FRONTIERS SYMPOSIUM in Biology

IISER THIRUVANANTHAPURAM

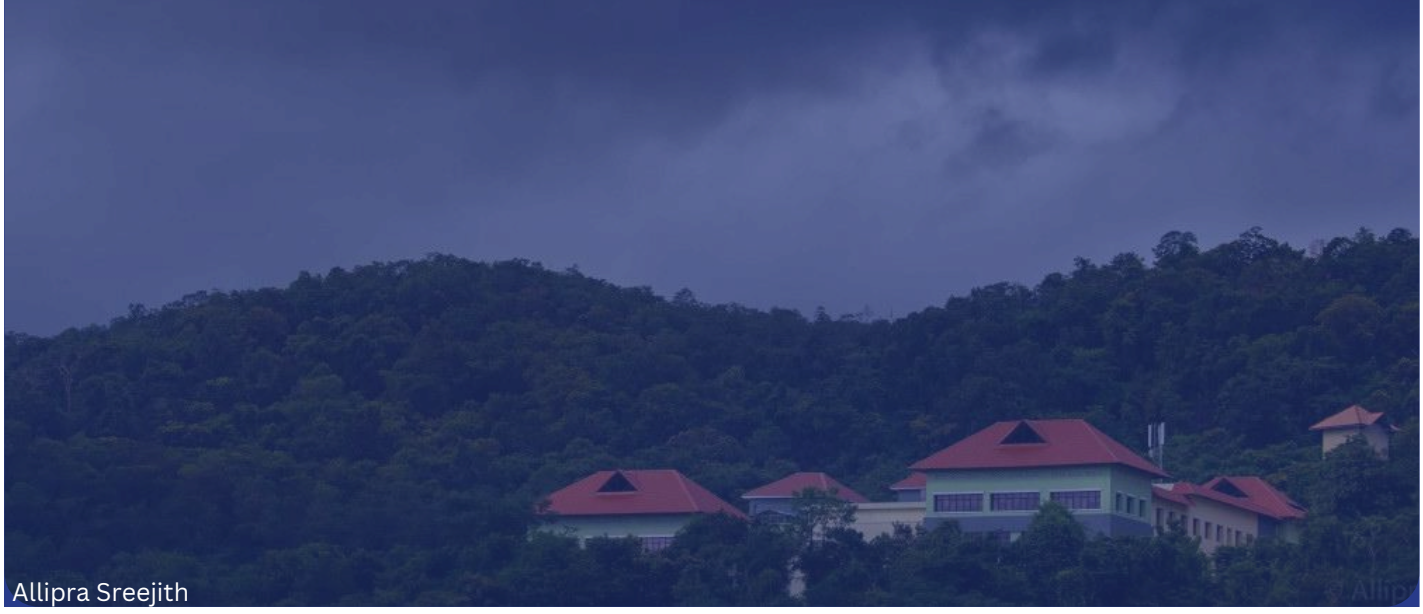
FS-BIO 2025

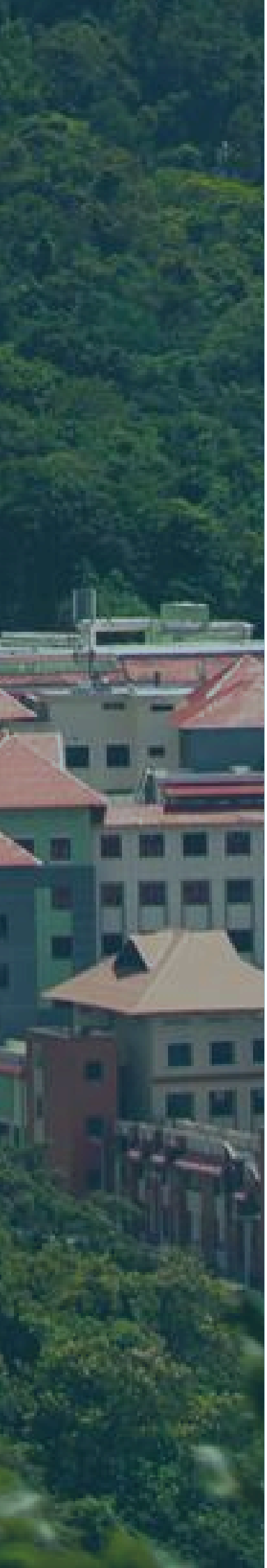
07-09 February, 2025

School of Biology,
Indian Institute of Science Education and Research,
Thiruvananthapuram

ABOUT FS BIO 2025

The Frontiers Symposia in Biology are annual conferences organized by the School of Biology, IISER Thiruvananthapuram. The 2025 symposium will be held from 7th to 9th February at our campus. The meetings cover a wide range of cutting-edge research topics in all fields of biology. Students and researchers from across the country come together to meet and discuss science in our picturesque campus in the foothills of the Western Ghats.





CONTENT

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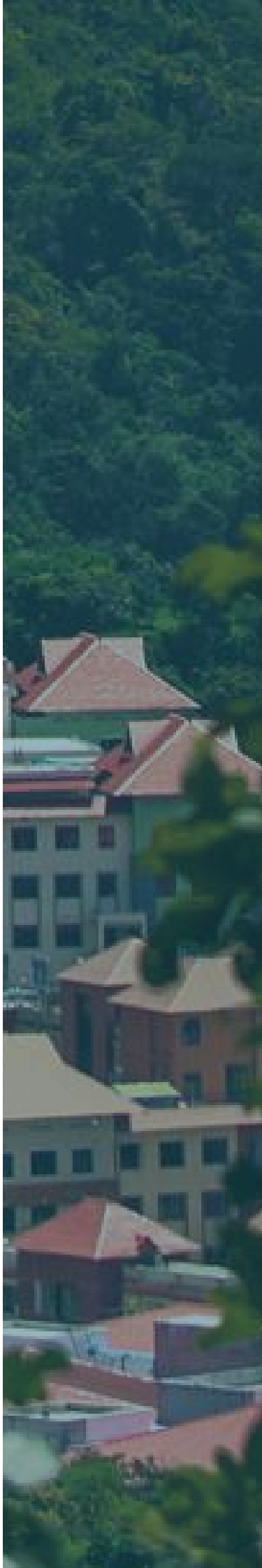


SCHEDULE
AND LISTS

DAY 1
Friday, 7th Feb, 2025

11:00 - 15:00	**REGISTRATION**
15:00 - 15:10	**Welcome Address:** Dr Ravi Maruthachalam, Head, School of Biology, IISER TVM
15:10 - 15:20	**Opening Remarks:** Prof J. N. Moorthy, Director, IISER TVM
	SESSION 1 Chair: Dr Satish Khurana
15:30 - 16:00	Prof Sanjeev Das, NII, New Delhi
16:00 - 16:30	Prof Pradip Sinha, IIT Kanpur
16:30 - 17:00	**ANNOUNCEMENTS AND REFRESHMENTS**
	SESSION 2 Chair: Dr Ravi Devani/Dr Nitin Uttam Kamble
17:00 - 17:30	Dr Ashish Ranjan, NIPGR, New Delhi
17:30 - 18:00	Dr Annapurna Devi Allu, IISER Tirupati, Tirupati
18:00 - 18:30	Dr Hemanth Medidhi, Sr. Application Specialist, Qiagen
18:30 - 20:00	**POSTER SESSION: LHC Corridor**
20:00	**DINNER**

DAY 2

Saturday, 8th Feb, 2025

	SESSION 3 Chair: Dr Vijay Jayaraman
09:30 - 10:00	Dr Ramanathan Natesh, IISER TVM
10:00 - 10:30	Prof Athi Naganathan, IIT Madras
10:30 - 11:00	**ANNOUNCEMENTS AND REFRESHMENTS**
	SESSION 4 Chair: Dr N. Sadananda Singh
11:00 - 11:30	Prof K. Thangaraj, CCMB, Hyderabad
11:30 - 12:00	Prof Madan Rao, NCBS-TIFR, Bengaluru
12:00 - 13:30	**ANNOUNCEMENTS AND LUNCH**
	SESSION 5 Chair: Dr Sandhya Ganesan
13:30 - 14:00	Prof Chandan Goswami, NISER Bhubaneshwar
14:00 - 14:30	Dr Nagaraj Balasubramanian, IISER Pune
14:30 - 15:00	Dr Minhaj Sirajuddin, inStem, Bengaluru
	SESSION 6 Chair: Dr Amrutha Swaminathan
15:00 - 15:30	Prof Pankaj Seth, NBRC
15:30 - 16:00	Dr Poonam Thakur, IISER TVM
16:00 - 16:30	**ANNOUNCEMENTS AND REFRESHMENTS**

DAY 2
Saturday, 8th Feb, 2025

	SESSION 7 Chair: Dr Amrutha Swaminathan
16:30 - 18:00	**FLASH TALKS BY STUDENTS**
18:00 - 20:00	**POSTER SESSION: LHC Corridor**
20:00	**DINNER**

DAY 3
Sunday, 9th Feb, 2025

	SESSION 8 Chair: Dr Nisha N Kannan
9:30 - 10:00	Dr Tina Mukherjee, inStem, Bangalore
10:00 - 10:30	Dr Vatsala Thirumalai, NCBS-TIFR, Bangalore
10:30 - 11:00	Prof Utpal Nath, IISc, Bangalore
11:00 - 11:30	**ANNOUNCEMENTS AND REFRESHMENTS**
11:30 - 12:00	**VALEDICTORY FUNCTION**

List of Invited Speakers

1. Dr Aashish Ranjan
Photosynthesis at the interface of leaf developmental features: A genomic perspective

2. Dr Annapurna Devi Allu
Using insult to overcome injury: Mechanisms to cope heat stress in plants

3. Prof Athi Naganathan
DNA vs Polyphosphate in Condensates: A Kutti Story

4. Prof Chandan Goswami
TRP channels in sub-cellular organelle structure and functions: Importance in mitochondrial and lysosomal biology

5. Dr Hemant Medidhi
Advance Technology for Molecular Biomarker Screening and QIAGEN solutions for NGS

6. Prof Madan Rao
How do cells accurately infer their position in a developing tissue?

List of Invited Speakers

7. Dr Minhaj Sirajuddin
Functional and chemical diversity of cytoskeleton

8. Dr Nagaraj Balasubramanian
Matrix - Mechanosensing - More : A Golgi Story

9. Dr Natesh Ramanathan
Role of unique loops in structure and function of Plasmodium falciparum Gyrase B

10. Prof Pankaj Seth
Viruses and the Brain: What We Knew and What is New?

11. Dr Poonam Thakur
Modelling PD pathology by combinatorial injection of α-synuclein preformed fibrils and over-expressing virus in mouse

12. Prof Pradip Sinha
When biomedical challenges seem insurmountable, dial D for Drosophila

List of Invited Speakers

13. Prof Sanjeev Das
PARP1: emerging link between DNA repair and cancer metabolism

14. Dr Kumaraswamy Thangaraj
Our origin, society and disease

15. Dr Tina Mukherjee
Sensory perception in defining immune potential: a role beyond its senses

16. Prof. Utpal Nath
Shaping up a leaf - How genes control growth and geometry

17. Dr Vatsala Thirumalai
Developmental synaptic pruning in the olivo-cerebellar circuit sculpts predictive processing.

List of Flash Talk Speakers

1. Sachin Bhaskar

Flowering in the dark: Influence of lunar phases on flowering patterns and plant-pollinator interactions of nocturnal flowers

2. Anindita Rao

Unraveling the Hexamerin Code to Development and Nutritional Homeostasis in Drosophila melanogaster

3. Maria Jacob

Uncovering the Role of QPCTL gene in Microtubule Cytoskeleton Regulation Using CRISPR-Cas9 Screening

4. Sameer Joshi

Irc20 modulates LOH frequency and distribution in S. cerevisiae

5. Swetha Gopalakrishnan

Probing the role of CCHamide-1 in the interplay between circadian clock and metabolism in Drosophila melanogaster

6. Akshaya Rajan

Influence of glycation on α-synuclein structure and Parkinson's disease pathology in Vivo

List of Flash Talk Speakers

7. Yash Misra

Decoding transcription regulation by Mycobacterium smegmatis Gre factor homologue

8. T. M Tejas

Unlocking enhanced haploid induction: Epigenetic control of uniparental genome elimination

9. Nikhil Dev Narendradev

E3 ligase substrates and where to find them

10. Dhanagovind P T

Oxygen sensing pathway in the maintenance of neural stem cell pool

11. Ushma Anand

Plk4-dependent degradation of STIL-SAS6 axis by FBXW7 controls centriole duplication

12. Akhil Sadiq

Decoupling detection and recognition in animal camouflage

13. Kavitha Sethumadhavan

Self-assembling protein nanoparticle vaccine elicits potent humoral responses against three emerging coronaviruses

List of Poster Presenters

1. Aakash Kumar Pathak
Genomic interrogation of morphological plurality reveals a species complex in the social spider Stegodyphus sarasinorum

2. Amal K Vyas
Genetic and Morphological diversity of native honey bee; Apis cerana in India

3. Amamah Farzlin Farnaz
Association of the Class II crossover protein (Mms4) with meiotic chromosomes in the baker's yeast.

4. Ananda Krishnan M
Systematic Identification of Antagonyms and their Bifunctional variants in Metabolism

5. Anaswara K S
Testing the preference-performance hypothesis in butterflies

6. Anjitha Kotharambath
Targeting the Mycobacterium tuberculosis evolvability factor Mfd

List of Poster Presenters

7. Anu P V

Unraveling the effect of maternal diabetes on murine hematopoietic emergence

8. Anuraag Nallan Chakravarthi

Modulation of gene expression by replication-transcription collisions

9. Arnav Lakhdive

Putative Inhibitors for M. smegmatis Mfd

10. Ashvitha Balaji

The molecular circadian clock and light input pathway evolve in the Drosophila melanogaster populations selected for the timing of adult emergence

11. Aswathy BJ

Micro-managing the mind: Decoding the role of miR-986 in the fly brain

12. Aswathy V S

Evolution of carbon source preference in Bacillus

List of Poster Presenters

13. Bhanu Bhakta Sharma

Can butterflies use visual memory to improve pupal camouflage?

14. Diya Elizabeth Shaji

Inducible multicellularity and its effect on coexistence between two antagonistic species

15. Harsh Agrawal

Cellular morphometric analysis of mouse fetal liver identifies hepatoblastic niche for hematopoietic stem cells

16. Hrithik Kumar

Infection-Induced exocytosis promotes replication of a lysosomal adapted pathogen, Coxiella burnetiid

17. Jacob Gigi Kurian

Spicing up the centromere : The holocentromere in Nutmeg is not based on major satellite repeats.

18. Jyoti Prakash Bhoi

Genomic ultraconserved elements refute monophyly of Acari

List of Poster Presenters

19. Krishanu Dey Das

Regulation of Golgi architecture and function by novel ubiquitin E3 ligase

20. Krishna M Nair

Diurnal converse with plant-emitted light unfolded potential targets for improving rapeseed-mustard biological yield

21. Kulkarni Gopal

Agent based modelling of Granuloma formation during Mycobacterium tuberculosis infection

22. Manpreet Kaur

The Role of Nuclear Transport in Mediating DNA Repair Following DOX-Induced Topoisomerase II Inhibition

23. Muhammed Naseem

A screen to identify novel roles of microRNAs in the Drosophila prothoracic gland

24. Nidhi S. Kumar

New insights into the photosynthetic thermotolerance of Sorghum bicolor under progressive drought

List of Poster Presenters

25. Parnika Sahoo

Exploiting polypharmacology of kinase inhibitors to identify host regulators of Toxoplasma gondii infection

26. Parul Jain

Novel role for nuclear DUB, USP28 in Parkin-mediated mitophagy

27. Poorvishaa V. Muthusamy

Genomic profiling reveals the genetic foundation for enhanced productivity and adaptability in Sunandini cattle

28. Sandra SN

Decoding host-parasite interactions in Plasmodium vivax infections using Genome-scale metabolic models and Single-Cell RNA sequencing data.

29. Santhosh Kumar Subramanya

A relevant α-synuclein-based mouse model of PD displays neuroprotection upon PD180970 administration

30. Sidharth K A

A cell geometry-based mechanism for controlling organ shape during plant morphogenesis

List of Poster Presenters

31. Soujatya Banerjee

Uncovering the Role of CHD2 in Neurodevelopmental Disorders

32. Swarnendu Mukhopadhyay

Regulation of Centriole duplication: Role of SAS-6 and γ-tubulin ring complex interaction

33. Sweta Chandana Acharjyai

Deep Learning Unlocks Peptide Characterization in the Enigmatic Scorpion Venom Cocktails

34. Tiyas Sengupta

Deciphering the molecular pathways underlying chromatinopathies in neurological disorders

35. Unnati Agrawal

Lipidomic analysis of the midbrain region in an early-stage PD mouse model

36. Vaishak K P

Co-evolution of DSN1 and TTN9 in flowering plants and its Potential role in Kinetochore Assembly in Arabidopsis

List of Poster Presenters

37. Vartika Srivastava
Understanding the Bermuda Triangle of Stress, Sociality, and Aggression in Danio rerio

38. V. Vipina
Metabolic modeling reveals the role of vacuolar citrate and isocitrate in CAM chlorenchyma

39. Dr Barun Mahata
DRIMER: An Optimized Programmable RNA Scaffolds for Multivariate CRISPR/Cas-based Effector Recruitment

40. Dr Vino Udappusamy
Immunomodulatory Action of Coccinia grandis Bioactive Compounds Against Hepatocellular Carcinoma: A Computational Approach

41. Jeena TM
miR200a regulates matrix metalloproteinases and fibrinolytic system during pulmonary fibrosis

42. Susmi Varghese
A multi-PTM landscape of metabolic enzymes

43. Yuvarajan S
Altered Urological Metabolites Differentially Modulate the Agr Quorum-Sensing System in Uropathogenic Staphylococcus aureus

44. Delvin K Pauly
Understanding the mechanisms underlying temporal regulation of Kinetochore size


INVITED
SPEAKERS

DR AASHISH RANJAN

NIPGR, Delhi

Photosynthesis at the interface of leaf developmental features: A genomic perspective

The importance of increasing photosynthetic efficiency for sustainable crop yield increases is well recognized. Optimizing leaf developmental features holds enormous potential for increasing photosynthetic efficiency, as leaves are the prime site of photosynthesis. The natural genetic variation in leaf photosynthesis and its underlying developmental basis is an overlooked and untapped resource. The genus Oryza, including cultivated rice and wild relatives, offers tremendous genetic variability to explore photosynthetic differences and underlying developmental attributes. Investigation of the variations in photosynthesis across multiple wild and cultivated rice accessions identified several photosynthetically efficient wild rice accessions. Leaf morphological traits, such as wider and thicker leaves, and anatomical features, such as mesophyll features and chloroplast surface area exposed to intercellular space, contribute to higher photosynthetic efficiency in wild rice accessions. Moreover, large-scale field phenotyping exhibited remarkable variation in leaf photosynthesis and related leaf physiological and developmental traits among cultivated Indian rice accessions. While comparative transcriptomics involving wild and cultivated rice identified genetic regulators of rice leaf size and transition from development to photosynthesis, GWAS with cultivated landraces identified the genetic loci regulating the desirable leaf developmental and physiological features. We identified a genetic loci on chromosome 1, strongly enriched in photosynthetic genes and regulators, that significantly associated with photosynthesis rate as well as associated physiological traits. These regulators are being targeted for increasing the photosynthetic efficiency of cultivated rice varieties.

