ABSTRACTS

CSIR-Central Drug Research Institute

SBC(I)2026

95th ANNUAL MEETING & CONFERENCE OF THE SOCIETY OF BIOLOGICAL CHEMISTS (INDIA)

On

"Advancing Biochemistry and Translational Research To Address Evolving Challenges in Healthcare"

Jointly organized by CSIR-CDRI and SBC(I)

October 28-30, 2026





CSIR-Central Drug Research Institute, Lucknow

सीएसआईआर - राष्ट्रीय रासायनिक प्रयोगशाला, पुणे
CSIR - NATIONAL CHEMICAL LABORATORY, PUNE

Catalysing Innovation

The CSIR - NCL founded in the year 1950 has contributed significantly to the growth and development of the Chemical industry in India. It has partnered research with some of the largest companies in the world. Many of the processes and products that have come out of CSIR-NCL have been successfully commercialized by the industry for domestic consumption and exports.

CSIR-NCL serves sectors such as

- **Advanced Materials**
- **Clean Energy & Environment**
- **Sustainable Chemical Industry**
- **Drugs & Pharmaceuticals**
- **Chemical & Polymer Engineering**

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The roadmap aims to leverage the laboratory's scientific excellence and passion for translation along with key stakeholder connects to develop technologies for public, private, societal and strategic goods.



Central Analytical Facility (CAF)

A sophisticated analytical facility that hosts an array of state-of-the-art analytical equipment. It is dedicated to providing high-quality research and technical services, along with expertise and guidance to its users



Microscopes
Confocal, AFM, Fluorescence SEM, ESEM, FESEM, TEM, EDX, HRTEM

Thermal Analyzers
TGA, DTA, DCS, DMA, TMA, STA, SDT

Chromatography Equipment
GC, GC-MS, LC-MS, MS-TOF, MALDI-TOF-MS, GPC, HTGPC, HDMS, FPLC, HRMS

BET and magnetic measurement facility
VSM, SQUID, PPMS

Biochemical Characterization
Genetic analyzer, microinjection system, SPR, FPLC

Spectrometers
UV-Vis, IR-NIR, Time-Resolved IR, Raman, Fluorescence, CD, XPS (ESCA)

X-ray Facility
Variable temperature powder and single crystal XRD, XRF, SAXS, WAXD

NMR
200 MHz (H, C), 300 MHz (Solid State-Multinuclear), 400 MHz (Solution-Multinuclear), 500.13 MHz (Solution & Solid State - Multinuclear)

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Message
President, SBC (I)



The Society of Biological Chemists (India), popularly known as **SBC(I)**, was founded in 1930, with its headquarters at the Indian Institute of Science (IISc), Bangalore. Over the years, SBC(I) has played an important role in the growth of biological sciences in India. There have been three phases of growth of SBC(I): First, it started as a small society with around 40 members. Since then, the growth of SBC(I) has been dramatic. Second, SBC(I) has played national roles by supporting the establishment of laboratories and associating with CSIR in publishing the Indian Journal of Biochemistry and Biophysics (IJBB). Third, SBC(I) has participated in setting up and is part of the current FAOBMB organization. In addition, IUBMB coordinates with INSA and SBC(I) is the official scientific society.

One of the major activities of the Society is holding symposia and annual meetings. The 2024 meeting was held at M.S. University of Baroda, and last year, the University of Hyderabad organized the meeting.

Another activity of the annual meeting is to recognize scientists for their work. This year, we are happy that four scientists will be recognized in distinct categories. One award needs a special mention as it will be given for the first time. This award is in the name of Dr. Kamala Sohonie, who was one of the earliest Indian women scientists to earn a PhD for her research in biochemistry. Importantly, she opened the door for women to enter and study at IISc, Bangalore. We need to acknowledge the efforts of Prof. Hema Balaram and Dr. Saman Habib in supporting this initiative.

2030 is the centenary year of SBC(I), and we plan to host the FAOBMB Congress at IISc. Thus, we need to expand our base and reinvigorate our society. It is important to restart several dormant SBC chapters with younger members taking the lead. Some progress has been made, but more effort is required.

In addition, I request you to please read the latest SBC(I) newsletter, which has several write-ups for senior faculty who are part of the growth of SBC(I). There are some write-ups by students on their research. I will request students, especially poster awardees, to submit short write-ups on their work by email to the SBC office (sbcihq@gmail.com), which may be selected for the next newsletter. All SBC(I) life members are encouraged to send short write ups and suggestions to make the Newsletter more attractive and reader friendly!

Finally, we are delighted that CDRI, Lucknow, will be hosting the annual meeting this year. Saman, Ravi and their team have worked hard to draw up a well-balanced program on a wide array of research in biological chemistry and from various parts of India. On behalf of the entire SBC(I) team, I thank and wish them a great success and am sure that the meeting will be enriching for all.

One last word for the student participants in this meeting. I urge you all to make full use of this meeting, listen to talks, interact with speakers, present your work and ask questions. Certainly, you must have fun but have learning as a priority.

Dipankar Nandi
President, SBC (I)

Message
Director, CSIR-CDRI



It is a matter of great pride for CSIR–Central Drug Research Institute (CSIR-CDRI), Lucknow, to host the 95th Annual Meeting of the Society of Biological Chemists (India) [SBC(I)].

The objectives of SBC(I) are to promote research and collaboration in biochemistry and allied fields in India. Established in 1930, the organization provides scientists with opportunities to present their research and engage in discussion through its publications and annual meetings.

I am confident that this meeting will be a scientific feast, given the number of distinguished scientists, academicians, and young researchers who are attending. It will serve as a platform to exchange ideas, explore emerging frontiers, and forge meaningful collaborations. Such interactions are essential to strengthening the scientific ecosystem and translating knowledge into solutions for societal well-being.

I extend my sincere appreciation to SBC(I), the organising committee and all those who have contributed to making this event possible. CSIR and SBC(I) have had a long history of association and hosting the 95th Annual meeting cements the rich legacy.

I warmly welcome all delegates to CSIR-CDRI and the historic city of Lucknow. I wish the 95th Annual Meeting of SBC(I) great success and hope that its deliberations inspire new ideas, lasting collaborations, and meaningful scientific breakthroughs.

Radha Rangarajan
Director, CSIR-CDRI, Lucknow

Foreword

Organising Secretary, 95th SBC (I) Meeting & Conference



It is our privilege and immense pleasure to welcome you to the 95th Annual Meeting and Conference of the Society of Biological Chemists (India), hosted at *CSIR-Central Drug Research Institute*, Lucknow, from October 28–30, 2026.

For nearly a century, the SBC(I) conference has served as the premier forum for charting the frontiers of Biological Chemistry research and Molecular Biosciences. This year's milestone edition convenes over 500 delegates from across the Nation, bringing together leading investigators, clinicians, postdoctoral fellows, and young scholars. Under the overarching theme of *"Advancing Biochemistry and Translational Research to Address Evolving Healthcare Challenges,"* the scientific program features comprehensive deliberations spanning Structural biology, Drug discovery, AI-ML in therapeutics, Immunobiology, Metabolism, RNA biology, Infection biology and other allied exciting areas.

As Biomedical Research stands at an unprecedented intersection of computational power and molecular precision, this gathering provides an invaluable platform to foster multidisciplinary collaborations, ignite new ideas, and translate fundamental biochemical discoveries into tangible healthcare solutions.

We extend a warm welcome to all participants to CSIR-CDRI and to the historic city of Lucknow, wishing you an intellectually stimulating and deeply engaging conference.

Organizing Secretary

Ravishankar Ramachandran

Co-organizing Secretaries

Saman Habib

Sabyasachi Sanyal
Biochemistry and Structural Biology Division
CSIR-Central Drug Research Institute, Lucknow

We are grateful to the Conference Sponsors



Local Organising Committee

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and team

Scientific Programme

DAY 1, Oct 28

Session 1 Venue: Main auditorium	
8.30 am – 9.30 am	Registration
9.30 am-9.35 am	Welcome by Director, CSIR-CDRI
9.35 am – 9.55 am	Presidential Address
9.55 am- 10.40 am	Plenary Lecture: Raghavan Varadarajan Design of efficacious vaccines against respiratory viruses
10.40 am-11.00 am	*Tea*
11.00 am – 11.30 am	Dr. Kamala Sohonie Memorial Lecture Award: Sandhya S. Visweswariah Fundamental 3Gs: Gut reactions, gut instincts and cGMP
11.30 am – 12.00 pm	Prof. I. S. Bhatia Award Lecture: Kaustuv Sanyal Emergence of anti-fungal drug resistance: Novel strategies adopted by *Candida auris*
12.00 pm – 12.30 pm	Sanjay Singh (ImmunoScript Life Science)** The mRNA vaccine revolution: Core principles, safety, and regulatory pathways of platform technologies
12.30-1.30 pm	*Lunch*

Session 2A Cancer Biology Venue: Main auditorium Chairpersons: Dipankar Nandi & Saman Habib		
1.30- 1.55 pm	Shilpak Chatterjee, CSIR-IICB	S1P-S1PR1 axis drives $CD8^+$ T Cell dysfunction in the tumor microenvironment
1.55-2.20 pm	Sorab Dalal, ACTREC	Iron homeostasis, tumour progression, and therapy resistance
2.20-2.45 pm	Shaida Andrabi, Kashmir Univ	FAK and PCTAIRE promote resistance against anticancer agents in ovarian cancer
2.45-3.10 pm	Dipak Datta, CSIR-CDRI	CXCR4 in cancer metastasis: Beyond GCPR signaling

Session 2B Applied Structural Biology & Drug Discovery Venue: Hall 3 Chairpersons: Vivek Natarajan & R. Ravishankar		
1.30- 1.55 pm	Manidipa Banerjee, IIT-Delhi	Therapeutic and preventive strategies against arboviruses
1.55-2.20 pm	Deepti Jain, RCB	From inhibition to initiation: Regulation of late flagellar gene expression in *Pseudomonas aeruginosa*
2.20-2.45 pm	Saikrishnan Kayarat, IISER-Pune	Mode of substrate binding by the SARS-CoV-2 NIRAN domain and the mechanism of modulation of its activities during RNA capping
2.45-3.10 pm	Mahavir Singh, IISc	Mechanisms of RNP assembly and toxin control in Type III toxin–antitoxin systems

Session 2C Metabolism and Lifestyle Diseases Venue: Hall 2 Chairpersons: Madhu Dikshit & Ravi Manjithaya		
1.30- 1.55 pm	Nikhil Gandasi, IISc	Understanding targets at single-islet-cells for anti-diabetic treatment
1.55-2.20 pm	Naresh C Bal, KIIT	Targeting skeletal muscle to treat metabolic diseases: An exercise-mimetics approach
2.20-2.45 pm	Partha Chakrabarti, JCMLRI-Kolkata	Complement Factor D/Adipsin is a Novel Hepatic Glucose Effector
2.45-3.10 pm	Rohit Anthony Sinha, SGPGI	Hormonal therapy of MASH: An emerging hepato - endocrine disorder

3:10 pm – 3:30 pm: *Tea Break*

Session 3A Immunobiology Venue: Main auditorium Chairpersons: Manidipa Banerjee & Monika Sachdev		
3.30-3.55 pm	Nimesh Gupta, BRIC - NII	The T cell blueprint of protective immunity : Lessons from human immunology
3.55-4.20 pm	Imroze Khan - Ashoka Univ.	Mutation load, pathogen growth and virulence dynamics drive immune adaptations against coinfections
4.20-4.45 pm	Karthika Rajeeve, BRIC-RGCB	Pathogen associated neutrophils shapes an immune-silent milieu
4.45-5.10 pm	Tripti Shrivastava, BRIC-THSTI	Translating virus biology from structural transition to transient conformational changes: key to vaccine design

Session 3B Bone and Reproductive Biology Venue: Hall 2 Chairpersons: Sorab Dalal & Atul Goel		
3.30-3.55 pm	Rupesh Srivastava, AIIMS-New Delhi	Delineating the autoimmune nature of inflammatory bone loss in post-menopausal osteoporosis
3.55-4.20 pm	Aritra Chatterjee, IIT - Guwahati	Multiscale structure –property relationships between knee joint function and tissue mechanics
4.20-4.45 pm	Geetanjali Sachdeva, ICMR-NIRRCH, Mumbai	Novel insights into the pathophysiology of endometriosis
4.45-5.10 pm	Ashish K. Tripathi, IIT - Bhilai	Beyond hematological benefits: Impact of hydroxyurea on bone health in Sickle Cell Disease

Session 3C Biochemistry of Rare Diseases Venue: Hall 3 Chairpersons: Deepti Jain & Akhilesh Tamrakar		
3.30-3.55 pm	Vivek Natarajan, CSIR-IGIB	Epigenetics of cellular identity: How melanocyte cell fates are specified, maintained, and lost
3.55-4.20 pm	Ravi Manjithaya, JNCASR	How to build and move autophagosomes
4.20-4.45 pm	Sandeep Eswarapa, IISc	Forbidden translation: Protein synthesis from the 'untranslated' regions of mammalian mRNAs
4.45-5.10 pm	Anshika Srivastava, SGPGI	PRUNE1 splice variant mediated AURKA upregulation dysregulates RNA metabolism as a novel pathogenic mechanism in NMIHBA

5:10 pm – 7:15 pm	**Poster Session**
5:15 pm – 6:15 pm	**EC Meeting**
7:15 pm – 8:15 pm	**Cultural Program**
8:15 pm Onwards	***Dinner***

DAY 2, Oct 29

Session 4 Venue: Main auditorium	
9:30 am– 10:00 am	Sreenivasaya Memorial Award: Sunil Laxman The cellular metabolic economy
10:00 am– 10:30 am	Prof. A. N. Bhaduri Memorial Lecture Award: Satish Mishra Molecular determinants of *Plasmodium* development and transmission

10.30 am -10.45 am	*Tech Talk:* Subir Biswas, Cytiva Deciphering Host-Parasite Molecular Interactions Using Label -Free SPR and Advanced Protein Analytics
10.45 am – 11.00 am	*Tea Break*

Session 5A **The Microbiome and its Interactions** **Venue: Hall 2** **Chairpersons: Radha Rangarajan & Partha Chakrbarti**		
11.00-11.25 am	Souvik Mukherjee, NIBMG Kalyani	Metagenome Wide Association Studi es (MWAS) on vaginal and oral microbiome in preterm birth and infant gut microbiome in growth failure: Precision microbiomics in developing the BHARAT webtool for rapid analysis of microbial WGS data
11.25-11.50 am	Amit Lahiri, CSIR-CDRI	Mitochondrial citrate exporter regulates dysbiosis and stress response outcome in Ulcerative colitis
11.50-12.15 pm	Vivek Rao, CSIR-IGIB	Metabolism as an immune strategy in fighting TB
12.15-12.40 pm	Prasenjit Bhaumik, IIT - B	Molecular insights of plasmepsins for understa nding their inactivation mechanism and developing antimalarial inhibitors
12.40-1.05 pm	Prabhakar Tiwari, AIIMS-New Delhi	Gut microbiome and host metabolism: Metagenomic and metabolomic findings in Alzheimer's disease

Session 5B **Fungal and Parasite Biochemistry** **Venue: Hall 3** **Chairpersons: Krishnapal Karmodiya & Niti Kumar**		
11.00-11.25 am	Anindita Ukil, Univ of Calcutta	Silent sabotage: How *Leishmania* reprograms host immune metabolism for its sustained survival
11.25-11.50 am	Nishith Gupta, BITS - Hyd	Optogenetic illumination of cyclic nucleotides signaling in the intracellular pathogen *Toxoplasma gondii*
11.50-12.15 pm	Sneha Sudha Komath, JNU	The catalytic subunit of GPI-N-acetylglucosaminyltransferase which initiates GPI biosynthesis in Candida albicans also transcriptionally regulates the enzyme

12.15-12.40 pm	Srimonti Sarkar, Bose Instt	Trafficking Without a Golgi: Presence of a Divergent TRAPP Complex in *Giardia lamblia*

Session 5C **Cell and Developmental Biology** **Venue: Main auditorium** **Chairpersons: Nikhil Gandasi & JV Pratap**		
11.00-11.25 am	Saravanan Matheswaran, IIT-K	SWR1 chromatin remodeling regulates development, effector expression, and virulence in *Ustilago maydis*
11.25-11.50 am	Devanjan Sinha, BHU	Beyond Complex I: Mitochondrial electron flux plasticity in tumour cells
11.50-12.15 pm	Parul Mishra, UoHyd	Rewriting protein fate: The hidden regulatory language of Ubiquitin
12.15-12.40 pm	Sujit Kumar Bhutia, NIT Rourkela	Distinct molecular signaling pathways governing mitochondrial fission and their roles in mitochondrial biogenesis and mitophagy
12.40-1.05 pm	Abdur Rahaman, NISER-Bhubaneswar	A novel endocytic route delivers cardiolipin from plasma membrane to nuclear envelope: A role in nuclear expansion

Session 6A **Plant Biology and Defences 1** **Venue: Hall 2** **Chairpersons: Satish Mishra & Vidhu Sane**		
2.00- 2.25 pm	Gopalji Jha, BRIC-NIPGR	Molecular insights into fungal-eating properties of *Burkholderia* bacteria and utilizing them for the mitigation of fungal infections
2.25-2.50 pm	Jitendra Thakur, ICGEB	A molecular switch for survival: How mediator subunit MED14 couples cell-cycle control to DNA damage response
2.50-3.15 pm	Samir Sawant, CSIR - NBRI	Epigenetic landscape regulating fibre development in cotton
3.15-3.40 pm	Madhumita Barooah, Assam Agricultural Univ., Jorhat	Retention versus exclusion: Convergent and divergent mechanisms of Fe and Al toxicity tolerance in Assam's rice landraces

Session 6B Neurobiology and Aging Venue: Main auditorium Chairpersons: Naresh Bal & PN Yadav		
2.00- 2.25 pm	Anirban Basu, BRIC - NBRC	Neuroimmune circuits in brain health and disease:From neurotropic viral Infections to gut brain crosstalk
2.25-2.50 pm	Geetanjali Chawla, Shiv Nadar Univ (IoE)	MicroRNA pathways in aging and dietary restriction
2.50-3.15 pm	Sumantra Chattarji, CHINTA, TCG CREST	Tiptoeing into translational neuroscience in India: a small example
3.15-3.40 pm	Nihar Ranjan Jana, IIT-Khrg	Repurposing Ube3a imprinting biology for a neurodegenerative target

Session 6C Clinical Biochemistry, Biomaterials and Tissue Engineering Venue: Hall 3 Chairpersons: Siddharth Jhunjhunwala & Manish Chaurasia		
2.00- 2.25 pm	Biman B. Mandal IIT - Guwahati	Bioengineered *in vitro* liver models for high throughput drug screening applications
2.25-2.50 pm	Indranil Bannerji, IIT - Jodhpur	NIR-responsive multifunctional phototherapeutics
2.50-3.15 pm	V Padmanaban, CMC Vellore	Proteogenomic analysis identifies type 2 diabetes - influenced plasma proteins causally associated with microvascular and macrovascular complications of diabetes mellitus
3.15-3.40 pm	Satyaprakash Pandey, TIGS, Bangalore	Cervical cancer screening using HPV genotyping panel

Session 7A Flash Talks (Infectious diseases) Venue: Hall 2 *Coordinator: Niti Kumar*	Session 7B Flash Talks (Non-communicable diseases) Venue: Main auditorium *Coordinator: Dipak Datta*	Session 7C Flash Talks (Structural, computational and molecular biology) Venue: Hall 3 *Coordinator: Tejender Thakur*
3.55-5.20 pm	3.55-5.20 pm	3.55-5.20 pm
Time: 7 (5+2) min each	Time: 7 (5+2) min each	Time: 7 (5+2) min each
Presenters: Arunima Biswas Priyanka C. Yadav	Presenters: Arya Devi K P Shashi K. Gupta	Presenters: Imran Ansari Yogananda S M

Amanullah Sayeed	Bibhukalyan Mohapatra	Alok Kumar Mishra
Krishan Kumar	Udita Jindal	Sandipan Mukherjee
Sainath Polepalli,	Nitish Kumar Bhol	Samriddhi Thakur
Gurvinder Kaur	Priya Saha	Shubham Krushna Talware
Kanchan Bhardwaj	Dipanjana Ghosh	Shalini Singh
Simmi Pradhan	Debasree Dutta	Sudarshan Gadadhar
Deneshraj Srinivasan	Syed Musthapa Meeran	Abhijeet Mishra
Tashi Palmo	Shagun	Abdul Basit Khan
Manisha Ghosh	Bhupesh Mehta	Atul Kumar

5.25 pm – 7:15 pm	**Poster Session**
7.15 pm-8.00 pm	**SBC General Body Meeting**
8.00 pm Onwards	**Dinner**

DAY 3, Oct 30

Session 8 **Venue : Main auditorium**	
9:30 am – 10:10 am	Plenary Lecture : Soniya Nityanand Beyond regeneration/repair: Emerging role of stem cells in disease pathogenesis
10.10 am – 10.20 am	**Tech Talk: HiMedia**
10.20 am – 10.30 am	**Tech talk:Leica**
10.30 am-10.40 am	**Tech talk: Nucleome Informatics**
10.40 am-11.00 am	***Tea Break***

Session 9A **Biotherapeutics** **Venue: Hall 2** **Chairpersons: Dipak Datta & PK Singh**		
11.00-11.25 am	Siddharth Jhunjhunwala, IISc	Neutrophils drive immunopathology in chronic inflammatory states
11.25-11.50	Ashis Kumar Mukherjee, IASST-Guwahati	Snake venom Nerve Growth Factor-derived peptides impede the progression of oxidative stress-induced neurodegenerative diseases
11.50-12.15 pm	Bhavana Muralidharan, inStem, Bangalore	Chromatinopathies, ciliopathies, and brain malformations: From genetic mechanisms to disease models
12.15-12.40 pm	Suktilang Majaw, NEHU	From natural products to molecular targets: Linking Metabolic regulation to cancer cell survival
12.40-12.55	Durgesh Kumar, Immunoscript Life Sciences	Self-Amplifying RNA Vaccines: Harnessing Durable and Multifunctional T-Cell Immunity for Next-Generation Therapeutics

Session 9B Structural Biochemistry Venue: Hall 3 Chairpersons: Aravind Penmatsa & Sohail Akhtar		
11.00-11.25 am	Tanweer Hussain, IISc	Unique strategy and structural mimicry by viral mRNA help hijack host ribosomes
11.25-11.50	Prem Kaushal, BRIC-RCB	Cryo-EM studies of ribosome assembly in mycobacteria
11.50-12.15 pm	Mahipal Ganji, IISc	Biochemistry in singulo: A single -molecule view of bacterial genome organization
12.15-12.40 pm	Sujata Sharma, AIIMS-New Delhi	From mother's milk to molecular medicine: Lactoferrin from structure to patient care

Session 9C Viruses and Phage Therapy Venue: Hall 3 Chairpersons: Jayanta Sarkar & Meetali Singh		
11.00-11.25 am	Vikas Jain, Krea Univ.	Antiphage defense in mycobacteria through a phage-derived protein domain
11.25-11.50 am	Rajesh Ringe, NIPER - Mohali	Escape from neutralization: The role of differential sugarcoating of SARS-CoV-2 Spike protein
11.50-12.15 pm	Syamala Maitreyi Rajala, JNU	Recombinant measles virus with a pro-apoptotic gene: A potential therapeutic approach to target breast cancer
12.15-12.40 pm	Sutharsan Govindarajan, SRM Univ., Guntur	From mechanism to medicine: Translating Jumbo Phage biology into clinical potential against drug resistant pathogens

12:45 pm – 2:15 pm: ***Poster Session and Lunch***

Session 10A Parasite Biology Venue: Hall 2 Chairpersons: Tripti Shrivastava & Arun K. Haldar		
2:15-2:40 pm	Meetali Singh, IISc	Small RNA-mediated epigenetic regulation of pathogenesis and host-parasite interaction
2:40-3:05 pm	Budhaditya Mukherjee, IIT-Khrgpr	From dermal to visceral adaptation: Genome plasticity drives GP63 paralogue specialization in *Leishmania*
3:05-3:30 pm	Krishnapal Karmodiya, IISER-Pune	Non-coding RNAs in regulating gene expression and chromatin dynamics in *P. falciparum*
3:30-3.55 pm	Amit Prasad, IIT-Mandi	A fight for eradication of neurocysticercosis against all the odds: Immunology, inflammation, and epileptogenesis of *Taenia solium*

Session 10B RNA Biology in the Origin and Evolution of Life Venue: Hall 3 Chairpersons: Hamim Zafar & Arunava Dasgupta		
2:15-2:40 pm	Shovamayee Maharana , IISc	Role of RNA metabolism in controlling RNA -RBP condensate dynamics in ageing and inflammation
2:40-3:05 pm	Sudha Rajamani, IISER - Pune	The emergence and evolution of biomolecules on the early Earth: Implication for life's origin
3:05-3:30 pm	Soma Banerjee, IPGMER - Kolkata	The circular RNA–Stemness circuit: A hidden driver of Sorafenib resistance in hepatocellular carcinoma
3:30-3.55 pm	Amanjot Singh, MAHE	RNA-dependent regulation of ribonucleoprotein complex dynamics by an E3 Ligase

Session 10C Bacterial Infections and AMR Venue: Main auditorium Chairpersons: Suman K. Dhar & YK Manju		
2:15-2:40 pm	Vinay Nandicoori, CSIR-CCMB	Tuberculosis: From molecular mechanisms to genomic surveillance
2:40-3:05 pm	Raju Mukherjee, IISER - Tirupati	Induced innate immunity in *Mycobacterium* against mycophages
3:05-3:30 pm	Ashwani Kumar, CSIR - IMTech	Mycobacterial Biofilms; Another armor is rise of a superbug
3:30-3.55 pm	Tushar Kanti Beuria, ILS - Bhubaneshwar	Inhibition of efflux pumps: Making resistant bacteria susceptible to existing antibiotics

3.55 pm – 4:10 pm: *Tea Break*

Session 11A Towards Precision Medicine/Genomics and Metagenomics Venue: Hall 3 Chairpersons: Sudha Rajamani & Shakil Ahmad		
4:10-4.35 pm	Sauvik Maiti, CSIR-IGIB	Indigenous CRISPR-Cas9 Tools: Advancing Gene Therapy Through Precision
4:35-5:00 pm	Vinod Scaria, Karkinos Healthcare	Personal genomes for precision medicine
5:00-5:25 pm	Shankar Manoharan, IIT - Jodhpur	Genetic and physiological adaptations in *Klebsiella pneumoniae* customized for the bloodstream
5:25-5:50 pm	Ranjana Arya, JNU	Exploring pathomechanisms and potential therapeutic leads for rare diseases

Session 11B AI-ML in Biochemistry and Drug Discovery Venue: Hall 2 Chairpersons: Tanweer Hussain & MI Siddiqi		
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4:35-5:00 pm	Hamim Zafar, IIT-K	Computational analysis of single -cell and spatial omics datasets for elucidating cancer heterogeneity
5:00-5:25 pm	MS Madhusudhan, IIS ER-Pune	Reading Genomes with DNA motifs
5:25-5:50 pm	Kasturi Mitra, Ashoka Univ	Quantitative elucidation of mitochondrial structure - function heterogeneity to decipher specification of the potent mitochondria primed neoplastic stem cells and their therapeutic vulnerabilities

Session 11C Plant Biology and Defences 2 Venue: Main auditorium Chairpersons: Gopalji Jha & Samir Sawant		
4:10-4.35 pm	PK Singh, CSIR-NBRI	Engineering of a Bt protein for the development of pink bollworm-resistant transgenic cotton
4:35-5:00 pm	Hitendra Kumar Patel, CSIR-CCMB	Durable resistance to bacterial blight disease and development of super rice varieties
5:00-5:25 pm	Sridev Mohapatra., BITS - Hyd	Molecular mechanisms in plant- rhizobacterial interaction for abiotic stress tolerance
5:25-5:50 pm	T. Narender, CSIR-CDRI	Challenges in development of plant secondary metabolites as phytopharmaceuticals

5.50-6.20 pm	**Student Awards and Concluding Session**
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Plenary Lecture

Design of efficacious vaccines against respiratory viruses

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Viral acute lower respiratory infections directly or indirectly cause over a million deaths annually, with a substantially higher toll in pandemic years. A large fraction of these deaths occur in infants and the elderly in low and middle income countries. For most major respiratory viruses, vaccines either do not exist, are unaffordable, or have to be stored at ultralow temperatures. Enhancing vaccine stability is important for both vaccine efficacy and deployment. There have been recent, transformative advances in the area of protein structure prediction. However, even with state-of-the-art AI driven approaches, reliable prediction of stabilizing mutations for complex, viral surface proteins remains challenging. We have developed general methodology to rapidly isolate stabilized protein variants, including for metastable viral surface proteins. Our efforts to apply this to design and clinically test novel vaccines against important respiratory and other viruses will be discussed. An influenza vaccine formulation that we developed was shown to be safe in a human Australian Phase 1 trial, and clinical development in India is ongoing.

