protease inhibitors, respectively. Genetic variations in *MCP-1* and *PAI-1* may contribute to altered gene expression. The *MCP-1* promoter polymorphism (rs1024611) has been extensively studied in various inflammatory conditions, but only one report exists regarding its association with PCOS. The rs4586 polymorphism has not been previously studied in relation to PCOS. Hence aimed to investigate the association between *MCP-1* and *PAI-1* polymorphisms [*MCP-1* (rs1024611, rs4586) and *PAI-1* (rs1799889)] with PCOS. A case-control study was conducted with the participation of 1118 women aged between 15 and 35, including 538 PCOS patients and control subjects without PCOS. PCR-RFLP analysis was performed on selected samples, and 120 controls were selected with no family history of PCOS in their second-degree relatives. The distribution and association of rs1024611, rs4586, and rs1799889 with PCOS were analysed. In our study, we observed a statistically significant higher prevalence of the GG genotype for rs1024611 in PCOS patients compared to control samples, indicating an increased risk of the GG genotype in PCOS susceptibility (odds ratio [OR] = 2.203; 95% confidence interval [CI]: 1.008-4.814, $p < 0.04$). Apart from this, the rs4586 polymorphism demonstrated a statistically significant higher prevalence of the CC genotype in control samples compared to PCOS patients, suggesting a protective effect of the CC genotype against PCOS susceptibility (OR = 4.505;

95% CI: 1.763-11.514, $p < 0.001$). However, we could not find any significant relationship between the rs1799889 *PAI-1* polymorphism and PCOS. Our findings suggest an association between the *MCP-1* rs4586 and rs1024611 polymorphisms and PCOS, indicating their potential as predictive genetic markers for PCOS predisposition. Further research is needed to validate these findings and explore their clinical implications in diagnosing and managing PCOS.

Keywords

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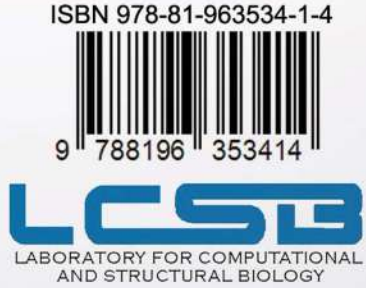

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