IISER THIRUVANANTHAPURAM

DR ANNAPURNA DEVI ALLU

IISER Tirupati

Using insult to overcome injury: Mechanisms to cope heat stress in plants

In response to heat stress, plants evoke a range of adaptive mechanisms, such as the induction of heat shock proteins, antioxidant systems, and osmoprotectants. However, repeated stress responses in biological systems come with a potential energy trade-off, impacting the overall energy budget of the organism. Our research explores the concept of stress memory-based priming in plants, where exposure to mild or non-lethal stress events equips plants to confront subsequent, more severe stressors better. We find that seedlings primed with mild heat stress exhibit enhanced tolerance to subsequent intense heat stress. This increased resilience can be attributed to establishment of efficient cellular homeostasis and a strategic balance between growth and defense mechanisms. We unravel how priming facilitates the rewiring of transcriptional regulatory networks to orchestrate a more organized stress response. We posit that employing priming (insult) could avoid the damaging effects of intense heat stress (injury), in the face of changing environmental conditions and therefore aid in sustainable agricultural practices aimed at ensuring food security.

IISER
THIRUVANANTHAPURAM

PROF ATHI NAGANATHAN

IIT Madras

DNA vs Polyphosphate in Condensates: A Kutti Story

Disordered proteins and domains often assemble into condensates with polyanionic nucleic acids, primarily via charge complementarity, regulating numerous cellular functions. However, the assembly mechanisms associated with the other abundant and ubiquitous, anionic, stress-response regulating polymer, polyphosphate (polyP), is less understood. Here, we employ the intrinsically disordered DNA binding domain (DBD) of cytidine repressor (CytR) from E.coli to study the nature of assembly processes and their maturation with polyP and DNA. Wild-type CytR forms metastable liquid-like condensates with polyP and DNA, while undergoing liquid-to-solid transition in the former and solubilizing in the latter. On mutationally engineering the ensemble to exhibit more or less structure and dimensions than the WT, the assembly process with polyP is directed to either condensates with partial time-dependent solubilization or spontaneous aggregation, respectively. On the other hand, the CytR variants form only liquid-like but metastable droplets with DNA which solubilize within a few hours. Polyphosphate induces large secondary-structure changes with two of the mutants adopting polyproline II-like structures within droplets, while DNA has only minimal structural effects. Our findings reveal how polyphosphate is able to more efficiently discern conformational heterogeneity in the starting protein ensemble, its structure, and compactness, with broad implications in assembly mechanisms involving polyP and stress response in bacterial systems.

IISER THIRUVANANTHAPURAM

PROF CHANDAN GOSWAMI

NISER Bhubaneswar

TRP channels in sub-cellular organelle structure and functions: Importance in mitochondrial and lysosomal biology

TRP channels are a family of non-selective cation channels that are present from single cell lower eukaryotes to human, but are absent in plant kingdom. This channels act as key molecules involved in sensory functions and induce diverse signalling events. Among all TRP sub-family, TRPV group of ion channels are very important as few members of this sub-family are thermo-sensitive in nature, i.e. regulated by temperature and show “thermo-gated behaviour”. Mutations in TRPV channels induce several physiological disorders commonly known as “channelopathies”. In 2021, Prof David Julius fetched the Noble Prize for demonstrating the importance of TRPV1 (also known as the “Capsaicin Receptor”) in sensory functions and the thermo-sensitivity of these channels.

Notably, majority of the TRP channels are described as ion channels present in plasma membrane and relevant for cytosolic Ca2+ regulation. In this context, our lab looked the presence of TRPV3 and TRPV4, two important members of TRPV that are activated by physiological temperature in sub-cellular organelles. We demonstrate that TRPV4 is present in a sub-set of mitochondria and TRPV3 is present in Lysosome. We also show that TRPV4 regulates a number of mitochondrial parameters, such as morphology, fission-fusion, ER-mito contact points, mitochondrial metabolism, and mitochondrial temperature. In a parallel manner, TRPV3 is present in lysosome and regulates lysosomal pH, Ca2+. Such findings suggest the critical involvement of TRPV4 in several channelopathies including Charcot Marie Tooth and different forms of Skeletal Dysplasia. We also propose that TRPV3 mutation induced channelopathies, such as “Olmsted Syndrome” (a rare genetic disorder) is a lysosomal disorder.

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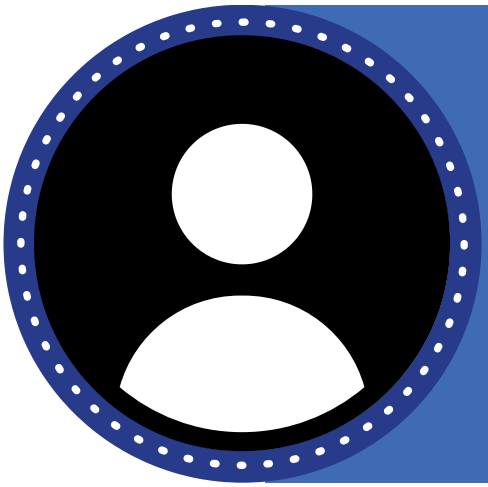

DR HEMANT MEDIDHI

Qiagen India PVT Ltd

Advance Technology for Molecular Biomarker Screening and QIAGEN solutions for NGS

Advanced genotyping technologies are essential for precision medicine, driving breakthroughs in cancer research, cell and gene therapy, infectious disease detection, and copy number variation (CNV) analysis. QIAGEN's advanced genotyping instruments, including real-time PCR, digital PCR, and next-generation sequencing (NGS) platforms, provide high sensitivity, accuracy, and reproducibility in genetic analysis. In cancer research, these instruments enable precise tumor profiling, minimal residual disease detection, and liquid biopsy applications. In cell and gene therapy, they support vector copy number quantification and genome integrity assessments. For infectious diseases, they facilitate rapid pathogen detection, strain differentiation, and antimicrobial resistance analysis. Additionally, their robust CNV detection capabilities are crucial for identifying genetic disorders and understanding disease mechanisms. By integrating automation, multiplexing, and bioinformatics solutions, QIAGEN's genotyping technologies empower researchers and clinicians with actionable insights for personalized medicine and translational research.

IISER THIRUVANANTHAPURAM

PROF MADAN RAO

National Centre for
Biological Sciences
TIFR, Bengaluru

How do cells accurately infer their position in a developing tissue?

A fundamental challenge in Cell Biology is to understand how physical and chemical processes get translated into information (Paul Nurse, 20020). During embryogenesis, cells in a developing tissue need to accurately infer their position from a noisy morphogen signal, for the accurate and reliable determination of cell fate. I will present a conceptual framework for the decoding of noisy molecular information in a developing tissue treated as a Distributed Computing System. We will explore strategies for optimal local (cellular) control that may achieve a global (tissue level) task, namely the accurate inference of cellular position in a tissue. This will lead to a discussion of the geometry of high dimensional inference landscapes, with implications for dimensional reduction, redundancy and robustness in biological networks. I will end with how one might extend this framework to address positional inference in a growing tissue, leading to a morphogen profile that exhibits dynamical scaling.

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THIRUVANANTHAPURAM

DR MINHAJ SIRAJUDHIN

iBRIC-inStem, Bengaluru

Functional and chemical diversity of cytoskeleton

Cytoskeletal components, including actin filaments, microtubules, and intermediate filaments, play a crucial role in mediating various cellular processes within eukaryotic cells. The functionality of these cytoskeletal elements is regulated by specific cytoskeleton-binding proteins, which are often influenced by genetic variations and post-translational modifications (PTMs). In this presentation, I will elucidate the technological platform that facilitated the development of live-cell sensors for microtubule PTMs and their application in investigating the chemical and functional diversity of the microtubule cytoskeleton. Notably, the live-cell sensor for microtubule glutamylation also labels another cytoskeletal element. I will further highlight the application of glutamylation sensors in identifying novel cytoskeletal PTMs and their functional implications in cellular processes.

IISER THIRUVANANTHAPURAM

DR NAGARAJ BALASUBRAMANIAN

IISER Pune

Matrix - Mechanosensing - More : A Golgi Story

Integrin-mediated adhesion regulates membrane trafficking to control anchorage-dependent signaling and growth that is deregulated in anchorage independent cancers. Cell organelles like the Golgi and mitochondria are vital regulators of cellular function, that could contribute to everything from cell migration to development. Loss of adhesion triggers a rapid and reversible disorganisation of the Golgi. This we find is mediated by differential activation of Arf1 regulated by Arf GEF, GBF1. This in turn causes the differential recruitment of microtubule motor proteins to regulate the Golgi. This regulatory pathway controls Golgi-dependent microtubule stability and cell surface glycosylation. My talk will discuss this pathway in cells, and how it can be used to understand the Golgi. I will also talk about its implications in cellular mechanosensing, particularly in context of diseases like cancers.

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DR NATESH RAMANATHAN

IISER Thiruvananthapuram

Role of unique loops in structure and function of *Plasmodium falciparum* Gyrase B

DNA Gyrase is a type II A ATP dependent topoisomerase that introduces negative supercoiling in the DNA. The importance of DNA Gyrase for the survival of the pathogens and its unequivocal absence in humans makes it an ideal drug target. DNA Gyrase is also found in apicoplast of apicomplexan parasites which has an irrefutable role in the survival of the pathogen. Gyrase B (GyrB) from Plasmodium falciparum (PfGyrB), an apicomplexan parasite, has unique biochemical characteristics that are different from its bacterial counterparts. In this work we identified two unique regions, termed as L1 and L2 region in Pf GyrB N-terminal domain (PfGyrBN) and studied them. Towards this aim, we cloned, expressed, and purified PfGyrBN, PfGyrBNΔL1 and PfGyrBNΔL1ΔL2 to demonstrate the effect of the unique stretches of amino acid residues that are present in Plasmodium falciparum Gyrase B but are absent in other bacterial species. Through a series of biophysical and biochemical experiments we have characterized the importance of L1 and L2 region in the role of ATP hydrolysis and dimeric state of the protein. We found that PfGyrBNΔL1 and PfGyrBNΔL1ΔL2 showed reduced ATPase activity in comparison with PfGyrBN, indicating that the L1 region of PfGyrB is essential for ATP hydrolysis. We demonstrate that the binding affinity of ATP is decreased in the absence of L1 and L2 regions. We also find that the L1 region plays a role in the dimerisation of PfGyrBN and may provide a unique dimer interface than the GyrB from other bacterial species. Hence, L1 region has an indispensable role in the function of the protein and is unique to PfGyrB. Based on our results, we propose that this region provides a unique drug target to design drugs specific to Plasmodium falciparum Gyrase B.

IISER THIRUVANANTHAPURAM

PROF PANKAJ SETH

NBRC,
Gurgaon

Viruses and the Brain: What We Knew and What is New?

The consequences arising from the relationship between viruses and the brain have always intrigued basic and clinical researchers of the field of neuroscience and virology. Although rare, infections of the central nervous system (CNS) can have fatal outcomes or life-crippling disorders with acute neurological conditions such as encephalitis, meningitis, and neurodevelopmental disorders etc. Recent advancements in research from our lab and others have provided novel insights into cellular and molecular mechanisms, revealing how viruses and their proteins can impact brain health. It is now evident that viral infections can contribute to neuroinflammation, immune dysregulation, and the long-term degeneration of brain cells. Emerging research also highlights how viruses, such as HIV-1, Zika and SARS-CoV2, may influence brain function through persistent or latent infections, leading to neurocognitive disorders and irreversible damage to neuronal cells. Our laboratory at NBRC has established a unique in vitro model of human fetal brain-derived neural stem cells that we use to study the effect of different viral proteins on human astrocytes, neurons, and human neural stem/progenitor cells. We use this cell culture model in 2D and 3D systems. Research findings from our group have immensely contributed towards understanding how HIV-1 Tat protein modulates neuron-glia interactions that culminate into neurocognitive and motor deficits in HIV/AIDS patients and how certain structural and non-structural proteins cause damage to human neural stem cells affecting in-utero development. We have identified novel roles of several miRNAs that are pivotal in viral neuropathogenesis. The findings have far-reaching implications for cases of viral infection of CNS. Funding from national and international funding sources and NBRC core funds is gratefully acknowledged.

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DR POONAM THAKUR

IISER Thiruvananthapuram

Modelling PD pathology by combinatorial injection of α-synuclein preformed fibrils and over-expressing virus in mouse

Parkinson's disease (PD) is a neurodegenerative disorder caused by the loss of dopaminergic neurons of the substantia nigra (SN). The pathological hallmark of PD is aggregation of α-synuclein (α-syn) proteins in Lewy bodies and their progressive spreading in the brain. 60% of neuronal death occurs before motor symptoms appear. Successful recapitulation of progressive PD features in animal models is vital to understanding disease progression mechanisms.

In our study, we injected AAV-SNCA and α-syn pre-formed fibrils (SynFib) into medial and lateral SN to generate PD models. Also, a set of mice injected with AAV-GFP, AAV-SNCA (Syn) and PFFs (Fib) were compared with the SynFib group. The behavioral outcomes were evaluated using wirehang, cylinder, openfield corridor tests. We studied the extent of neurodegeneration, α-syn aggregation and neuroinflammation at 4W in all the groups and at 4W (early), 12 (intermediate) and 24W (late) in the SynFib group. SynFib model displayed significant neurodegeneration and striatal fibre loss at 4W with increased accumulation of p-syn aggregates in SN, which progressed with time in SynFib group. Further, we observed trans-synaptic spread at striatum and cortex in SynFib group. We also observed a significant increase in activated microglia and astrocytes, strongest at early time points and attenuated over time. Also the model displayed mild motor deficits in mice consistent with other synuclein-based models. The model also showed reduced stride length at 24W. The model replicated various distinct pathological signatures at early and late timepoints. Studying the mechanisms behind progression would lead to identification of therapeutic targets.

IISER THIRUVANANTHAPURAM

PROF PRADIP SINHA

IIT Kanpur

When biomedical challenges seem insurmountable, dial D for Drosophila

In recent years, the tiny fruit fly, Drosophila, has emerged as an unexpected yet powerful tool in biomedical research. Advances in genetics and genome editing have revealed three striking facts: most developmental genes in Drosophila are shared with humans and other species, over 70% of genes linked to human diseases exist in Drosophila, and various diseases can be modeled in this organism by expressing human disease-linked genes. As a result, Drosophila has become an invaluable system for modeling human diseases, identifying drug targets, and exploring therapeutic strategies.

Building on these insights, I will first explore how we identify human oncogene targets, then delve into the connection between cancer and metabolic syndromes. Finally, I will discuss our work on COVID-19 and long-COVID. These findings deepen our understanding of disease mechanisms and offer novel insights for therapeutic interventions.

IISER
THIRUVANANTHAPURAM

PROF SANJEEV DAS

NII, New Delhi

PARP1: emerging link between DNA repair and cancer metabolism

The metabolic requirements of cancer cells are unique as characterized by enhanced nutrition uptake and shunting of metabolic intermediates into the biosynthesis of macromolecules for rapid proliferation. There is also significant crosstalk between the rewired metabolic pathways and the cellular signaling networks. Poly(ADP-ribose) polymerase 1 (PARP1) is an abundant nuclear protein involved in DNA repair, chromatin structure, and transcription. PARP1 activated in response to genotoxic insult catalyses PARylation, which uses NAD+ as substrate. NAD+ serves as a cofactor for several enzymes involved in cellular energy metabolism. However, the role of PARP1 in metabolic rewiring in tumor cells is not well-explored. Here, we report the role of its acetylation status in modulating its DNA repair and transactivation functions. We demonstrate that HDAC5 determines PARP1 acetylation at Lys498 and Lys521 sites. HDAC5-mediated deacetylation at the Lys498 site regulates PARP1 DNA damage response and facilitates efficient recruitment of DNA repair factors at damaged sites, thereby promoting cell survival. On the other hand, HDAC5-mediated deacetylation at the Lys521 site promotes PARP1 coactivator function, resulting in the induction of proliferative and metabolic genes in ATF4-dependent manner. PARP1-ATF4 regulated metabolic genes promote the glutamine anaplerotic pathway to maintain cellular energetics. Glutamine also serves as the nitrogen source for amino acid and nucleic acid biosynthesis. Thus, PARP1-mediated transactivation is critical for metabolic adaptation to spur malignant phenotype. Our studies in mouse tumor models suggest that pharmacological inhibition of PARP1 enzymatic activity does not block tumor progression robustly as transactivation function remains unperturbed. These findings, which shed light on the intricate regulatory mechanisms that determine the impact of PARP1 acetylation status on DNA damage response and metabolic adaptation, will be discussed.