Dr. Kamala Sohonie Memorial Lecture Award

Fundamental 3Gs: Gut reactions, gut instincts and cGMP

Sandhya S. Visweswariah

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Cyclic AMP and cyclic GMP were the first second messengers discovered, and cAMP is used for signaling in all domains of life. Cyclic GMP, however, appears to play a role in cellular physiology predominantly in higher eukaryotes. I will speak on our research in understanding the role of cGMP in modulating mammalian gut function via a receptor guanylyl cyclase, GC-C. I will describe our efforts to understand the molecular basis of regulation of this receptor by its ligands, the consequences of its activation in the gut, and characterisation of human mutations in the receptor that cause severe familial and congenital diarrhoea. Finally, I will describe our recent observations on novel transgenic mice that we have generated to understand the physiology of human disease at the molecular level.

Prof. I. S. Bhatia Award Lecture

Emergence of anti-fungal drug resistance: Novel strategies adopted by *Candida auris*

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The fungal kingdom comprises a minimum of 2.5 million eukaryotic species. Fungi can adapt to various selection pressure by changing their karyotypes. The unusual karyotype plasticity of fungal pathogens plays a significant role in driving reproductive isolation and increased resistance to antifungal drugs. Candida auris, a World Health Organisation–listed critical priority fungal pathogen, causes frequent multidrug-resistant outbreaks worldwide. While point mutations underlying antifungal resistance are well characterised, the contribution of structural genomic variation to antifungal responses remains poorly defined. We integrate whole-genome sequencing, a genome-wide copy number variation (CNV) screen, electrophoretic karyotyping, and mutation-accumulation analyses to investigate the role of structural variation in antifungal susceptibility across a clinical cohort of C. auris isolates collected from Indian hospitals. We identify recurrent CNV hotspots, with segmental duplications representing a predominant mode of genome variation. Small duplications encompassing ERG11 arise at high frequency and frequently co-occur with resistance-associated ERG11 mutations, collectively enhancing azole resistance. In addition, large centromere-inclusive duplications of chromosome 1 generate supernumerary chromosomes, leading to paradoxical growth and reduced susceptibility to the echinocandin caspofungin. At the population level, these structural variants frequently arise alongside mutations in FKS1, suggesting coordinated genetic mechanisms underlying reduced drug susceptibility. Together, our findings establish segmental aneuploidy as a major, non-mutational driver of antifungal resistance, highlighting the need to consider structural genomic variation in both resistance surveillance and clinical susceptibility testing.

Invited Lecture

The mRNA vaccine revolution: Core principles, safety, and regulatory pathways of platform technologies

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Messenger RNA (mRNA) vaccine technology has transformed the landscape of vaccine development by enabling rapid, adaptable, and scalable approaches to disease prevention and therapeutic intervention. The success of mRNA vaccines during the COVID-19 pandemic has established nucleic acid-based platforms as a promising new generation of vaccine technologies. This talk will explore the fundamental principles of mRNA vaccine design, antigen expression, and immune activation, with particular emphasis on the evolution of vaccine platforms, clinical safety, and regulatory pathways.

The presentation will discuss the development of self-amplifying RNA (saRNA) technology as an extension of conventional mRNA platforms, highlighting its potential for dose efficiency and broad applicability. Findings from ImmunoScript Life Sciences' vaccine development programmes, including COVID-19, rabies, Nipah, and tuberculosis, will illustrate the versatility of this platform. Comparative preclinical studies have demonstrated that the saRNA platform can elicit immune responses comparable to those induced by conventional mRNA vaccines at substantially lower doses. In addition, findings from rabies vaccine studies highlight the potential of single-dose vaccination strategies and intradermal administration for optimizing immunogenicity and dose efficiency.

The talk will also address clinical safety considerations, regulatory pathways, and India's progress in developing indigenous mRNA vaccines, including the GEMCOVAC vaccine programme. Furthermore, it will examine key challenges associated with manufacturing scalability, thermostability, supply-chain resilience, and technology transfer, alongside emerging opportunities in infectious diseases and precision therapeutics.

Overall, the presentation will highlight the potential of mRNA and saRNA technologies as flexible, disease-agnostic platforms for the development of next-generation vaccines and therapeutics.

Invited Lecture

S1P-S1PR1 axis drives CD8⁺ T cell dysfunction in the tumor microenvironment

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Sphingosine-1-phosphate receptor 1 (S1PR1) signaling regulates diverse cellular processes and plays a pivotal role in T cell trafficking and differentiation. Recent studies indicate that S1PR1-mediated activation of JAK2/STAT3 signaling is essential for the accumulation of regulatory T cells (Tregs) at tumor sites. However, the precise role of the S1P-S1PR1 signaling cascade in shaping the functional outcomes of anti-tumor CD8⁺ T cells remains unclear. Here, we demonstrate that S1PR1 expression in CD8⁺ T cells is predominantly confined to a subset co-expressing multiple inhibitory receptors. Functionally, S1PR1-S1P signaling in CD8⁺ T cells induces endoplasmic reticulum (ER) stress, triggering PERK-mediated activation of CHOP. We further found that CHOP activation transcriptionally regulates MAP kinase kinase kinase (MAP3K) expression, which leads to the upregulation of MAP kinase cascades and subsequent activation of p38 MAPK signaling. Activation of p38 MAPK in CD8⁺ T cells results in apoptosis, mitochondrial dysfunction, and functional impairment. Our findings identify the S1PR1-S1P signaling axis as a key driver of CD8⁺ T cell dysfunction in tumors and suggest it as a potential target to enhance the efficacy of CD8⁺ T cell-based immunotherapies.

Invited Lecture

Iron homeostasis, tumor progression, and therapy resistance

Bhagyashree Choudhary, Prerana Uttankar, Bushra Khan, Nazia Chaudhary and Sorab N. Dalal

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A major focus of the laboratory is the identification of mechanisms underlying tumor progression and therapy resistance in colorectal cancer. I will focus on how iron homeostasis regulates invasion and migration. Over the course of this talk, I will describe our journey, from a story about how epithelial cells form adhesive structures to how Lipocalin2 (LCN2), a protein that regulates iron homeostasis, is elevated in colorectal cancer and promotes therapy resistance by inhibiting ferroptosis. We have demonstrated that LCN2 promotes invasion and migration by preventing actin glutathionylation and by promoting focal adhesion formation. The first mechanism depends on LCN2's ability to bind iron, while the second is independent of iron binding and focuses on LCN2's ability to stimulate c-Src activity. Finally, I will present some unpublished data that illustrate how this story, which began with the most basic of biological questions, has reached the point where we now have multiple options that can be exploited in the clinic.

Invited Lecture

FAK and PCTAIRE1 promote resistance and tumorigenesis against anti-cancer agents in ovarian cancer

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Using a high throughput screening strategy, we have previously screened a kinase library and identified several protein kinases that promote survival against anti-mitotic agents like polyoma virus small T antigen. Among them, FAK/PTK2, CDK16/PCTAIRE1 and PLK1 showed the strongest survival also against several anti-mitotic/anti-cancer agents including paclitaxel and nocodazole. Using several genetic, biochemical and proteomic approaches, we identified PCTAIRE1/CDK16 as a novel kinase that promotes resistance against anti-cancer agents. Interestingly, we showed that it as a downstream target of FAK/PTK2. Further experiments showed that these kinases (FAK and PCTAIRE1) are activated by netrin-1, an extracellular growth factor that promotes survival, and is overexpressed in several types of cancers. Our results showed that netrin-1 binds to cell surface receptors like UNC5B, which potentially recruits FAK/Src on the cytoplasmic side, and initiates a signaling cascade. Immunofluoresence results revealed that both FAK and CDK16 play an important role in the mitotic progression, and localize to the mitotic spindle. Overexpression of these kinases promoted survival of cancer cell lines against several anti-cancer agents while knockdown or inhibition made them sensitive to such agents. Inhibitors against these kinases are already in clinical trials and hold a lot of promise in the treatment of ovarian cancer. Interestingly, the expression levels of FAK/PTK2, PCTAIRE1/CDK16 and netrin-1 are also substantially elevated in ovarian cancer tumors, as compared to the normal tissues, at both mRNA and protein levels. These findings therefore underscore the significance of such mitotic kinases in tumorigenesis, and can be very useful in designing targeted strategies for the treatment of cancer and more importantly, overcoming resistance against anti-cancer agents.

Invited Lecture

CXCR4 in cancer metastasis: Beyond GCPR signaling

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Triple-negative breast cancer (TNBC) remains a major clinical challenge due to the absence of targeted therapies. We have uncovered a previously unrecognized, non-canonical (intracellular) function of the chemokine receptor CXCR4 that drives metastatic progression in TNBC through direct coupling with the ribosomal protein RPL35A. Integrative proteomic and transcriptomic analyses, reveal that CXCR4 overexpression selectively enhances protein-level signatures of ribosome biogenesis and translation, without corresponding transcriptional changes. Mechanistically, CXCR4 binds RPL35A via residues 66–71, stabilizing it and promoting its ribosomal association to sustain global translation. Disruption of this interaction by targeted mutagenesis, impairs protein synthesis, tumor cell invasiveness, and metastatic dissemination in vivo. Notably, high CXCR4–RPL35A co-expression in matched TNBC patient metastases correlates with elevated translational competence and poor clinical outcomes. Our findings identify an intracellular receptor–ribosome coupling mechanism that sustains translational output and metastatic competence, establishing the CXCR4–RPL35A axis as a therapeutically targetable vulnerability in TNBC.

Invited Lecture

Therapeutic and preventive strategies against arboviruses

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Arthropod-borne viruses or arboviruses cause significant morbidity and mortality among the global population, particularly in the African and South Asian regions. We are attempting to develop broadly applicable therapeutic and prophylactic strategies against the alphavirus family, which includes mammalian pathogens such as Chikungunya Virus. All alphaviruses produce a 6 kDa protein (6K) and its transframe variant (TF) during cellular infections, whose roles in host interaction is unknown; although it has been shown that loss of the 6K gene affects both virus assembly and propagation. Given the essentiality of 6K/TF in the virus life cycle, these can serve as druggable targets for repurposing or development of broad range antivirals. We show that both 6K and TF are virus-encoded membrane proteins or viroporins, which carry out membrane alteration/remodelling for facilitating virus assembly and egress. The 6K protein forms ion channels in membranes that can be blocked by amantadine, a generic inhibitor of other virally encoded, channel forming proteins. Inhibition of 6K channel activity appears to cause anomalies in virus structure. The translation of 6K from CHIKV genome is accompanied by ribosomal slippage leading to production of TF. While 6K has the propensity to localize in ER membranes, TF appears to localize on the cellular membrane and cause the punctation of Scribble, a cellular junction protein, which results in large-scale host membrane remodelling and propagation of CHIKV. Removal of TF from CHIKV results in an attenuated virus which shows reduced propagation, and can therefore be a vaccine candidate. The essential roles of 6K/TF in budding and egress of alphaviruses indicate that they may be excellent targets for development of broad-spectrum strategies against alphaviruses

Invited Lecture

From inhibition to initiation: Regulation of late flagellar gene expression in *Pseudomonas aeruginosa*

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Pseudomonas aeruginosa is a gram-negative opportunistic pathogen that possesses a single polar flagellum. The flagellum is important for virulence, motility, and biofilm formation. The group 3 sigma factor ^{28} (FliA), plays a central role in regulating the expression of late flagellar genes, while its activity is inhibited by its cognate anti-sigma factor FlgM. The X-ray crystal structure of σ^{28}-FlgM complex reveals that FlgM binds wraps around σ^{28} in a manner that blocks its association with promoter DNA and RNA polymerase inhibiting transcription initiation. Additionally, a single particle cryo-EM structure of the σ^{28}-RNA polymerase-promoter complex discloses molecular basis of promoter recognition and transcription initiation by σ^{28}. Structure guided mutagenesis supports the importance of key interface residues in maintaining motility, flagellar phenotypes and transcription initiation. Together these structures divulge new insights into transcription of late flagellar genes.

Invited Lecture

Mode of substrate binding by the SARS-CoV-2 NiRAN domain and the mechanism of modulation of its activities during RNA capping

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The RNA dependent RNA polymerase of Nidovirus, to which SARS CoV-2 belongs, are unique in having a fused N-terminal pseudokinase like domain called NiRAN (Nidovirus RdRP Associated Nucleotidyltransferase). This is a versatile enzyme capable of performing nucleotide transfer reactions with a variety of substrates and is essential for catalyzing the first two steps of 5'-end RNA capping. It covalently bonds nsp9 to the 5'-pppA-end of the genome (RNAylation). Subsequently, nsp9 is delinked from the RNA by GDP-polyribonucleotidyltransferase reaction (deRNAylation), forming capped GpppA-RNA. Additionally, NiRAN NMPylates nsp9 using NTP and deNMPylates nsp9 to form GpppN. Based on cryo-EM structures from different laboratories, it is observed that the nucleotides can sit in three different poses inside the NiRAN domain – base-in, base-out and base-up. However, the precise pose adopted by the nucleotide for the different enzymatic reactions carried out by NiRAN is unclear. Our study aims to clarify the pose adopted by a nucleotide during different reactions carried out by NiRAN. We also aim to understand how the essential step of RNAylation and deRNAylation that leads to the viral genome capping occur despite NMPylation being kinetically more efficient. We have used a combination of structure-guided mutagenesis and biochemical assays using the reconstituted replication machinery of SARS-CoV-2 in vitro. Our study reveals that the NiRAN-bound NTP's orientation during NMPylation is in the base-out pose, similar to that seen in the evolutionarily related pseudokinase Selenoprotein-O. However, during RNAylation the RNA's 5'-pppA-end is in the base-up pose. In addition, we also identify the role of a base-up residue in the exclusive selection of 5'-adenine-containing RNA. We find that GpppN can also be a substrate for NMPylation, but not its methylated form. nsp13 NTPase flips NiRAN's preference for NMPylation over RNAylation, while RdRp's substrate engagement diminishes RNAylation. Our study reveals mechanistic details of NiRAN's substrate binding during different reactions carried out by the enzyme, with implications to therapeutic. The study also suggests how the activities of RNAylation, NMPylation, deRNAylation and deNMPylation are orchestrated leading to capping of the viral genomic RNA.

Invited Lecture

Mechanisms of RNP assembly and toxin control in type III toxin–antitoxin systems

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Toxin-antitoxin (TA) systems are genetic modules in bacteria that play roles in plasmid maintenance, persister cell formation, drug tolerance, and phage resistance. TA modules contain a toxin gene and an antitoxin gene as an operon under the same promoter/operator control. The toxin is toxic for bacteria in its free form. Therefore, it is kept inactive by forming a complex with antitoxin. Based on the nature of the toxin's activity and the mechanism of the toxin's inactivation by antitoxin, TA systems have been classified into eight types. Type III TA complex consists of a protein toxin and an RNA antitoxin. Structures of type III TA complexes have revealed a unique pseudoknot structure at the core of antitoxin RNA that is essential for toxin inhibition by forming a closed TA assembly. In this talk, I will present recent results from our laboratory on understanding the role of antitoxin RNA pseudoknot structure in the formation of closed TA RNP assembly and control of toxin's activity. Understanding the TA complex assembly is important, as specific disruption of TA complexes, thereby releasing free toxins in pathogenic bacteria, has been envisioned as a potential antibacterial strategy.

Invited Lecture

Understanding targets at single-islet-cells for anti-diabetic treatment

Nikhil R Gandasi

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Type 2 diabetes (T2D) arises fundamentally from a failure of pancreatic β-cells to secrete adequate insulin in response to glucose, yet the molecular events underlying this failure remain incompletely resolved at the level of individual cells and secretory vesicles. We have used high-resolution single-cell and single-vesicle imaging approaches, including TIRF microscopy and single-cell amperometry to dissect the exocytotic machinery of human and mouse β-cells with unprecedented spatial and temporal precision. These studies show that glucose-dependent docking of insulin granules limits secretion, revealing a defect in exocytosis that is a feature of type 2 diabetic β-cells. Complementary work at the single-fusion-pore level demonstrates that impaired pore expansion restricts insulin exocytosis in human type 2 diabetes, pointing to fusion pore dynamics as a discrete therapeutic target. Beyond exocytosis itself, the lab has characterized how dynamic GLUT transporter trafficking at elevated glucose enhances insulin secretion, with its dysregulation contributing to reduced secretion in T2D, and how islet amyloid polypeptide aggregation contributes to β-cell loss and diminished insulin output. Additional avenues of investigation include the role of multivesicular bodies and exosome release in islet cell signalling offering distinct nodes for pharmacological intervention.

Together, these findings position single-islet-cell and single-vesicle analyses as powerful platforms for identifying discrete molecular checkpoints in granule docking and priming, fusion pore regulation, glucose transporter cycling, vesicular trafficking, and receptor-mediated modulation that are selectively disrupted in T2D. By resolving these events at sub-cellular resolution in human islets, this body of work provides a mechanistic foundation for designing anti-diabetic therapies that restore insulin secretory capacity at its most fundamental level, the individual secretory event.

Invited Lecture

Targeting skeletal muscle to treat metabolic diseases: An exercise-mimetics approach

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Skeletal muscle is the largest organ of the body and contributes to ~40-50% of total energy expenditure of the mammalian body. Discovery of mechanisms nonshivering thermogenesis in the skeletal muscle demonstrated that function of sarcoendoplasmic reticulum calcium ATPase (SERCA) can be recruited by a small interacting protein called sarcolipin (SLN) in a futile manner to cause energy dissipation. We have explored the possibility of enhance SLN action on SERCA to boost energy expenditure. Based on previous literature we have taken capsaicin, an ingredient of chili, as the lead molecular scaffold to stabilize the SERCA-SLN complex. In vitro and in silico studies showed that capsaicin can stabilize SLN binding to SERCA. We applied chemical biology idea to design 11 analogs to identify the ones with lowered cytotoxicity and improved ability to enhance SERCA-mediated ATP hydrolysis. Then we identified two analogs (A8 and A10) with improved ability to increase glucose uptake into the insulin resistance muscle cells. Next we analyzed if A8 and A10 (named DiaSpiceRx) administration in mice skeletal muscle can counter chemical induced diabetes. Intramuscular injection of DiaSpiceRx showed enhanced substrate utilization in the muscle leading to reduction in diabetic phenotype. This is the first study demonstrating muscle as a targetable organ countering metabolic diseases mimicking the beneficial effects of exercise.

Invited Lecture

Complement factor D/Adipsin is a novel hepatic glucose effector

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Complement factor D, also known as adipsin, is produced by adipose tissue and the liver, which links metabolic regulation with innate immunity. Despite its established systemic functions, the regulation of hepatic adipsin expression and its contribution to metabolic disease remain poorly defined. Here, we show that hepatic adipsin protein abundance is markedly increased in individuals with type 2 diabetes (T2D), and positively correlates with glycated hemoglobin, despite unchanged mRNA expression. Concordantly, hepatic adipsin protein levels were elevated in multiple murine models of hyperglycemia, including type 1 diabetes (T1D), T2D, and following fasting–refeeding transitions. In cultured hepatocytes, glucose exposure induced a rapid, dose-dependent increase in adipsin protein without altering transcript abundance, demonstrating post-transcriptional regulation. Mechanistically, glucose stimulates adipsin translation via dephosphorylation of eukaryotic initiation factor 2α (eIF2α), and activation of the mammalian target of rapamycin, mediated by the 5′ untranslated region of adipsin mRNA. Functionally, hepatocyte-specific depletion of adipsin impaired postprandial glucose tolerance, with reduced glucose uptake and a marked downregulation of glucose transporter type 2 (GLUT2). Taken together, these findings identify hepatic adipsin as a glucose-responsive translational target that couples nutrient availability to metabolic adaptation, revealing a new layer of regulation with potential relevance to diabetes pathogenesis.

Invited Lecture

Hormonal therapy of MASH: An emerging hepato-endocrine disorder

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Metabolic dysfunction-associated steatohepatitis (MASH) results from dysregulated endocrine and metabolic signaling linking steatosis, cellular stress, inflammation, ductular remodeling, and fibrosis. Our work has explored hormonal pathways as therapeutic modulators of these interconnected processes, including thyroid hormone receptor-β signaling, vitamin D/VDR signaling, and emerging DHEA based therapies. Our lab investigates how hormonal interventions influence hepatic lipid metabolism, mitochondrial and cellular stress responses, inflammation, and fibrosis. This talk will integrate our experimental observations with emerging clinical evidence to discuss how liver-directed and pathway-selective hormonal therapies could reshape precision treatment of MASH.

Invited Lecture

The T Cell blueprint of protective immunity: Lessons from human immunology

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Optimal T-cell–B-cell crosstalk is central to the development of durable humoral immunity, but dysregulated interactions can also contribute to pathological antibody responses. Dengue provides a unique model to understand this balance, where humoral immunity can be both protective and associated with severe disease. In this talk, I will discuss our studies deciphering how T-cell responses shape germinal-centre (GC) and extrafollicular humoral immunity during dengue infection. In longitudinal patient cohorts, we identified a dominant peripheral IL-21$^+$ helper T-cell population that accumulates in severe dengue and promotes B-cell differentiation through IL-21-dependent mechanisms. Single-cell transcriptomic and T-cell receptor profiling revealed the dynamics, clonotypic architecture, and transcriptional features of this population and its relationship with conventional T follicular helper (Tfh) cells. I will further discuss our work on the metabolic regulation of Tfh differentiation and function, showing how glycolytic and lipid metabolic programs influence Tfh functional phenotype and their capacity to provide B-cell help. Together, these findings provide an integrated view of how T-cell states and metabolic programs regulate GC and extrafollicular humoral responses in dengue, with implications for understanding disease pathogenesis and designing vaccines that induce durable and protective immunity.

Invited Lecture

Mutation load, pathogen growth and virulence dynamics drive immune adaptations against coinfections

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Coinfection is widespread in nature and significantly impacts global health. However, the lack of a robust empirical framework has hindered our understanding of how coinfecting pathogens might influence host adaptation and the evolution of immunity. Our study, which utilised mathematical modelling and experimental evolution with an insect model, shows that the individual growth and virulence patterns of coinfecting pathogens, along with mutational load, critically regulate host adaptation to coinfections. Pathogens that grow rapidly, cause rapid mortality, and lead to germline mutations impede the host's ability to adapt successfully to coinfection. Furthermore, detailed comparative analyses of immune gene expression support our model predictions and observed phenotypic patterns, advancing our understanding of evolutionary patterns and processes in complex real-world coinfection scenarios.

Invited Lecture

Pathogen associated neutrophils shapes a immune-silent milieu

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Chlamydia trachomatis, a major cause of sexually transmitted infections, is an intracellular pathogen known for its asymptomatic mode of infections. Neutrophils, key immune cells fail to detect and clear Chlamydia. Surprisingly, on encountering Chlamydia, neutrophils turn paralysed and fail to respond to any external stimuli. Interestingly, regardless of the multiplicity of infection Chlamydia infects only a small subset of neutrophils. We employed single-cell sequencing to discover that Chlamydia-infected neutrophils segregate into distinct clusters. PI3 is significantly up-regulated protecting cells from cell death, entailing a long-living phenotype to the neutrophils. Further, we show that the Chlamydial deubiquitinase transcriptionally enhance PI3 expression. Chlamydial deubiquitinase deficient bacteria fail to induce this protective phenotype. This discovery is a paradigm shift in neutrophil biology as it reveals the existence of a sub-population of pathogen-associated neutrophils (PAN) with an unexpected role in nurturing Chlamydia thus supporting its replication and spread.

Invited Lecture

Translating virus biology from structural transition to transient conformational changes; key to vaccine design

Puneet Srivastav[1], Ankit Gupta1, Raja Mani Tripathi[2], Rakesh Chaudhary[1], Ravishankar Ramachandran[2] and Tripti Shrivastava[1*]

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Viral surface protein structural transitions are the prime events driving the infection and are the prime target for protective intervention development. Such intervention is often outpaced by the antigenic variability of continuously emerging and reemerging pathogens, causing compromised effectiveness. Influenza contineous to emerge and reemerge due to antigenic shift/drift and reassortment, with novel influenza viruses posing significant pandemic threst. Here, leveraging on the virus biology; transient "breathing" conformation of influenza hemagglutinin (HA), we developed a next-generation universal influenza vaccine candidate targeting conserved, structurally occluded epitopes. The selected conformation displays highly conserved epitopes, across thousands of circulating and historical influenza strains, including H1N1, H3N2, H5N1, and H7N9 subtypes, spanning approximately a century of influenza evolution. Immunization induced robust humoral and cellular responses with increased frequencies of IFN-γ-producing CD4+ and CD8+ T cells, provided complete protection against homologous and heterologous mouse-adapted challenge viruses, PR8 (H1N1) and X31 (H3N2). SAXS analyses demonstrated structural stability of the candidate in solution and its ability to bind occluded-epitope-directed antibodies. Serum-depletion studies further confirmed accessibility of the targeted conserved epitopes on diverse influenza subtypes. Collectively, these findings demonstrate a virus-biology-guided strategy for developing a broadly protective universal influenza vaccine with potential utility for pandemic preparedness.

Invited Lecture

Delineating the autoimmune nature of inflammatory bone loss in post-menopausal osteoporosis

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Post-menopausal osteoporosis (PMO) affects a major fraction of women, due to enhanced bone resorption, primarily triggered by lack of estrogen. Our scientific contributions have shifted the field of osteoporosis toward "Immunoporosis," highlighting the pivotal role of immune cell dysregulation in its pathophysiology. We have previously demonstrated that both the number and function of regulatory B cells (Bregs) is compromised in PMO (in pre-clinical model and clinics). Given the critical role of Bregs in maintaining immune tolerance and preventing autoimmunity, their dysregulation in PMO suggests its autoimmune nature. Beyond Bregs, pathogenic memory B-cell subsets, metabolic alterations and gut microbiome changes have emerged as central features of autoimmune diseases including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and experimental autoimmune encephalomyelitis (EAE). Although, PMO and autoimmunity share a common burden characterized by female predominance and increasing prevalence with age, the contribution of autoimmune B-cell responses in PMO remains largely unexplored. We employed an integrated multi-omics approach to characterize the unique immune, metabolic, and gut-microbial landscape of PMO. B-cell heterogeneity was resolved using single-cell AbSeq and plasma metabolomics was performed using untargeted LC-MS/MS. In parallel, gut-microbial composition was characterized by 16S rRNA sequencing. Taken together, our findings identify a previously unexplored autoimmune-spectrum in PMO characterized by B cell remodelling, metabolic changes, and gut-immune-bone dysfunction.

Invited Lecture

Multiscale structure–property relationships between knee joint function and tissue mechanics

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Joint stability depends on various properties that include the bone anatomy, joint capsule geometry and stiffness, and soft tissues within. The multiscale biomechanical relationships between the whole joint and individual tissues are useful in estimating the physiological condition of the knee. To better understand these relationships, we evaluated multiple structural and mechanical parameters in healthy ovine stifles, specifically joint laxity, joint morphology, individual tissue T_2^* relaxation and mechanical properties of ligaments (ACL, PCL, MCL, LCL), patellar tendon, menisci, and cartilage. By combining mechanical testing at two length scales and magnetic resonance imaging (MRI) scans, we quantify the strength of correlation coefficients between measured metrics, among joint size, whole joint and individual tissue properties. We observe positive correlations between joint laxity forces and the inter-epicondylar distance. Further, the viscoelastic properties of the tendons and ligaments correlate positively with joint laxity forces; however, no such correlations were observed for the cartilage and menisci. We also found weak inverse correlation between tissue viscoelasticity and T_2^* for MCL; and positive correlations for cartilage and menisci, LCL and PCL respectively. These results can provide insights into the differential role of individual tissue properties to the overall joint responses, which can help with designing subject-specific multiscale computational models to simulate joint biomechanics more accurately. Additionally, we will also present some preliminary results on the role mechanical stimuli including matrix stiffness and external loading in influencing chondrocyte mechanobiology that can regulate cartilage health and regeneration. From a clinical perspective, the framework of these studies can be extended in future to humans to develop improved patient-specific treatment strategies for improved joint health care.

Invited Lecture

Novel Insights into the Pathophysiology of Endometriosis

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Endometriosis, a benign gynaecological condition, affects approximately 10% of reproductive- age group women worldwide. Endometriosis is characterized by the presence of endometrium-like cells at ectopic sites and is classified into three subtypes based on the anatomical locations of ectopic lesions. These subtypes include Superficial Peritoneal lesion (SUP), Endometrioma (OMA), and Deep Infiltrating Endometriosis (DIE). The disease is further staged from I to IV based on the size, depth, and extent of adhesions of the ectopic lesions. It has been unequivocally established that the molecular phenotype of not only ectopic lesions but also of their eutopic counterparts differs in women with endometriosis compared to the eutopic endometrium of women without endometriosis. Taking these leads further, our investigations have revealed that ectopic lesions in women with endometriosis adopt a strategy to counteract the stress conditions, i.e., oxidative stress, inflammation, and replicative stress. Our investigations further revealed that the cellular composition of the eutopic endometrium, especially the proportion of specific cell states, differs in eutopic women with endometriosis compared with women without the disease. Further, it was observed that the proportion of endometrial mesenchymal stem cells also differs in eutopic women with endometriosis, compared to women without endometriosis. It is likely that the eutopic endometrium has a different cellular composition in women with endometrium and on retrograde menstruation, the eutopic endometrium with altered cellular composition thrives at ectopic sites.

Invited Lecture

Beyond hematological benefits: Impact of hydroxyurea on bone health in Sickle Cell disease

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Sickle cell disease (SCD) is a severe inherited hematological disorder associated with multisystem morbidity, including impaired bone health and increased fracture risk. Hydroxyurea (HU), a cornerstone of SCD therapy, increases fetal hemoglobin and reduces disease severity; however, its effects on skeletal health remain incompletely understood.

Using the humanized Townes mouse model of SCD, we investigated the effects of HU on bone mass and remodeling. In skeletally mature sickle (SS) mice, HU mitigated cortical bone loss but paradoxically aggravated trabecular bone loss. HU similarly reduced trabecular bone mass in wild-type C57BL/6 mice, suggesting direct skeletal effects independent of SCD. Histomorphometric analyses revealed suppression of osteoblast and osteoclast indices, consistent with low bone turnover. Mechanistically, HU reduced RANKL expression by bone marrow stromal cells, impaired mature osteoclast resorptive activity, and inhibited stromal cell proliferation and early osteogenic differentiation. HU also suppressed mitochondrial respiration and ATP production and decreased mitochondrial membrane potential, accompanied by increased mitochondrial superoxide production.

Together, these findings reveal a complex skeletal response to HU, whereby improvement of SCD may benefit cortical bone, while direct effects on bone cells and mitochondrial energy metabolism may adversely affect trabecular bone, highlighting the need to monitor skeletal health during long-term HU therapy

Invited Lecture

Epigenetics of cell identity: How melanocyte cell fates are specified, maintained, and lost

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How cells navigate competing lineage programs to establish and maintain specific fates remains a central question in developmental biology. Neural crest cells (NCCs), which traverse sequential and often opposing lineage trajectories to generate diverse derivatives, provide a powerful system to address this question. Here, using CUT&RUN in zebrafish, we show that deposition of the histone variants H2A.Z and H3.3 across the neural crest genome is highly structured and preferentially marks functionally relevant chromatin in a cell-state-specific manner. Integrated single-cell transcriptomic and epigenomic analyses reveal that depletion of either H2A.Z or H3.3 disrupts NCC lineage fidelity, resulting in loss of specific derivatives and aberrant activation of alternative fate programs. Depletion of selective histone variants remodels chromatin accessibility and regulatory activity at loci controlling aberrant cell identity, promoting inappropriate activation of programs. We identify a combinatorial role for these two histone variants whose co-occupancy constitutes a “histone code” required for melanocyte specification and regeneration. Together, our findings define a histone variant-driven chromatin framework that resolves competing developmental programs and stabilizes cell identity.

Invited Lecture

How to build and move autophagosomes

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Autophagy is an evolutionary conserved intracellular process that plays pivotal role in maintaining cellular homeostasis. Macroautophagy (herein autophagy) involves *de novo* formation of double membrane vesicles called autophagosomes. These vesicles capture cellular material and deliver it to the lysosomes for degradation and recycling to generate building blocks. While it has implications for lifespan extension, healthy aging, it can also clear intracellular infections and toxic protein aggregation. In certain autophagy-addicted cancers, immune evasion tactics and fuelling cancer growth is powered by autophagy. Therefore, understanding fundamental mechanisms that contribute to autophagosome biogenesis and turnover provide therapeutic solutions to several diseases. In my talk, I will highlight how the humble yeast can shed light on these processes and how extension of some of the findings can also be seen in higher eukaryotic model systems.

Invited Lecture

Forbidden translation: Protein synthesis from the 'untranslated' regions of mammalian mRNAs

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Protein synthesis is conventionally thought to be restricted to annotated coding sequences, leaving untranslated regions (UTRs) largely outside the translational landscape. Our work challenges this view by uncovering diverse modes of translation within mammalian UTRs. We have identified stop-codon readthrough events that extend proteins into the 3′UTR, as well as downstream open reading frames (dORFs) translated independently within 3′UTRs. These events can generate functional protein extensions, short peptides, or regulate the expression of the canonical protein. Mechanistically, they involve cis-regulatory RNA elements, ribosome reinitiation or leaky scanning, and RNA structures such as G-quadruplexes. Together, these findings reveal UTRs as active and functionally important translational territories

Invited Lecture

PRUNE1 loss dysregulates the cAMP–SOX4/SOX11 axis to impair progenitor fate and neuronal migration in NMIHBA

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NMIHBA (OMIM #617481) is a severe autosomal recessive neurodevelopmental disorder caused by biallelic *PRUNE1* variants encoding a dual-function DHH-superfamily enzyme with exopolyphosphatase and cyclic nucleotide phosphodiesterase activities essential for cortical development. Affected individuals present with progressive microcephaly, profound intellectual disability, and truncal hypotonia. We identified two variants c.40-2A>G (novel splice) and c.933G>A (synonymous) in unrelated individuals and functionally confirmed synonymous variant-driven loss of phosphodiesterase activity with no change in total cellular polyphosphate. Transcriptomic profiling of patient fibroblasts revealed upregulation of SOX4, SOX11, adenylyl cyclases (ADCY1/3/4/5/9), PKA catalytic subunit PRKACA, and regulatory subunits PRKAR1B/PRKAR2B, consistent with cAMP elevation from PRUNE1 PDE loss. Antisense oligonucleotide-mediated exon 7 rescue achieved 29% exon inclusion in c.933G>A fibroblasts providing proof-of-concept for splicing correction. *In vivo*, Prune1-RNAi delivered by in utero electroporation at E15.5 produced an aberrant SOX2$^+$/Tbr2$^+$ hybrid progenitor state with elevated Ki67$^+$ cells, indicating failure of the radial glia-to-intermediate progenitor transition and blocked cell cycle exit. NeuN immunostaining revealed reduced mature neurons and NeuN-negative cells in deep cortical layers, reflecting impaired differentiation and radial migration arrest recapitulating NMIHBA pathology. These findings identify SOX4/SOX11 upregulation as a novel transcriptomic signature of PRUNE1 loss and implicate the cAMP/PKA–SoxC axis as a therapeutic target.

Sreenivasaya Memorial Award

The cellular metabolic economy

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Our goal is to understand biochemical constraints, bottlenecks, evolution and design principles of cellular metabolic networks. In the first part of this talk, I will outline our recent studies addressing aspects how the mitochondria functions as both a dynamic metabolic engine, and a cell within a cell that competes and cooperates for resources. This includes findings on metabolic state-based control of mitochondrial form, compositional heterogeneity, and decoupling respiration from other functions. In the second part of my talk, I will highlight ongoing efforts to understand the cell as a metabolic economy, with resource allocations constrained either by supply challenges, or biochemical demand. Here, we address how cells prioritize different amino acids, identify hierarchies of responses constrained by demand, and then build a quantitative understanding of the intra and extracellular amino economy of a proliferating cell. By defining the nature and amounts of amino acids that can be exchanged, we now design robust synthetic yeast communities based on metabolite exchange. I will end with how divison of metabolic labor can be used to build effective synthetic cell communities, with diverse application.

Prof. A. N. Bhaduri Memorial Lecture Award

Molecular determinants of *Plasmodium* development and transmission

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Malaria transmission requires *Plasmodium* parasites to undergo highly coordinated developmental transitions between vertebrate and mosquito hosts. Our studies have identified diverse molecular pathways that regulate parasite fitness, sexual development, mosquito-stage progression, and sporozoite infectivity. We demonstrate that the *Plasmodium*-specific actin-like proteins Alp5a and Alp5b are individually dispensable for blood-stage growth but collectively essential for parasite viability and male-gamete DNA segregation. Their loss compromises male-gamete integrity and consequently impairs oocyst development. We further establish post-translational modifications as critical regulators of parasite development and transmission. Nedd8 and its conjugating enzyme Ubc12 are dispensable for blood-stage propagation and gametogenesis but are essential for ookinete formation and maturation, revealing a stage-specific requirement for neddylation. Similarly, C-mannosyltransferase is required for ookinete gliding and oocyst formation, whereas POFut2-mediated O-fucosylation regulates TRAP abundance, sporozoite motility, and hepatocyte infectivity. Our studies further identify TKL3 as a regulator of blood-stage proliferation, male-gamete fertility, and ookinete development, while PFTP coordinates parasite fitness, schizont maturation, gametocytogenesis, immune evasion, and mosquito transmission. At the sporozoite stage, the inner membrane complex protein S14 is essential for gliding motility and invasion of mosquito salivary glands and hepatocytes. Collectively, these findings reveal that *Plasmodium* development and transmission are governed by interconnected mechanisms involving cytoskeletal dynamics, protein phosphorylation, post-translational modification, and glideosome function. Defining these stage-specific molecular dependencies provides fundamental insights into malaria transmission biology and highlights molecular vulnerabilities that may be exploited for transmission-blocking interventions.

Invited Lecture

Metagenome wide association studies (MWAS) on vaginal and oral microbiome in preterm birth and infant gut microbiome in child growth failure: Precision microbiomics in developing the BHARAT webtool for rapid analysis of microbial WGS data

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Human microbiome is considered as the 'forgotten organ' with a tremendous potential for understanding both health and disease conditions in humans. Almost 50% cells in the human body are microbial in nature, the total genetic material in all these cells are collectively termed as the Second Genome. The Human Microbiome Project (HMP) has unravelled healthy human microbiome from different parts of the human body in Western populations. However, there are significant differences in the composition and diversity of the healthy human microbiome in other world populations.

Our human microbiome research (HMR) laboratory at BRIC-NIBMG is an integral part of multi-institutional, multi-omics consortiums on maternal and child health research using large maternal and child cohorts in India. Metagenome wide association study (MWAS) on the vaginal microbiome of pregnant women enrolled in GARBHINI cohort identified non-commensal, inflammogenic microbial taxa and their differentially enriched gene families and pathways in the first and second trimesters of pregnancy that triggers premature cervical ripening leading to preterm birth. We also characterized that longitudinal shifts in oral microbiome of pregnant women may also trigger preterm birth.

Preterm born infants are mostly predisposed to malnutrition and child growth failure (CGF). Currently, child malnutrition rates are significantly high in India. To understand the role of infant gut microbiome in child growth failure (CGF), we characterized the changes in microbiome composition between normal and CGF infants at 3 and 6 months of age enrolled in the largest mother and child cohort, the WINGS cohort. Gut microbiome of normal growing children was replete with *Bifidobacterium longum* and *Bifidobacterium breve* whereas pathogenic microbes like *Escherichia-Shigella coli* and *Escherichia-Shigella fergusonii* were higher in the gut of CGF infants. Interventions during preconception, pregnancy and postpartum increased beneficial bacterial taxa in the infant gut microbiome and decreased the rate of child growth failure compared to the routine care group.

The results obtained from MWAS studies are often validated by culturomics studies of clinical isolates obtained directly from patient samples. The analysis of bacterial WGS data requires several softwares for assembly, alignment and annotation in a time-consuming manner. To address this problem in a user-friendly manner, we have developed an automated microbial WGS analysis pipeline BHARAT (Bacterial Hybrid Assembly and Rapid Annotation Toolset) for rapidly identifying AMR genes, virulent factors, secondary metabolites and biosynthetic gene clusters produced by those bacteria. The pipeline operates approximately twice as fast as existing web-based platforms while delivering comprehensive results in a consolidated manner.

Invited Lecture

Mitochondrial citrate exporter regulates dysbiosis and stress response outcome in Ulcerative colitis

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Ulcerative colitis (UC) is a chronic inflammatory disorder marked by persistent mucosal inflammation and mitochondrial dysfunction. However, the molecular basis underlying impaired mitochondrial function and effect on UC pathology remains poorly understand. Using human UC patient derived colon biopsy samples, primary macrophages, mouse model of colitis and loss/gain of function studies, we have identified mitochondrial dynamics as a previously unrecognized regulator of immune and mitochondrial stress response in UC. We demonstrate that disruption of mitochondrial quality-control pathways leads to altered cellular metabolism, changes in microbiome population, enhanced inflammatory signaling, and excessive production of pro-inflammatory cytokines. Reduced expression or dysfunction of key mitochondrial regulators is associated with heightened mucosal inflammation and impaired immune balance, suggesting a mechanistic link between mitochondrial stress, gut dysbiosis and chronic intestinal pathology. Collectively, these findings support a model in which mitochondrial dysfunction acts as a central driver of aberrant immune responses in IBD. Our work provides new insights into disease mechanisms and highlights mitochondrial regulatory pathways as promising biomarkers and therapeutic targets for the treatment of chronic intestinal inflammatory disorders.

Invited Lecture

Metabolism as an immune strategy in fighting TB

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Macrophage physiology critically determines the dynamics and specificity of host responses to infection. Using sertraline (SRT), an FDA-approved antidepressant with host-directed therapeutic potential, we identify macrophage cholesterol metabolism as central to bacterial control. SRT modulates cholesterol homeostasis by inducing lysosomal cholesterol accumulation, lysosomal membrane permeabilisation, and mitochondrial ROS production. We identify SREBP2 as a key transcriptional regulator driving inflammasome-mediated IL-1β release and K^+ efflux, suppressing infection-induced type I interferon responses. Together, these processes enhance macrophage-mediated bacterial killing and potentiate anti-tubercular therapy. We thus uncover an important role for host sterol metabolism in regulating macrophage-mediated drug control of *Mycobacterium tuberculosis* (Mtb). Together, our findings define a novel metabolic–immune axis in macrophages linking cholesterol biosynthesis and inflammasome activation to improved control of Mtb, and highlight sertraline as a valuable tool and adjunct in host-directed tuberculosis therapy.

Invited Lecture

Molecular insights of plasmepsins for understanding their inactivation mechanism and developing antimalarial inhibitors

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Malaria is responsible for infecting 300-500 million people annually and the death of 1-3 million. The causative agents responsible for human malaria are five Plasmodium species (*P. vivax*, *P. ovale*, *P.malariae*, and the most lethal *P. falciparum*). Due to the emergence of *P. falciparum* strains which are resistant to inexpensive antimalarial agents such as chloroquine and sulfadoxine/pyrimethamine, there is a constant pressure to find new and long lasting chemotherapeutic agents. The Plasmodium pepsin-like aspartic proteases, known as plasmepsins (PMs), are involved in important processes such as hemoglobin degradation, invasion and egress for the survival of the parasites. Inhibition of the functions of these PMs would kill the parasites. Therefore, these PMs are considered as promising targets for the development of novel antimalarial drugs. We have demonstrated that the plasmepsin zymogens have novel inactivation mechanism and get matured by a trans auto-activation process not reported before for any other pepsin-like aspartic proteases. We have studied KNI inhibitors and our data on PM inhibition indicated that these inhibitors have the Ki values in the nanomolar range. We determined high resolution crystal structures of active PMII as

complexed with different derivatives of KNI-inhibitors revealing non-planarity of two catalytic aspartates (D32 and D215). Further QM/MM calculations have provided novel insights into the catalytic mechanism of the pepsin-like aspartic proteases. Among the tested inhibitors, KNI-10743 and KNI-10333 exhibited significant antimalarial activity, blocked hemoglobin degradation inside the food vacuole, and showed no cytotoxicity on human cells. Subsequently, new generations of KNI derivatives have been synthesized and those show broader inhibitory activity against multiple PMs, significant antimalarial activity and capability of inhibiting growth of other apicomplexan parasites like *Toxoplasma gondii*. These new KNI inhibitors are promising candidates for further optimization as future antimalarials and antiparasitic drugs. We have also explored the possibility of using marketed anti-HIV drugs as antimalarials. HIV-1 drugs ritonavir (RTV) and lopinavir (LPV) inhibited activity of vacuolar and non-vacuolar PMs. We have determined the first crystal structures of PMs complexed with antiretroviral drugs RTV and LPV. High resolution crystal structures and extensive molecular dynamics (MD) simulations revealed the mechanism of inhibition of PMs by antiretroviral drugs and would aid in drug repurposing. Our structural data, biochemical studies and antiparasitic assays on the novel KNI derivatives with improved antimalarial activity present solid foundations for antimalarial and antiparasitic drug development.

Invited Lecture

Gut microbiome and host metabolism: Metagenomic and metabolomic findings in Alzheimer's Disease

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The metabolic functions of the gut microbiome provide a framework for investigating interactions between microbial communities and host physiology. Characterising microbial functional potential alongside circulating metabolites may offer complementary insights into biochemical disturbances associated with Alzheimer's disease (AD).

Objective: To describe differences in gut microbial composition, functional potential and plasma metabolic profiles between patients with AD and cognitively healthy controls, highlighting their relevance to microbiome–host interactions. Findings from two published studies conducted at AIIMS, New Delhi, were considered together. Baseline gut microbiome profiling included 16 patients with mild AD and 17 healthy controls. Stool samples underwent shotgun metagenomic sequencing for taxonomic analysis, microbial diversity assessment and functional annotation using COG and KEGG databases. The metabolomics study included 25 patients with AD and 25 healthy controls. Untargeted plasma liquid chromatography–mass spectrometry was combined with ELISA-based assessment of disease-related, inflammatory, oxidative stress and neurotrophic biomarkers. Statistical analyses included differential abundance testing, multivariate analysis, metabolic pathway enrichment and exploratory assessment of metabolite discrimination. Gut microbial alpha diversity did not differ significantly between AD and healthy controls. However, baseline compositional profiles showed reduced representation of Faecalibacterium, *Lachnospira eligens* and *Bifidobacterium catenulatum*, alongside enrichment of *Prevotella copri* and Veillonella species in AD. Functional annotation indicated lower representation of microbial metabolic genes, with differences involving carbohydrate, amino acid and energy metabolism. Plasma metabolomics identified 75 significantly altered metabolites among 530 evaluated following false discovery rate correction. Selected increased metabolites included leucine, ascorbic acid and guanine, whereas valine, nicotinamide, octadecanedicarboxylic acid and prolinamide were reduced. Pathway analysis implicated branched-chain amino acid metabolism, nicotinamide metabolism, the tricarboxylic acid cycle and neurotransmitter-related pathways. Octadecanedicarboxylic acid and prolinamide distinguished AD from controls within the study cohort, with areas under the receiver operating characteristic curve of 0.917 and 0.908, respectively. Elevated C-reactive protein and 8-hydroxy-2′-deoxyguanosine, together with reduced brain-derived neurotrophic factor, indicated accompanying inflammatory, oxidative and neurotrophic alterations. These complementary studies identify differences in gut microbial composition and functional potential alongside systemic metabolic disturbances in AD. Amino acid and energy metabolism emerge as biochemical domains for further investigation of microbiome–host interactions. The findings do not establish direct microbe–metabolite relationships or microbial origins of circulating metabolites. Matched stool–plasma analyses, targeted metabolite measurements and longitudinal validation are required to investigate these connections and their biological significance.