IISER
THIRUVANANTHAPURAM

PROF KUMARASWAMY THANGARAJ

CCMB, Hyderabad

Our origin, society and disease

Indian subcontinent / South Asia is a region of remarkable cultural, linguistic, and genetic diversity with over 4,500 anthropologically well-defined groups. We have been studying various South Asian populations to understand their origin, affinities, and impact of endogamy. One of our studies established that the contemporary Indian populations have descended 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 the Indian subcontinent have been practising endogamy. To assess the impact of endogamy, we have analysed 275 distinct South Asian groups and found that 81 out of 275 groups have stronger founder events than the one that occurred in both Finns and Ashkenazi Jews (Nat. Genet., 2017). Further, we went back to the populations that have strong founder event and found that they have a high prevalence of population-specific diseases. Notably, one of the populations has a high frequency of Junctional Herlitz Epidermolysis Bullosa disease, characterized by vesicobullous skin lesions, oral mucositis, congenital heart disease, and premature death. Subsequently, we performed exome sequencing and found a novel mutation in the LAMB3 gene of the patients, whereas the parents were heterozygous for this deletion. CRISPR/Cas9 mediated knockout of the above mutation exhibits the same phenotype in mouse (C57BL/6NJ) (unpublished data). Our continuing effort is to identify recessive mutations in the populations with strong founder event, and provide prenatal and premarital counseling, which would help eliminate the pathogenic mutation(s) from the population.

IISER
THIRUVANANTHAPURAM

DR TINA MUKHERJEE

INSTEM, Bengaluru

Sensory perception in defining immune potential: a role beyond its senses

Our past work has alluded to sensory control of immunity in Drosophila, where our findings elucidated the influence of environmental odor perception in the development of a competent repertoire of blood progenitor cells. The findings put forth a neuro/immune cross-talk in hematopoiesis. They revealed the impact of environmental odor detection and their sensing modules as determinants of defining the immune potential of the animal. Taking forward our observations, we have embarked on an exploration to address the influence of odor-based immune priming across systems. My talk will share some of our recent and unpublished findings on how odors influence mosquito immunity. Given that both Anopheles and Aedes are potent vectors for many parasitic and viral infections, the implications of odor sensing are central to their blood-feeding and vector potential. Our current findings reveal an interesting insight into the implications of sensing human volatiles on their internal physiology and unveil how odors might have led to the emergence of their vector competency. From flies to mosquitoes, using a model system has lent us an edge to uncover newer principles, and my talk will highlight the sensory routes underlying immune potential.

IISER THIRUVANANTHAPURAM

PROF UTPAL NATH

IISc Bengaluru

Shaping up a leaf – How genes control growth and geometry

How shape evolves during organ growth is an important question in developmental biology. We address this by analyzing the growth of plant leaves in the planar dimension. Leaves are initiated as mounds of cells (primordium) at the flank of the shoot apical meristem, a stem cell niche that generates all above-ground parts of a plant. At the inception, growth is uniform throughout the primordium. In certain species, such as Arabidopsis, growth stops towards the distal end as development progresses while the base continues to grow, thus creating a base-to-tip polar growth pattern. Analysis of leaf growth in 75 diverse plant species using the law of allometry revealed that, although leaves of some species grow from the base, others grow from the tip. In contrast, another group of leaves grows with no apparent polarity, generating a natural diversity in growth polarity. The plant-specific microRNA miR396 regulates this growth diversity.

Despite their anisometric growth as described above, how leaves retain their surface flatness is still an open question. Studies from several laboratories, including ours, have identified two groups of genes that control surface curvature: one group codes for miR319-regulated TEOSINTE BRANCHED1, CYCLOIDEA, PROLIFERATING CELL FACTORS (also called JAW-TCP) transcription factors that suppress marginal growth, while the other group encodes proteins involved in proteasome-mediated protein-degradation and suppress growth at the center. Mutations in either group result in the loss of leaf flatness. Genetic interaction studies reveal that these two genetic pathways function independently.

IISER
THIRUVANANTHAPURAM

PROF UTPAL NATH

IISc Bengaluru

Shaping up a leaf – How genes control growth and geometry Contd.

Leaves show extensive shape diversity and are broadly divided into two forms: simple leaves with intact lamina and compound leaves with lamina dissected into leaflets. The mechanistic basis of margin dissection and leaflet initiation has been inferred primarily by analyzing compound-leaf architecture, and thus, whether the intact lamina of simple leaves has the potential to initiate leaflets upon endogenous gene inactivation remains unclear. We have shown that the JAW-TCP transcription factors activate the class II KNOTTED1- LIKE (KNOX-II) genes, and the JAW-TCP and KNOX-II proteins together redundantly suppress leaflet initiation in simple leaves. Simultaneous downregulation of JAW-TCP and KNOX-II in Arabidopsis leads to the reactivation of the stemness genes KNOX-I and CUPSHAPED COTYLEDON (CUC). It triggers ectopic organogenesis, eventually converting the simple lamina to a super-compound form that appears to initiate leaflets indefinitely. Thus, a conserved developmental mechanism promotes simple leaf architecture in which JAW-TCP–KNOX-II forms a strong differentiation module that suppresses the KNOX-I-CUC network and leaflet initiation.

These findings help us understand how genes regulate biological shape. We are currently studying the regulation of leaf shape in other species to test whether the molecular mechanisms underlying organ geometry are evolutionarily conserved.

IISER
THIRUVANANTHAPURAM

DR VATSALA THIRUMALAI

NCBS, Bangalore

Developmental synaptic pruning in the olivo-cerebellar circuit sculpts predictive processing

Synaptic pruning is a dominant process of circuit assembly known to eliminate a large proportion of synapses formed during development. In humans, approximately 50% of all formed synapses are estimated to be eliminated in early childhood. Yet, very little is understood about how the drastic elimination of a large number of synapses affects circuit computation and behavior. Here, using the olivocerebellar system of larval zebrafish, we first establish the timelines of olivary climbing fiber to Purkinje neuron synaptic pruning. We then show that during this window, encoding of sensory-motor mismatches is improved, sensory representations are fine-tuned, and predictive signals are more robust. All of these lead to faster and better behavioral responses adaptable to current sensory input. Thus, developmental synaptic pruning makes circuits fit for complex computations like predictive processing.

IISER THIRUVANANTHAPURAM


FLASH
TALKS

1

Sachin Bhaskar
BEE Lab

Flowering in the dark: Influence of lunar phases on flowering patterns and plant-pollinator interactions of nocturnal flowers

The night shows remarkable physical environmental changes, compared to the day. Certain angiosperms show nocturnal flowering to combat water-stress, by reducing evapo-transpiration. Bat-pollinated flowers are specialised, pale, with a musty odour and copious nectar. These species show a big-bang strategy of flowering, where they flower for 4-6 weeks. Small frugivorous bats show increased foraging on new moon nights, and reduce their foraging on moonlit nights, thereby exhibiting light-avoidance behavior. Moth-pollinated flowers are often sweet-scented, with a long corolla tube with nectar. Nocturnal hawkmoths depend on visual and odour cues primarily to locate flowers at night, directing their dependence on light for foraging and thereby are expected to show peak foraging around relatively lit nights. This suggests a lunar-phase-specific foraging activity in the major nocturnal pollinators. However, we don't know if the flowering and pollinator activity of bat/moth-pollinated species is in synchrony. We hypothesised that bat-pollinated flowers would show peak flowering, reward levels, and receive higher pollinator visits around new moon nights; and the same with moth-pollinated flowers around full moon, to maximise the reproductive success of plants. We studied twelve nocturnal flower species to test our hypotheses. Here, we present the results of Pajanelia longifolia (bat-pollinated) and Tabernaemontana alternifolia (moth-pollinated). We estimated the flower abundance, quantified the reward levels (both nectar and pollen), and observed the flower-pollinator interactions every lunar phase of a lunar cycle. We find that bat and moth-pollinated species show increased flowering, and nectar levels on the nights of new moon and full moon respectively. This study presents evidence that the flowering patterns of nocturnal flowers are in synchrony with lunar phases (and foraging activity of pollinators).

IISER
THIRUVANANTHAPURAM

2

Anindita Rao
DREAM Lab

Unraveling the Hexamerin Code to Development and Nutritional Homeostasis in *Drosophila melanogaster*

Organisms rely on a variety of physiological and biochemical mechanisms to maintain nutrient homeostasis under fluctuating environmental conditions - a critical process for survival. At the heart of this adaptive machinery lies the adipose tissue, a dynamic hub that orchestrates the organism's response to stresses. We aimed to identify key regulatory factors that govern nutrient equilibrium within the fat body of Drosophila melanogaster using a targeted genetic screening approach.

Through this investigation, we highlight the role of a fascinating family of storage molecules - Hexamerins (Larval Serum Proteins in fruitflies), as important mediators of nutritional homeostasis. The Drosophila genome encodes two hexamerin genes, Lsp1 and Lsp2, which are predominantly expressed in the larval fat body. These proteins serve as amino acid reservoirs, playing a key role during metamorphosis to support the transition from larva to adult. While much of the scientific focus on hexamerins has revolved around their biochemical roles, their functional significance has remained an elusive puzzle—until now.

To address this gap, we knocked down larval hexamerin (LSP) expression, specifically in the fat tissue, and analysed its impact on development and metabolism. Contrary to what we anticipated, silencing LSP triggered unexpected growth surges accompanied by altered energy levels. Its downregulation activated the Target of Rapamycin (TOR) signaling, a crucial nutrient-responsive pathway, to fuel growth, even so under nutrient-limiting conditions. Intriguingly, LSP-deficient adults exhibited sexual dimorphism in fitness outcomes. We are currently teasing apart the stage-specific and sex-specific roles of these remarkable proteins in the maintenance of overall organismal fitness, whilst also exploring trade-offs that might accompany this metabolic rewiring.

In summary, our study shows the impact of hexamerin disruption, revealing a riddling interplay of resilience and adaptation in Drosophila, which shifts the balance toward unforeseen benefits. These findings provide novel insights into the regulatory mechanisms by which hexamerins contribute to nutrient homeostasis and organismal fitness, expanding our understanding of metabolic adaptation in response to environmental challenges.

IISER
THIRUVANANTHAPURAM

3

Maria Jacob
Genome Editing Lab

Uncovering the Role of QPCTL gene in Microtubule Cytoskeleton Regulation Using CRISPR-Cas9 Screening

Cell division, a tightly regulated process, involves microtubules forming the mitotic spindle to ensure accurate chromosome segregation, governed by the spindle assembly checkpoint (SAC). Microtubules play essential roles in diverse cellular processes and are important pharmacological targets for treating human disease. Dysregulated mitosis is a cancer hallmark, making it a therapeutic target. Microtubule-targeting agents (MTAs), like nocodazole, disrupt microtubule dynamics, causing mitotic arrest and cell death. However, certain genes confer resistance to MTA therapy when downregulated. To identify key regulators of this system, we conducted a CRISPR-Cas9 positive screen using nocodazole, a microtubule destabilizer, to select for genes involved in microtubule cytoskeleton regulation. Next-generation sequencing (NGS) coupled with MAGeCK analysis identified few sgRNAs conferring survival advantage under nocodazole treatment. Our study investigates the role of QPCTL, a gene identified via CRISPR-Cas9 screening, conferring nocodazole resistance. We observe that QPCTL knockout (KO) cells showed increased survival, faster wound closure, and bypassed nocodazole-induced G2/M arrest, confirmed by fluorescence-activated cell sorting (FACS). Reintroducing QPCTL cDNA reversed these effects, restoring G2/M arrest. Immunostaining results indicated that QPCTL KO cells had less prometaphase arrest, bypassing the cell cycle, possibly due to mitotic slippage or improved spindle assembly. The cold-stable assay showed better-assembled microtubules in QPCTL KO cells compared to wild-type (WT) cells. Additionally, MAD2L2, a SAC component and reported QPCTL interactor, showed increased levels in QPCTL KO cells in preliminary western blot analysis. This suggests that QPCTL KO may enhance microtubule assembly through MAD2L2 modulation. Further studies are required to elucidate the precise mechanism by which QPCTL KO confers resistance to nocodazole and improves microtubule dynamics, potentially employing therapeutic strategies against mitotic dysregulation in cancer.

IISER
THIRUVANANTHAPURAM

4

Sameer Joshi
Genome Stability Lab

Irc20 modulates LOH frequency and distribution in *Saccharomyces cerevisiae*

Loss of Heterozygosity (LOH) due to mitotic recombination is frequently associated with the development of various cancers (e.g. retinoblastoma). LOH also affects genetic diversity, especially in organisms where meiosis is infrequent. Irc20 is a putative helicase and E3 ubiquitin ligase involved in DNA double-strand break repair pathway. We analyzed genome-wide LOH events, gross chromosomal changes, small insertion-deletions and single nucleotide mutations in eleven S. cerevisiae mutation accumulation lines of irc20Δ, which underwent 50 mitotic bottlenecks. LOH enhancement in irc20Δ was small (1.6 fold) but statistically significant as compared to the wild type. Short (≤ 1 kb) and long (> 10 kb) LOH tracts were significantly enhanced in irc20Δ. Both interstitial and terminal LOH events were also significantly enhanced in irc20Δ compared to the wild type. LOH events in irc20Δ were more telomere proximal and away from centromeres compared to the wild type. Gross chromosomal changes, single nucleotide mutations and in-dels were comparable between irc20Δ and wild type. Even though Irc20 is expressed in meiosis, locus-based and genome-wide analysis of meiotic recombination showed that meiotic crossover frequencies are not altered in irc20Δ. These results suggest that Irc20 primarily regulates mitotic recombination and does not affect meiotic crossovers. Our results suggest that the IRC20 gene is important for regulating LOH frequency and distribution.

IISER
THIRUVANANTHAPURAM

5

Swetha Gopalakrishnan
Chronobiology Lab

Probing the role of CCHamide-1 in the interplay between circadian clock and metabolism in *Drosophila melanogaster*

Circadian clocks are molecular machines that help most organisms maintain 24-hour daily rhythms and regulate a myriad of physiological processes, including metabolism and sleep-wake cycles. In the fruit fly Drosophila melanogaster, about 150 clock neurons in the brain constitute the central clock. To maintain homeostasis, the central circadian clock communicates with the many peripheral clocks in different tissues. Our study focuses on a relatively less studied neuropeptide, CCHamide-1 (CCHa1), expressed in a subset of the clock neurons in the Drosophila brain and recently shown to affect the activity-rest rhythms in Drosophila. CCHa1 is also expressed abundantly in the mid-gut. In this study, we aimed to investigate the role of CCHa1 on sleep and metabolism in the fruit fly and how CCHa1 could be involved in the bidirectional interaction between the central and peripheral clocks. We assayed sleep under ad libitum fed and starved conditions using CCHa1 mutant males and found that the mutants showed decreased sleep when fed ad libitum and increased sleep loss under starvation compared to the controls. The CCHa1 mutants also exhibited a delay in pupariation and fared better under starvation stress. Upon tissue-specific downregulation of CCHa1 in central circadian clock neurons and in the mid-gut, we observed that the CCHa1 expressed in the central clock affects both sleep and survival under starvation, and CCHa1 expressed in the gut majorly affects the survival of the flies under starvation and does not impact sleep. These results suggest a possible role for CCHa1 in relaying information about the nutrient status between the brain and gut in Drosophila, thereby affecting sleep, development, and metabolism. We will be doing further studies to understand the molecular underpinnings.

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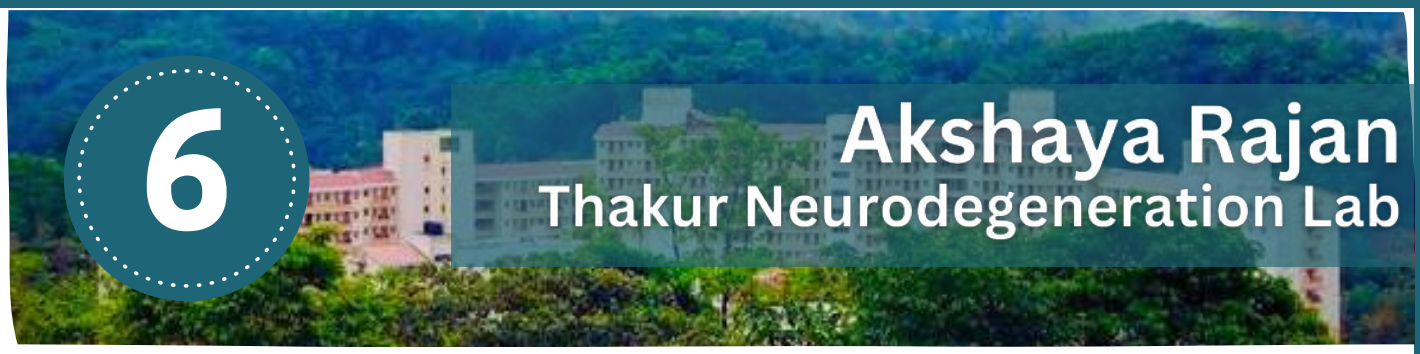

6

Akshaya Rajan
Thakur Neurodegeneration Lab

Influence of glycation on α-synuclein structure and Parkinson's disease pathology in Vivo

Parkinson's disease (PD) is a common neurodegenerative disorder that is prevalent in millions worldwide. A main factor that drives the disease pathogenesis is aberrant misfolding and aggregation of Alpha-synuclein (α-Syn) protein. Several factors, including post-translational modifications (PTMs), influence its aggregation propensity and pathogenicity. Glycation is a non-enzymatic PTM elevated with aging and in hyperglycemic condition, both of which are risk factors for PD. In the current study, we aim to investigate the structural alteration induced on α-Syn upon glycation. We also scored for its effect on the progression of PD and its pathological outcomes in-vivo.

Glycation of purified human α-Syn using Methylglyoxal causes distinct deviation from its ability to form beta-sheet-rich aggregates in-vitro. These heterogeneously-sized, non-fibrillar assemblies were then injected into the substantia nigra region of the C57Bl/6 mouse brain. Earlier deterioration of neuromuscular grip strength and anxiety behavior was observed in these mice compared to the control group. The former also exhibited a similar extent of TH cell loss and neuroinflammation in SN compared to mice that received non-glycated fibrils. The glycated assemblies were potent to cause enhanced inflammation in the striatal dopaminergic nerve endings, which might also fasten these neurons towards degeneration.

Thus, glycation promotes the toxicity of α-Syn towards dopaminergic neurodegeneration with earlier risk for motor and non-motor symptoms. Glycation of α-Syn due to hyperglycemia might be a reason for channeling the increased risk of PD in the diabetic population. Thus, therapeutics that can target glycation can be of high value as a cure for PD.