Invited Lecture

Silent sabotage: How *Leishmania* reprograms host immunometabolism for its sustained survival

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Early phase *L. donovani* infection upregulates glycolysis, resulting in faster ATP production through lactate pathway than oxidative phosphorylation (OXPHOS). Excess ATP is effluxed extracellularly and converted to adenosine, which activates $A_{2A}R$ receptor, a GPCR. $A_{2A}R$ activation dampens pro-inflammatory cytokines in infected macrophages and promotes infection. We showed $A_{2A}R$ blockade reduces expression of heme oxygenase-1 (HO-1), an enzyme which reduces pro-inflammatory cytokines. We showed infection-mediated $A_{2A}R$ activation increases intracellular cAMP, activates PKA, which activates two major transcription factors of HO-1, CREB and NRF2. During late phase infection, increased cellular energy demand may drive metabolic shift toward OXPHOS. This shift can possibly reduce adenosine supply and inactivate $A_{2A}R$ signalling, raising question of how the parasite-favourable environment is maintained. Metabolic shift is marked by fluctuating ratio of NAD+/NADH. Our preliminary study showed this ratio increasing during late phase infection, indicating shift to OXPHOS. NAD+ is a co-factor for sirtuin (SIRT) family deacetylases which regulate stress, metabolism and post-translational modifications. NQO1 is an antioxidant enzyme that produces NAD+ and activates SIRT1. We hypothesized, *L. donovani* may induce NOQ1-NAD+-SIRT1 axis during late phase infection and deacetylate NRF2, increase its activity and stronger binding to target gene HO-1, and establish positive feedback loop which maintains parasite survivability.

Invited Lecture

Optogenetic illumination of PKG-dependent cGMP-calcium signaling in the obligate intracellular pathogen *Toxoplasma gondii*

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Toxoplasma gondii, an obligate intracellular parasite of global medical importance, relies on orchestrated signaling cascades to control its life cycle in mammalian cells. Cyclic GMP is a critical actuator of Ca^{2+}-regulated parasite motility and ensuing egress and invasion events. Likewise, protein kinase dependent on cGMP (PKG) is the primary signaling mediator; yet its downstream effectors and hierarchical integration with Ca^{2+} homeostasis and signaling remain unresolved. Investigating such second messenger events has conventionally been challenged by the slow kinetics and irreversibility of currently-available genetic and pharmacological tools. To overcome these constraints, we engineered an optogenetic system for fast, efficient, reversible and spatiotemporal control of cGMP *via* a fungal-derived light-activated guanylate cyclase (RhoGC). While parasites maintained in dark replicate normally, a green-light (530 nm) pulse induces robust reversible elevation of parasite cGMP. The activation of cGMP-PKG potentiated gliding motility, egress and invasion by mobilizing Ca^{2+}, revealing a direct coupling of these signaling systems. Quantitative phosphoproteomics profiling of light-stimulated and PKG-inhibited parasites revealed extensive remodeling of the phospho-signaling network. We discovered novel effector proteins functionally linking cGMP and Ca^{2+} cascades. We are now examining the impact of these factors on calcium homeostasis and lytic cycle. Collectively, our work exemplifies a versatile system for studying cGMP-PKG-Ca^{2+} axis in genetically-tractable and clinically-relevant intracellular pathogens.

Invited Lecture

The catalytic subunit of GPI-N-acetylglucosaminyltransferase which initiates GPI biosynthesis in Candida albicans also transcriptionally regulates the enzyme

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Candida albicans exists as a commensal in healthy individuals and occupies several different niches such as the skin, nail, mouth, gut and the female reproductive tracts. But when an opportunity presents itself, such as due to steroidal or immunosuppressive therapy or when the microbiota of the gut is disturbed by long-term proton pump inhibitors/ antibiotic treatment, then the organism switches on its pathogenic traits and begins to aggressively invade the host tissue. One of the characteristic traits that enables this transformation is the expression of factors/ proteins that contribute to adhesion and virulence, many of which are GPI anchored. Work from my lab over the past two decades has demonstrated that GPI biosynthesis responds to stimuli that induce filamentation dues to at least 2 factors: 1) an unusual Ras-dependent upregulation of the activity of GPI-*N*-acetylglucosaminyltransferase (GPI-GnT), the enzyme that initiates GPI biosynthesis in *Candida albicans* and, 2) a unique inter-subunit transcriptional cross-talk within the GPI-GnT [1-3]. Using published and more recent, unpublished, data from my lab for two of the GPI-GnT subunits, I hope to provide some clues on the mechanisms by which these two processes occur and dwell upon its likely consequences for *Candida albicans* infections.

Invited Lecture

Trafficking without a golgi: Presence of a divergent TRAPP complex in *Giardia lamblia*

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The intestinal protozoan pathogen *Giardia lamblia* possesses a highly reduced endomembrane system and lacks a distinct Golgi apparatus. How cargo sorting and membrane trafficking are organized in the absence of this canonical sorting compartment remains poorly understood. While several Golgi-associated SNAREs and Rab GTPases have been identified in *Giardia*, the TRAPP (TRAnsport Protein Particle) complex, a key guanine nucleotide exchange factor for Golgi-associated Rabs, has not been characterized. We report that *Giardia* expresses a minimal repertoire of TRAPP components comprising GlBet3, GlBet5, GlTrs23, and GlTrs31. Protein interaction analyses revealed associations of selected TRAPP components with the Rab GTPases GlRab1a and GlRab11, as well as the COPII coat protein GlSec23. Colocalization and co-immunoprecipitation studies further established interactions between GlBet3 and GlBet5, supporting the existence of a functional TRAPP complex in *Giardia*. Our findings indicate that this complex possesses a distinct architecture relative to its yeast counterpart, displaying both conserved and lineage-specific interactions. TRAPP genes are upregulated during encystation, and GlBet3 and GlBet5 localize to encystation-specific vesicles, implicating the complex in developmental trafficking. Additionally, both components localize to the plasma membrane, ventral disc periphery, and median body suggesting previously unrecognized roles in maintaining unique cellular structures and functions of this early-diverging eukaryote.

Invited Lecture

SWR1 chromatin remodeling regulates development, effector expression, and virulence in *Ustilago maydis*

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Chromatin remodeling plays a central role in regulating fungal adaptation and pathogenicity, yet its contribution to effector regulation during plant infection remains poorly understood. Here, we investigate the role of the SWR1 chromatin-remodeling complex in the maize pathogen *Ustilago maydis* using the haploid FB1 and solopathogenic backgrounds. SWR1 deletion causes pronounced developmental and morphological phenotypes, including enhanced melanization, highlighting its role in fungal cellular homeostasis. Notably, the phenotypic consequences of SWR1 loss differ between FB1 and the solopathogenic strain, suggesting that SWR1 function is influenced by fungal developmental state. Importantly, SWR1 deletion alters the expression of plant infection-associated effector genes, indicating that SWR1 contributes to transcriptional reprogramming during host colonization. Consistent with these molecular changes, loss of SWR1 affects maize infection and disease development. Together, our findings identify SWR1 as a chromatin-based regulatory hub connecting fungal development, effector expression, and plant pathogenicity in *U. maydis*.

Invited Lecture

Beyond complex I: Mitochondrial electron flux plasticity in tumour cells

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The fundamental concept of heightened OXPHOS activity driving tumour growth is derived from effective channelling of electrons through Complex I. It has been the basis of conceptualizing mitochondrial metabolism with cancer progression. However, the existence of bioenergetic plasticity in cancer cell mitochondria and its consequences in tumorigenesis is underexplored. Our study provides proof-of-concept evidence that tumour cell mitochondria can adapt its preferential electron flux through succinate dehydrogenase complex (Complex II) to promote tumour growth by inducing fatty acid metabolism. Despite Complex I uncoupling, cells showed better respiratory output and preserved NADH pool. Our observations indicate that effective mitochondrial respiration may not be a direct manifestation of Complex I activity and suggest that proliferating cells exhibit bioenergetic rewiring through alterations in the levels of a regulatory protein, Methylation-Controlled J-protein (MCJ) that in turn, induces reprogramming towards lipid metabolism. Elevated MCJ levels promoted aggressive proliferative and migratory phenotypes, leading to increased primary tumour burden, by enabling a preferential rerouting of electron flux through Complex II. This study invokes an important consideration in designing future therapeutics and inhibitors, which presently centres around Complex I dependent respiratory activity.

Invited Lecture

Rewriting protein fate: The hidden regulatory language of ubiquitin

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Ubiquitin is an evolutionarily conserved molecular tag that directs protein fate within cells. Despite its central role in regulating diverse biological processes, how ubiquitin encodes functional and interaction specificity with the myriad of its interactors remains poorly understood. We employed comprehensive deep mutational scanning to systematically delineate the functional landscape of ubiquitin and identified a spectrum of dominant-negative variants that perturb ubiquitin signaling through altered interactions with conjugating enzymes, substrates, and deubiquitinases (DUBs) with remarkable specificity. Our analysis revealed that functional residues extend beyond the canonical chain-building sites, uncovering an underappreciated regulatory layer encoded within the amino acid sequence of ubiquitin. Recently, we have demonstrated how a precise single-residue substitution selectively impairs ubiquitin chain processing by the deubiquitinase Ubp14 and its human homolog USP5. Through integrated biochemical, structural and genetic analyses, we have shown how this substitution remodels the ubiquitin-DUB interface, promoting high-affinity engagement and effectively converting the ubiquitin variant into a substrate-trapping inhibitor inside cells. The perturbed DUB activity consequently alters ubiquitin homeostasis and reshapes protein degradation pathways inside cells. Taken together, our findings establish ubiquitin variants as valuable molecular probes for dissecting and potentially rewiring the ubiquitin network inside cells and also lay the foundation for use of ubiquitin-DUB interfaces as a tractable framework for mechanism-guided therapeutic discovery.

Invited Lecture

Distinct molecular signaling pathways governing mitochondrial fission and their roles in mitochondrial biogenesis and mitophagy

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MTP18 (also known as MTFP1), a nuclear-encoded inner mitochondrial membrane protein, is crucial for mitochondrial integrity. MTP18 is found to promote mitochondrial fission. However, there are limited studies on the mechanistic role of MTP18 in contributing to mitochondrial fission. The current study found that MTP18 regulates the DRP1-MFF-FIS1 signaling axis to regulate mitochondrial fission. In this connection, MTP18 overexpression elevated mitochondrial biogenesis, DNA content, and ATP level and upregulated the symmetric mitochondrial fission by phosphorylating MFF, a DRP1 receptor. MTP18 also increased the recruitment of cytosolic DRP1 to mitochondria by phosphorylating DRP1 at Ser616 to initiate fission. In addition, MTP18 was also found to stabilize MFF by inhibiting its priming with ubiquitin and further proteasomal degradation. In addition, MTP18 induced FIS1-mediated asymmetric mitochondrial fission and mitophagy to clear mitochondrial damage induced by CCCP-mediated mitochondrial uncoupling. Moreover, we found that MTP18 functions as a mitophagy receptor that targets CCCP-induced dysfunctional mitochondria for elimination via autophagosomes. Interestingly, MTP18 interacts with members of the LC3 (also known as MAP1LC3) family through its LC3-interacting region (LIR) to induce mitochondrial autophagy. A mutation in the LIR motif (mLIR) inhibited that interaction, thus suppressing mitophagy. The study establishes that MTP18 signals distinct fission events for mitochondrial biogenesis or elimination, thereby maintaining mitochondrial homeostasis.

Invited Lecture

A novel endocytic route delivers cardiolipin from plasma membrane to nuclear envelope: A role in nuclear expansion

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Nucleus is a dynamic organelle that undergoes remodelling including nuclear expansion during cellular growth. Tetrahymena is a single cell ciliate that involves drastic nuclear expansion (10-15-fold increase in volume) at a particular stage of sexual conjugation. This requires rapid supply of lipid supply. Nuclear envelope relies on endoplasmic reticulum for the membrane lipids. However, a vesicular route delivering lipid to the nuclear envelope remains unknown. We have discovered a novel endocytic pathway to deliver specific phospholipid, cardiolipin (CL) from plasma membrane to the nuclear envelope essential for rapid nuclear expansion. CL undergoes rapid, late endosome-mediated accumulation at the nuclear envelope after incorporation at the plasma membrane. Inhibition of endocytosis or late endosome function by pharmacological agents as well as by genetic disruption of Rab7 function, markedly impairs nuclear expansion. Further, selective inhibition of plasma membrane CL synthesis blocks nuclear development, a defect that is substantially rescued by exogenous CL, establishing the plasma membrane as a physiologically important CL source for rapid nuclear expansion. Our findings support the presence of an endosomal pathway that carries lipids from plasma membrane to the nuclear envelope to meet massive lipid demands during nuclear biogenesis.

Invited Lecture

Molecular insights into fungal-eating properties of Burkholderia bacteria and utilizing them for the mitigation of fungal infections

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Controlling plant diseases in an eco-friendly and sustainable manner remains a challenge for sustainable agriculture. We have isolated a novel bacterium, *Burkholderia gladioli* strain NGJ1, from rice that demonstrates fungal-eating properties. We demonstrated that the bacterium delivers a prophage tail-like protein (Bg_9562) using a specialized secretion system (Type III secretion system) into the fungal hyphae to forage over them. The purified Bg_9562 protein demonstrates broad-spectrum antifungal activity. Notably, the heterologous overexpression of Bg_9562 or exogenous treatment with purified protein not only imparts fungal disease tolerance but also bacterial disease tolerance in tomato. The defense-inducing ability of the protein lies within the 18-51 aa region and is due to sequence homology with the bacterial flagellin epitope. Our data emphasize that, on one hand, Bg_9562 is important for the endophytic growth of B. gladioli, while on the other hand, the plant perceives it as a MAMP (microbe-associated molecular pattern) via a specialized receptor and elicits an immune response. We are currently exploring ways to deploy the Bg_9562 protein/peptide for controlling fungal and bacterial diseases in crop and horticultural plants.

Invited Lecture

A molecular switch for survival: How mediator subunit MED14 couples cell-cycle control to DNA damage response

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Mediator is an important component of transcription regulation as it serves as a connecting link between transcription factor and transcriptional machinery. Our studies show that this multi-subunit complex rely on structural flexibility and key architectural subunits like MED14 and MED17 to coordinate plant growth and stress responses. In *Arabidopsis thaliana*, root meristems require tight coordination between cell proliferation and genome maintenance to withstand environmental threats. Here, we demonstrate that MED14 cooperates with the transcription factor ELONGATED HYPOCOTYL 5 (HY5) to safeguard root development. MED14 is essential for flavonoid biosynthesis; its disruption impairs reactive oxygen species (ROS) homeostasis and triggers oxidative DNA damage. Mechanistically, the MED14–HY5 axis operates as a molecular switch governing cell-cycle progression. Under normal conditions, MED14 and HY5 promote growth by activating *CYCD1;1*. Concurrently, they repress the DNA damage-responsive transcription factors *NAC044* and *NAC085*. Under genotoxic oxidative stress, this repression is relieved, leading to *CYCD1;1* downregulation and cell-cycle arrest. Together, our findings reveal a crucial MED14–HY5 regulatory module that couples metabolic redox balance with cell-cycle control to ensure root plasticity and genomic stability.

Invited Lecture

Epigenetic landscape regulating fibre development in cotton

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The cotton ovule epidermal cell that commits to fibre development provides an excellent model for studying the transcriptional and epigenetic control of cell differentiation. Inhibition of histone acetyltransferase activity by Anacardic acid (AA), a p300/PCAF inhibitor, in *in vitro* cotton ovule culture promotes cotton fibre development. ChIP sequencing showed that AA treatment of developing cotton fibres reduced H3K9ac levels, indicating chromatin hypoacetylation. Transcriptome and ChIP-Seq analyses revealed that AA enhances fibre initiation and rapid elongation by increasing the expression of genes involved in the auxin pathway while suppressing cell-cycle genes. Concurrently, we identified that cotton histone deacetylase 5 (HDA5) positively regulates cotton fibre development. The MALDI-based *in vitro* activity assay suggested that GhHDA5 primarily deacetylates H3K9-acetylated marks. Downregulation of *GhHDA5* inhibits fibre initiation, resulting in decreased lint yield in its RNA interference (RNAi) lines through altered reactive oxygen species homeostasis and increased autophagic cell death in developing fibres. Further, co-expression network analysis suggests that GhHDA5 functions as a multi-protein repressor complex comprising other chromatin-modifying proteins, including HDACs, histone methyltransferases (SUVH1), and heat shock proteins (HSPs). The expression analysis also revealed that several members of GhHSP70 and GhHSP90 were significantly expressed during the different stages of fibre development. Inhibition of HSP70 and HSP90 activity resulted in retardation of fibre growth at the early and late stages of fibre development, respectively. Suppression and overexpression lines of these Heat Shock Proteins showed decreased fibre growth during initiation and elongation.

The promoter analysis of the histone methyltransferase gene *GhSUVH1* shows that it is expressed at higher levels at the initiation stage of cotton fibre development. RNAi lines of the *GhSUVH1* gene showed earlier flowering, more boll setting, and higher seed number, lint weight, and harvesting index than the overexpression lines and the control. We further investigate whether GhSUVH1 is localised in the nucleus and interacts with key TFs, including MYB2, MYB25L, and PDF2, that are involved in cotton fibre development. Transcriptome and ChIP-Seq analyses suggest that GhSUVH1 downregulation alters the expression of various genes, including fibre-development-associated genes, and promotes genome-wide H3K9 trimethylation. Thus, our study provides a comprehensive landscape of epigenetic regulation, including histone modifications and modifiers, during cotton fibre development.

Invited Lecture

Retention versus exclusion: Convergent and divergent mechanisms of Fe and Al toxicity tolerance in Assam's rice landraces

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Acidic, waterlogged soils of Northeast India expose rice to two co-occurring but chemically distinct metal stresses: iron (Fe^{2+}) and aluminium (Al^{3+}) toxicity. This study synthesizes findings from two parallel screens of indigenous Assamese rice landraces (55 genotypes for Fe, 53 for Al) under hydroponic stress, integrating morphophysiological, biochemical, SSR-marker, and gene-expression data to compare how a shared genetic background manages both toxicities. Both stresses cause comparable growth inhibition, chlorophyll loss, and oxidative damage, countered by a similar antioxidant/osmoprotective response (SOD, CAT, POD, APX induction; proline accumulation). However, the underlying tolerance logic diverges sharply: Fe tolerance relies on retention and compartmentalization root iron-plaque formation, restricted shoot translocation, and intracellular sequestration via *OsVIT2*/*OsFer1* despite high root Fe accumulation, whereas Al tolerance relies on true root-surface exclusion through organic-acid chelation (*OsFRDL4*) and cell-wall modification (*OsSTAR1*/*OsSTAR2*), with vacuolar sequestration (*OsNRAT1–OsALS1*) acting only as a weaker fallback in susceptible lines. SSR marker–phenotype concordance is strong for Fe but weak for Al. The landrace Ahom Sali tolerates both stresses through independent mechanisms, while Mahsuri is Fe-tolerant but Al-susceptible, showing these traits are genetically separable with direct implications for multi-stress acid-soil rice breeding.

Invited Lecture

Neuroimmune circuits in brain health and disease: From neurotropic viral infections to gut brain crosstalk

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The brain is an immunologically active organ whose function and integrity are shaped by complex interactions between neural cells, innate immune responses, and signals originating from peripheral tissues. The gut-brain-axis has emerged as a critical integrative network linking the gut microbiome, intestinal barrier function, immune signalling, and central nervous system (CNS) homeostasis. Disruption of these interconnected pathways may contribute to the pathogenesis of infectious, inflammatory, and age-associated neurological disorders.

This presentation will explore how studies of neurotropic viral infections, particularly Japanese encephalitis virus (JEV), provide insights into the molecular and cellular mechanisms underlying neuroimmune dysfunction and gut brain crosstalk. Viral infection can alter gut microbial composition, intestinal barrier integrity, and microbial metabolite profiles, potentially influencing peripheral immune responses and CNS inflammation. Within the brain, microglia and other innate immune components act as critical regulators of the inflammatory response, shaping neuronal injury and disease progression. These observations raise important questions about how signals originating in the gut interact with virus-induced neuroimmune pathways to influence the severity and outcome of encephalitis, as well as longer term neurological consequences.

The presentation will also discuss emerging microbiome-targeted and nutritional strategies, including probiotics, prebiotics, and bioactive microbial metabolites, as potential approaches to modulate host immunity and restore gut–brain homeostasis. By integrating findings from viral neuropathogenesis, neuroimmunology, microbiome research, and nutrition, this talk will highlight the biochemical and immunological circuits connecting the gut and brain and their potential relevance to the prevention and management of neurological disease.

Invited Lecture

MicroRNA pathways in aging and dietary restriction

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Aging is characterized by a progressive decline in physiological function and an increased risk of chronic degenerative diseases. Dietary restriction (DR) promotes healthspan and delays the onset of age-related chronic conditions. Micro-ribonucleic acids (miRNAs) function as critical post-transcriptional components of signaling pathways that modulate lifespan by regulating mRNA turnover and translation. Using the *Drosophila melanogaster* model system, we identified miR-125 and miR-375 as two conserved miRNAs modulated by DR. The DR phenotype associated with miR-125 loss of function results from deregulation of its target, *Chronologically Inappropriate Morphogenesis* (*chinmo*), which alters fat metabolism when upregulated in the nervous system. Using overexpression and knockout lines, we show that miR-375 modulates DR-dependent lifespan extension by targeting the circadian gene *timeless*. Competitively inhibiting miR-375 or overexpressing *timeless* in the adult fat tissue increased longevity under *Ad libitum* conditions. Increasing miR-125 dosage and decreasing miR-375 dosage increased longevity under *Ad libitum* conditions. Furthermore, circulating miR-375 levels decrease significantly in prediabetic individuals undergoing DR prior to any changes in anthropometric parameters, indicating that miR-375 could serve as a biomarker to track the effect of diet in prediabetic individuals. In summary, we have identified conserved miRNA pathways that mediate the effects of DR by promoting tissue-tissue communication.

Invited Lecture

Tiptoeing into translational neuroscience in India: A small example

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Brain disorders pose a major public health threat, especially in India. The urgent unmet need is for overcoming bottlenecks at pivotal stages of translating "discovery" to "delivery". Over the past few decades, there have been exciting new breakthroughs in neuroscience, but these do not lead easily to successful treatments. This is due to a breakdown in translating promising new targets from pre-clinical, animal models to human trials. This highlights the need for understanding how the disease affects brain cells of human origin. There is also a need to bridge the wide gap between fundamental and clinical neuroscience research in India. In my talk I will present an example of a uniquely "Indian" neurodegenerative disorder that addresses some of these challenges and opportunities.

Invited Lecture

Repurposing Ube3a imprinting biology for a neurodegenerative target

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The gene whose maternal-allele loss causes Angelman syndrome (AS) encodes the ubiquitin ligase Ube3a, the same enzyme degrades α-synuclein, the protein that aggregates in Parkinson's disease (PD), dementia with Lewy bodies (DLB), multiple system atrophy (MSA), and other synucleinopathies. This rare coincidence led us to investigate whether the typical phenotypic features of synucleinopathies can be seen in Ube3a-maternal knockout mouse, a model mouse for AS. Interestingly, because the Ube3a gene is paternally imprinted in neurons, its reactivation could be a breakthrough in developing novel therapeutics for synucleinopathies.

Patients with AS have been shown to manifest typical features of PD, like tremors, cogwheel rigidity, and bradykinesia, and these motor abnormalities were responsive to levodopa, which is widely used for the symptomatic treatment of PD and subsequently, our group, followed by others, demonstrated that the motor deficits exhibited by AS mice are due to the dysfunction of the nigrostriatal dopaminergic pathway. Our recent in depth study revealed that α-synuclein-mediated pathology could be one of the major underlying cause of progressive nigrostraital dysfunction and motor deficits observed in AS mice. Based on our observations, we also speculate that Ube3a could be a novel modifier of synucleinopathies. In my talk, I will first demonstrate the progressive development of various motor deficits in AS mice, and subsequently, I will provide our recent evidence that strongly indicate α-synuclein-mediated pathology might contribute to the progressive motor and other behavioral deficits observed in these mice.

Invited Lecture

Bioengineered *in vitro* liver models for high throughput drug screening applications

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The development of physiologically relevant human in vitro liver models is crucial for understanding liver diseases, evaluating drug efficacy and hepatotoxicity, and reducing reliance on animal experimentation. Prof. Biman B. Mandal and his research group at IIT Guwahati are advancing biomaterial-driven tissue engineering approaches to develop next-generation liver models for drug screening and disease modelling. A key focus is the use of silk-derived biomaterials, particularly non-mulberry silk fibroins, to engineer three-dimensional cellular microenvironments with tunable properties and potential to support hepatic cell function.

By integrating silk-based biomaterials with 3D bioprinting, microfluidic technologies, and dynamic culture systems, the research aims to recapitulate essential features of native liver architecture and physiology. Three-dimensional bioprinting enables spatially controlled organization of cells and biomaterials, while microfluidics and dynamic perfusion culture facilitate controlled nutrient transport, oxygenation, and physiologically relevant fluid flow. These integrated approaches offer opportunities to improve cellular viability, hepatic functionality, and the maintenance of complex multicellular constructs.

The resulting platforms have potential applications in drug metabolism studies, drug-induced liver injury assessment, hepatotoxicity screening, and disease modelling. By combining indigenous silk-based biomaterials with advanced biofabrication and microphysiological technologies, this research seeks to establish scalable, human-relevant testing platforms that accelerate translational biomedical research and support alternatives to animal testing.

Invited Lecture

NIR-responsive multifunctional phototherapeutics

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Antibiotic-resistant infections, ischemia, and fibroblast senescence are major causes of failed healing in chronic wounds. To address this, we developed a near-infrared (NIR)-responsive supramolecular complex composed of bovine serum albumin (BSA), indocyanine green (ICG), and Cu(II) as a multifunctional therapeutic platform. Supported by in-silico data, the platform was designed by exploiting the high affinity of BSA toward ICG and Cu(II) in an aqueous environment. Rigorous screening identified a fatty acid-, protease-, and globulin-free BSA variant (BSA-A7030) as the optimal carrier, exhibiting the highest Cu(II) affinity and enhanced ICG optical properties. Synthesized via room-temperature green chemistry, the BSA-ICG-Cu(II) complex generated photothermal hyperthermia and photodynamic antibacterial effects under 808 nm NIR laser exposure, eradicating *Staphylococcus aureus*, *Escherichia coli*, and methicillin-resistant *S. aureus* (MRSA) in vitro. Additionally, the complex promoted human dermal fibroblast migration, elevated VEGF expression, and enhanced HUVEC tube formation. In a *S. aureus*-infected diabetic mouse model, NIR-irradiated treatment accelerated wound closure and achieved >90% bacterial reduction by day 7, demonstrating a promising strategy combining phototherapy, angiogenesis, and tissue regeneration.

Invited Lecture

Proteogenomic analysis identifies type 2 diabetes-influenced plasma proteins causally associated with microvascular and macrovascular complications of diabetes mellitus

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The molecular mechanism of chronic complications of type 2 diabetes mellitus (T2DM) is not fully understood. Integrative proteogenomic analysis provides an opportunity to explore the proteins playing a role in T2DM induced complications. We used a two-step Mendelian randomization (MR) framework to identify plasma proteins causally influenced by type 2 diabetes mellitus (T2DM) that are, in turn, causally associated with the risk of microvascular and macrovascular complications of T2DM.

In step 1, we used genome-wide association (GWAS) summary data from DIAGRAM consortium (for T2DM) and deCODE genetics to identify which of the 4907 plasma proteins (available in deCODE genetics data) is causally affected by T2DM using Mendelian randomisation. In the second step, after rigorous quality control and filtering, GWAS summary data from proteins that are causally influenced by T2DM were used to identify which of the proteins mediate the chronic complications of T2DM using data from CARDIoGRAMplusC4D for coronary artery disease, the Million Veteran Program for microvascular complications, and Malik et al. for stroke subtypes. Significant associations were replicated in the Fenland cohort and evaluated for genetic colocalization.

Of the 4,907 candidate proteins, 97 were causally influenced by T2DM after passing all the criteria of step 1. Step 2 analysis identified five significant protein-complication pairs: PCBD1 (diabetic neuropathy), LGALS3BP (stroke), F11 (cardioembolic stroke), ESAM (large-artery stroke), and NMB (ischemic stroke). Colocalization showed strong evidence of a shared causal variant for F11 with cardioembolic stroke (PP.H4 = 0.97) and ESAM with large-artery stroke (PP.H4 = 0.82), while colocalization was inconclusive for PCBD1, LGALS3BP, and NMB.

This two-step MR study identifies five T2DM-influenced proteins causally associated with distinct chronic complications, of which F11 and ESAM are additionally supported by genetic colocalisation. Several of these proteins (PCBD1, LGALS3BP, F11) correspond to existing or emerging therapeutic targets.

Invited Lecture

Cervical cancer screening using HPV genotyping panel

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Cervical cancer remains one of India's most preventable yet persistently lethal cancers, driven largely by silent, high-risk HPV infections that current screening infrastructure struggles to catch early or characterize accurately. Most clinically available HPV tests are either genotype-restricted, or too costly for large-scale, low-resource screening - a critical translational gap given India's disproportionately high cervical cancer burden. To address this, we developed and clinically validated a multiplex PCR assay that simultaneously detects fifteen HPV high-risk genotypes, delivering broad-spectrum genotyping without specialized instrumentation. The assay achieved a limit of detection as low as 10 copies/μL, and is validated in clinical validation benchmarked against the predicate kit. Beyond diagnostic accuracy, its ability to resolve co-infections and genotype-specific risk profiles positions this assay as a scalable, cost-effective tool for population-level cervical cancer screening, vaccine-impact surveillance, and precision triage in Indian clinical settings- directly answering the need to translate it into real-world solutions for evolving healthcare challenges.

Plenary Lecture

Beyond Regeneration/Repair: Emerging role of stem cells in disease pathogenesis

Soniya Nityanand
King George's Medical University, Lucknow

Invited Lecture

Neutrophils drive immunopathology in chronic inflammatory states

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Chronic inflammatory diseases shorten healthy lifespan and increase vulnerability to secondary insults such as infection or tissue injury. Disentangling which immune components drive this excess morbidity is difficult because few preclinical systems permit selective testing of individual cell populations. I will present experimental approaches developed in my laboratory that combine disease-relevant mouse models with biomaterial implant associated inflammation to probe causality. Using models of type 2 diabetes and sterile implant–associated inflammation, we identify immature neutrophils as central mediators of inflammation-associated tissue damage. Integrating single-cell RNA sequencing, multiparameter flow cytometry, and ex vivo functional assays, we characterize a distinct immature neutrophil program linked to enhanced tissue-destructive activities. Mechanistic studies show that blocking specific neutrophil effector functions reduces injury in chronically inflamed hosts without broadly suppressing host defence. These findings establish immature neutrophils as actionable drivers of immunopathology in chronic inflammatory settings and suggest targeted neutrophil modulation as a therapeutic strategy to limit collateral injury following infection or trauma in patients with chronic inflammatory disease. I will discuss translational implications, potential biomarkers for patient stratification, and ongoing efforts to develop selective inhibitors that preserve antimicrobial immunity while preventing neutrophil-mediated tissue injury in clinical settings.

Invited Lecture

Snake venom nerve growth factor-derived peptides impede the progression of oxidative stress-induced neurodegenerative diseases

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The nerve growth factor (NGF), a small constituent of snake venom (SV), induces neuritogenesis by interacting with the TrkA receptor on nerve cells. We revealed the TrkA binding locations of SV NGFs. Following this, two innovative synthetic peptides, Tribeca-neuropeptide (TNP) and Heptadeca-neuropeptide (HNP), were developed from the binding domains of SV NGF TrkA by computational techniques. These bespoke peptides (CPs) facilitated neuritogenesis upon binding to TrkA receptors in PC-12 cells and mitigated the toxicity and oxidative stress induced by paraquat and commercial pesticides. Proteomic, transcriptomic, and qRT-PCR analyses demonstrated an alteration in the expression profiles of pesticide-induced oxidative stress-associated genes in PC-12 cells that were pre-treated with TNP and HNP. The in vivo defensive strategies of these tailored peptides against paraquat (PT)-induced neurodegeneration in the *Caenorhabditis elegans* model revealed their ability to obstruct PT attachment to the CAM-1 receptor in *C. elegans* (similar to the TrkA receptor), thereby preventing increased ROS generation and mitochondrial impairment. CPs significantly obstruct pesticide-triggered degeneration of dopaminergic neurons and the clustering of alpha-synuclein in transgenic *C. elegans* strains. Transcriptomic, functional proteomics, and miRNA investigations revealed that CPs can inhibit alterations in gene expression linked to oxidative stress and apoptosis in worms. In a murine model, CPs effectively repair PT-induced neuronal injury without eliciting toxicity or inflammatory responses.

Invited Lecture

Chromatinopathies, ciliopathies, and brain malformations: From genetic mechanisms to disease models

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Chromatin modifiers orchestrate neurodevelopmental gene expression, and their dysfunction gives rise to a spectrum of brain malformations and psychiatric disorders.

KDM1A or Lysine-specific demethylase 1 (LSD1) is a key epigenetic regulator that orchestrates gene expression through histone demethylation, playing a pivotal role in neurodevelopment. In addition to developmental delay and cognitive impairments, some patients with LSD1 point mutations exhibit ventriculomegaly- a common brain abnormality during early development. However, how LSD1 regulates ventricular morphology, and cortical architecture remains poorly understood.

In my talk, I will present our efforts to dissect the mechanisms of dysregulation caused by the epigenetic regulator LSD1 (KDM1A).

We investigated how loss of LSD1 leads to ventriculomegaly using a cortex-specific LSD1 knockout mouse model, which exhibited fetal ventriculomegaly phenotype persisting into adulthood, with some cases progressing to hydrocephaly. Our results demonstrate that loss of LSD1 impairs ependymal ciliogenesis, contributing to ventriculomegaly independently of CSF overproduction and highlight its critical role in cortical and ventricular development. These insights may facilitate future epigenetic strategies for treating ventriculomegaly and associated neurodevelopmental disorders.

Invited Lecture

From natural products to molecular targets: Linking metabolic regulation to cancer cell survival

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Natural products provide a valuable source of bioactive molecules for the identification of molecular targets and development of therapeutic leads. Our investigations integrate experimental models, bioinformatics, molecular docking, lead optimization and *in vivo* validation to explore metabolic targets with therapeutic relevance. Initial studies with *Potentilla fulgens* in experimental models of diabetes and high-fat diet-induced metabolic dysfunction demonstrated its potential to modulate metabolic abnormalities and provided a basis for investigating the underlying molecular mechanisms. Integration of bioinformatic approaches and molecular docking identified ursolic acid as a potential bioactive molecule, with a predicted interaction with AMP-activated protein kinase (AMPK), a key regulator of cellular energy metabolism. This observation led to further investigation of ursolic acid and the development and evaluation of its derivatives. Subsequent studies focused on angiopoietin-like protein 4 (ANGPTL4), an important regulator of lipid metabolism and lipoprotein lipase (LPL) activity. Computational analysis of the ANGPTL4–LPL axis, followed by experimental evaluation, identified a promising derivative that was further investigated in an *in vivo* model. These findings provided a basis for exploring ANGPTL4 as a therapeutically relevant metabolic target. In parallel, the poor aqueous solubility of ursolic acid has prompted the development of nanoparticle-based delivery approaches aimed at improving its physicochemical properties, solubility and potential bioavailability. The biological relevance of the ANGPTL4 axis is now being extended to cancer biology, where its potential role in cancer cell survival and anoikis resistance is under investigation. This integrated approach illustrates how molecular targets emerging from natural-product-based metabolic research can be progressively investigated to understand their relevance to cancer cell survival.

Invited Lecture

Self-amplifying RNA aaccines: Harnessing durable and multifunctional T-cell immunity for next-generation therapeutics

Durgesh Kumar, Sanjay Singh
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Self-amplifying RNA (saRNA) technology offers a promising approach for generating sustained antigen expression and robust cellular immunity. We evaluated the immunogenicity of an saRNA-based COVID-19 vaccine in phase-III clinical trial, with particular emphasis on the quality, breadth, and durability of antigen-specific T-cell responses. The vaccine induced robust Omicron spike-specific polyfunctional CD4+ and CD8+ T-cell responses, characterized by coordinated production of IL-2, TNF-α, and IFN-γ. Compared with a conventional adenoviral vaccine cohort, enhanced central memory and effector memory T-cell responses were observed, together with increased stem-like T-cell populations. These findings demonstrate the potential of the saRNA platform to generate multifunctional and durable cellular immunity beyond conventional antibody-focused vaccine responses (PMID: 38637636, 40025095).

The ability to induce sustained, antigen-specific T-cell responses provides a compelling foundation for applying saRNA technology to challenging antigens and therapeutic settings. Building on these observations, the platform is being explored for applications where strong and durable cellular immunity may be critical, including difficult-to-target infectious diseases and tumor-directed therapeutics. Collectively, these findings highlight the potential of saRNA as a versatile platform for developing next-generation preventive and therapeutic biotherapeutics.

Invited Lecture

Unique strategy and structural mimicry by viral mRNA help hijack host ribosomes

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Protein synthesis and its regulation is a fundamental process in all life forms. Although translation initiation is an indispensable process, many of its aspects are poorly understood. Our research interest lies in understanding the molecular details of the translation initiation using biochemical, mutational and structural biology approaches. The initial steps of protein synthesis in eukaryotes require various eukaryotic initiation factors (eIFs) namely, eIF1, eIF1A, eIF3, eIF5 and the eIF2-GTP-initiator tRNA ternary complex to form the 43S pre-initiation complex (PIC). The mRNA is activated for initiation by eIF4 factors, which help in recruiting mRNA-eIF4 complex to the 43S PIC resulting in the formation of the 48S PIC.

Viruses employ internal ribosome entry sites (IRESs) in their genomic RNA to hijack the host's translational machinery. The picornavirus, Encephalomyocarditis virus (EMCV), employs a type 2 IRES present in its 5'UTR and requires 43S ribosomal preinitiation complex (PIC), the central domain of eIF4G, eIF4A, and an essential ITAF (IRES trans-acting factor)-polypyrimidine tract binding protein 1 (PTB1) to form 48S PIC. Using cryogenic electron microscopy (cryo-EM) we determined the structure of EMCV IRES-bound mammalian 48S PIC, which revealed a unique strategy used by viral IRES to capture host translational apparatus for making viral polypeptide.

Invited Lecture

Cryo-EM studies of Ribosome assembly in mycobacteria

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Ribosomes are the cell's protein synthesis machinery of mega Dalton sizes and consist of three ribosomal RNAs along with approximately 55 ribosomal proteins in prokaryotic. The ribosomal components must assemble accurately to perform error-free protein synthesis. Our study mainly focuses on GTPases, crucial assembly factors believed to play a role in cell growth, and genetic perturbations in their genes lead to defects in ribosomal assembly and rRNA processing. In mycobacteria, one such class of protein that belongs to the GTPase family is EngA, which is known to be involved in 50S ribosome assembly. However, the exact mechanism of how the EngA protein assists in 50S ribosomal subunit biogenesis remains a mystery. Our preliminary studies showed that the EngA protein possesses GTPase activity. Further, binding studies and cryo-EM have identified its putative binding site on the ribosomal subunit. The single-particle reconstruction analysis of 50S-EngA with bound GTPγS and GDP at ~3 Å resolution has revealed that H89 undergoes substantial conformational changes and forms an intermediate assembly state featuring a kissing-stem loop-like motif. Furthermore, rRNA and EngA undergo extensive rearrangement during assembly. These latest findings from the lab. will be presented.

Invited Lecture

Biochemistry in singulo: A single-molecule view of bacterial genome organization

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Biochemical studies of protein-DNA interactions are typically performed on relaxed, linear DNA, whereas DNA in the cell is always supercoiled. I will present our single-molecule data on supercoiled DNA showing that DNA helicity dictates a protein's binding mode and, in turn, its function. Specifically, we studied the *E. coli* xenogeneic silencer H-NS and its functional ortholog Lsr2 from *Mycobacterium tuberculosis*. H-NS binds relaxed or positively supercoiled DNA in an oligomerization mode that acts as a torsional constraint on supercoiling. On negatively supercoiled DNA, it instead bridges juxtaposed DNA strands within plectonemes, which allows it to act as a transcriptional silencer. Lsr2, in contrast, binds AT-rich sequences through a physical mechanism we call sequence-dependent co-condensation, sensing the overall local AT content rather than individual binding sites. Together, these studies highlight the power of single-molecule imaging.

Invited Lecture

From mother's milk to molecular medicine: Lactoferrin from structure to patient care

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Lactoferrin is a multifunctional iron-binding glycoprotein with antimicrobial, anti-inflammatory, immunomodulatory and tissue-protective properties. Our work on lactoferrin began with an effort to understand its three-dimensional structure and gradually evolved towards exploring how structural insights could be translated into therapeutically relevant applications. Particular attention was directed towards the C-terminal lobe (C-lobe), a structurally and functionally distinct region of the molecule. Structural and biochemical studies revealed a striking feature: diverse proteases cleave lactoferrin at a remarkably conserved region, reproducibly generating an intact C-lobe. The persistence of this proteolytic pattern suggests that evolution may have preserved a structurally accessible cleavage site that permits generation and functional retention of the C-lobe under different biological conditions.

These observations prompted us to examine whether the C-lobe could retain biologically important protective functions outside the context of the intact protein. One such application was explored in non-steroidal anti-inflammatory drug (NSAID)-induced gastropathy, where disruption of the gastric mucosal barrier, oxidative stress and inflammation contribute to tissue injury. Structural and animal studies demonstrated a protective role of the lactoferrin C-lobe in reducing NSAID-associated gastric damage. These findings extended the significance of the C-lobe beyond structural stability, suggesting that this proteolytically generated fragment may retain important tissue-protective properties and could serve as a biologically active entity in its own right.

The translational potential of lactoferrin was subsequently explored in human disease. A randomized, placebo-controlled clinical trial was undertaken to investigate oral lactoferrin supplementation in patients developing dry eye following refractive surgery. The study combined patient-reported symptoms with objective measures of tear-film stability, tear production and lipid-layer integrity. Lactoferrin supplementation resulted in faster and sustained improvement in dry-eye symptoms, accompanied by improvement in multiple objective indicators of ocular-surface health. These findings provided evidence that the anti-inflammatory, antioxidant and tissue-protective properties of lactoferrin can translate into measurable clinical benefit.

Taken together, this journey from the three-dimensional structure of lactoferrin and the unusual biology of its C-lobe, through experimental studies of NSAID-induced gastropathy and clinical evaluation in dry eye, to its emerging application in diabetes illustrates how structural biology can progressively inform therapeutic questions. It also highlights the growing opportunity to integrate structural biology, experimental models, clinical research and AI-assisted analysis as a continuum. Lactoferrin provides a compelling example of how understanding a molecule at atomic resolution can ultimately lead to interventions and outcomes that matter at the patient level.

Invited Lecture

Antiphage defense in mycobacteria through a phage-derived protein domain

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Encounters between bacteria and bacteriophages have led to the evolution of phage and counter-defense arsenals, respectively. Despite tremendous research in antiphage defense, the mechanisms by which mycobacteria resist such infections remain poorly understood. Mycobacteria-encoded multicopy phage resistance protein (Mpr) is known to provide antiphage defense against D29 and L5 mycobacteriophages. However, the molecular basis of Mpr-mediated antiphage defense remains unclear. Here, we explored the molecular basis Mpr-mediated antiviral immunity in mycobacteria. We show that DUF4352 of Mpr originates from mycobacteriophages, and is adopted by Msm, which is later repurposed for defense against related mycobacteriophages. Furthermore, DUF4352 domain-containing Mpr and other similar phage-encoded hypothetical proteins are nucleotide hydrolases, and synthesize an unusual guanosine nucleotide – ppGp. Through domain shuffling, we demonstrate that DUF4352 can be replaced with those coded by mycobacteriophages, suggesting that it is structurally and functionally conserved during evolution. Lastly Oligomerized Mpr is sensitive to GDP concentration, which maintains Mpr oligomers and mediates ppGp synthesis, thus bridging the structural and functional regulation of Mpr. In summary, we demonstrate that Mpr is a host-engineered, phage derived antiphage protein. Our study highlights the nucleotide-driven regulation of oligomerization and the alarmone-mediated toxic signaling in the host bacterium and phages.

Invited Lecture

Escape from neutralization: The role of differential sugarcoating of SARS-CoV-2 spike protein

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Viral surface glycoproteins mediate host-cell entry and are major targets of antibody-mediated immunity, placing them under continuous selective pressure. Viruses evade neutralization through multiple mechanisms, including epitope shielding by glycosylation, conformational masking, and genetic variation that alters antibody epitopes and reduces neutralization potency and breadth. While genetic variation is a well-established mechanism of antibody escape in viruses such as SARS-CoV-2 and HIV, post-translational modifications of viral glycoproteins may also contribute substantially to immune evasion.

We developed a novel approach to isolate and characterize SARS-CoV-2 viral populations with enhanced resistance to antibody-mediated neutralization. These viruses differed in glycosylation patterns and conformational states, revealing an additional layer of immune escape beyond genetic variation. The antigenic heterogeneity may allow the virus to persist for longer period of time especially in non-immunocompetent people and contribute to pathogenesis. These findings highlight the importance of evaluating therapeutic antibodies and vaccines not only for potency and breadth but also for the completeness of neutralization across diverse viral genetic and conformational landscape.

Invited Lecture

Recombinant measles virus with a pro-apoptotic gene: A potential therapeutic approach to target breast cancer

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Virotherapy is an emerging cancer therapy using genetically engineered viruses. The oncolytic effect of a virus can be achieved either through its inherent characteristics or by altering its genetic makeup. We have engineered the measles virus for oncolytic purpose by incorporating a pro-apoptotic gene of human origin. The anti-tumor effects of modified virus were evaluated in breast cancer cell lines. The replication-competent engineered virus infection had shown promising results in triple-negative breast cancer cells, representative of an invasive and aggressive sub type. The mechanism by which the recombinant virus induces anti-tumor effects was further investigated; genes that are involved in the tumor progression were found to be affected. Of which, CTNNB1 gene encoding β-catenin was the significant one. β-catenin pathway is known to be a driver of tumor cell invasion and migration; thus, the impact of the engineered virus on this pathway was investigated. The results had demonstrated a notable decrease in β-catenin expression and its downstream targets, reducing the migration potential of triple-negative breast cancer cells following infection. Our findings imply that the engineered measles virus may serve as a promising biotherapeutic agent for targeting breast tumors, and our validation studies are ongoing.

Invited Lecture

From mechanism to medicine: Translating jumbo phage biology into clinical potential against drug resistant pathogens

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Jumbo-bacteriophages are bacterial viruses with exceptionally large genomes. These phages are amongst the popular bacteriophages that is part of several phage therapy cocktails targeting *P. aeruginosa*. Recently, it has been discovered that jumbo-bacteriophages, upon infecting their hosts, can produce unique sub-cellular structures including a tubulin-like cytoskeletal complex and a protein-based DNA compartmentalizing organelle named as phage nucleus. These structures are essential for their life cycle, but also contribute in protecting injected phage DNA from host immune systems like CRISPR-Cas and restriction modification systems through intriguing mechanisms. Our research suggested that jumbo bacteriophages have extraordinary potential to evade CRISPR-Cas and other DNA targeting immune systems of bacteria. We have uncovered novel components of jumbo phages contributing to its immune evasion properties. Furthermore, through a collection of clinical *P. aeruginosa* isolates, we have isolated novel jumbo phages and explored its clinical potential through multipronged approaches including infection studies, genomics, and resistant mutant analysis. Overall, our investigations into jumbo bacteriophages, from fundamental science to translational applications, contribute to advancing the relatively unexplored role of viral genes in cellular evolution, while also offering innovative approaches to tackling antibiotic resistance towards a sustainable One Health future.

Invited Lecture

Small RNA-mediated epigenetic regulation of pathogenesis and host-parasite interaction

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Small RNAs are among the main drivers of epigenetic gene regulation. There are three main categories of small RNAs: microRNAs, piRNAs, and endogenous siRNAs. These various small RNA pathways are conserved across most eukaryotes. I will discuss the lessons learned about the biogenesis and function of small RNAs across different models. Briefly, I will discuss the role of small RNAs in the inheritance of stress memory using the nematode model, followed by our findings on the role of microRNAs in host-pathogen interactions. Lastly, I will highlight our group's new ventures aimed at understanding the role of small RNAs in host-parasite interactions, using the eukaryotic parasite *Toxoplasma* as a model.

Invited Lecture

From dermal to visceral adaptation: genome plasticity drives GP63 paralogue specialization in Leishmania

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Highly plastic genome of Leishmania is thought to underlie its remarkable ability to adapt to diverse host microenvironments, yet how this plasticity translates into dermal versus visceral persistence remains unclear. GP63, a zinc metalloprotease, is a well-established determinant of promastigote infectivity, particularly in cutaneous leishmaniasis. Despite this, its role in amastigote stage and in visceral disease caused by *Leishmania donovani* (Ld) remains undefined. Using an integrated approach combining phylogenetics, CRISPR-mediated genome editing, and biochemical analyses, we demonstrate that GP63 paralogues in Ld have undergone independent evolutionary diversification to support visceral infection. While GP63-paralogues encoded on chromosome 10, previously implicated in cutaneous manifestation caused by *L. major* were found severely truncated and dispensable in Ld two distinct GP63-paralogues encoded on chromosome-28 (GP63_28) and-31 (GP63_31) were found 'essential' to establish visceral infection. LdGP63_31 facilitates promastigote attachment to macrophages by promoting lipid raft engagement and complement inactivation, thereby enabling host entry. LdGP63_28 is essential for intracellular amastigote survival by suppressing host inflammatory pyroptosis. Structural and enzymatic analyses revealed preferential host localization and substrate specificities, possibly resulting from distinct amino acid substitution within conserved motifs of these proteases, indicating independent evolutionary adaptations. Together, these findings reveal coordinated functional specialization of GP63-paralogues ensuring visceral adaptation.