IISER
THIRUVANANTHAPURAM

7

Yash Misra
NSMB Lab

Decoding transcription regulation by *Mycobacterium smegmatis* Gre factor homologue

Rise in Anti-Microbial Resistance (AMR) of Mycobacterium tuberculosis (Mtb), the causative agent of TB against first-line drugs, Rifampicin and Isoniazid, has led to complications in tackling AMR Mtb. Rifampicin targets RNA polymerase (RNAP), making it a highly druggable target. Gre factors are a group of regulatory proteins that bind to the secondary channel of RNAP to promote the rescue and reactivation of the stalled elongation complex by enhancing the RNAP transcript cleavage activity. Mycobacterium smegmatis (Ms) Gre factor homologue (Gfh) MSMEG_6292 (MsGfh) competes with its Gre factor, to bind to the RNAP secondary channel. However, despite having a high sequence identity with mycobacterial Gre factors (MtbGre/MsGre), MsGfh does not show transcript cleavage activity. We have expressed, purified, and crystallised MsGfh and its selenomethionine(SeMet) derivative MsGfhSe. MsGfhSe crystals belonging to the P3221 space group with a = 82.9 Å, b = 82.9 Å, c = 107.1 Å and gamma = 120 degrees, Z = 12 could diffract to better than 2.9 Å resolution. The structure was solved by ab initio SAD phasing using a SeMet Single wavelength Anomalous Data (SAD) collected at the ESRF MASSIF-I Synchrotron beamline. MsGfh does not inhibit transcription, although has structural similarity to TthGfh, an RNAP secondary channel inhibitor. MtbGfh (Rv3788) on the other hand was shown to inhibit RNAP. The talk will focus on structural and functional characterization of MsGfh using various biophysical and biochemical techniques such as CD, DLS/MALS, and activity assays, to understand the significance of Gre factors and their connection to AMR.

IISER
THIRUVANANTHAPURAM

Unlocking enhanced haploid induction: Epigenetic control of uniparental genome elimination

Haploid production in plants is a million-dollar industry with significant applications in plant genetic research and crop breeding. Uniparental genome elimination (UGE), a highly sought-after method to produce haploid plants, is an artificially induced phenomenon where one parent's genome is selectively eliminated during early embryogenesis, resulting in a haploid plant. Central to UGE-based haploid production methods are genetically engineered plants termed haploid inducers. Haploid inducer(HI) plants manipulated at the centromeres, when crossed with wild-type (W.T.) plants, trigger UGE by eliminating their gametic chromosome set after fertilization. In the model plant Arabidopsis thaliana, the HI plant possesses an engineered chimeric variant of CENH3(centromeric histone3 protein) known as GFP-tail swap, yielding 30% haploid progeny, 30% hybrid diploids, and 40% aneuploid progeny when crossed with W.T plants.

Recent studies have shown that the genotype of the W.T. parent also affects UGE efficiency. Notably, crossing a HI plant(GFP-tail swap) with a vim1 (variant in methylation) null mutant plant results in ~70% haploid progeny. Here we discuss, 1. How epigenetic factors, particularly DNA methylation status at the centromeres, play a crucial role in haploid induction 2. Hypomethylated centromeres as a quantitative trait enhancing UGE, and 3. The paradoxical effect of DNA hypomethylation on haploid inducer centromeres vs wild-type centromeres during the genome elimination process. Understanding these molecular mechanisms and identifying key factors that improve UGE efficiency could revolutionize plant breeding, offering a powerful tool for producing haploids across a variety of commercial crops.

IISER
THIRUVANANTHAPURAM

9

Nikhil Dev
Laboratory of Immune Cell Biology

E3 ligase substrates and where to find them

Abnormal protein regulation drives many diseases, making targeted protein degradation a promising therapeutic strategy. The ubiquitin-proteasome system, one of the cell's intrinsic pathways for protein quality control, relies on E3 ubiquitin ligases for substrate specificity. Here, I focus on RFFL, an endosome-associated RING E3 ligase involved in mitochondrial homeostasis and the clearance of misfolded cystic fibrosis transmembrane conductance regulator proteins. Using label-free quantitative mass spectrometry-based proteomics for interactome and differential expression analyses, I systematically investigated and identified putative substrates of RFFL. For more confident identifications, we performed these analyses on three cell lines we generated: an RFFL knockout cell line generated using CRISPR/Cas9, another cell line rescuing RFFL expression when complemented with stably expressing RFFL cDNA and wild-type cells. Orthogonal validation confirmed two substrates, including JMJD6, an enzyme linked to Alzheimer's disease, which RFFL ubiquitinates and degrades via the proteasome. Additionally, our investigation revealed a hitherto unknown role for RFFL in lipid metabolism and observed tissue-specific proteoforms of RFFL in human brain tissue compared to A549 lung carcinoma cells. In brief, the study provides the first comprehensive analysis of RFFL substrates, offering insights into its diverse biological roles and therapeutic potential. In this talk, I will be discussing the methodology used here and how it can be applied to other E3 ligases to identify their potential substrates.

IISER
THIRUVANANTHAPURAM

Oxygen sensing pathway in the maintenance of neural stem cell pool

Neurogenesis is a well-orchestrated process by which the cells of the central nervous system are generated. Postnatally, there are two major neurogenic niches in the mammalian brain – the Subgranular Zone (SGZ) and the Subventricular Zone (SVZ), both considered to be hypoxic. Disruption of the hypoxia pathway through loss-of-function studies has previously been shown to result in defective neural stem cell (NSC) pool maintenance and also defective neurogenesis. HIF-1α is one of the primary mediators of hypoxia signaling, whose activity is tightly regulated by Prolyl hydroxylase domain (PHD) enzymes, integral players in the oxygen sensing pathway. We sought to examine the effect of HIF-1α stabilization by disrupting the oxygen-sensing pathway. Long-term deletion of the prolyl hydroxylase domain (PHD) proteins 1 and 3 (Phd1-/-,3-/-; dKO) led to enhanced activation of hypoxic signaling. Against our expectations, we observed a substantial loss of proliferative activity of cells in the SGZ. The NSC population displayed dramatic changes whereby the total pool size was reduced. In addition, dKO SOX2+GFAP+ adult NSCs displayed pronounced alterations in their morphology with a shortened arbor-like appearance of radially oriented fibers. Concomitantly, we observed a marked decrease in proliferative neural progenitors, which was reflected in a decrease in the number of DCX+ newborn neurons. Contrarily, there was a significant increase in the number of astrocytes, indicating a predisposition of the NSC population towards astroglial differentiation at the expense of neurogenesis. Overall, we report the involvement of the oxygen-sensing pathway in the stem cell fate decisions of the adult NSC population.

IISER
THIRUVANANTHAPURAM

11

Ushma Anand
Cytoskeleton and Cell Division Lab

Plk4-dependent degradation of STIL-SAS6 axis by FBXW7 controls centriole duplication

Centriole amplification and resulting supernumerary centrosomes are associated with abnormal cell division and cancer. Polo-like kinase 4 (Plk4), SCL/TAL1 interrupting locus (STIL), Spindle assembly abnormal protein 6 homolog (SAS6), and F-box and WD repeat domain (FBXW) containing E3 ubiquitin ligases are implicated in centriole amplification. However, the underlying mechanism, particularly cross-talk between F-box ligases and the Plk4-STIL-SAS6 axis, remains elusive. Here, we show that depletion of FBXW7 induces over-production of centrioles, due to abnormal stabilization of STIL and SAS6 at the centrosomes in human cells. Multiple mother-daughter centriole pairs are evident in FBXW7-depleted cells, suggesting an aggravated centriole reproduction cycle. Over-expressed FBXW7 inhibits centriole amplification induced by ectopic STIL expression. FBXW7 interacts with STIL and induces its ubiquitin-mediated degradation. We further reveal that Plk4 inhibition abolishes FBXW7-mediated degradation of STIL and SAS6 and centriole copy number control. Mutations in Plk4-phosphorylating sites in a conserved motif in the SAS6-interacting STAN domain of STIL abrogates FBXW7-mediated STIL degradation, suggesting its role as a phosphodegron for the ligase. In summary, the results demonstrate that FBXW7 controls aberrant centriole duplication by degrading the centriole assembly-competent STIL-SAS6 axis in a Plk4-dependent manner.

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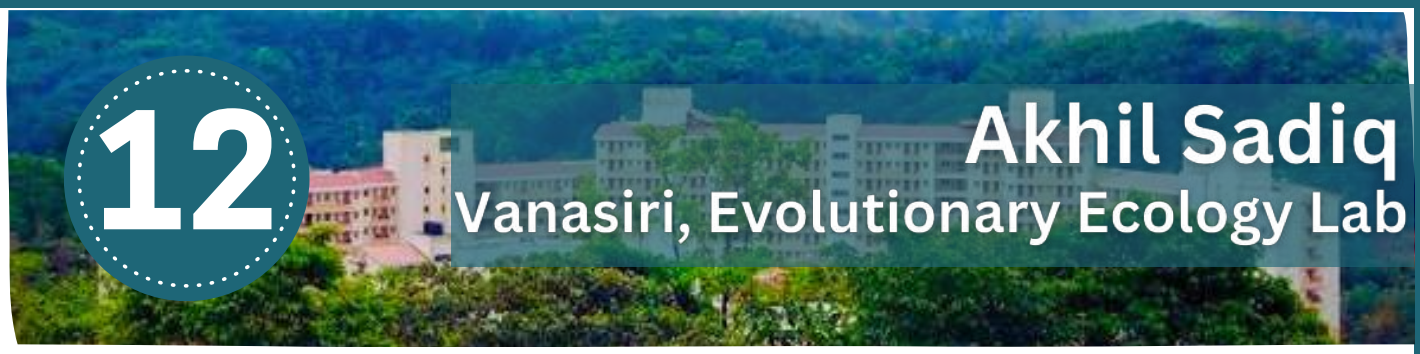


12

Akhil Sadiq
Vanasiri, Evolutionary Ecology Lab

Decoupling detection and recognition in animal camouflage.

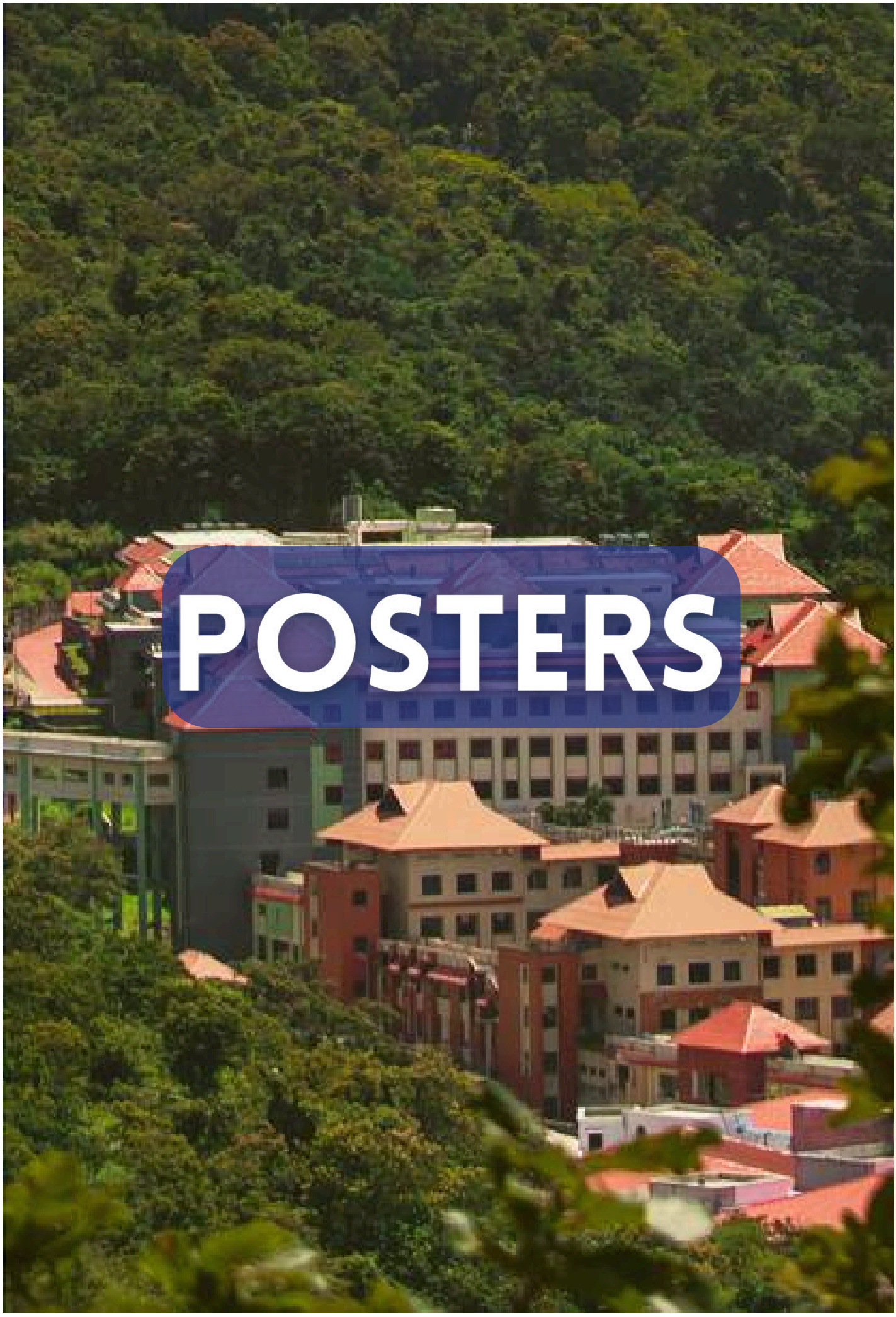
Camouflage involves diverse strategies that aid animals in obscuring their presence to potential threats. These strategies inhibit detection (locating the animal) and, if detected, prevent recognition (determining the animal's identity) of the bearer. Disruptive colouration, characterised by high-contrast markings that perceptually break up the animal's shape, is one of the most widespread camouflage strategies. While numerous studies have investigated how disruptive colouration impedes detection, its effect on recognition remains poorly understood, with many studies implicitly assuming that patterns hindering detection also inhibit recognition. Here, using human volunteers as 'predators' of virtual targets, we tested the effectiveness of disruptive colouration on detection and recognition. We demonstrate that detection and recognition are not fully coupled. Specifically, we found that patterns effective at hindering detection did not necessarily impede recognition, and conversely, patterns that inhibited recognition were not always effective at preventing detection. Furthermore, we show that the location of the high-contrast markings on the animal's outline influenced recognition but not detection. Our study demonstrates that obscuring detection and recognition are independent strategies. Our results also underscore the importance of recognition in studies of animal camouflage.

IISER
THIRUVANANTHAPURAM

Self-assembling protein nanoparticle vaccine elicits potent humoral responses against three emerging coronaviruses.

Emerging and re-emerging infectious diseases ranked as one of the leading causes of mortality pose a significant threat to global health. An undeniable example is the coronavirus outbreaks, SARS-CoV-1 in 2003, followed by MERS-CoV in 2012, and SARS-CoV-2 in 2019. Currently, there are no approved vaccines for SARS-CoV-1 and MERS-CoV. Although vaccines against SARS-CoV-2 are available, the continuous circulation of the virus has resulted in the emergence of variants posing challenges to long-term immunity. Nanoparticle-based vaccines are an emerging platform for vaccine delivery reported to show enhanced immunogenicity and durability of immune responses. Lumazine synthase (LS), a bacterial protein, naturally forms self-assembling nanoparticle cages displaying sixty symmetric projections. This property of multivalent projections allows the presentation of high local density of antigenic epitopes. Taking advantage of its property, the LS nanoparticle was extended with domain B of Protein-A (pA-LS) which allows the binding of spike S1 protein of coronaviruses tagged with human IgG-Fc tag (S1-Fc). First, pA-LS was conjugated with spike S1-Fc protein of SARS-CoV-2 (mono-conjugation) for studying its immunogenicity. We observed that the pA-LS-S1-Fc complex was able to elicit humoral response and was able to neutralize the infection of pseudoviruses not only of SARS CoV-2 wild type (WT) but also of the Delta and Omicron variants. Further, live virus challenge study in mice immunized with the pA-LS-S1-Fc complex showed that it conferred protection, indicated by maintained body mass, reduced viral load and significantly less lung infectivity against Wuhan, Delta, and Omicron strains. These results show the advantage of the LS nanoparticle in orderly projecting the antigenic epitopes resulting in high avidity interactions, followed by potent immune response. Further, we expanded the applicability by conjugating the pA-LS nanoparticle with spike S1-Fc proteins of two coronaviruses- SARS-1 and MERS-CoV (multi-conjugation). Binding and co-localization assays showed the decoration of both the spike proteins. The immunization of this multi-conjugated complex in mice showed that the mice sera was able to recognize the confirmational and linear epitopes of the corresponding full-length spike protein as well as significantly neutralize the pseudovirus infection of both SARS-1 and MERS-CoV. These results demonstrate the potential of using a single nanoparticle vaccine against two different coronaviruses which broadens the protective coverage against multiple pathogens through a single vaccine.

IISER
THIRUVANANTHAPURAM


POSTERS

1

Aakash Kumar Pathak
BEE Lab

Genomic interrogation of morphological plurality reveals a species complex in the social spider *Stegodyphus sarasinorum*

Sociality in spiders has evolved ca. 23 times convergently, independently thrice in the genus *Stegodyphus*. The permanent non-territorial social spider, S. sarasinorum, is distributed across the Indian subcontinent. This species exhibits limited dispersal, high female-biased sex ratios, reproductive skew, and high inbreeding, providing an excellent model for exploring how geographic and ecological factors shape population structure and genetic diversity. These traits are often associated with reduced effective population sizes and are hypothesised to be an evolutionary dead-end. However, the Indian subcontinent's diverse geographic features, including mountain ranges, river systems, plateaus, and climatic gradients, create a complex landscape that can restrict gene flow and shape genetic differentiation. These barriers, limited dispersal, isolation by distance, and inbreeding, likely contribute to genetic differentiation and clustering. These factors show remarkable examples of genetic differentiation, such as laughing thrushes and shortwings of the Western Ghats, vine snakes, the Bengal Tiger, centipede Digitipes, etc.. Propitiously, we hypothesised that limited dispersal ranges, combined with inbreeding and isolation, can lead to reproductive isolation. To test this, we targeted ultraconserved elements from de novo low-coverage genomes from seven samples of S. sarasinorum across its range. We found evidence of phylogenetic relationships concordant with the ecological and biogeographic regions. We are performing further analysis on species complex with morphological comparisons. The results will offer valuable phylogeographic insights into how environmental and physical barriers shape the evolution of S. sarasinorum, advancing our understanding of evolutionary processes in social species.