Invited Lecture

Non-coding RNAs in regulating gene expression and chromatin dynamics in *P. falciparum*

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Non-coding RNAs (ncRNAs) are increasingly recognized as important regulators of gene expression, yet their functional roles in the malaria parasite *Plasmodium falciparum* remain incompletely understood. Despite its compact genome and limited repertoire of canonical transcriptional regulators, *P. falciparum* exhibits highly coordinated and dynamic control of gene expression in response to environmental stress and during antigenic variation. Here, we investigate diverse classes of non-coding transcripts and their contribution to transcriptional, post-transcriptional, and chromatin-based regulation. We identify widespread and regulated antisense transcription, which responds to environmental stresses and can generate sense–antisense RNA duplexes that influence transcript stability and translational engagement. In parallel, we identify short-lived non-coding transcripts arising from heterochromatic regions that interact with the chromatin regulator PfHP1 and contribute to the dynamic organization and maintenance of repressive chromatin domains. Together, these findings reveal that ncRNAs function at multiple regulatory levels in *P. falciparum*, linking RNA metabolism, translation, chromatin organization, and gene expression plasticity. Rather than representing transcriptional by-products, ncRNAs emerge as dynamic regulatory molecules that help the parasite adapt to changing environments while maintaining tightly controlled expression of genes involved in virulence and survival. These findings expand our understanding of RNA-mediated regulation in malaria parasites and highlight non-coding transcription as an important layer of parasite gene regulation.

Invited Lecture

A fight for eradication of neurocysticercosis against all the odds: Immunology, Inflammation, and Epileptogenesis of *Taenia solium*

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Neurocysticercosis (NCC) is considered as the most common parasitic infestation of the central nervous system, caused by larval stage of *Taenia solium*. Within endemic regions, the parasite contributes to approximately 30% of acquired epilepsy cases, but in areas with a higher frequency, this proportion can reach up to 70%. NCC is frequent in regions with insufficient sanitation amenities, high rates of improperly prepared pork consumption, and where pigs roam freely. It is believed that the overall number of people affected by cysticercosis globally lies between 2.56 and 8.30 million, comprising both symptomatic and asymptomatic cases.

Demographic, clinical and epidemiological data from rural pig farming community in North India, showed alarmingly high rates of active epilepsy and *T. solium* taeniasis. Our investigation reveals that many individuals with diverse stages of cysticerci in their brains are symptomatically unaffected, thereby disputing the idea that the degenerative or calcified stages of the parasite predominantly trigger seizures in NCC. The immunopathogenesis associated with NCC is mostly ambiguous. The Th1 and Th2 immune responses are active in proximity to metacestodes, and the specific immune response type could determine the severity of the disease. The Secretome of *T. solium* cyst may induce immunosuppression during the initial viable phase of the parasite in NCC, which is predominantly asymptomatic. The degenerating parasite releases fluid which is inflammatory in nature and produces strong Th1 immune response leading to epilepsy.

Neuroimaging tools are viewed as gold standards for NCC diagnosis, although their availability is constrained in underdeveloped nations. Our findings show cyst fluid antigen-based lymphocyte transformation test (LTT) and Enzyme-linked immunoelectrotransfer blot (EITB) serves as a key diagnostic tool for NCC. Further investigations are required to deeply understand the immunomodulatory and epileptogenic role of the parasite for better clinical management.

Invited Lecture

Role of RNA metabolism in controlling RNA-RBP condensate dynamics in ageing and inflammation

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RNA-protein condensates, such as stress granules, help cells adapt to stress and maintain RNA homeostasis. However, how age-related changes in RNA metabolism affect these condensates and contribute to chronic inflammation remains unclear. Here, we show that cellular RNA abundance is a key regulator of condensate assembly, dynamics, and function during ageing and inflammatory stress.

We find that ageing is associated with a progressive decline in cellular RNA levels, which compromises the formation and material properties of RNA-RBP condensates. RNA loss shifts condensates toward aberrant protein-rich states with reduced dynamics, limiting their ability to respond effectively to stress. Functionally, impaired condensate behavior disrupts RNA buffering and promotes the accumulation of endogenous double-stranded RNA (dsRNA), a potent trigger of innate immune pathways.

Importantly, we identify stress granules as protective compartments that restrict dsRNA-induced mitochondrial fragmentation and inflammatory signaling. When stress granule integrity is compromised, dsRNA-driven mitochondrial dysfunction and inflammation are exacerbated. Restoration of RNA homeostasis rescues condensate dynamics and mitigates these defects.

Together, our findings reveal a direct link between age-associated RNA depletion, dysfunctional RNA-RBP condensates, and chronic inflammation, establishing RNA metabolism as a central regulator of cellular resilience during ageing.

Invited Lecture

The emergence and evolution of biomolecules on the early Earth: Implication for life's origin

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How life originated on our planet continues to be an enduring scientific mystery. At the COoL Lab @IISER Pune, our goal is to understand how first cellular life emerged on the early Earth. Delineating the various steps of this process involves studying the fundamental components of a putative protocell, both, independently and when they interact with each other. In this regard, we have been characterizing the outcome(s) of different prebiotically pertinent reactions, which would have resulted in the emergence of informational/catalytic polymers and protocellular entities. The results we have gleaned thus far underscore the importance of accounting for prebiotic soup heterogeneity while discerning life's origin and for characterizing co-evolutionary processes (e.g. oligomer synthesis and membrane assembly). I will give a flavour of our work that has fundamental implications for delineating the emergence of functional protocellular systems on the early Earth.

Invited Lecture

The circular RNA–stemness circuit: A hidden driver of sorafenib resistance in Hepatocellular Carcinoma

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Chemoresistance remains a major challenge in hepatocellular carcinoma (HCC), contributing to poor clinical outcomes and high mortality. Although circular RNAs (circRNAs) are increasingly recognized as regulators of tumor progression, their role in chemoresistance remains poorly understood. This study investigated the functional significance of DKK1 pre-mRNA derived circRNA, circ_DKK1 (hsa_circ_0018414) in making HCC resistant to sorafenib, one of the most effective first-line chemotherapeutics for HCC.

Differential circRNA analysis of sorafenib-sensitive and resistant (SR) HCC patient-derived organoids (GSE182593) using CIRI2 identified 101 dysregulated circRNAs, among which circ_DKK1 was markedly downregulated in resistant organoids. Its differential expression in HCC-SR cell lines was validated by RT-qPCR using divergent primers while actinomycin D treatment confirmed its higher stability compared to linear RNA. Cellular fractionation and RNA-FISH demonstrated predominant cytoplasmic localization. Restoration of circ_DKK1 in Huh7-SR cells reduced stem-like cell populations, suppressed spheroid formation and migration, and re-sensitized cells to sorafenib.

Mechanistically, circ_DKK1 acted as a molecular sponge for oncogenic miR-140-3p, restoring PTEN expression and attenuating PI3K/AKT signaling. In silico analysis and ChIRP further identified interactions with transcripts involved in Wnt signaling, cell survival, and drug efflux, including VCAN, WNT5A, and ABCB10.

Collectively, these findings identify circ_DKK1 as a key regulator of stemness-associated sorafenib resistance and a potential therapeutic target in advanced HCC.

Invited Lecture

RNA-Dependent regulation of ribonucleoprotein complex dynamics by an E3 ligase

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Stress granules (SGs) are ribonucleoprotein (RNP) complexes that assemble in the cytoplasm in response to cellular stress, viral infection, and disease states including cancer and neurodegeneration. Notably, the pathological protein aggregates characteristic of age-related neurodegenerative diseases share both molecular composition and assembly mechanisms with SGs, underscoring the importance of understanding how SG dynamics are regulated.

We have identified TRIM3 (TRIpartite Motif Containing 3) as a novel SG-associated protein. TRIM3 is an RNA-binding E3 ubiquitin ligase previously implicated in breast cancer progression through stabilization of estrogen receptor alpha. We find that upon oxidative stress, TRIM3 is recruited to SGs, where it co-localizes with G3BP1 and other canonical SG markers. Strikingly, overexpression of TRIM3 delays SG assembly, whereas TRIM3ΔNHL- a mutant that retains E3 ligase activity but cannot bind RNA- fails to do so, establishing that the RNA-binding function of TRIM3, is as important as its ubiquitin ligase activity, for this effect.

To define the mechanistic basis of this regulation, we examined the RNA targets of TRIM3. TRIBE analysis revealed that TRIM3 binds preferentially within the open reading frames of target mRNAs. Consistent with a role in promoting translation, reporter constructs in which the ORFs of TRIM3 target mRNAs were fused to GFP showed enhanced chimeric protein expression. Together, these findings suggest that TRIM3 both delays SG assembly as well as is capable of SG disassembly, by sustaining the translation of specific target mRNAs, using RNA as a scaffold to coordinate protein production. We are further exploring if TRIM3 modulates the balance between polysome-engaged and SG-sequestered transcripts.

Invited Lecture

Tuberculosis: From molecular mechanisms to genomic surveillance

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Tuberculosis remains a major global health challenge, driven in part by the remarkable ability of *Mycobacterium tuberculosis* (*Mtb*) to persist in the host, evade immune defences, and acquire drug resistance. My laboratory investigates the kinase-mediated signalling networks that govern *Mtb* growth, cell division, cell-wall biogenesis, and survival under host-imposed stress, with particular emphasis on PknA, PknB, PknG, PstP, and associated pathways. More recently, we have expanded our work to examine the regulation of translation initiation. In this presentation, I will discuss how initiation factor 3 (IF3) controls initiation-codon fidelity and how this regulation, in turn, influences its own translation. Complementing these mechanistic studies, my group contributes to whole-genome sequencing efforts through the DBT-funded Indian Tuberculosis Genomic Surveillance (InTGS) Consortium, which is cataloguing drug-resistance mutations and lineage diversity across thousands of clinical *Mtb* isolates from India. Together, these efforts bridge molecular mechanisms and population-scale genomic surveillance, providing an integrated framework to understand, track, and combat drug-resistant tuberculosis in India and beyond.

Invited Lecture

Induced innate immunity in Mycobacterium against mycophages

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Mycobacteriophages are promising alternatives to antibiotics for treating drug-resistant mycobacterial infections, but the emergence of phage-resistance limits their therapeutic potential. Our group has recently identified the transcriptional regulator *xylR* as a critical host determinant required for productive infection by mycobacteriophage TM4 in *Mycobacterium smegmatis*. Through spontaneous mutant isolation, transcriptomic profiling and lipid analyses, we have demonstrated that an in-frame deletion in *xylR* confers robust TM4 resistance through a remodeled cell envelope that obstructs phage DNA injection without affecting phage adsorption. Mechanistically, *xylR* deficiency promotes the accumulation of surface lipooligosaccharides, creating an envelope barrier that restricts phage genome delivery. TM4 infection further enhances lipooligosaccharide biosynthesis, reinforcing this as a phage-responsive innate resistance mechanism. The talk will attempt to redefine *xylR* as a key regulator linking cell envelope lipids to phage susceptibility and uncover a previously unrecognized mechanism by which host lipid homeostasis regulates phage infection.

Invited Lecture

Mycobacterial biofilms; another armor is rise of a superbug

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Mycobacterium tuberculosis (Mtb) is one of most successful pathogens. The capability of Mtb to form the biofilm could explain the phenotypic drug tolerance displayed by Mtb in humans. Recent literature points to the drug tolerance observed in biofilms that may help in the evolution of drug resistance. Here, I will highlight that intracellular thiol reductive stress (TRS) induces Mtb biofilm formation. TRS-induced biofilms harbor drug-tolerant but metabolically active bacteria with comparable levels of ATP/ADP, NAD^+/NADH, and $NADP^+$/NADPH. Evidence generated through electron microscopy and confocal microscopy revealed that cellulose is a major component of Mtb biofilms. Further analyses suggest that cellulose is universally used as a major component of different types of biofilms across slow and fast-growing mycobacterial species. Using cellulose as a biomarker, we demonstrate that Mtb forms biofilms in infected mice's lungs, non-human primates, and human lungs. We have observed that cellulose protects resident bacilli from the host immune system and antimycobacterial agents. Interestingly, new modes of drug resistance/tolerance were observed inside the biofilms. Further studies indicate that Mtb forms intracellular biofilms, although the significance of these intracellular biofilms in TB pathogenesis remains to be analyzed.

Invited Lecture

Inhibition of efflux pumps: Making resistant bacteria susceptible to existing antibiotics

Suvendu Ojha, Simran Sinsinwar, Puja Chatterjee, Sarmistha Biswal, Pinkilata Pradhan and Tushar Kant Beuria*

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Efflux pumps in *Staphylococcus aureus* are membrane transport systems that actively expel antibiotics and other toxic compounds, lowering their intracellular concentrations and reducing treatment effectiveness. Major pumps, including NorA, NorB, AbcA, and MepA, contribute to resistance against fluoroquinolones, β-lactams, antiseptics, and other antimicrobials. Their expression is regulated by global factors such as MgrA and can be enhanced by environmental stress. Efflux pump inhibitors may restore antibiotic susceptibility and improve therapeutic outcomes in resistant infections. We evaluated FDA-approved drugs as potential efflux pump inhibitors (EPIs) to restore antibiotic activity. Our Screening identified several molecules that can inhibit the efflux pump activity or expression in *S. aureus*. One of such molecule is montelukast, a leukotriene receptor antagonist, effectively inhibits the *S. aureus* efflux pumps and showed synergy with moxifloxacin in vitro and reduced bacterial burden in a murine skin-infection model. Moxifloxacin is an antibiotic that actively expelled out through norB efflux pump. The norB efflux pump is regulated by MgrA, the master regulator that controls several efflux pumps. Its phosphorylation form can interact to the promoter region of the norB and inhibits its expression. Our study showed that montelucast strongly binds to the MgrA and enhanced its phosphorylation leading to the inhibition of the expression of *norB* gene.

Invited Lecture

Indigenous CRISPR-Cas9 tools: Advancing gene therapy through precision

Souvik Maiti

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The advent of CRISPR-Cas9 has revolutionized the field of gene therapy, offering unprecedented precision in genome editing. While significant progress has been made globally, the development of indigenous CRISPR tools tailored to address region-specific challenges holds immense potential for advancing therapeutic applications. This talk will delve into the journey of developing an indigenous CRISPR-Cas9 platform optimized for treating genetic disorders prevalent in India, such as sickle cell disease and beta-thalassemia.

Key highlights will include the engineering of the CRISPR-Cas9 system to enhance target specificity and reduce off-target effects, ensuring safety and efficacy in clinical settings. Additionally, I will discuss the biophysical insights gained during this development, particularly in understanding the interaction of CRISPR components.

The talk will also provide an overview of ongoing academic clinical trials utilizing this indigenous tool, addressing challenges such as scalability, regulatory pathways, and ethical considerations. By integrating cutting-edge science with regionally relevant solutions, this initiative exemplifies how homegrown innovations can transform healthcare and make gene therapy accessible on a global scale.

Invited Lecture

Personal genomes for precision medicine

Vinod Scaria,
Karkinos Healthcare

One of the major advances that happened in the last decade has been the availability of fast, efficient and cost-effective DNA sequencing which has seen tremendous applications in healthcare and research. This has been largely possible with the advent of newer sequencing approaches which offer a higher throughput, lower cost and faster turnaround times, and appropriate computational tools to enable the handling, processing and mining of information from them. On one end, this technology enables one to elucidate the genomes of individuals and how genomic variations could influence the life of the individual, while on the other side, it enables one to peek into the pathophysiology of diseases and have a mechanistic view of the disease processes. It is widely believed that these advances would be immensely useful in healthcare through Predictive, Preventive, Precise, Personalised and Participatory Medicine. In the present talk, we would describe our experiences with personal genome sequencing and use of genomics approaches and model systems towards this end. We have employed a number of novel approaches towards harnessing the BigData challenge including involvement of students towards analysis and model-building. Systematic annotation of datasets for personalised genomics for the OpenPGx consortium and analytical tasks through the 2C4C programme for Cheminformatics could be crowdsourced through the platform.The talk would also discuss the way forward, detailing the ongoing initiatives including the GUaRDIAN Consortium involving a large clinical network towards realising the dream.

Invited Lecture

Genetic and physiological adaptations in *Klebsiella pneumoniae* customized for the bloodstream

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Klebsiella pneumoniae (Kpn) is one of the notorious causes of infant mortality, especially in low-resource settings. Genomic and virulence phenotyping of three neonatal sepsis outbreak isolates from Jodhpur identified a Kpn isolate BC135 carrying a capsule-inactivating insertion, resulting in a hypomucoid phenotype. As the Kpn capsule confers resistance to complement killing, permitting bloodstream survival, the finding was intriguing. Even more so because the BC135 isolate remained fully resistant to the antimicrobial effects of human serum despite losing its capsule. Subsequent comparative genomic analyses suggest that capsule inactivation may be a common adaptation in neonatal sepsis-causing Kpn isolates, although there may be evolutionary preferences in how capsule inactivation is achieved. To understand the physiological adaptations of BC135 to human serum, its transcriptome was profiled after exposure to non-immune human serum. We show that Kpn BC135 undergoes extensive transcriptional rewiring to overcome host nutritional immunity and the oxidative stress induced by host antimicrobial peptides present in human serum. In addition, we identified metabolic shifts and key pathways that could be exploited as targets to tackle this formidable pathogen. Taken together, our data suggest a model in which the non-capsulated Kpn BC135 seamlessly adapts to attacks by innate immune factors in serum by fine-tuning its metabolism and defences. This expanded understanding of the physiological adaptations of clinical Kpn isolates to bloodstream-like conditions will enable the development of more effective strategies to prevent or treat Kpn infections.

Invited Lecture

Exploring pathomechanisms and potential therapeutic leads for rare diseases

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Rare Diseases represent more than 8000 diseases with prevalence less than 10/10000 that are incurable due to challenges in diagnostics and therapeutics as a result of phenotypic heterogeneity and lack of effective clinical trials. One such rare neuromuscular genetic disorder is GNE Myopathy (GNEM) characterized by anterior tibialis muscle weakness and atrophy progressing to wheel-chaired bound patients. GNEM is caused due to mutations in bifunctional GNE gene (UDP-N-acetylglucosamine 2 epimerase/N-acetyl mannosamine kinase) affecting sialic acid biosynthesis. Pathologically the disease is characterized by presence of rimmed vacuoles with protein aggregates and upregulation of muscle atrophy markers. Poor understanding of pathomechanisms at cellular and molecular level limits drug development for GNEM. Our laboratory has focused on establishing the cellular models to study GNEM disease in HEK cells harbouring recombinant GNE mutant proteins of Indian origin. Further the mechanisms were validated in L6 skeletal muscle cells exhibiting GNE knock out at exon 3 (Heterozygous). The cytoskeletal network was found to be altered with reduced cell migration and actin dynamics severely affected in absence of functional GNE. ER Stress and UPR pathway leading to protein aggregation was found to be upregulated along with mitochondrial dependent apoptosis in GNE mutant cells. HSP70 was found to be GNE interacting partner and was downregulated. Studies indicated reduced cytosolic calcium that may affect autophagic flux reducing autophagy. Further muscle atrophy markers and their regulatory signaling cascades were affected in GNE dysfunctional cells. Repurposing of drugs such as CGA (activator of cofilin affecting actin dynamics), BGP15 (activator of HSP70) and IGF1 (Insulin Growth factor reduced apoptosis and muscle atrophy) successfully demonstrated significant rescue of cellular phenotype in GNEM cellular model. New small effector molecules as substrate analogs are being explored as potential therapeutic agents. Our study provides insights into the understanding of pathomechanisms of GNEM at molecular and cellular level and opens up new areas of drug design for rare genetic disorder.

Invited Lecture

Beyond adhesion: Active cell sorting

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Sorting or segregation of two cell types is a mechanism of pattern formation in multicellular organisms. What drives cell sorting remains an open question. The classical answer to this question is the Differential Adhesion Hypothesis (DAH), which suggests that adhesion energy between cell types differs and that sorting occurs within an ensemble of cells as the system moves from a high-energy state to a minimum-energy state. This is analogous to the separation of oil and water. However, unlike oil and water, living cells are not passive, but active agents. They sense their neighbors, generate forces, change shape, and move in preferred directions. Treating their motion as largely passive or random may therefore miss an important part of the physics. In this talk, I will discuss a different way of thinking about cell sorting. We explore simple models in which individual cells use local information to bias their movement. Collective organization then emerges from many such active decisions, without requiring the entire population to behave as if it were minimizing a global energy. Our aim is not to reproduce any particular experimental system. Instead, we propose generic, non-equilibrium models of active cellular organization as an alternative to the DAH model.

Invited Lecture

Computational analysis of single-cell and spatial omics datasets for elucidating cancer heterogeneity

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Recent advances in single-cell and spatial genomics have fundamentally expanded our ability to resolve tumor heterogeneity and cellular interactions within complex tissue microenvironments. Single-cell sequencing enables the detection of somatic variants and reconstruction of tumor phylogenies, which are essential for understanding intra-tumor heterogeneity that drives drug resistance and cancer relapse. However, emerging large-scale single-cell panel sequencing technologies introduce substantial computational challenges due to amplification biases and data scale, limiting the performance of existing variant calling and phylogenetic methods. Beyond genetic heterogeneity, cellular communication within tissues critically shapes disease progression and therapeutic response and spatial transcriptomics datasets can be utilised for mapping the cellular communication in the tissue. In this talk, I will present two statistical frameworks - PHALCON and Renoir for resolving tumor heterogeneity and cellular interactions from single-cell and spatial omics datasets. PHALCON is a statistical framework for scalable mutation detection from single-cell panel sequencing data that models tumor evolution under a finite-sites model along a clonal phylogeny. Applications of PHALCON to triple-negative breast cancer and acute myeloid leukemia uncover novel high-impact somatic mutations, resolve rare and clinically relevant clonal substructures, and identify poor-survival AML subgroups characterized by chromatin, cohesin, and DNA methylation pathway alterations. Renoir is a framework for charting ligand–target activities across spatial topologies, identifying spatial communication niches and pathway-level activity landscapes. Across spatial datasets spanning development and disease, Renoir reveals context-specific ligand–target programs and cellular crosstalk, including hepatocyte–macrophage interactions in fetal liver and interactions between oncofetal and bipotent cell populations in hepatocellular carcinoma.
Together, these approaches integrate clonal evolution with spatially resolved signaling, providing a unified framework for dissecting tumor biology and tissue organization from single-cell and spatial genomics data

Invited Lecture

Reading genomes with DNA motifs

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We read the genome as proteins in the cell would – by studying the distributions of 5–6 base motifs of DNA in the whole genome or smaller stretches such as parts of, or whole chromosomes. This led us to some interesting findings about motif clustering and chromosome organization. It is quite clear that the motif distribution in genomes is not random at the length scales we examined: 1 kb to entire chromosomes. The observed-to-expected (OE) ratios of motif distributions show strong correlations in pairs of chromosomes that are susceptible to translocations. With the aid of examples, we suggest that similarity in motif distributions in promoter regions of genes could imply co-regulation. A simple extension of this idea empowers us with the ability to construct gene regulatory networks. Further, we could make inferences about the spatial proximity of genomic fragments using these motif distributions. Spatially proximal regions, as deduced by Hi-C or pcHi-C, were ~3.5 times more likely to have their motif distributions correlated than non-proximal regions. These correlations had strong contributions from the CTCF protein recognizing motifs which are known markers of topologically associated domains. In general, correlating genomic regions by motif distribution comparisons alone is rife with functional information.

Invited Lecture

Quantitative elucidation of mitochondrial structure-function heterogeneity to decipher specification of the potent mitochondria primed neoplastic stem cells and their therapeutic vulnerabilities

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Mitochondria are heterogenous within and between cells, tissues, and individuals, which is further influenced by intracellular and extracellular milieu. Untangling of mitochondrial heterogeneity is required to elucidate the complex role of multifaceted mitochondria and knowledge translation for precision medicine. Mitochondria can exist in elaborate networked or non-networked structures, which is modulated by their fission and counteracting fusion events governed by key molecules. A high-potency stemness state with characteristic mitochondrial structure-function properties 'primes' stem cell activation. Earlier, we isolated such mitochondrial primed stem cells (mpSCs) of ~10 folds higher potency from neoplastic populations and reported that precise tuning of mitochondrial structure by the mitochondrial fission protein, Drp1, can prime an mpSC state for neoplasticity. More recently, we developed mito-SinComp quantitative profiling to untangle mitochondrial structure-function heterogeneity by analyzing their single component organization. Our data demonstrates that a Drp1 regulated subpopulation of Small-Mitochondrial-Networks (SMNs) with precise properties is linked to specification of an early mpSC state. Hierarchical analyses of Drp1 linked heterogeneity of a transcriptomic signature of mitochondria-primed neoplastic stem cells to mitochondrial ATP hotspots explains the heterogeneous vulnerability of cancer cells to mitochondrial energy-metabolic inhibitors. We reported a proof of concept of mitochondrial function can be predicted from their structure by using machine learning algorithm on data generated from mito-SinComp profiling of organizational structure-function of mitochondria. Currently, we are attempting to employ AI-ML strategies to identify mitochondrial structural biomarkers for neoplastic states, towards developing a personalized/targeted approach for eliminating the potent neoplastic mpSC state.

Invited Lecture

Engineering of a Bt protein for the development of pink bollworm-resistant transgenic cotton

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Transgenic crops expressing *Bt*-insecticidal proteins have revolutionised agriculture by effectively controlling major lepidopteran pests. However, field-derived resistance in pink bollworms against Bollgard II transgenic cotton has threatened the technology's long-term sustainability. As a result, cotton lint productivity in India has stagnated below 500 kg/hectare over the last decade.

Earlier, we developed a chimeric Cry protein, Cry1EC, and expressed it in transgenic cotton to confer resistance to leaf armyworm. This protein was not toxic to pink bollworm. We compared its domain III sequence with other Cry1-class δ-endotoxins and identified variations at a few positions. We substituted these amino acids in Cry1EC with those found in other Cry1 proteins using site-directed mutagenesis and tested the mutants for larvicidal activity against pink bollworm. A series of experiments led to the development of a highly toxic triple-mutant variant, named mCry1EC, against the target pest. We expressed mCry1EC in transgenic cotton under the regulation of a wound-specific promoter, named *RbPCD1*. The selected transgenic line expresses mCry1EC at ~0.1% of total soluble protein for up to 160 days. It provides complete protection against both susceptible and field-derived Bt-resistant pink bollworm populations by causing over 90% larval mortality, while retaining toxicity against leaf armyworm. Expression in major insect feeding tissues, including leaves, squares, flowers, and bolls, ensures season-long yield protection. Comprehensive molecular and phenotypic characterization identified three promising transgenic events. Detailed genetic analysis of event NBRI-PGK-519 confirms T-DNA integration into an intergenic region of chromosome A08, with no vector backbone sequences. Event NBRI-PGK-519 is selected for further advancement and is currently undergoing open-field trials across major cotton-growing zones of India as part of the regulatory evaluation process for deregulation and potential commercial cultivation.

Invited Lecture

Durable resistance to bacterial blight disease and development of super rice varieties

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Rice crop is affected by several biotic and abiotic stresses. Bacterial Blight (BB) caused by *Xanthomonas oryzae* pv. *oryzae* (*Xoo*) is one of the most serious bacterial diseases of rice, which can result in up to 50% yield loss. Towards a molecular understanding of rice-*Xoo* interactions, we conducted a meta-analysis of transcriptomic data and identified a rice *flavone synthase* (*OsFNS*) gene. *OsFNS* is targeted by a type III effector protein of *Xoo* and is a susceptibility factor for *Xoo* in rice. We have further characterised the *OsFNS* gene through various functional assays. Currently, using marker-assisted selection, functional genomics and genome editing approaches, we are developing durable resistance to BB disease in rice. Improved Samba Mahsuri (ISM), jointly developed by CSIR-CCMB and ICAR-IIRR is a BB disease-resistant derivative of Samba Mahsuri (SM) and low GI (diabetic-friendly) rice. We are working towards the development of super (trait-added) rice varieties of ISM that possess additional important climate-resilient [resistance to blast (a fungal disease), gall midge, brown planthopper (insect pests), submergence, drought, salinity, and low soil phosphorus etc.] and high-yielding traits. Furthermore, we have identified EMS mutant lines of SM that exhibit several important agronomic traits. These mutants and identified markers will serve as a technology package for the development of climate-resilient, high-yielding and healthier super rice varieties.

Invited Lecture

Molecular mechanisms in plant-rhizobacterial interaction for abiotic stress tolerance

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Plant growth promoting rhizobacteria (PGPR) are beneficial soil bacteria that associate with plant roots and help in plant growth promotion and stress tolerance. There is relatively low understanding of the molecular mechanisms involved in such beneficial interactions, especially for abiotic stress tolerance. Our laboratory is focused on delineating these mechanisms by studying the interaction between various rhizobacteria with the model plants, *Arabidopsis thaliana* and rice. In this regard, I will be highlighting our studies on two PGPR strains, *Bacillus endophyticus* J13 and *Pseudomonas putida* AKMP7. We have established that J13 positively influences drought tolerance in *A. thaliana* by (a) increasing the soil water potential (precluding the necessity of ABA-signalling) (b) accelerating the plant auxin-dependent auxin conjugation pathway and (c) modulating cell-wall ligno-cellulosoic composition. J13 helps in salinity amelioration of *A. thaliana* by positively regulating ethylene and brassinosteroid signalling. AKMP7, a multiple abiotic stress tolerant PGPR, imparts drought tolerance to rice plants by tightly regulating the homeostasis of polyamines, and related metabolites, such as, GABA and proline. It induces proteome-wide changes in rice roots under saline conditions and positively regulates the signalling pathways that lead to Na^+ exclusion and sequestration in plant cells. However, this strain becomes conditionally pathogenic towards Arabidopsis under drought conditions by negatively regulating the salicylic acid-mediated SAR pathway and induction of T6SS-mediated pathogenesis.

Invited Lecture

Challenges in development of plant secondary metabolites as phytopharmaceuticals

T. Narender
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Plant secondary metabolites are organic compounds produced by plants through subsidiary pathways (such as the shikimic acid or mevalonate pathways) that are not directly involved in basic growth or reproduction, but serve vital roles in defense, signaling, and environmental adaptation. When extracted and utilized in medicine, these compounds function as phytopharmaceuticals—standardized, plant-derived therapeutic agents that target specific human biological receptors and disease processes. Development of phytopharmaceuticals from plant secondary metabolites for non-communicable diseases such as diabetes, osteoporosis, benign prostatic hyperplasia, polycystic ovary syndrome and challenges in their development will be discussed.

Abstracts of Flash Talks

Flash Talk FT-01

Mechanism-guided drug repurposing across infectious disease and oncology: Kinome-guided targeting in *Leishmania* and PDE inhibitor repurposing in cancer

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Abstract: Drug repurposing can shorten timelines and reduce cost compared with de novo drug discovery. We applied this strategy in two disease settings-*Leishmania* and cancer. For *Leishmania*, we started with a large kinase-focused computational screen, analyzing around 350 parasite kinases and prioritizing almost 180 high-value candidates based on phosphorylation-related scoring. We then tested whether approved tyrosine kinase inhibitors-such as sorafenib and imatinib-could engage these parasite targets. Promising in silico hits were moved to in vitro testing, creating a practical pipeline from digital triage to biological validation. In parallel, for cancer, we repurposed phosphodiesterase (PDE) 4 and 5 inhibitors rolipram and sildenafil respectively by screening for anticancer activity in breast and cervical cancer, selecting druggable leads, and validating cell-killing effects through key signaling pathways. To move beyond single-target interpretation, we performed off-target interrogation to identify auxiliary liabilities of rolipram in binding with MMP2/MMP9 that could reinforce anti-cancer activity, including processes relevant to EMT transition and metastasis. Together, these studies represent convergent repurposing paradigm: (i) broad target-space computation, (ii) clinically informed molecule matching, and (iii) mechanism-resolved biological validation. By reusing pharmacologically characterized compounds against carefully prioritized disease biology, effective, affordable, and translational therapeutics in both neglected parasitic disease and oncology can be achieved.

Flash Talk FT-02

Structural and biophysical insights into Histo-Aspartic protease inhibition by repurposed antiviral peptidomimetics

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Abstract: The emergence of multidrug-resistant *Plasmodium falciparum* strains necessitates the identification of new molecular targets and therapeutic scaffolds for antimalarial drug discovery. The acidic food vacuole of the parasite contains a cascade of proteolytic enzymes responsible for hemoglobin degradation, providing attractive targets for structure-based inhibitor development. Histo-Aspartic Protease (HAP), an atypical member of the plasmepsin family, is involved in hemoglobin processing and represents a promising target for exploring novel antimalarial inhibitors. In the present study, a structure-guided drug repurposing strategy was employed to evaluate antiviral peptidomimetic compounds as potential inhibitors of HAP. Recombinant HAP was successfully expressed and purified, followed by biochemical and biophysical characterization of its interactions with selected antiviral inhibitors. Molecular docking was employed to investigate inhibitor recognition within the HAP active-site region and to identify the molecular interactions contributing to ligand binding. Fluorescence spectroscopy was used to characterize inhibitor-induced changes in the intrinsic fluorescence of HAP, while isothermal titration calorimetry provided quantitative thermodynamic parameters governing protein– inhibitor

association. Enzyme inhibition studies further demonstrated the ability of the repurposed compounds to modulate HAP catalytic activity. The integration of recombinant protein technology, molecular docking, fluorescence spectroscopy, calorimetry, and enzyme kinetics provides a multidisciplinary framework for understanding the structural and thermodynamic basis of HAP inhibition. These findings demonstrate the potential of antiviral peptidomimetic scaffolds as repurposed candidates for targeting plasmepsin-mediated hemoglobin degradation and highlight the utility of structure-guided and biophysical approaches in accelerating antimalarial drug discovery.

Flash Talk FT-03

Coordination between HSP40-HSP70-HSP110 and mechanochemical GTPases in the human malaria parasite

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Abstract: *Plasmodium falciparum* possesses a highly divergent proteome rich in low-complexity regions, making maintenance of protein homeostasis particularly challenging during its complex lifecycle. The parasite relies on an evolutionary diverged proteostasis machinery, including the HSP40-HSP70-HSP110 tri- chaperone system, which coordinates folding and degradation quality control processes. We checked the expression and localization of plasmodial HSP40-HSP70-HSP110 under different proteotoxic stress conditions. We observed stress-induced differential partitioning, with HSP70 and HSP110 both in soluble and detergent-insoluble fractions. Whereas HSP40 showed stress-specific redistribution, predominantly in insoluble fraction suggesting stress-dependent differences in their client substrate interactions. These chaperones sediment into higher order complexes and co-interact with each other. LC-MS analysis of HSP110 immunoprecipitates identified interaction with plasmodial dynamins. To validate this interaction, pull downs were performed with his-tagged *Pf* DYN1-3 and *Pf* DYN2 and *Pf* DYN3 showed enrichment of HSP40, HSP70 and HSP110, suggesting a potential functional connection between Plasmodial dynamins and the HSP chaperone network. These interactions raise the possibility that the HSP machinery may contribute to the folding, stability or quality control of dynamins, or that dynamins may participate in the trafficking or organization of chaperone-associated complexes. Further studies are required to determine the molecular nature and functional significance of these associations.

Flash Talk FT-04

Differentially regulated M32 Metallo Carboxypeptidase of *Leishmania* controls miltefosine induced apoptosis and protects parasite against oxidative stress

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Abstract: Visceral leishmaniasis, caused by *Leishmania* parasites, remains a major global health concern, with limited therapeutic options. Miltefosine (MIL), an effective oral antileishmanial drug, is threatened by emerging resistance, although the underlying mechanisms remain poorly understood. This study investigated the functional role of differentially expressed carboxypeptidase (*Ld*CP), a metallopeptidase

M32 family protein, in MIL-resistant *Leishmania donovani*. *Ld*CP knockdown in MIL-resistant BHU875 parasites increased MIL sensitivity and susceptibility to oxidative stress. Silencing *Ld*CP in BHU875 and DD8 parasites attenuated cell-cycle progression and growth and reduced intracellular thiol and ATP levels. Conversely, *Ld*CP-overexpressing parasites exhibited enhanced growth, maintained mitochondrial membrane potential, neutralized MIL-induced reactive oxygen species, and showed elevated thiol and ATP levels. *Ld*CP knockdown also induced MIL-associated apoptosis-like cell death, with increased intracellular calcium levels. Furthermore, *Ld*CP-knockdown parasites displayed impaired macrophage infectivity, reduced intracellular parasite burden, and increased expression of apoptotic markers and inducible nitric oxide synthase. Overall, these findings demonstrate that *Ld*CP contributes to parasite survival by maintaining cellular redox balance, energy metabolism, mitochondrial integrity, and resistance to MIL- induced stress. Thus, *Ld*CP may regulate MIL-induced apoptosis and represents a potential therapeutic target for combating MIL resistance in *Leishmania* parasites.

Flash Talk FT-05

Towards Understanding *Mycobacterium tuberculosis* Cystathionine β-synthase Inhibition

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Abstract: The reverse transsulfuration pathway enables *Mycobacterium tuberculosis* (*Mtb*) to metabolize sulfur-containing amino acids, maintain redox homeostasis, and combat antibiotic- induced oxidative stress. Cystathionine β-synthase (*Mtb*CBS), a pyridoxal-5′-phosphate (PLP)- dependent enzyme, catalyzes the rate-limiting step of this pathway and exists as a functional tetramer, making it an attractive target for host-directed, combination-based TB therapy. Using cryo-electron microscopy, site-directed mutagenesis, spectroscopy, and molecular dynamics (MD), density functional theory (DFT), and preliminary quantum mechanics/molecular mechanics (QM/MM) calculations, we dissect the determinants underlying inhibition of *Mtb*CBS by aminooxyacetic acid (AOAA), a classical broad-spectrum PLP-enzyme inhibitor, using the full- length tetrameric enzyme. The high-resolution structure of AOAA-bound *Mtb*CBS reveals a covalent PLP–oxime adduct anchored by conserved active-site residues T75 and Q147, locking the enzyme in a catalytically inert state. Through a molecular-mimic approach, we further decode the molecular features governing inhibition and identify a structural mimic that occupies the substrate channel entrance, suggesting a route to non-covalent inhibition. Extending these insights, we identify non-reacting polar substrate analogues that occupy the active site, offering non-toxic scaffolds for selective inhibitor design. Together, this integrated structural, chemical, and scaffold- based study provides a mechanistic framework for targeting *Mtb*CBS and related PLP-dependent enzymes implicated in infectious diseases.

Flash Talk FT-06

Exploring a novel cholesterol-recognition motif in the pore-forming toxin *Vibrio cholerae* cytolysin

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Abstract: *Vibrio cholerae* cytolysin (VCC) is a β-barrel pore-forming toxin. VCC is secreted as soluble monomers, which upon encountering cholesterol-containing cell membranes form transmembrane oligomeric β-barrel pores. VCC employs multiple strategies to interact with distinct cell membrane components, which include phospholipids, cholesterol, as well as non-lipid components, such as cell-surface glycans. However, exact description of the structural motifs, in VCC, responsible for such multi-faceted membrane interaction mechanisms still remains incomplete. In this direction, our structure-guided mutagenesis approach has identified crucial role(s) of a loop sequence, in the upper part of the so-called 'rim' region of VCC, alterations of which compromise pore-forming cytotoxic functions of the toxin. Modifications of a specific residue within this loop sequence impair the ability of the toxin to bind to cholesterol, and cholesterol- containing lipid vesicles. Interestingly, these loop mutants of VCC retain the ability to associate with the biomembranes of mammalian cells, presumably through glycan-dependent interaction, but fail to execute efficient oligomeric pore-formation. Taken together, our results imply that the said loop sequence could act as a potential cholesterol-recognition motif in VCC that has not been appreciated earlier. Our study provides crucial new insight into how VCC structure could sense membrane cholesterol, and translate into pore- formation execution.

Flash Talk FT-07

Targeting coronavirus Nsp15 for antiviral development: Insights from biochemical analysis and *in silico* screening

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Abstract: Coronavirus Infectious Disease (COVID) has had a global impact, causing widespread morbidity and mortality, affecting economies, healthcare systems, and social structures. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of COVID is a positive-sense, single-stranded RNA virus. SARS-CoV-2 belongs to the Betacoronavirus genus within the family *Coronoviridae*. SARS- CoV-2 remains a serious concern due to the propensity of the virus to evolve to highly virulent variants. Preparedness to control the virus is highly desirable. However, no specific approved antivirals are currently available. Several viral proteins are targets for the development of direct-acting antivirals against SARS- CoV-2. Nsp15 is one such target candidate protein. SARS-CoV-Nsp15 is a multifunctional protein, and its orthologs are found in other viruses, which are of public health and economic importance. We have screened a large library of small molecules to identify potential inhibitors and evaluated them by molecular docking, pharmacophore modeling, MD simulation, and ADMET analysis. Identification of the inhibitors and the development of biochemical and cell-based assays to monitor the various activities of Nsp-15 will be discussed. Inhibitors of Nsp15 are expected to prevent viral evasion, improve host response, and reduce viral pathogenesis. The identified inhibitors will also be useful for use against multiple coronaviruses.

Flash Talk FT-08

The essential mitochondrial LetM1-like transporter of the malaria parasite has diverged metal ion specificities

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Abstract: Metal ion concentrations vary during *Plasmodium falciparum* asexual blood stage growth and are regulated by surface and organellar transporters. Organellar metal ion transporters are not well- characterized. LetM1 is an inner mitochondrial Ca^{2+}/H+ or K^{+}/H^{+}antiporter in yeast and humans. The *P. falciparum* genome encodes a LetM1-like protein (*Pf*LetM1) lacking the EF hand Ca^{2+}binding domain; it has a long N-terminal extension, LETM domain, a conserved TMD1, and two putative TMDs. We expressed recombinant *Pf*LetM1 in *E.coli*. IFAs confirmed its localization to the parasite mitochondrion. BN-PAGE analysis showed that *Pf*LetM1 forms an oligomer, held together through disulfide bonds. Spectrofluorimetry at different pH indicated that *Pf*LetM1 binds Fe^{2+} and Zn^{2+}, with higher K_{sv} for Fe^{2+}, but not Ca^{2+}/K^{+}/Na^{+}/Mg^{2+}/Mn^{2+}, thus exhibiting differential ion selectivity from known homologs. Deletion analysis showed that Zn^{2+} binding was abolished in *Pf*LetM1$_{\Delta N\Delta C}$ but not in *Pf*LetM1$_{\Delta N}$ indicating a role for the C-ter domain in Zn^{2+} interaction. In *E. coli*, *Pf*LetM1 conferred tolerance to high iron and reduced quenching of PhenGreen SK in flux assays, confirming its role in Fe^{2+} efflux. *Pf*LetM1 levels were also reduced upon iron chelation in the parasite. Our results suggest a role for *Pf*LetM1 in Fe^{2+}/Zn^{2+}homeostasis in the *P. falciparum* mitochondrion.

Flash Talk FT-09

Exploring selective lipid trafficking, tethering and transfer mechanism in providing fitness gain to drug resistant clinical isolates of *Leishmania donovani*

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Abstract: Visceral leishmaniasis (VL) remains a life-threatening disease, predominantly affecting South Asia and East Africa. *Leishmania donovani* is the primary causative agent of VL in the Indian subcontinent. Although the annual incidence of VL has declined over the past decades, the persistence of antimony-resistant *L. donovani* (SSG-R) raises concern of epidemic outbreaks, despite the discontinuation of antimonial treatments. Notably, SSG-R parasites exhibit enhanced survival fitness compared to antimony-sensitive strains (SSG-S). As lipid auxotrophs, SSG-R relies on host-derived lipids for survival. Interestingly, SSG-R parasites demonstrate increased infectivity and intracellular multiplication over time relative to SSG-S. A distinctive feature of SSG-R infection is the accumulation of lipid droplets (LDs) around the parasitophorous vacuole (PV), which can act as an excess lipid source to support its pathogenesis. To investigate this, we performed high resolution imaging on SSG-R infected macrophages, revealing a well-defined LD-PV contact site. Currently, we are characterising the lipid droplets in infected conditions. Further, we aim to isolate LDs for Proteo-Metabolic studies to identify key molecules, executing this contact site formation and possibly ensuring lipid transfer for SSG-R amastigotes. The identified targets will be subjected to functional validation via knockdown/Knock out approaches to elucidate their role in SSG-R fitness and survival.

Flash Talk FT-10

Unveiling the antibacterial potential of cannabinoid-derived scaffolds targeting drug-resistant *Staphylococcus aureus*

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Abstract: *Cannabis sativa* is a phytochemically rich plant producing over 500 compounds, among which cannabinoids are recognized as a major bioactive constituent. However, the natural exploration and exploitation of novel, pharmacologically active cannabinoids remain limited due to their trace abundance in the plant. To address this challenge, we employed an extract engineering strategy which enabled purification of seven cannabinoid analogs, including rare and previously undescribed compounds, in appreciable quantities. Antibacterial susceptibility assay revealed Compound **1**, **5**, and **7** exerted inhibitory activity against both *Staphylococcus aureus* and methicillin- resistant *S. aureus* (MRSA). A Checkerboard study revealed the synergistic interaction between active hits and Rifampin against both pathogens. The biofilm-based assay demonstrated the antibiofilm potential of the identified hits. Mechanistic investigations indicated bacterial cell membrane targeting, which was further supported by scanning electron microscopy. Propidium iodide uptake assay using flow cytometry and fluorescence microscopy revealed the membrane disruption effect of the identified hits. In addition, the ATP quantification study demonstrated a major decline in ATP levels along with an augmentation in ROS production in the MRSA pathogen. Thus, this work establishes extract engineering as a powerful strategy to unlock rare cannabinoid scaffolds and highlights their potential as leads for combating multidrug-resistant *Staphylococcus* infections.

Flash Talk FT-11

Role of CgSnf1 kinase in *Candida glabrata*-host interaction

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Abstract: *Candida glabrata* (*Nakaseomyces glabratus*) is a haploid budding yeast that usually exists as a commensal on human mucosal surfaces, including the oral cavity, gastrointestinal tract and vagina. However, it becomes invasive in hospitalized and immunosuppressed individuals and has been classified as a high-priority fungal pathogen by the World Health Organization. *C. glabrata* is efficiently phagocytosed by both murine and human macrophages, and after internalisation, it inhibits acidification of the phagolysosome and is sustained within the non-acidified phagosome organelle. Previously, we have shown that CgVps34 is the sole PI3P kinase in *C. glabrata*, with *Cgvps34Δ*- infected macrophages displaying enhanced phagolysosomal acidification and *Cgvps34Δ* mutant displaying impaired intramacrophage survival. In the current study, through affinity purification-MS analysis approach, we have identified CgVps34 interactors, and established CgSnf1, the yeast homolog of the mammalian AMPK kinase, as an interactor and a kinase of CgVps34. We also generated a knockout strain for *CgSNF1*, and found that it exhibits impaired extracellular pH modulation, including colocalization with the acidified phagolysosomes in macrophages. Further, through genetic, biochemical, transcriptional, and protein-protein interaction analysis, we have uncovered the mechanistic basis underlying CgVps34-CgSnf1 axis-mediated acidification of the extracellular environment, which may be important for *C. glabrata* adaptation to varied host niches.

Flash Talk FT-12

Therapeutic potential of taurine in the management of Polycystic Ovary Syndrome: Evidence from a preclinical study

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Abstract: Polycystic Ovary Syndrome (PCOS) is a common endocrine-metabolic disorder characterized by hyperandrogenism, insulin resistance, and disrupted folliculogenesis. Taurine is a sulfur-containing amino acid recognized for its antioxidant and insulin-sensitizing properties. This study aimed to assess the protective effect of taurine as a dietary intervention in the management of PCOS in a rodent model. P COS was induced in female Wistar rats using Letrozole (1 mg/kg BW) with a high-fat diet for 21 days. PCOS induction was confirmed by daily monitoring of the estrous cycle through vaginal cytology. Treatment groups received low and high doses of taurine (50 and 250 mg/kg) and standard drug metformin (150 mg/kg). Serum insulin, testosterone, estrogen, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and Sex hormone binding globulin (SHBG) were measured by ELISA. Ovarian histopathology was assessed by Hematoxylin and & Eosin staining. The PCOS untreated group showed markedly elevated levels of insulin, testosterone, and LH, with reduced FSH, estrogen, and SHBG, along with a 4-fold increase in HOMA-IR and extensive ovarian cystic follicle formation. Treatment with taurine significantly reduced insulin, HOMA-IR, testosterone, and LH levels, restored FSH and SHBG levels, and markedly reduced ovarian cystic follicles. Taken together, taurine supplementation ameliorated the hormonal, metabolic, and histopathological abnormalities associated with letrozole-induced PCOS, supporting its potential as a dietary supplement in PCOS management.

Flash Talk FT-13

LncRNA Lockd promotes cardiomyocyte proliferation via Eno1/beta-catenin/Myc axis

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Abstract: Neonatal mouse hearts have demonstrated the ability to regenerate and restore cardiac function in response to various injuries and to pathological stimuli such as TAC. However, the neonatal heart's response to pathological hypertrophic stimuli, such as isoproterenol, remains unknown.

Here, we aimed to investigate whether neonatal hearts during the regenerative window are protected from pathological hypertrophic insults, such as those induced by isoproterenol.

In methodology, neonatal hearts within the regenerative window were protected from pathological hypertrophy and preserved cardiac function, showing resistance to isoproterenol. On the other hand, isoproterenol induced pathological cardiac hypertrophy and impaired cardiac function in neonatal hearts during the non-regenerative phase. This resistance in the regenerative phase was driven by robust cardiomyocyte proliferation, which was markedly absent in the non-regenerative phase. Global transcriptomic analysis revealed that Lockd (Long non-coding downstream of Cdkn1b) was the top upregulated transcript in the regenerative phase, and its upregulation was E2F1-dependent. AAV9-mediated cardiomyocyte-specific overexpression of Lockd during the non-regenerative phase blunted isoproterenol-induced hypertrophy, preserved cardiac function, and promoted cardiomyocyte proliferation. Mechanistically, Lockd physically interacted with and stabilised α-enolase (ENO1), as

shown by RNA and protein pull-down assays. ENO1 stabilization increased β-catenin stability and promoted its nuclear accumulation, leading to strong induction of Myc, a key β-catenin target gene required for cardiomyocyte proliferation. Furthermore, Eno1 knockdown reduced Myc expression, β-catenin stability, and cardiomyocyte proliferation.

Neonatal hearts during the regenerative window resist isoproterenol-induced pathological hypertrophy by activating proliferative programs. Lockd functions as a critical regulator of this regenerative resistance via the ENO1-β-catenin-Myc axis.