IISER
THIRUVANANTHAPURAM

Genetic and Morphological diversity of native honey bee; *Apis cerana* in India

Honeybees are important pollinators across different habitats globally. Their declining numbers are a cause of increasing global concern, making studies on their population level critical. This is especially true for the tropical species of honeybees, about which little is known. One among the native is Apis cerana which is an important pollinator that is also widely distributed throught India. However, despite their value in providing ecosystem services to wild and crop plants, their ecology and population structures remain largely understudied.

This study aims to investigate the population structure using morphological variation and genetic diversity of A. cerana populations across different geographical regions of India using morphological traits and genome-wide single nucleotide polymorphism (SNP) markers. We measured 24 traits from 235 individuals from all over the mainland India and did multivariate analysis for understanding the morphological variation. Further, we employed ddRAD sequencing on 59 samples and bioinformatics pipelines to analyze genetic variation and populations across the distribution.

Our findings reveal morphologically as well as genetically distinct population clusters corresponding to geographic gradients. Population structure analysis using NGSadmix revealed the presence of three distinct genetic clusters, suggesting significant population differentiation across sampled regions. Additionally, our results provide insights into the evolutionary processes shaping A. cerana populations in India. These findings have significant implications for the conservation and sustainable management of A. cerana.

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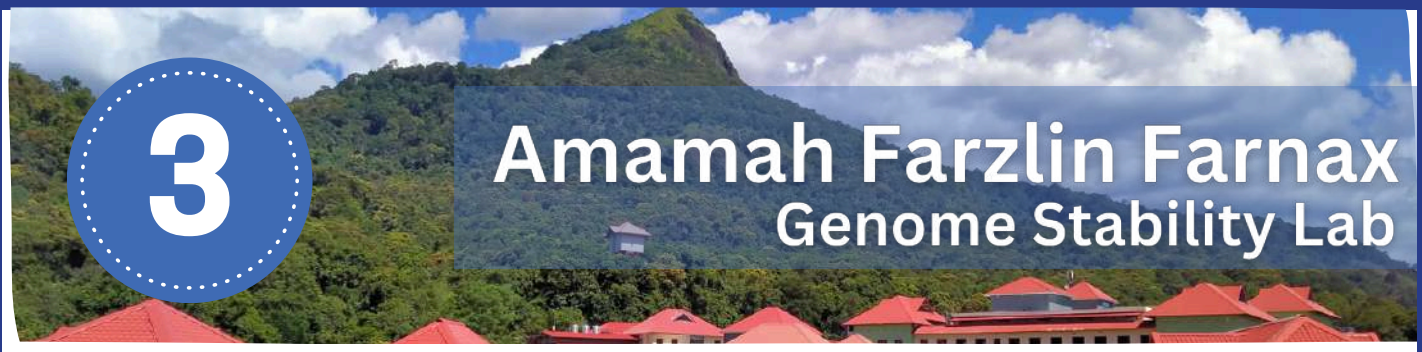

3

Amamah Farzlin Farnax
Genome Stability Lab

Association of the Class II crossover protein (Mms4) with meiotic chromosomes in the baker's yeast.

The accurate segregation of homologous chromosomes at Meiosis I is facilitated by crossovers. Meiotic crossovers are generated from the repair of programmed DNA double-strand breaks (DSBs). Most of the meiotic crossovers in the baker's yeast Saccharomyces cerevisiae and mammals are made through the mismatch-repair related protein complexes Msh4-Msh5 and Mlh1-Mlh3 (Class I pathway). The Mms4-Mus81 (Class II) pathway generates a minor set of crossovers. We investigated genome-wide localization of the Mms4 protein during meiosis to understand how the choice to repair meiotic DSBs through Class I or Class II crossover pathways is made. To determine Mms4 localization, the Mms4 gene was tagged at the C terminus with a 9 Myc tag. Mms4 binding was analyzed by ChIP-qPCR and ChIP-seq in wild type and in mutants - spo11Δ and red1Δ, where DSB formation and the meiotic chromosome axes are affected. Previous published work from our lab showed that Msh5 binding at DSB hot spot sites is markedly reduced in both spo11Δ and red1Δ mutants. ChIP-Seq analysis in meiotic time courses showed Mms4 binding to DSB hotspots, axes, and centromeres on all chromosomes similar to the Class I crossover protein -Msh5. However, Mms4 showed preferential binding to weak DSB hotspots compared to the Msh5 protein which is associated with strong DSB hotspots. Mms4 peak width at DSB hotspots was significantly smaller (mean : 0.9kb, median : 0.6 kb) than Msh5 (mean : 1.2 kb, median : 0.8kb) suggesting differences in their mode of association on meiotic chromosomes. Compared to the wild type, Mms4 binding is significantly in red1Δ but maintained in spo11Δ. This implies axis proteins may be directly or indirectly involved in the localization of Mms4 to the meiotic chromosomes. Consistent with this, we observed direct protein interactions between Mms4 and Red1. Previous published data from our lab showed that Msh5 binding in the hybrid strain S288C-sp/YJM789 showed decreased enrichment at high heterozygous regions as compared to the homozygous SK1 strain. No such difference was seen for Mms4 binding which implies heterozygosity does not have an effect on its localization. Overall, these results suggest differences in the localization of Mms4 and Msh5 proteins.

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4

Ananda Krishnan M
Evo Sys Bio Lab

Systematic Identification of Antagonyms and their Bifunctional variants in Metabolism

A pair of enzymes where one enzyme catalyses the forward reaction and the other enzyme catalyses the reverse reaction are referred to as Antagozymes. Bifunctional variants of Antagozymes where a single enzyme catalyses both the forward and reverse reaction using two different catalytic sites present in it, are called Antagonistic Bifunctional Enzymes. So far a systematic method to profile such enzymes are lacking, making it difficult to estimate their prevalence in nature. In this study we developed a constraint-based method to identify all the Antagozymes in metabolism, and have discovered 42 Antagozymes. Using these identified pairs as basis we searched the genomic database to identify Antagonistic Bifunctional Enzymes, and have discovered a wide variety of them in a diverse set of organisms. We have proposed several utilities for these co functional antagonistic enzyme pairs. Knowledge of Antagozymes and their bifunctional variants can further our understanding of metabolism and can be useful for synthetic biology applications.

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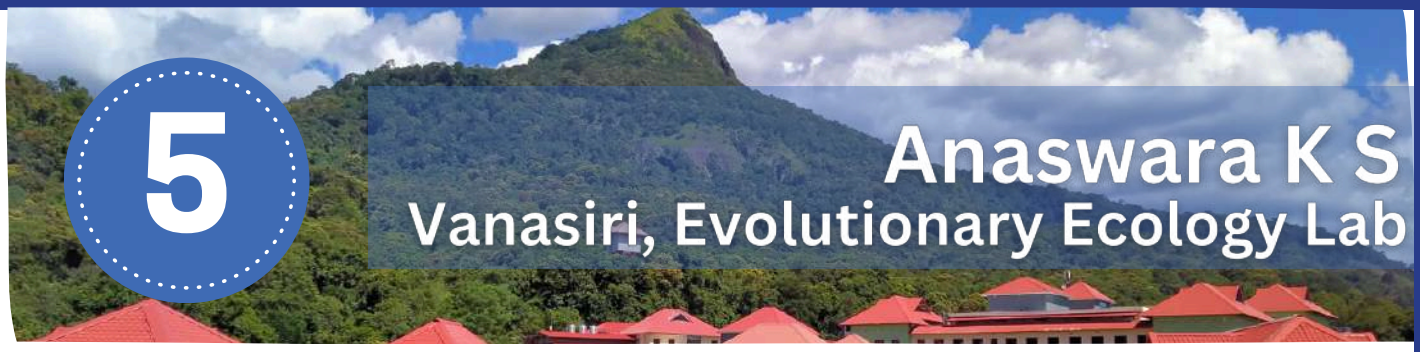

5

Anaswara K S
Vanasiri, Evolutionary Ecology Lab

Testing the preference-performance hypothesis in butterflies

In herbivorous insects, the choice of ovipositing substrate by females significantly impacts the fitness of offsprings, as newly hatched larvae are relatively immobile and thus rely heavily on the maternal selection of host plants. The 'preference–performance hypothesis' predicts that females prefer to oviposit on the host plant where larval survival is highest. We tested the preference–performance hypothesis in two populations of a polyphagous butterfly species, Acraea terpsicore, across six reported host plant species. The Trivandrum population of A. terpsicore showed highest oviposition preference and their larvae performed best on the same host plant, Passiflora foetida. For the Tiruppur population, the oviposition preference and larval performance were highest on Turnera ulmifolia.

The preference–performance hypothesis has been applied widely to include not only host plant species but also to different parts of the same host plant, such as flowers and leaves. A previous study (Sahoo & Kodandaramaiah 2018) showed that larval survival of A. terpsicore was higher when flowers were provided alongside leaves. However, it is unclear if females prefer plants with flowers while oviposition. We tested if oviposition preference and larval performance are highest when flowers are presented alongside leaves. Experiments were done with the Tiruppur population of A. terpsicore and two plants - T. subulata and T. ulmifolia. Surprisingly, in contrast to Sahoo and Kodandaramaiah (2018), larvae performed better when flowers were absent. In summary, my experiments support the preference-performance hypothesis in Acraea terpsicore. However, populations of the species appear to have diverged in their host use.

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6

Anjitha Kotharambath
NSMB Lab

Targeting the *Mycobacterium tuberculosis* evolvability factor Mfd

Mycobacterium tuberculosis (Mtb) is one of the most successful pathogens that can adapt and survive within host intracellular microenvironments even when continuously exposed to many DNA damaging agents. Mutation Frequency Decline (Mfd), the bacterial transcription-coupled repair factor, plays a critical role in nucleotide excision repair. In addition to its role in DNA damage repair, there are recent reports of Mfd's role in prokaryotic virulence, and survival by promoting mutations. This has led to Mfd being called as a "proevolutionary factor" or "evolvability factor". Bacterial evolution drives Antimicrobial Resistance (AMR) development through chromosomal mutations. This necessitates the development of novel drugs that can effectively diminish the crisis. In this context, targeting the evolvability factor Mfd represents a promising target for the development of innovative antimicrobial drug.

We have solved the crystal structures of MtbMfd and Mycobacterium smegmatis Mfd (MsMfd) (PDB: 6ACA, 6AC6) and nucleotide bound MsMfd (PDB 6ACX). Using Structure-Based Drug Discovery tools we are targeting an inhibitor for MtbMfd. Molecular docking studies using a library of small molecules targeting MtbMfd, showed several promising hits. Out these hits, Compound5 emerged as the positive candidate in in vitro screening. In vitro binding studies, including Isothermal Titration Calorimetry and Intrinsic Tryptophan Fluorescence confirmed the interaction between MtbMfd and Compound5, providing key thermodynamic parameters like dissociation constant. We have crystals of MtbMfd in complex with Compound5 complex. The in vitro interaction studies indicate that Compound5 functions as a weak inhibitor of MtbMfd. However, its structural framework will provide a foundation for further modifications to improve binding affinity and inhibitory potency.

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7

Anu P V
Stem Cell Biology Lab

Unraveling the effect of maternal diabetes on murine hematopoietic emergence

Hematopoiesis is an intricate process by which diverse blood cells are formed, ensuring a continuous supply to meet the body's pathophysiological requirements. Formation of these definitive hematopoietic stem cells (HSCs) occurs during early embryonic development within the aorta-gonad-mesonephros (AGM) region. A subset of endothelial cells that line the blood vessels undergo endothelial-to-hematopoietic transition (EHT), giving rise to intra-aortic hematopoietic clusters, which contribute to hematopoietic stem cells and progenitor cells. This complex process is orchestrated by an interplay of signaling pathways, transcription factors, and interactions with surrounding tissues. Recent studies have highlighted the role of metabolism in regulating hematopoiesis. HSCs that reside in the bone marrow primarily rely on glycolysis for energy production, and a metabolic shift determines their stem cell fate. The role of metabolic pathways in the early emergence of the hematopoietic system in mammalian embryos had not been previously explored. Our recent research has demonstrated that a glycolytic state of the aortic endothelium is essential for the EHT process (Anu PV et al. Sci. Adv. 2024). This suggests that metabolic regulation plays a key role in the earliest stages of HSC formation. The present study extends these findings to understand if maternal metabolic aberrations during the gestation period impact hematopoietic emergence during development. Here, we show that maternal hyperglycemia increases hematopoietic emergence with the formation of functionally impaired HSCs. These findings further emphasize the impact of glucose metabolism on HSC development in the foetus. Future studies include exploring the long-term effects of gestational diabetes on adult hematopoiesis.

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8

Anuraag Nallan Chakravarthi
Mutations Lab

Modulation of gene expression by replication-transcription collisions

Replication-transcription collision occurs when the replication fork collides with the transcription machinery as they traverse the DNA template in the same direction on the leading strand (co-directional) or opposite direction on the lagging strand (head-on). Most studies focus on the aftereffects of collisions on replication, while very few studies suggest the possible effects of collisions on gene expression. Some of the known effects include RNA polymerase dislodgement (Sarah French, 1992), loss of gene expression by mutagenesis in the promoter (Sankar et al, 2016), and possibly premature transcription termination (Rocha EP and Danchin. A, 2003). It has been proposed that orientation-specific effects on gene expression could drive the gene-strand bias of operons in prokaryotes (Price et al, 2008). Further transcription-translation coupling has also been proposed to have negating effects on collisions (Dutta. D et al, 2011).

In order to systematically study the effects of collisions on gene expression, a single-cell gfp reporter system was developed, where the reporter is chromosomally inserted in either the co-directional or head-on orientation in B. subtilis, keeping the genomic loci constant in both conditions. We observed an orientation-specific variation in gene expression levels at varying degrees of transcriptional and translational strengths, implicating the influence of collisions on gene expression. We also found with increased translational strength, head-on gene expression is promoted, whereas an increased transcriptional strength is detrimental to head-on gene expression. In summary, our results highlight the impact of collisions on gene expression in an orientation-specific manner.

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9

Arnav Lakhdive
NSMB Lab

Putative Inhibitors for *M. smegmatis* Mfd

MFD protein in Mycobacterium and other prokaryotes, is a transcription coupled repair protein, involved in rescuing backtracked or stalled RNA polymerase. It is implicated as a 'evolvability factor' due to an increase in mutations and greater antibiotic resistance. We use computational methods to find chemically viable inhibitors that might hinder the functioning of Mfd. We have found 3 ligand candidates using HADDOCK and AutoDock Vina. We have also conducted preliminary MD simulations for msMFD

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10

Ashvitha Balaji
Chronobiology Lab

The molecular circadian clock and light input pathway evolve in the *Drosophila melanogaster* populations selected for the timing of adult emergence

Circadian clocks, crucial intrinsic timekeeping systems, provide organisms with significant adaptive advantages . However, the empirical evidence for the evolutionary mechanisms shaping precise circadian clocks over millions of years remains limited, necessitating the need for further studies. Our present study focuses on the Drosophila melanogaster populations that have evolved with a precise circadian clock as a correlated response to selection for adult emergence in a narrow window of time over 350 generations. The results of our study showed that flies from populations selected for the timing of adult emergence sleep more and possess a faster-running circadian clock than those from control populations. These flies from the selected population exhibited higher sleep under a reduced light intensity of 1 Lux in a 12h light: 12h dark cycle. Furthermore, a significantly higher percentage of these flies exhibited free-running period rather than arrhythmicity compared to the control flies under constant light 1 Lux. Moreover, the larvae from selected populations exhibited an increased preference towards darkness than light. We examined the transcript oscillation of the circadian photoreceptor cryptochrome (cry), along with the core clock genes period (per) and timeless (tim)in adult flies to explore the molecular basis of the evolved precise circadian clocks and to determine whether selection influences the circadian light input pathway. Flies from the selected population exhibited a phase advance in the transcript oscillation of per, tim and cry, indicating that the molecular circadian clock and its light input pathway evolve as a correlated response to the selection for the timing of adult emergence in Drosophila melanogaster populations.

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THIRUVANANTHAPURAM

Micro-managing the mind: Decoding the role of miR-986 in the fly brain

MicroRNAs (miRNAs) constitute a class of small, non-coding RNA molecules that post-transcriptionally regulate the expression of their target genes. miRNAs act akin to a thermostat and help buffer large-scale changes in gene expression, thereby limiting inadvertent effects on various biological functions. The capacity of miRNAs to simultaneously regulate multiple targets makes them essential modulators of various physiological processes, including cellular differentiation, development, and metabolic regulation. Despite the significant implications for microRNAs in metabolic regulation and development, the role of brain-derived endogenous microRNAs involved in regulating lifespan and metabolic homeostasis has yet to be fully deciphered. To fill this lacuna, a functional screen was performed, wherein 30 microRNAs were downregulated in adult Drosophila neurons, from which miR-986 emerged as a physiologically relevant microRNA. The functional significance of miR-986 was elucidated by examining its influence on critical metabolic parameters, its involvement under differing nutrient conditions, locomotion, and aging, thereby shedding light on the underlying mechanisms through which miR-986 modulates these vital processes. Our results reveal that the knockdown of miR-986 confers the flies with enhanced resistance to starvation alongside significant changes in triglyceride homeostasis and feeding patterns, collectively underscoring its pivotal role in maintaining a metabolic equilibrium. The miRNA also shows a sexually dimorphic phenotype under low nutrient conditions and has a significant role to play in the aging process. The elucidation of the targets of miR-986 will further provide insights into the organismal response to nutrient deprivation and other metabolic stresses.

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Evolution of carbon source preference in *Bacillus*

When multiple carbon sources are available in a growth environment, bacteria use their preferred carbon source first, followed by consumption of other non-preferred sugars. While glucose is the preferred carbon source in many bacterial species, there are enough examples of other preferred carbon sources. Decades of research have given us insights into the molecular basis of this preference, which is captured in the umbrella term Carbon catabolite repression. We are trying to understand how carbon source preference evolves and how quickly the preference changes with changes in the environment. We are also interested in the molecular mechanism behind such preference changes. The Bacillus phylum is composed of organisms thriving in diverse environmental conditions and presents a valuable model system to study the evolution of carbon source preference. In this poster, I have given a brief background of the field, discussed the methods we have chosen to address this goal, and finally present the results we have obtained.

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THIRUVANANTHAPURAM

13

Bhanu Bhakta Sharma
Vanisiri, Evolutionary Ecology Lab

Can butterflies use visual memory to improve pupal camouflage?

Pupal color plasticity is widespread in butterflies. In many species, pupal color varies from green to brown depending on the substrate where the larvae pupate. Larvae on green substrates, such as leaves, typically develop into greener pupae, whereas those on non-leaf substrates, such as twigs or bark, become brown pupae. It is hypothesized that matching the substrate color helps pupae camouflage against visually oriented predators. Larvae of butterfly species, including Eurema blanda, generally pupate at night when substrate color cues are minimal. Despite the limited visual cues at night, the resulting pupal color often matches the substrate. These observations suggest that wandering larvae may retain the memory of visual cues of the substrate observed during the day and use this memory to regulate the pupal coloration at night. To test this hypothesis, wandering larvae of E. blanda were briefly exposed to green or brown substrates under illuminated conditions. These larvae were transferred to dark conditions, and 50% of each of the green and brown exposed larvae were exposed to green, while the remaining were exposed to brown. All larvae pupated in complete darkness. Larvae exposed to green substrate under illuminated conditions were significantly greener than those exposed to brown, regardless of the substrate on which they pupated. This finding suggests that larvae can retain visual memory of substrate cues and may confer adaptive advantages. While deciding the pupal color under natural conditions, larvae may rely on the substrate color if available; if not, they rely on the memory of the substrate.

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14

Diya Elizabeth Shaji
CLUE

Inducible multicellularity and its effect on coexistence between two antagonistic species

Explaining how antagonistic species manage to coexist with each other is a longstanding challenge in evolutionary ecology. Here we address this question in the context of the medically relevant pair of opportunistic human pathogens *Pseudomonas aeruginosa* (Pa) and *Staphylococcus aureus* (Sa), which are routinely found together in septic wounds and cystic fibrosis lungs, but are extremely difficult to co-culture in the laboratory. We show that in highly saline environments, both Pa and Sa individually form phenotypically plastic multicellular collectives. Next, we show that in high salinity static co-cultures, such induced multicellularity leads to spatial niche partitioning: while Pa inhabits the air-liquid interface and forms a thick multicellular mat, Sa grows from the bottom of the tube and forms a vertical submerged multicellular filament. We also established that high salinity environments led to better Sa-Pa coexistence than habitual salinity environments. We also proved that, counterintuitively, this increase in Sa-Pa coexistence was solely due to high salinity and not because of spatial niche separation between Sa and Pa. This is because high salinity environments could lead to an even greater coexistence (with Sa counts almost the same as Pa counts) if the multicellular structures were periodically broken by vortexing in high salinity environments. Interestingly, such vortexing failed to increase Sa-Pa coexistence under habitual salinity. This proves that phenotypically plastic multicellularity plays opposite roles in Sa-Pa interactions: It is maladaptive for Sa but adaptive for Pa. We also found that such plastic multicellularity was also adaptive for Pa in monocultures. Overall, our data suggest that the amount and activity of a diffusible toxin produced by Pa for killing Sa is the major determinant of Sa-Pa ratios.

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THIRUVANANTHAPURAM

Cellular morphometric analysis of mouse fetal liver identifies hepatoblastic niche for hematopoietic stem cells

The fetal liver (FL) is a critical hematopoietic niche during embryonic development, enabling the expansion and differentiation of hematopoietic stem cells (HSCs). Despite its importance, the mechanisms governing HSC interactions within the FL niche remain poorly understood. Here, we investigated the spatiotemporal dynamics of HSC localization and their microenvironmental interactions at embryonic days 14.5 (E14.5) and 18.5 (E18.5). Using high-resolution immunofluorescence microscopy and three-dimensional tissue reconstruction, we found that HSCs at E14.5 preferentially associate with DLK1+ hepatoblasts and CD31+ endothelial cells, forming a supportive microenvironment for proliferation and expansion. By E18.5, HSCs migrate toward sinusoidal regions as the influence of hepatoblasts diminishes. Analysis of single-cell RNA sequencing data from mouse FL corroborated these findings, revealing that hepatoblasts at E14.5 exhibit enriched expression of hematopoietic regulators, significantly declining by E17.5 as hepatoblasts differentiate into hepatocytes. This study demonstrates the dynamic nature of the FL niche, where early-stage hepatoblasts play a pivotal role in HSC support, transitioning to a sinusoidal-dominant niche as development progresses. These insights deepen our understanding of fetal hematopoiesis and the evolving microenvironment that shapes HSC behavior. By elucidating these temporal changes in the FL niche, our findings offer valuable perspectives on HSC biology and potential strategies for enhancing ex vivo HSC expansion for therapeutic purposes.

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16

Hrithik Kumar
Host Pathogen Interaction Lab

Infection-Induced exocytosis promotes replication of a lysosomal adapted pathogen, *Coxiella burnetii*

Coxiella burnetii is an obligate intracellular bacterium that causes a worldwide zoonosis known as Q fever. Upon internalization into host cells, Coxiella extensively remodels host vesicle trafficking and replicates within spacious, acidic, lysosome-derived vacuoles. However, how fundamental lysosomal functions, such as exocytosis, are affected during Coxiella infection remains unknown. In this study, we aimed to investigate the dynamics of lysosomal exocytosis in the context of Coxiella infection. Our findings reveal that C. burnetii infection triggers increased release of extracellular vesicles with endolysosome proteins and elevated surface LAMP1 expression in both phagocytic and non-phagocytic cells during later stages of infection. This infection-induced exocytosis is found to be dependent on the type IVB secretion system, which the bacteria use to secrete effectors and hijack host cell machinery. We also explored the role of exocytosis in cell-autonomous defence mechanisms against intracellular pathogens. Notably, STX11, a SNARE protein with a well-established role in exocytosis, is known to restrict C. burnetii, but its underlying molecular mechanisms remain poorly characterized. Our study demonstrates that STX11 inhibits infection-induced exocytosis in C. burnetii-infected cells. Further, we also evaluated the effects of modulating TRPML1, a lysosomal calcium channel, during infection. Using TRPML1 antagonist ML-SI3, we demonstrate that decreased TRPML1 activity leads to decreased C. burnetii replication. In addition, the depletion of TFEB, a master regulator of lysosomal biogenesis, increased Coxiella replication and further exocytosis, suggesting a negative regulatory role for TFEB activation. Overall, our data highlights the temporal regulation of exocytosis in C. burnetii-infected cells and provides new insights into the cell-intrinsic modulation occurring during infection.

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17

Jacob Gigi Kurian
Plant Haploid Genetics Lab

Spicing up the centromere : The holocentromere in Nutmeg is not based on major satellite repeats.

Holocentric species are characterized by the presence of centromere throughout the length of the chromosome. We confirmed the holocentricity in *Myristica fragrans* (Nutmeg) based on chromosome wide distribution of centromere specific KNL1 protein, alpha-tubulin fibres and the cell cycle dependent histone H3 Serine phosphorylation (H3S28ph) mark. Each holocentromere of nutmeg is likely composed of on an average 10 centromeric units. Centromeres in most organisms are composed of satellite repeats. None of the identified and in-situ hybridized high-copy satellite repeats in Nutmeg were centromere specific.

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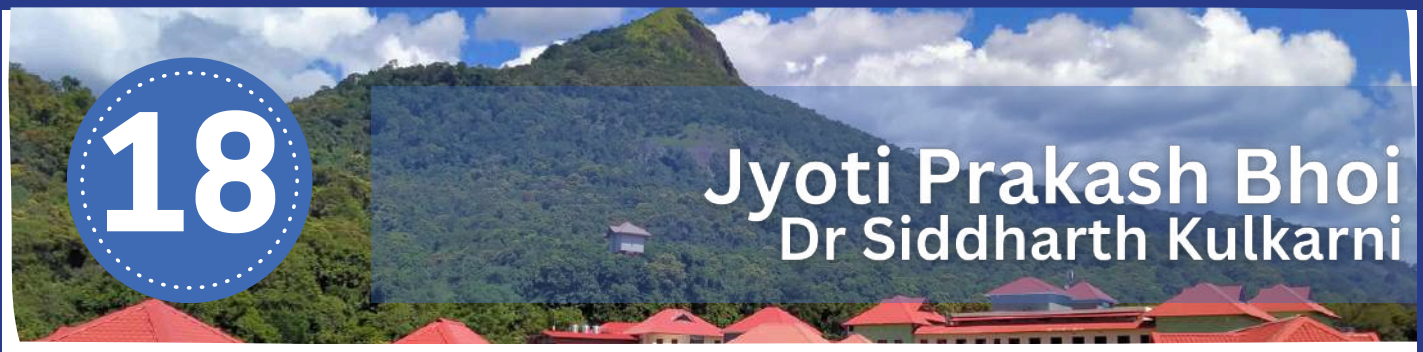

18

Jyoti Prakash Bhoi
Dr Siddharth Kulkarni

Genomic ultraconserved elements refute monophyly of *Acari*

Acari, which includes ticks and mites, is a hyperdiverse group of miniature bodied arachnids with over 40,000 described (540 families) and an estimated 1–3 million undiscovered species. Over their circa 430 Ma (Silurian period) evolutionary history, they have occupied both terrestrial and aquatic habitats. Most Acari have fewer chromosomes with miniaturized genomes (ca. 200 Mb) as compared to other arachnid genomes averaging 1.5 Gb. A multitude of medically important ticks and mites are known, however, their evolutionary relationships remain contentious due to their small body size, deep divergence, and miniaturized genomes. Various phylogenetic hypotheses range from a monophyletic to polyphyletic Acari, primarily classified into Acariformes (mites) and Parasitiformes (ticks and parasitiform mites). We capitalized on the deep diverging Acari to target the ultraconserved elements (UCE) regions of de novo generated and publicly available 91 arachnid genomes including 48 Acari genomes. To optimize Acari placement within Arachnida, we developed a UCE bait set using six chromosomal-level arachnid genomes that can target 3,294 UCE loci. We establish that Acari is not monophyletic with robust support. Parasitiformes are monophyletic with Solifugae as their close relative. We recovered the Acariformes clade with the Trombidiformes sub-clade, however, with non-monophyletic Sarcoptiformes and Orbatida. The Opiliones resembling opiliocarid (Indiacarus sp.) mite was placed as a sister group of Parasitiformes suggesting a convergent evolution of the harvestmen phenetic makeup.

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19

Krishanu Dey Das
Laboratory of Immune Cell Biology

Regulation of Golgi architecture and function by novel ubiquitin E3 ligase

Organelle homeostasis is crucial for proper functioning of cells and dysregulation of which often leads to pathophysiological conditions. Organelle functions and homeostasis are influenced by dynamic interactions between diverse compartments like the ER, mitochondria, endosomes, lysosomes and the Golgi. This study focuses on regulation of Golgi architecture which is poorly understood. Golgi is the central organelle in sorting and trafficking of protein and lipid, controlling many other functions. In mammalian cells the Golgi appears as a ribbon, and is dynamically altered to cater to the physiological needs of cell functions like migration, proliferation.

Recently, Golgi has been shown to be controlling inflammasome activation, regulating mTORC1 activation, microtubule organization indicating its previously unrecognized role in cell signaling pathways. Several pathophysiological conditions like Alzheimer's, Parkinson's, Cancer, Diabetes Golgi architecture have been shown to be disturbed indicating its importance in maintaining normal physiological functions. Several studies have shown molecular regulation of Golgi architecture by phosphorylation though the role of other post translational modifications (PTM) like ubiquitination is not well explored. It is mainly of E1, E2 and several E3 ligases (~700) which help in conjugating Ub molecules to target proteins. Different Ub conjugation promotes cell signaling, stability, degradation of target proteins and in-turn control its functions. Role of ubiquitination in Golgi dynamics is less studied. Some Golgi structural proteins like Golgin45, GRASP55/65, have been shown to be ubiquitinated and degraded. Recent studies have shown interplay of poly-ADP-ribosylation, ubiquitination and SUMOylation in maintaining Golgi structural protein Golgin45, indicating existence of many complex unexplored regulators of these structural proteins.

Here, we establish an E3 ligase RNF34, as a novel regulator of the Golgi architecture and function. Our investigations into the mechanisms revealed that RNF34 targets one of the Golgi structural proteins and regulates Golgi function under stress conditions.

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20

Krishna M Nair
Dr Anirban Guha

Diurnal converse with plant-emitted light unfolded potential targets for improving rapeseed-mustard biological yield

Recognition of the untapped potential of photosynthesis to improve yield has spurred research to identify novel photosynthetic targets. Advances in photosynthesis phenotyping technologies including chlorophyll a fluorescence (ChlF) and photosynthesis models have made 'direct improvement of photosynthesis' a relatively new frontier in increasing crop yield. As the average mustard yield in India has stagnated at 1.0-1.3 tons/hectare, improving its biological yield is critical. Using ChlF approaches we aim to identify, leaf photosynthetic traits that could enhance the selection of high yield rapeseed-mustards. We investigated: (1) diurnal leaf ChlF responses, (2) relationships of ChlF responses with growth & yield performance and (3) genotypic variations in photosynthetic thermotolerance (PT) in 17 rapeseed-mustard genotypes. PSII maximal efficiency (FV/FM) and performance index (PIabs) displayed a bimodal pattern, with a midday drop at ~14:00 hrs. The minimal fluorescence (Fo) remained largely stable, while maximal fluorescence (FM) showed a significant midday drop. In contrast, dissipation per reaction center (DI/RC) exhibited a midday rise, suggesting dissipation of excess energy as heat is likely a photoprotective strategy. Importantly, rapeseed-mustard yield correlated positively with PIabs and negatively with DI/RC. We investigated PT by determining the temperature at which FV/FM drops to 50% (T50) of its maximum and the temperature at which Fo begins to rise (TC). The mean T50 ranged from 42.43°C to 44.03°C & mean TC ranged from 40.59°C to 42.82°C. The indices of PT did not correlate with yield but we need further assessment under field warming and drought events.

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21

Kulkarni Gopal
Sim.Bio.Sys lab

Agent based modelling of Granuloma formation during *Mycobacterium tuberculosis* infection

The formation of granuloma following a cascade of immunological events is the hallmark of Mycobacterium tuberculosis (MTB) infections. The granuloma are known to undergo necrosis in oxygen-deficient conditions and immune cells are involved in the formation of necrotizing granuloma. With cellular crowding leading to reduction in the efficacy of anti-MTB drugs to resolve the infection. Understanding the origins of development of a necrotic granuloma is cornerstone for designing new therapy regimens. This study focuses on building an agent-based model for necrotic granuloma formation to understand the underlying mechanism of the formation of a necrotic core and quantify the effects of anti-MTB drugs in granuloma resolution.

To model the granuloma formation, we use an agent-based modelling framework, CompuCell3D, based on the cellular Potts model. This multi-scale virtual tissue modelling framework allows integration agent-based cell phenotypes and PDE based continuum fields. The initial model consists of bacteria, non-infected and infected macrophages and T cells with the oxygen and chemokine continuum fields. Non-infected macrophages and neutrophils are recruited by the secretion of chemokines by infected macrophages. MTB and immune cells interact with the oxygen field by consumption and diffusion. Immune cells undergo necrosis when the concentration of the oxygen field dips below critical thresholds.

Modelling of the necrotic granuloma using an agent-based framework lets us identify the relevant parameters that underlie the formation and resolution of such structures under the influence of anti-MTB drugs. Our model results propose key interventional strategies in terms of combination therapies that lead to efficient resolution of granuloma.

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The Role of Nuclear Transport in Mediating DNA Repair Following DOX-Induced Topoisomerase II Inhibition

Topoisomerase II (TopoII) plays a crucial role in relieving torsional stress on tightly folded DNA during key cellular processes such as replication, transcription, and segregation. TopoII manages this by cutting, re-winding, and re-ligating DNA strands. Failures in re-ligation, however, can result in DNA breaks and cell death. While the response to such stress is not well understood, recent studies suggest sumoylation and ubiquitination remove covalently linked TopoII, followed by DNA repair and proteasome inhibition to reverse these breaks. To investigate additional regulators involved in the DNA damage response, we used the anticancer drug Doxorubicin (DOX), a TopoII inhibitor commonly used in cancer treatment. We performed genome-wide CRISPR knockout screens in AC16 and HEK293T Cas9-expressing cell lines, targeting all human protein-coding genes followed by DOX treatment. Comparative analysis with other DOX CRISPR screens revealed enrichment in nuclear transport and DNA repair processes. Nuclear transport, mediated by karyopherin alpha, karyopherin beta, and cargo complexes, relies on the Ran-GTP gradient and nucleoporins for nuclear membrane passage. Focusing on the importin beta family, we identified a karyopherin beta protein, IPO5 as one of the top negatively selected genes in our screens. Knockout of IPO5 increased DOX sensitivity and led to higher levels of DNA breaks compared to wild-type cells. Additional analysis showed elevated 53BP1 foci at DNA damage sites post-DOX treatment, suggesting enhanced non-homologous end joining (NHEJ) activity. In conclusion, our CRISPR screens targeting TopoII with DOX suggest nuclear transport, particularly IPO5, plays a key role in mediating DNA repair and cytotoxicity. Future research will explore how karyopherin beta proteins regulate DNA repair pathway selection.

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Muhammed Naseem
DREAM Lab

A screen to identify novel roles of microRNAs in the *Drosophila* prothoracic gland

Prothoracic gland, an endocrine organ responsible for producing the molting hormone ecdysone, plays a critical role in insect larvae's growth and developmental transitions. Coordinated growth and development of the prothoracic gland and the timely release of ecdysone are essential for ensuring proper organismal development. Various external signaling factors, along with intrinsic factors, are known to regulate both the growth of the prothoracic gland and the release of ecdysone. Among the intrinsic factors, microRNAs (miRNAs), i.e., 21-23 nucleotide-long short noncoding RNAs, that regulate the expression of their target mRNAs could play a crucial role in the prothoracic gland. A microRNA (miRNA) knock-out screen identified several miRNAs that cause delays in development. Target prediction analyses suggest that these miRNAs may be involved in regulating various downstream signaling cascades and the growth of the prothoracic gland, with further investigation being carried out to confirm these findings

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Nidhi S. Kumar
Dr Anirban Guha

New insights into the photosynthetic thermotolerance of Sorghum bicolor under progressive drought

Photosynthetic thermotolerance (PT) is the ability of plants to prevent high-temperature induced damage to the photosystems. Acclimation in PT is critical to cope with increasing warming and drought events. A large number of economic crops in the tropics belong to the grass family – Poaceae and their intrinsic PT and acclimation responses are less understood.

We investigated the acclimation in PT to increasing drought severity in sorghum in a semi-controlled greenhouse environment. Plants were exposed to dry-down and were allowed to lose only a certain amount of water per day. Relationships between normalized transpiration ratio (NTR) and fraction of transpirable soil water (FTSW) and the FTSW breakpoints where NTR initiated its decline were estimated using a sigmoidal non-linear model. The NTR started declining at FTSW values ranging between 0.44 and 0.34, and the genotypes varied in FTSW thresholds. At different stages of FTSW (moderate and severe), we quantified PT using T50, the leaf temperature at which Fv/Fm (photosystem-II maximal efficiency) decreases to 50% from its initial reference value. We used a four-parameter logistic model to estimate T50.

The T50 ranged from 45.9 to 48.1°C and 47.6 to 49.4°C in moderate and severe FTSW stages. A drought-induced 2.2°C acclimatory rise in PT was found in one genotype. Interestingly, genotypes with lower FTSW thresholds showed lesser tendency of acclimation in PT. Overall, our results suggest that some sorghum genotypes can exhibit acclimation in PT under drought, making them more resilient to future climate extremes.

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Parnika Sahoo
Laboratory of Parasite Diseases

Exploiting polypharmacology of kinase inhibitors to identify host regulators of *Toxoplasma gondii* infection

Intracellular pathogens, which invest minimally in their own genome, are known to commandeer the host cell machinery to thrive in the hostile cellular environment. Kinases, being master regulators of the cell, are expected to play a major role in establishing infection. Currently, most drugs in use target multiple kinases simultaneously, resulting in polypharmacological effects. In this study, we aim to leverage such polypharmacological effects of kinase inhibitors to identify the specific host kinases that regulate the survival and development of intracellular pathogens. We utilize the pre-existing activity profiles of a small subset of kinase inhibitors to develop a predictive computational model capable of identifying host kinases (~300 kinases) that play a role in facilitating Toxoplasma infection. Using KIR on Hela and HFF cells, we have predicted four novel kinases (ACVR1, MET, CDK3 and NEK2) that impact T.gondii infection alongside other kinases that were previously known to regulate T. gondii infection . During the development of the parasite within the host, we observed significant increase in pSMAD-1,5 & 9, a downstream regulator of ACVR1. Pharmacological inhibition of ACVR1 has significantly reduced the parasite development by reducing the pSMAD-1,5,9 levels. In the future, we aim to elucidate the mechanistic role of ACVR1 and other kinases identified in the screen in regulating the infection and translate these findings into the development of host-targeted therapeutics.

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Parul Jain
Laboratory Immune Cell Biology

Novel role for nuclear DUB, USP28 in Parkin-mediated mitophagy

One way mitochondrial homeostasis is maintained is by eliminating damaged mitochondria by a catabolic process known as mitophagy. .mitophagy is critical for cellular health, and defects in mitophagy have been implicated in neurodegenerative disorders. The cell utilizes the ubiquitin-proteasome system (UPS) and the autophagy machinery to maintain a healthy pool of mitochondria, where upon mitochondrial damage, mitochondrial proteins are ubiquitinated, signalling the autophagosome machinery to engulf the damaged mitochondria. Thus, mitophagy can conceptually be organized in various steps: 1) activation and recruitment of Parkin, 2) ubiquitination of mitochondrial proteins, and 3) recruitment of the autophagosome machinery. Both ubiquitination and deubiquitination play critical roles in ensuring homeostasis, Multiple mitochondrial resident and non-mitochondrial resident deubiquitinating enzymes (DUBs) have been shown to affect one of these processes by removing ubiquitin from Parkin or mitochondrial proteins. In our study, we identified one of the nuclear DUBs - USP28, which can regulate Parkin-mediated mitophagy. Knock-down of USP28 promoted Parkin translocation to damaged mitochondria compared to control. Also, the knockdown of USP28 led to increased Parkin ubiquitination suggesting the effect of USP28 on Parkin recruitment is via Parkin ubiquitination. USP28 has mainly been studied in the context of DNA damage and cell cycle progression, and little is known about its function outside the nucleus. I present data to establish USP28 as a regulator of mitophagy.

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Poorvisha V. Muthusamy
Genome Editing Lab

Genomic profiling reveals the genetic foundation for enhanced productivity and adaptability in Sunandini cattle

India's native cattle are renowned for their adaptability and disease resistance but have limited genetic potential for high milk production, posing challenges to meet growing dairy demands. To address this, the Indo-Swiss Project Kerala (ISPK), initiated in 1963, developed the Sunandini breed by crossbreeding Kerala's indigenous cows with Brown Swiss, Jersey, and Holstein Friesian cattle. This composite breed combines the milk productivity of Bos taurus with the resilience of Bos indicus, refined over decades to enhance yield and adaptability to tropical climates.

To better understand its genetic potential, we performed hybrid de novo and haplotype-resolved genome assemblies, producing a 2.67 Gb genome with distinct maternal and paternal haplotypes, an N50 value of 102 Mb, and 95.4% completeness based on the BUSCO score. Comparative genomic analyses identified 6,151 structural variants and 9,187,816 SNPs, many linked to immune function and milk quality traits. Population genotype data revealed that the Sunandini breed exhibits closer genetic proximity to taurine breeds. Local ancestry analysis further showed that taurine-derived genomic regions span 1.72 Gb (69.2% of the genome), including 147 genes previously associated with milk production, which likely contribute to the breed's enhanced milk yield. Indicine-derived regions, spanning 46.6 Mb (1.87% of the genome), contain over 100 genes, including heat shock proteins and cellular stress response genes, along with 203 immune-related genes, contributing to the breed's disease resistance and adaptability.

These findings highlight the Sunandini breed's genetic potential and the importance of genomics-based breeding. By identifying markers linked to key traits, this research supports developing superior cattle that merge the best attributes of Bos taurus and Bos indicus, advancing sustainable dairy production and improving livelihoods in tropical regions.

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Sandra SN
Sim.Bio.Sys and LaPD Lab

Integration of Genome-scale metabolic model and Single-Cell RNA sequencing to identify the metabolic triggers of Plasmodium Vivax liver dormancy

One of the major challenges to malaria eradication is the ability of Plasmodium vivax to form dormant hypnozoite forms within the liver. These parasite forms can be reactivated, leading to recurring infection, are resistant to most antimalarials, and are difficult to culture in the lab. It has been hypothesized that a large majority of infections originate from reactivated parasites, so effective control of these forms would have major clinical impact. Clinical observations suggest that both host and parasite-intrinsic regulators can alter the state of dormancy in the liver stage parasite, but the molecular underpinnings of dormancy and reactivation remain largely unexplored. Here, we generate a liver-stage metabolic model for P. vivax using the liver-stage metabolic models of P. berghei and P. falciparum. In future, we aim to integrate the metabolic model of P. vivax and with its hepatocyte host metabolic model to identify key host metabolic enzymes critical for regulating the dormancy of the parasites. The generated P. vivax shows an accuracy of ~70% in predicting essentiality of Plasmodium genes. While refining the model, we concurrently analyzed the existing single-cell RNA sequencing data and identified a distinct set of metabolites uniquely overproduced in infected hepatocytes harboring the dormant form, underscoring the upregulation of these pathways compared to hepatocytes hosting active form thereby exposing the vulnerable targets of hypnozoite. In addition, we identified a unique set of active- and dormant-form-induced hypomorphs in the hepatocytes and their druggable synthetic lethal partner genes, enabling the targeted elimination of infected cells harbouring each of these forms.

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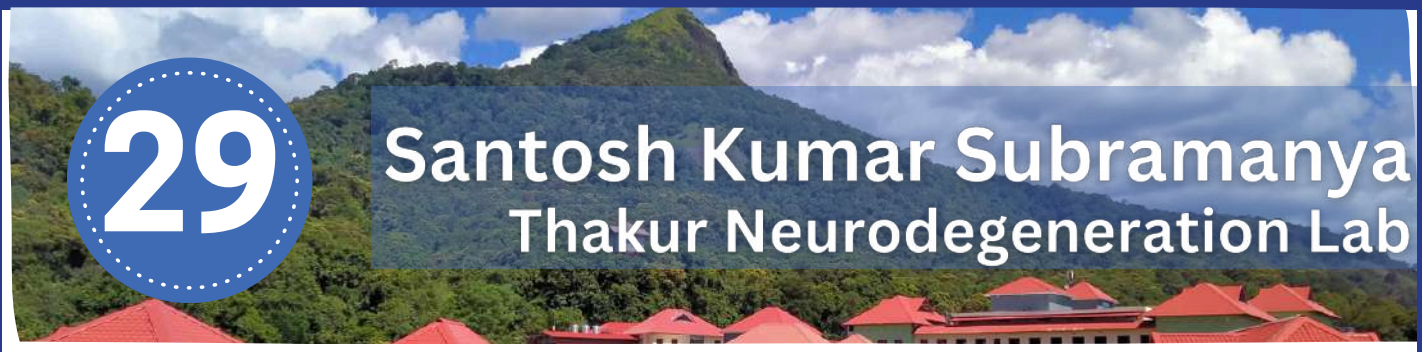

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Santosh Kumar Subramanya
Thakur Neurodegeneration Lab

A relevant α-synuclein-based mouse model of PD displays neuroprotection upon PD180970 administration

Parkinson's disease (PD) is an age-related movement disorder characterized by the loss of dopaminergic neurons (DA) of substantia nigra (SN) and accumulation of α-synuclein aggregates in lewy bodies. A faithful model that closely mimics the relevant pathological signatures is necessary to understand the disease progression and underlying mechanisms. We have developed a model by combinatorial injection of AAV6 overexpressing α-synuclein and pre-formed fibrils (PFF) called SynFib model.

The model exhibited significant neurodegeneration accompanied by striatal (STR) projection loss compared to relevant control groups (GFP, PFF and Syn). We also observed progressive motor behavioral deficits with gait abnormality in the SynFib group at 24W. This was associated with accumulation of aggregates in SN and STR compared to other groups. A time-dependent loss of SN-DA neurons and fibre density of STR was also captured. The model displayed progressive worsening of p-syn pathology at SN with aggregates spreading to the STR and also to the medium spiny neurons of STR and cortical regions. We also observed lewy-like features of aggregates which were proteinase K-resistant, ubiquitinated and thioflavin S positive. Further the model showed an elevation of neuroinflammation that reduced with time. Interestingly, the aggregates spread contralaterally, which elevated ubiquitin puncta structures and were colocalizing with Iba1 neurons. The model displayed neuroprotection and reduction of aggregates upon administration of PD180970.

The SynFib model captures various pathological signatures of PD that may be useful in studying mechanisms driving disease over time and the model displays its usefulness in pre-clinical therapy

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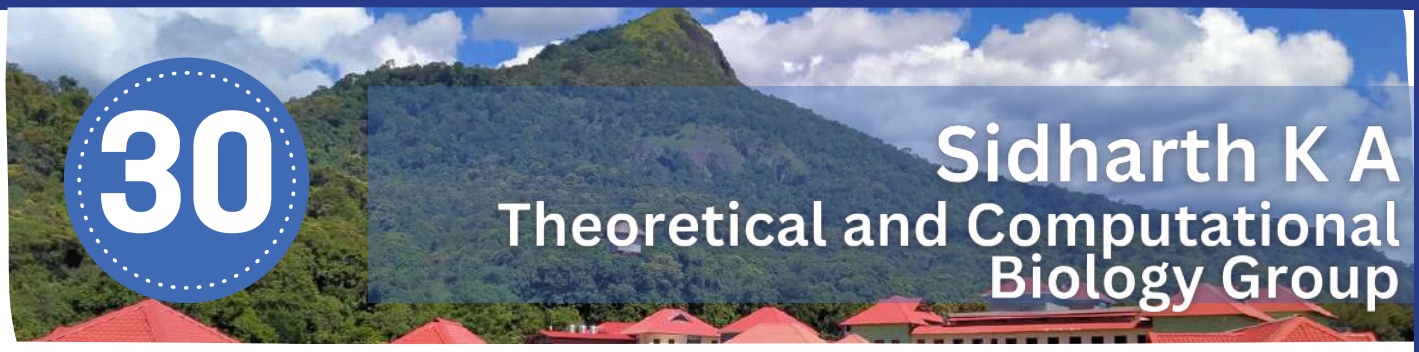

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Sidharth K A
Theoretical and Computational Biology Group

A cell geometry-based mechanism for controlling organ shape during plant morphogenesis

Multiple studies have shown how plant tissue and organs regenerate. However, how the lost organ regains its shape remains unknown, and how the plant knows which part of the organ to regenerate. In animals, cell migration near the cut site facilitates regeneration. However, in plants, cells are cemented together, and cell migration does not occur. Then, what mechanism facilitates the regeneration of lost tissue in plants? We performed experiments using Arabidopsis root tip resection as a model to answer this. We observed that post-resection (injury) when tissue regenerates, cell shape changes from elongated cube to rhomboid cell shape, where the former goes through horizontal division and the latter goes through oblique division. We hypothesize that in the resected root tip, the creation of rhomboid cells and their oblique division, along with cell growth, plays a vital role in the restoration of the U-shape morphology of the root tip. We developed a multiscale (cellular to tissue scale) computational framework to simulate differential growth that couples cell geometry, mechanics, and biochemical signals. Notably, microtubule (MT) orientation follows cell division orientation. Considering this fact, we simulated MTs on elongated cube and rhomboid cell surfaces. Our simulation predicted cell geometry alone can produce the observed division orientation. Interestingly, reducing MT stability at the cell edges significantly improved the prediction of oblique cell division in rhomboid cell shapes. Further, we explored the impact of the cell aspect ratio of the rhomboid cells, which predicted improved accuracy in the oblique division for a higher aspect ratio value. Our experimental quantification of the rhomboid cell division orientation confirmed the model predictions.

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Soujatya Banerjee
Molecular Neurodevelopmental Lab

Uncovering the Role of CHD2 in Neurodevelopmental Disorders

Mutations in the ATP-dependent chromatin remodeller CHD2 have been shown to result in severely impaired neurodevelopment leading to epileptic seizures, mental retardation, etc. However, the mechanism by which CHD2 mutations result in the aforementioned phenotypes is unclear. CHD2 is known to bind to bivalent regions of chromatin, having both active and repressive markers, a hallmark of undifferentiated cells. Thus, it is likely to have a role in controlling the expression of genes crucial in directing neurodevelopment. Most studies on the role of CHD2 have been performed on cells in culture or mice models, and it is challenging to study early development in either system. In contrast, zebrafish undergo external development, facilitating detailed analysis of developmental processes in a vertebrate system.

In order to understand the mechanisms by which CHD2 mutations lead to defective neurodevelopment, we are generating a knockout model of CHD2 in zebrafish using CRISPR/Cas9 technology. Founder fish capable of transmitting the mutation to the next generation will be screened for and mutant fish from the F2 generation will be used to characterise epileptic phenotypes. The sensitivity of chd2 knockout larvae to proconvulsant drugs like pentylenetetrazol and photosensitivity will be tested. Local Field Potential will also be recorded and analysed for bursts of neuronal firing. Finally, in order to understand the molecular mechanisms, RNA-seq and ChIP-seq data from CHD2 knockout mice and mESC were analysed to obtain target genes that are likely to be regulated by CHD2 and mediate the effects on neurodevelopment.

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Swarnendu Mukopadhyay
Cytoskeleton and Cell Division Lab

Regulation of Centriole duplication: Role of SAS-6 and γ-tubulin ring complex interaction

Centrosome assembles microtubules in animal cells and is required for cell division. During G1/S, centrosome including its two centrioles are duplicated, which serve as spindle poles during mitosis. Deregulation of centriole duplication links to diseases including cancer, ciliary dysfunctions. Centrioles are microtubule-based structures, assembled via nine SAS-6 dimers forming a cartwheel-like structure on the pre-existing centriole followed by polymerization of nine microtubule triplets around the cartwheel. While the N-terminal globular domain and the following coiled-coil central region constitute the cartwheel central hub and connecting spokes, the role of the extended C-terminal region remained unclear. Recent studies in human cells implicated an essential role of the C-terminus in the nucleation of microtubules of the new centriole by stabilizing centriolar recruitment of the γ-tubulin ring complex. However, the mechanisms of how γ-TuRC is recruited, stabilized and activated to assemble centriolar microtubules are poorly understood. We show that SAS-6 C-terminus mediates interaction with the component GCP4 of the γ-TuRC. Deletion of SAS-6 C-terminus results in substantial loss of centriolar localization of GCP4 and GCP6. While depletion of GCP6 leads to substantial loss of SAS-6 from the centrioles and results in centriole duplication defect, depletion of GCP4 did not impair centriolar association of SAS-6. We also find that aa 1400-1501 region of GCP6 is essential for SAS-6 localization at the centrioles and formation of bipolar mitotic cells. Molecular pathways regulating SAS-6 interaction with the γ-TuRC and their recruitment to the cartwheel are being explored.

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Sweta Chandana Acharjya
Siddharth Kulkarni Lab

Deep Learning Unlocks Peptide Characterization in the Enigmatic Scorpion Venom Cocktails

Toxin peptides extracted from venom are vital to drug discovery owing to their functional nature and site specificity. Parallel sequencing technologies have expedited discovery of new toxins across the tree of life, with efforts concentrated on vertebrate toxins. In the megadiverse invertebrates, characterizing toxins of several lineages continues to be a challenge due to their sheer number and narrow distribution of key lineages. To mitigate this knowledge gap, we interrogated the RNASeq data of a venomous arachnid group– Scorpiones. We developed a transfer learning pipeline for predicting the medical nature of venom peptides. The peptides collected from UniProt were converted to a vector format of similar dimensions using ProteinBERT for pretraining, and a simple 1D CNN classifier to classify the data. We trained the neural network with experimentally reviewed data from UniProt, as well as augmented data, obtaining a validation accuracy of 89.7%. Toxins and toxin-like polypeptides were collected from multiple arachnid transcriptomes using a transdecoder and filtering the toxins using toxify. Using the trained classifier, we assigned one potential class out of the three therapeutic classes for toxins and toxin-like polypeptides present across multiple arachnid species based on the probability assigned by the algorithm. With the artificially annotated dataset, we provide a starting point for a deeper exploration of the therapeutic properties of scorpion venom.

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Tiyas Sengupta
Chromatin Biology Lab

Deciphering the molecular pathways underlying chromatinopathies in neurological disorders

Cohesin, a multi-subunit protein, takes part in the cohesion of sister chromatids, segregation of chromosomes during cell division, DNA replication, and DNA repair. It has been recently discovered that cohesin takes part in the formation of topologically associating domains (TADs). TADs are regions where enhancer and promoter interactions occur for gene expression. Cohesin-mediated loop extrusion forms the TAD. Two DNA-bound convergently oriented CCCTC-binding factor (CTCF) interacts with cohesin to stop loop extrusion. Cohesin mutations are reported in a wide range of diseases including cancer, developmental disorders and neurological disorders. They are broadly termed as cohesinopathies. We aim to study the effect of cohesin mutations on molecular pathways leading to neurological disorders. RAD21 is a cohesin subunit which is frequently mutated in cohesinopathies. RAD21 joins SMC ATPase heads and also regulates the ATPase activity. It also interacts with CTCF to pause loop extrusion. During cell division, cleavage of RAD21 by separase leads to segregation of chromatids. Here in this study, we will be focusing on RAD21(D541_Q568del) mutation, reported in Cornelia de Lange Syndrome, a classical cohesinopathy and neurological disorder. This mutation was reported in a patient who inherited the mutation from his mother. The patient showed developmental delay, mental retardation and autistic features while his mother had mild symptoms. This mutation has been classified as pathogenic, but the molecular pathway behind its pathogenicity is unknown. We intend to study how RAD21 mutations can affect genome architecture and other cohesin functions which lead to disease progression.

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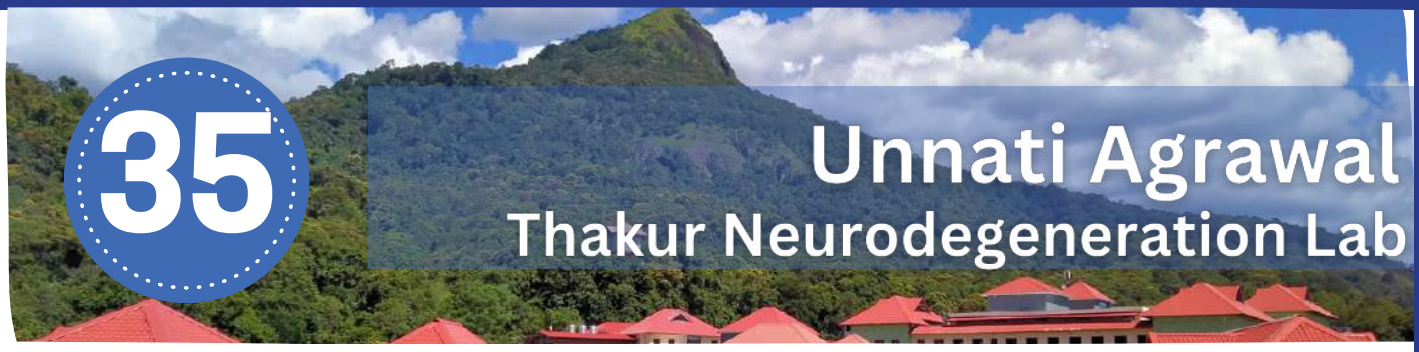

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Unnati Agrawal
Thakur Neurodegeneration Lab

Lipidomic analysis of the midbrain region in an early-stage PD mouse model

Several post-mortem studies have indicated PD-specific lipid alterations in the later stages of the disease. Still, there is a knowledge gap in how these lipid profiles in specific midbrain regions are implied in PD progression. Considering that the majority of dopaminergic neurons (DN) are lost when the symptoms of PD arise, we aimed to study the midbrain lipid alterations in the early stages of a progressive PD mouse model.

In this study, α-synuclein pre-formed fibrils (PFFs) were injected stereotaxically in the substantia nigra (SN) region of the mice brain. To examine disease progression, behavioral tests were performed at different time points (4, 8, and 12 weeks), which included open field, wire hang, and gait analysis tests. Mice were sacrificed at a 12-week timepoint, and dissection of the brain was performed to extract the midbrain region along with our region of interest, i.e., SN. Lipids were extracted, and HPLC-Q-TOF-MS was performed, followed by analysis of peaks.

Despite the obvious lack of motor deficits, changes in lipid species were observed. PFF-injected mice showed an upregulation in glucosylceramide (Glccer) but a downregulation in phosphatidic acid (PA) species. Both of these changes were more obvious in male mice than female mice.

Our study corroborates the sex-specific changes in the levels of lipid species, mainly Glccer and PA, in the early stages of disease pathology. Thus, it implies that abnormal glycosphingolipid and phospholipid metabolism play an important role in driving PD pathology, and potential pathomechanisms will be further evaluated to understand disease pathology.

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Co-evolution of DSN1 and TTN9 in flowering plants and its Potential role in Kinetochore Assembly in *Arabidopsis*

The kinetochore, a multi-protein complex essential for accurate chromosome segregation, ensures proper centromere-microtubule attachment and facilitates cell cycle progression. While flowering plants exhibit remarkable diversity in centromere types, ranging from holocentromeres to monocentromeres, the functional architecture of the plant kinetochore remains less understood compared to its yeast and human counterparts.

In this study, we investigate the MIS12 sub-complex protein DSN1 to characterize its role and kinetochore-specific identity in Arabidopsis thaliana. We identify TTN9, a homolog of the yeast kinetochore protein Csm1, which is conserved across algae and plants but absent in humans. In yeast, Csm1 enhances kinetochore function by recruiting condensins and providing structural stability. Similarly, we find that TTN9, along with DSN1, localizes to the kinetochore in Arabidopsis thaliana and is critical for plant development, as evidenced by the embryo-lethal phenotypes of the ttn9 and dsn1 mutants.

Furthermore, our analysis reveals that TTN9 is recruited to the kinetochore via conserved domains in DSN1, highlighting a plant-specific mechanism of kinetochore assembly. TTN9 is widely conserved across flowering plants, suggesting an evolutionary adaptation that underscores the unique dynamics of plant chromosome segregation. These findings provide novel insights into the evolution and functional dynamics of the plant kinetochore complex, advancing our understanding of chromosome movements in plants. This work bridges gaps in knowledge about kinetochore diversity across eukaryotes and sheds light on plant-specific adaptations in chromosome segregation mechanisms.

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Vartika Srivastava
Molecular Neurodevelopmental Lab

Understanding the Bermuda Triangle of Stress, Sociality, and Aggression in *Danio rerio*

Brain function impacts behavioural outcomes. Though there is considerable interaction between individual behaviours, this crosstalk remains largely unexplored. Zebrafish are an effective model organism for studying physiology and behaviour due to their ease of handling, genetic manipulation, diverse behavioural repertoire, and 70% genetic homology with humans. In this study, we explore the effect of stress and aggression on social behaviour in zebrafish.

We established the social preference test in adult zebrafish and found a difference in the social preference between lab-grown strains and those sourced from local aquariums. One of the factors underlying these differences appeared to be environmental stress, since zebrafish subjected to two weeks of unpredicted chronic stress in the lab exhibited reduced social preference compared to unstressed controls. We speculated that aggression might be another factor influencing sociality in zebrafish. In order to test this, fish were classified as high-social and low-social and a negative correlation between aggression and social preference was observed. Based on these observations, we conclude that social behaviour is influenced by factors such as stress and the aggressive behaviour of fish. These observations would be crucial in interpreting behavioral variations in different populations; with broader implications in animal welfare.

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V. Vipina
Sim.Bio.Sys Lab

Metabolic modeling reveals the role of vacuolar citrate and isocitrate in CAM chlorenchyma

Crassulacean acid metabolism (or CAM photosynthesis) is a modified form of photosynthesis found in vascular plants adapted to arid conditions. In these plants, stomata are closed during the day to minimize transpiration loss. During the night when temperature and transpiration rate are lower, fixation of atmospheric CO2 allows the accumulation of organic acids in the vacuole. During the day, the accumulated organic acids are remobilized to generate CO2 for the C3 cycle and form carbohydrates (such as starch and sugars). Several studies have been made on the diurnal accumulation of malate. However, a comprehensive study on the accumulation of other organic acids is lacking. In this study, we focus on the accumulation of other organic acids, such as citrate, isocitrate, and fumarate, and its role in CAM metabolism. For this, we use a popular metabolic modeling approach called Flux Balance Analysis (FBA) and apply it to a diel CAM leaf model. Our results show that the NADPH requirements of the leaf can influence the citrate to malate accumulation ratio, and that contrary to popular belief vacuolar citrate can contribute to the CAM cycle in certain CAM subtypes. Our analysis also shows that citrate and isocitrate pools potentially act as intracellular buffers during the nocturnal acidification of CAM vacuoles.

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DRIMER: An Optimized Programmable RNA Scaffolds for Multivariate CRISPR/Cas-based Effector Recruitment

Rational engineering of RNA has enabled diverse applications ranging from COVID vaccines to improved guide RNAs (gRNAs) for CRISPR/Cas systems in vivo and in vitro. For instance, chemical modifications to gRNAs are often required for genome editing in cell and gene therapy contexts, as well as CRISPR activation (CRISPR a) strategies. Further, gRNAs are frequently modified to incorporate stem loops that can, in turn, recruit RNA-binding proteins fused to an array of enzymatic and/or regulatory domains. While powerful, these current platforms offer limited stoichiometric and spatiotemporal control and often interfere with gRNA function and/or editing efficacy. Here, we developed a designer multi-stem-loop RNA intermediated effector recruitment platform, called DRIMER, that permits robust stochiometric and spatiotemporal control over effector recruitment to targeted human loci when used with CRISPR/Cas systems. We show that DRIMER can recruit up to four unique effector domains to human loci and that these effectors can be functionally distinct and recruited in user-defined combinations. Using this platform, we demonstrate that combinations of key transcription factors and epigenetic modifiers harbor powerful synergies at endogenous human loci. Further, we demonstrate that DRIMER-mediated recruitment can be precisely tuned by incorporating chemically controlled riboswitches or ontogenetically regulated stem-loops. Overall, the DRIMER platform is a highly programmable CRISPR-based system that allows stoichiometric and combinatorial effector recruitment using designer, structured RNAs for the precise modulation of human gene expression and other genomic activities, which is an attractive new capability for a wide range of applications spanning complex epigenome editing as well as gene and cell therapies.

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Immunomodulatory Action of *Coccinia grandis* Bioactive Compounds Against Hepatocellular Carcinoma: A Computational Approach

Hepatocellular carcinoma (HCC), a subtype of liver cancer, is the fifth most common cancer and a leading cause of cancer-related deaths globally. Due to limited effective treatment options, the mortality rate of HCC remains high, necessitating novel therapies. Coccinia grandis contains several bioactive phytochemicals with anticancer properties that could be explored for HCC treatment. This study used network pharmacology and in silico tools to predict the potential bioactive compounds, target proteins, and molecular pathways of Coccinia grandis in treating HCC. Out of 100 compounds screened from Coccinia grandis using PASS, 40 demonstrated pharmacological activities, including anticancer, anti-neoplastic, hepatoprotective, and chemopreventive effects. Among these, 18 compounds satisfied Lipinski's rule of five, making them viable drug candidates. Network pharmacology revealed that 114 target genes intersected between HCC and Coccinia grandis, highlighting key targets such as AKT1, STAT3, VEGFR, BCL2, MAPK3, PPARG, and ESR1 involved in HCC pathogenic pathways. PPI network analysis identified 114 nodes and 1512 edges, showing interactions crucial for HCC treatment. GO analysis linked potential targets to gene regulation, programmed cell death, and cellular stress response, while KEGG pathway enrichment analysis elucidated the apoptotic mechanisms of Coccinia grandis via intracellular signalling pathways. In conclusion, Coccinia grandis shows promise as a potential anticancer agent against hepatocellular carcinoma, acting through multiple targets and pathways to induce apoptosis and inhibit tumor progression.

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Yenepoya University, Mangalore

miR200a regulates matrix metalloproteinases and fibrinolytic system during pulmonary fibrosis

Idiopathic pulmonary fibrosis (IPF) is a chronic lung disorder characterized by the replacement of normal lung tissue with collagen-rich extracellular matrices, the cause of which remains unknown. Inadequate diagnosis and treatment are connected to its high prevalence and fatality rates. According to recent research, the miR200 family controls the transition from epithelial to mesenchymal tissue in healthy people. Based on this background we try to explore the regulatory function of miR200a on matrix metalloproteinases (MMPs) in bleomycin induced PF in vitro (A549) and in vivo (C57BL/6 mice) models respectively.

In vitro, miR200a mimic was employed to analyze the expression of the fibrinolytic system and MMPs, with specific fibrinolytic markers, including collagen and vimentin, assessed using RT-PCR, western blotting, and immunofluorescence. In vivo, a lentiviral vector containing miR200a mimic was administered intranasally, and fibrosis was induced using bleomycin. Lung tissues were collected 14- and 21-days post-bleomycin induction, and subjected to H&E, Masson Trichrome (MT staining), and immunofluorescence staining to evaluate histopathological and fibrotic changes. RT-PCR and western blotting were performed to quantify the expression of relevant proteins and genes.

Our findings demonstrate that miR200a significantly regulates pulmonary fibrosis by modulating MMPs. Treatment with miR200a mimic alleviated bleomycin-induced fibrosis by increasing uPA and uPAR mRNA levels while decreasing PAI-1 and MMPs mRNA and protein expression. Furthermore, the study highlights the influence of miR200a on the epithelial-to-mesenchymal transition pathway, emphasizing the therapeutic potential of miR200 in treating pulmonary fibrosis.

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Susmi Varghese
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A multi-PTM landscape of metabolic enzymes

Metabolic enzymes play pivotal roles in cellular homeostasis, orchestrating complex biochemical pathways that sustain life. Post-translational modifications (PTMs) regulate the structure, activity, stability, and interactions of these enzymes, serving as molecular switches to fine-tune metabolic processes and thus maintaining cellular homeostasis and metabolic adaptability. Dysregulation of PTMs has been linked to a variety of metabolic disorders, including cancer, cardiovascular diseases, diabetes, and neurodegenerative conditions, underscoring their critical role in enzymatic regulation. However, the lack of a unified framework integrating multi-PTM landscapes across metabolic pathways limits our understanding of their regulatory roles. This study systematically mapped and analyzed PTM data from resources such as PhosphoSitePlus, dbPTM, and qPTM, focusing on 771 human metabolic enzymes. Using a novel PTM density metric, we evaluated the prevalence and distribution of 29 distinct PTMs across catalytic domains, disordered regions, and other functional sites. Rate-limiting enzymes in metabolic pathways were found to be critically influenced by these modifications, underscoring their regulatory importance. This integrated PTM landscape offers a platform for studying the dynamic regulation of metabolic enzymes, bridging signaling networks with metabolic pathways. Our findings lay the groundwork for advancing PTM-directed therapeutic approaches and interventions for metabolic disorders and unraveling the complexity of metabolic regulation

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Altered Urological Metabolites Differentially Modulate the Agr Quorum-Sensing System in Uropathogenic *Staphylococcus aureus*

Staphylococcus aureus (S. aureus) is a major pathogen responsible for complicated urinary tract infections (UTI) acquired from different transmission routes. The accessory gene regulator (Agr), a central quorum sensing (QS) system, along with urease, plays an important role in the pathogenicity of S. aureus in the urinary environment. Nutritional cues mainly regulate QS in S. aureus. Under pathological conditions, QS can be differentially regulated by elevated metabolites such as glucose, creatinine, albumin, and haem, as well as shifts in pH. In this study, we investigated the impact of altered metabolites and pH on the growth, biofilm formation, and urease activity of S. aureus strains isolated from different urological conditions. The expression levels of QS genes and urease genes were analyzed under different urinary conditions. Our results demonstrated across glycosuria, haematuria, creatininuria, and albuminuria significant differences in growth, biofilm formation, and urease activity in S. aureus strains ($p<0.001$). Significantly higher growth and urease activity were noted in glycosuria and haematuria-originated strains under the similar simulated conditions ($p<0.001$). The results highlighted the overexpression of QS-regulating genes and virulence in strains from similar metabolic environments in patients, suggesting niche adaptation. Acidic pH revealed the overexpression of Agr, urease, along with robust biofilm formation in presence of all the elevated metabolites compared to alkaline pH ($p<0.001$). This may pose considerable challenge in the management of S. aureus infection in urinary tract depending on the metabolic profile of urine and its pH. Understanding

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Understanding the mechanisms underlying temporal regulation of Kinetochore size

Proper chromosome segregation is crucial for an organism to ensure genomic stability during cell division. The outermost kinetochore layer, the fibrous corona, is a highly dynamic structure that acts as an interface for microtubule-chromosome interactions required for proper segregation. In the absence of microtubules, fibrous corona appears as an expanded crescent-shaped assembly of different proteins. This increase in kinetochore size provides more surface area, which enhances the microtubule capture and checkpoint protein assembly. CENP-E is enriched at the fibrous corona crescent structure during early prometaphase and facilitates microtubule capture and congression of polar chromosomes. Nevertheless, direct interacting partners of CENP-E in the fibrous corona have yet to be unraveled. Here, we aim to study the role of kinesin motor protein CENP-E in the dynamic size change of kinetochore. Our CENP-E depletion data showed that CENP-E might assist the crescent structure formation of RZZ proteins. In addition, we have also observed reduced kinetochore localization of checkpoint proteins such as MPS1 and MAD1. Similarly, our preliminary biochemical interactions showed that CENP-E can interact with MPS1 and MAD1 without microtubules. Our rescue experiments also indicate that CENP-E can save the loss of RZZ crescents and interact with its component ZW10 using its C-terminal domain. Although the C-terminal domain could rescue the RZZ crescents, it was not sufficient to save the inter-kinetochore tension at the aligned kinetochores during mitosis. The role of phosphorylation in CENP-E in regulating this function is being explored.

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CAMPUS MAP

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