Flash Talk FT-14

ETS1 promotes breast cancer cell migration via transcriptional activation of STAT3

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Abstract: The transcription factor ETS1 is highly expressed in almost of all types of cancers and is implicated in canccer progression but its role in breast cancer cell migration remains poorly understood. We recently identified a positive correlation between ETS1 and STAT3 expression in breast cancer patient datasets. Further, ETS1 overexpression and knockdown studies revealed that ETS1 regulates STAT3 expression, where ETS1 overexpression increased STAT3 expression while ETS1 knockdown significantly reduced STAT3 expression in breast cancer cells. Mechanistically, ETS1 was found to interact with RNA polymerase II and gets recruited to the human STAT3 promoter to drive STAT3 transcription. Furthermore, ETS1 not only regulated STAT3 expression but also modulated the expression of STAT3 downstream target genes involved in breast cancer cell migration. Collectively, these findings establish ETS1 as a transcriptional activator of STAT3 and reveal a novel ETS1–STAT3 regulatory axis that promotes breast cancer cell migration, providing novel insights into the molecular mechanisms underlying breast cancer progression.

Flash Talk FT-15

Targeting NCL–PARP1 DNA repair axis as a potential therapeutic vulnerability in DLBCL

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Abstract: DLBCL is the most common type of Non-Hodgkins Lymphoma and is both heterogeneous and aggressive. Disease relapse and treatment resistance remain major therapeutic challenges. Nucleolin (NCL) is a highly multifunctional protein involved in RNA metabolism and DNA repair, but its role in the DNA damage response of DLBCL has not been identified. We studied NCL expression, its interaction with poly(ADP-ribose) polymerase 1 (PARP1) and therapeutic implications of targeting this pathway in DLBCL models. NCL and PARP1 were upregulated in DLBCL cell lines and primary tumors, and physically interacted in lymphoma cells. NCL associated with PARP1 and chromatin after DNA damage, coincident with changes in DNA damage signaling and PARylation. Pharmacological inhibition or genetic

depletion of NCL disturbed PARP1-associated DNA damage responses, and upregulated γ-H2AX accumulation upon genotoxic stress. In addition, NCL inhibition synergized with PARP1 inhibition by talazoparib to induce apoptosis and inhibit DLBCL growth in vitro and in vivo. Analysis of primary DLBCL samples revealed a significant correlation of expression of NCL and PARP1, supporting the clinical relevance of this pathway. Together, our findings define an NCL–PARP1 axis that contributes to DNA damage response and lymphoma cell survival. Targeting this axis, particularly through combined NCL and PARP1 inhibition, provides a therapeutic vulnerability in DLBCL.

Flash Talk FT-16

Anti-Thyroid Drug Propylthiouracil Promotes *AP- Tau* Aggregation and Neuroepigenetic modification: Evidence from Computational and Experimental Studies

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Abstract: Neurodegeneration arises from a complex interplay of endocrine disruption, oxidative stress, inflammation, and epigenetic dysregulation. Thyroid hormones are essential for synaptic integrity, neuronal survival, and cognitive function. Propylthiouracil (PTU), a widely prescribed anti-thyroid drug, may perturb neuronal homeostasis by disrupting thyroid functions, redox balance and epigenetic plasticity. In this context, we aim to investigate the PTU-induced neuroepigenetic modifications and their complementary interplay with the amyloid-(A,B)-tau inflammatory axis. This may act as an upstream trigger for neurodegenerative cascades. We have tried to investigate this through multiple approaches including computational, biophysical and *in vivo* studies. Molecular docking and all-atom molecular dynamics simulations revealed stable and energetically favorable binding of PTU with both Aand tau, supported by MM/PBSA based binding free-energy analyses. *In vitro* fluorescence spectroscopy, Thioflavin-T aggregation assays, and circular dichroism spectroscopy demonstrated that PTU induces conformational changes and concentration-dependent modulation of tau aggregation dynamics. In animal studies, PTU-induced hypothyroid rats exhibited behavioral abnormalities, confirmed by open-field, elevated plus-maze, and Y-maze tests. This indicates alterations in locomotor activity, anxiety-like behavior, and cognitive impairment. Serum biochemical analysis depicted metabolic and inflammatory disturbances, including increased cholesterol, triglycerides, CRP, SGPT & SGOT, reduced HDL, and alterations in urea, creatinine, uric acid, and ALP. Furthermore, PTU treatment showed altered level of tau, *A,B,* and GPX-4 in blood serum. It further induced oxidative stress, characterized by increased ROS and lipid peroxidation (4-hydroxynonenal), accompanied by depletion of GSH and SOD levels in the brain (cerebral cortex). Global DNA methylation and the expression of epigenetic signature molecules such as DNMTl, DNMTI A, DNMT3B, MBD4 and MECP2 were increased, whereas BDNF was markedly decreased. Collectively, these findings suggest that PTU-induced thyroid disruption promotes behavioral, metabolic, redox, and epigenetic alterations that converge on A,B-tau-associated

inflammatory signalling, potentially accelerating neuronal dysfunction and neurodegenerative progression.

Flash Talk FT-17

CD73 promotes breast cancer development and progression by regulating macrophage homeostasis and T cell infiltration in tumor microenvironment

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Abstract: Breast cancer remains the most prevalent cancer in women worldwide. Even with advancements in treatment, improving patient outcomes requires early diagnosis and understanding of the tumor microenvironment (TME). The TME plays a crucial role in breast cancer progression by influencing immune responses and promoting tumor survival. Utilizing immunotherapy to modify the TME offers promising avenues for more effective and sustained breast cancer treatments. In recent years, the ectonucleotidase enzyme CD73 (NT5E) has emerged as a promising target in cancer immunotherapy. CD73 is a key factor in accumulation of extracellular adenosine, and thereby driving immune evasion. However, its precise role in orchestrating TME remodeling remains to be fully defined. In this study, we investigated in detail immunomodulatory activities of CD73 and its impact on tumor growth in syngenic mouse model of breast cancer. To this end, tumors were established using two different mouse breast cancer cell lines, EO771 and 4T1, with stable expression of the chili-luciferase (chili-luc) reporter so as to monitor tumor cell proliferation and migration. While EO771 was used to explore role of host derived CD73 regulating by implanting them in mice with CD73 WT (wild type) and null genetic background, 4T1 cells were subjected to CRISPR-CAS9 mediated deletion of CD73 to elucidate role of cancer cell intrinsic CD73 in modulating TME. Transgenic animals of CD73 null background (CD73 KO) exhibited significantly slower tumor growth than their wild type counterparts, underscoring pro-tumorigenic role of CD73. Comparison of tumor-associated macrophages (TAMs) between harvested tumors from CD73WT and CD73KO mice showed higher numbers of M1 (anti-tumor) populations in CD73KO groups than WT counterparts, and thereby emphasizing the role of CD73 in generating an immunosuppressive TME. Reciprocally, tumor cell intrinsic role of CD73 in modulation of immune cell functions in TME was investigated by deleting it using CRISPR-CAS9 gene editing tool. Additionally, CD73 loss significantly enhanced cytotoxic T cell infiltration into the tumor core, thus generating an immunologically active environment. Overall, our results demonstrate that CD73 promotes an aggressive phenotype, and thus significantly impacting breast cancer growth and progression. Therefore, targeting CD73 may represent an effective therapeutic strategy to hinder tumor advancement and enhance anti-tumor immune responses in breast cancer.

Flash Talk FT-18

Decoding hepato-erythroid crosstalk in β-thalassemia associated iron dysregulation

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Abstract: β-thalassemia is characterized by impaired synthesis of β-globin chains of hemoglobin, ineffective erythropoiesis, chronic anemia, and systemic iron overload driven by increased intestinal

absorption, transfusional burden, and disrupted iron homeostasis. Excess Iron perturbs cellular redox homeostasis and stress responses, thereby shaping erythroid cell fate. Our study aims to elucidate the intricate interplay between hepatic and erythroid compartments in context to β-thalassemia pathophysiology, emphasizing on iron overload and its cellular consequences. qPCR analysis of whole-blood RNA from well-characterized β-thalassemia cohorts, conducted with appropriate ethical approval and informed consent, revealed distinct oxidative stress, stress-adaptive, and cytoprotective responses, as compared to healthy volunteers reflected by relative expression patterns of HMOX1, GDF15, GPX1, GPX4, ATF4, ATF3 and FTH1. An in vitro indirect co-culture model had been established using condition media from iron-overloaded HepG2 hepatocytes, exposed to both transferrin-bound and non-transferrin-bound iron sources. This conditioned media (25%) had been employed to erythroid-differentiated K562 cells with 75% fresh media to investigate how iron-perturbed hepatic signaling influences erythroid stress responses and cell fate. qPCR analysis of RNA from co-cultured erythroid cells exhibited significant upregulation of GPX4/FTH1 under moderate iron exposure and reduced GDF15/ATF3 expression. These findings will be further validated at protein level by immunoblot analysis.

Flash Talk FT-19

Histone chaperone HIRA in regulation of chromatin architecture in leukemia

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Abstract: Hematopoiesis is a strictly regulated process mediated by intricate signalling pathways, transcription, and epigenetic factors. Histone cell cycle regulator A (HIRA) confers chromatin accessibility and regulates developmental hematopoiesis. Disruption of hematopoiesis results to unregulated proliferation, blocked differentiation, mutations, resulting in leukemia. However, the underlying mechanism that connects HIRA with chromatin reorganization and pathogenesis of leukemia remains unexplored. Proteome-wide analysis of K562 CML cell line, with maximal HIRA expression, demonstrated the association of HIRA with components of chromatin organization. FRAP and FLIM-FRET microscopy and molecular interaction studies revealed increased chromatin compaction and altered spatial distribution of chromatin towards the nuclear periphery HIRA-downregulated K562 cells. Mechanistically, enhanced chromatin compaction was attributed to increased histone H3K9me3 and HP1α levels mediated by histone methyltransferase SETDB1. The enrichment of histone H3.3 and the reduction in H3K27me3 levels, resulting from the loss of EZH2 recruitment at the SETDB1 and HP1α promoters in HIRA-knockdown cells, led to their enhanced expression. This HIRA-SETDB1-H3K9me3 axis led to loss in proliferation along with reduced expression of BCR-ABL1 fusion protein that causes CML. Interestingly, level of HIRA corroborated with BCR-ABL1 expression in CML patients vs. healthy individuals. Our findings highlight how elevated HIRA expression contributes to the pathogenesis of CML and establish a regulatory axis that could be further explored for therapeutic interventions.

Flash Talk FT-20

Dietary bioactives reprogram cancer metabolism through gut microbiome-mediated epigenetic regulation in TNBC

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Abstract: Triple-negative breast cancer (TNBC) cells undergo profound metabolic reprogramming to support rapid proliferation, survival, and metastasis, with enhanced aerobic glycolysis being a hallmark of this adaptation. Increasing evidence suggests that dietary bioactives can influence cancer progression through interconnected metabolic, epigenetic and gut microbiome pathways. Our findings demonstrated that dietary green tea polyphenols (GTPs) and diindolylmethane (DIM) markedly altered metabolic pathways associated with aerobic glycolysis in TNBC cells. Metabolomic analysis revealed substantial metabolic perturbations following treatment, accompanied by downregulation of key glycolytic regulators, including pyruvate kinase M2 (PKM2), glucose transporter 1 (GLUT1), and hypoxia-inducible factor-1α (HIF-1α). In vivo, oral administration of GTPs and DIM significantly suppressed TNBC tumor growth, supporting their potential as complementary dietary interventions. Notably, DIM increased intracellular accumulation of therapeutic agents by modulating drug-efflux proteins ABCB1/P-glycoprotein. Dietary bioactives shown to influence gut microbiome and its metabolite network. Microbiota-derived metabolites, including acetate and butyrate, can function as metabolic substrates and epigenetic regulators, thereby linking dietary inputs with cellular metabolism and gene regulation. Collectively, our findings suggest that dietary bioactives establish a functional link between the gut microbiome, epigenetic regulation, and cancer metabolism. Overall, dietary epigenetic modulators reprogram the metabolic regulation of TNBC by altering gut microbiome homeostasis.

Flash Talk FT-21

Effect of Calcium modulators in GNE deficient skeletal muscle cell function

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Abstract: Calcium ions (Ca^{2+}) are essential for a multitude of physiological processes, particularly in muscle cells where they play a critical role in contraction and development. Any alteration in calcium homeostasis may contribute to impairment of skeletal muscle development and function as observed in various neurodegenerative disorders. One such rare neuromuscular genetic disorder, GNE Myopathy (GNEM), is characterized by muscle weakness and atrophy. GNEM is caused due to mutation in sialic acid biosynthetic gene GNE. Our study in GNE deficient L6 skeletal muscle cell (SKM-GNEHz) myoblast and myotubes showed ~38% and ~56% reduction respectively in cytosolic calcium levels as measured by Fura-2AM dye. Additionally ~50% reduction was observed in Troponin C(TnC) levels with increase in Troponin I(TnI) (~35%) and Tropomyosin(TpM) (~40%) levels. Consequently, myosin ATPase activity was reduced by 40%. Treatment of SKM-GNEHz cells with caffeine and calcium ionophore resulted in ~2 fold increase in cytosolic calcium levels, ~0.8 fold increase in TnC and ~2 folds increase in myosin ATPase activity. Alteration in contractile machinery may affect the differentiation process of GNE deficient cells. We observed ~20%, 40% and 60% reduction in Pax7, MyoD and Myosin Heavy Chain(MyHC) differentiation marker expression, respectively. The transcription of MyHC is regulated by NFAT that translocates from cytoplasm to nucleus post-dephosphorylation by ca^{2+} dependent calcineurin. We observed ~40% reduction in NFAT translocation to nucleus was in SKM-GNEHz cells. Treatment with calcium modulators restored the differentiation defect of SKM-GNEHz by 4 days and MHC/Myo D levels by ~2 folds and ~1.5 folds, respectively. Additionally, cell proliferation with reduced MTOC formation and cyclin D levels was observed in GNE deficient cells. Treatment with caffeine resulted in ~50% increase in MTOC formation and cyclin D expression. Our study indicates that modulation of calcium signaling in GNE-deficient skeletal muscle cells can improve muscle function and motor activity, thereby providing

mechanistic insights towards understanding the disease and opening a new area of drug design.

Flash Talk FT-22

When the synapse runs dry: Presynaptic Ca^{2+} overload and vesicle depletion drive retinal dysfunction before diabetic retinopathy

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Abstract: Diabetic retinopathy (DR) remains a leading cause of preventable blindness. Although vascular lesions define its clinical staging, neural retinal dysfunction precedes detectable vasculopathy. Oscillatory potentials (OPs) — high-frequency wavelets on the scotopic ERG b-wave — show progressive implicit-time delay in early diabetes, implicating inner retinal synaptic circuits. We previously demonstrated that diabetes disrupts mitochondrial Ca^{2+} homeostasis and elevates reactive oxygen species in retinal neurons (Haider et al., 2019, Neuroscience). The present study identifies the synaptic biochemical mechanism underlying this electrophysiological signature at the rod bipolar cell (RBC)–AII amacrine cell ribbon synapse. Using the STZ Wistar rat model (60 mg/kg i.p.; confirmed >250 mg/dL), we performed in vivo scotopic ERG, retinal-slice whole-cell patch-clamp, presynaptic Ca^{2+} imaging (Fluo-4ff), synaptic protein immunofluorescence, and electron microscopy at 8 and 16 weeks post-induction. Vascular integrity was confirmed by Evans blue dye extravasation and VEGF ELISA. OP implicit times were significantly delayed from 8 weeks onward. Paired-pulse depression was markedly enhanced, revealing synaptic refractoriness consistent with vesicle pool depletion. Ca^{2+} imaging showed elevated presynaptic transients in RBC boutons — a biochemical correlate of chronic vesicle release and impaired replenishment. Postsynaptically, AMPAR-mediated currents in AII amacrine cells were reduced, indicating receptor downregulation. Synaptic scaffold proteins Ribeye, PSD-95, and Piccolo were downregulated despite preserved ribbon ultrastructure by electron microscopy — a structural-functional dissociation. Vascular permeability and VEGF remained unchanged at 16 weeks. These findings establish a biochemical cascade from presynaptic Ca^{2+} dysregulation to vesicle depletion, scaffold protein loss, and postsynaptic AMPAR downregulation, collectively driving OP delay prior to vascular disease. The RBC–AII ribbon synapse represents an early and tractable target for neuroprotective intervention in diabetic retinopathy.

Flash Talk FT-23

Molecular basis of abasic mRNA surveillance by bacterial Rps3 in reconstituted translation initiation complexes

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Abstract: Ribosome-mediated mRNA surveillance is critical for maintaining translational fidelity, especially when transcripts carry chemical lesions. We previously showed that ribosomal protein S3 (Rps3) has an intrinsic endoribonuclease activity within the bacterial 30S subunit, cleaving abasic (AP-site) mRNA with high specificity, with the cleaved product localized near the mRNA entry tunnel by cryo-EM (Afsar et al., Nucleic Acids Res., 2024). Here we investigated whether this activity holds up in higher-order complexes *viz,* the 30S pre-initiation complex (30S-PIC) and 70S initiation complex (70S-IC) which

represent the key checkpoints before translation commits. Using three AP-site mRNA constructs with the lesion placed at the A-site codon, near the Rps3 S3 domain and near its KH domain, we found that cleavage efficiency in reconstituted 30S-PIC and 70S-IC depends on where the AP site sits relative to Rps3: moderate-to-good at the A-site, highest near the S3 domain and reduced near the KH domain. This suggests that in these static, assembled complexes, cleavage efficiency depends on how accessible the lesion is to the enzyme's active region. Single-particle cryo-EM of the 30S-PIC with the A-site AP construct yielded a 2.77 Å reconstruction, with density at the AP site consistent with backbone cleavage. Together, these results extend Rps3-mediated abasic mRNA surveillance to initiation-stage complexes.

Flash Talk FT-24

Patient derived hiPSCs reveal epilepsy mechanisms: A precision model for drug testing

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Abstract: Epilepsy encompasses a spectrum of neurological disorders characterized by recurrent seizures arising from abnormal neuronal firing, often linked to genetic variations in voltage-gated ion channels. Mutations in sodium channels, particularly SCN1A encoding the α-subunit of Nav1.1, are frequently implicated in epileptogenesis, yet the functional impact of several missense variants remains unclear. We investigated the pathogenic role of a novel SCN1A missense variant, p.Ile227Thr, identified by next-generation sequencing in patients with Dravet syndrome. Patient-derived PBMCs and family controls were reprogrammed into hiPSCs, validated for pluripotency, and differentiated into neurons via dual SMAD inhibition. Site-directed mutagenesis introduced the variant into wild-type SCN1A plasmids expressed in HEK cells, enabling electrophysiological recordings of current density and gating kinetics, complemented by tetrodotoxin assays of surface channel expression. HEK cells revealed markedly reduced current density without altered gating, while hiPSC-derived neurons demonstrated a 74% reduction in peak sodium current compared to wild-type (0.75 pA/pF vs. 2.93 pA/pF), specifically in bipolar neurons. These findings indicate that p.Ile227Thr is pathogenic due to defective channel trafficking and diminished surface expression. This model highlights impaired sodium channel function in epilepsy, supports pharmacological rescue strategies targeting trafficking deficits, and provides a platform for personalized drug screening.

Flash Talk FT-25

CRISPR-DT: A functional genomic approach for therapeutic drug discovery in cancer

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Abstract: Tumor immune evasion remains a major challenge in cancer therapy, highlighting the need to identify actionable regulators of immune checkpoint pathways. CD24 is a GPI-anchored "don't-eat-me" signal that protects ovarian cancer cells from macrophage-mediated clearance through interaction with Siglec10. Here, we used functional genomics to identify mechanisms controlling CD24 surface presentation and uncovered glycosylphosphatidylinositol anchor attachment 1 (GPAA1), a component of the GPI transamidase complex, as a critical regulator of this immune-evasion pathway. A genome-wide CRISPR-Cas9 screen identified *GPAA1* as the top factor promoting CD24 cell-surface expression. Genetic ablation of *GPAA1* abolished surface CD24 without affecting CD24 transcript levels, redirected CD24 to the endoplasmic reticulum, and enhanced macrophage-mediated phagocytosis across multiple ovarian cancer models. *GPAA1* loss suppressed tumor growth and increased survival in both xenograft and immunocompetent syngeneic models, accompanied by increased tumor-associated macrophage phagocytosis and $CD8^+$ T-cell infiltration. Importantly, the structural similarity of GPAA1 to metallo-aminopeptidases led us to identify the clinically advanced small molecule *bestatin* as a pharmacological inhibitor of GPAA1. *Bestatin* reduced GPI anchoring and cell-surface CD24, enhanced macrophage phagocytosis, reduced tumor growth. Together, these findings identify GPAA1 and the GPI-anchor biosynthetic pathway as actionable regulators of tumor immune surveillance and provide a potential small-molecule strategy for targeting CD24- dependent immune evasion in ovarian cancer.

Flash Talk FT-26

Exploring potential role of post translational modification of RBMX in LINE-1 RNA homeostasis

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Abstract: Cellular stress can activate endogenous retroelements such as LINE-1, challenging genome stability and cellular homeostasis. RBMX, an RNA-binding protein involved in RNA metabolism and genome maintenance, may represent a critical cellular regulator of this stress response, yet its rol e in controlling LINE-1 activity has not been investigated.

In methodology, induction of cellular stress using multiple pharmacological stimuli consistently triggered robust LINE-1 activation. RIP–RT-qPCR was performed to examine RBMX association with LINE-1 transcripts. RNA-decay assays were used to assess LINE-1 RNA turnover. Immunoprecipitation and immunoblotting were performed to evaluate RBMX ubiquitination and its association with an E3

ubiquitin ligase implicated in retroelement biology.

RBMX was found to associate with LINE-1 transcripts, accompanied by evidence of its involvement in LINE-1 RNA decay and retroelement resolution. Immunoprecipitation further revealed that RBMX undergoes ubiquitination suggesting a potential link between ubiquitin signalling and RBMX- mediated LINE-1 regulation.

Our study suggests that cellular stress triggers LINE-1 activation, accompanied by a marked increase in ubiquitination of RBMX, thereby contributing to LINE-1 RNA homeostasis. These findings positioned RBMX as a potential molecular responder linking LINE-1 activation to downstream cellular signalling.

Flash Talk FT-27

Genomic epidemiology and phenotypic characterisation of *Salmonella enterica* serovar Panama in Victoria, Australia

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Abstract: *Salmonella enterica* serovar Panama, a causative agent of non-typhoidal salmonellosis (NTS), has been significantly associated with invasive NTS disease (iNTS) in humans. *S.* Panama is an understudied pathogen, with its pathobiology poorly understood. This study investigates the genomic epidemiology, AMR mechanisms and infection biology of *S.* Panama isolates recovered in Victoria, Australia, between 2000 and 2020. Multi-drug resistance (resistance to ≥3 drug classes) was detected in 46 (51.7%) Australian isolates. The plasmid-mediated colistin resistance gene, *mcr1.1*, was detected in one Australian *S.* Panama isolate, carried by an IncI plasmid previously reported in *Salmonella* and *Escherichia coli* isolates from poultry in South-East Asia. Examination of the intracellular replication dynamics of seven *S.* Panama isolates, representing the genetic diversity of the study population, demonstrated diverse phenotypes. In THP-1 derived macrophages, despite low host cell uptake, *S.* Panama showed higher replication rates over time compared to *S. enterica* serovar Typhimurium SL1344 strain. However, a causative genotype could not be identified to explain this observed phenotype. This study provides the first data on the AMR mechanisms and host-pathogen interactions of *S.* Panama in Australia, which will aid our collective understanding of the pathobiology of *S.* Panama and iNTS serovars more broadly.

Flash Talk FT-28

From transcriptomics profiling to AI-assisted drug discovery: Identifying potential COX-II inhibitors for ferroptosis-associated ischemic stroke

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Abstract: Ischemic stroke (IS) remains a major cause of mortality and morbidity worldwide. Ferroptosis, an iron- dependent form of programmed cell death, contributes to IS pathophysiology. Established ferroptosis- associated targets highlight emerging therapeutic opportunities across various cerebrovascular disorders. In this study, we analyzed transcriptomic data from IS and normal patients to

identify differentially expressed genes (DEGs). By overlapping DEGs with ferroptosis-related genes from FerrDb and GeneCards, we identified hub genes and prioritized PTGS2 (encodes COX-II) for the downstream bioinformatics analysis. Ten machine learning (ML) and five graph neural network (GNN) models were benchmarked using PTGS2/COX-II bioactivity data. The top-performing models screened the Maybridge library, and molecular docking prioritized the consensus hits for biological evaluation. We assessed the final compounds for ADMET properties and CNS-MPO scores. The transcriptomics analysis revealed 570 DEGs and19 ferroptosis-associated hub genes. We prioritized PTGS2 because of its relevance in oxidative stress and lipid peroxidation. In benchmarking, the LGBM and GraphSAGE models outperformed their ML and GNN counterparts. Molecular docking shortlisted 13 compounds for dose-dependent assessment of COX-II inhibition. All compounds exhibited optimal ADME/T profile and BBB permeation potential. This integrated transcriptomics, AI-driven cheminformatics, and structure-based framework successfully identified potential COX-II inhibitor scaffolds for further investigation in ferroptosis-associated IS.

Flash Talk FT-29

Curcumin reprograms TLR4/NF-κB-mediated macrophage polarization to attenuate paraquat-induced pulmonary injury and fibrotic remodeling

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Abstract:

Background: Paraquat (PQ) is a widely used herbicide that can cause severe toxicity and acute lung injury (ALI). Curcumin, a bioactive compound derived from *Curcuma longa*, possesses potent antioxidant and anti-inflammatory properties. This study investigated the protective effects of curcumin against PQ-induced pulmonary injury, focusing on macrophage polarization and TLR4/NF-κB signaling.

Methods: PQ-induced ALI was established in mice exposed to PQ (50 mg/kg, intraperitoneally; 20 mg/kg, intranasally), with or without curcumin pretreatment. Lung histopathology was assessed using histochemical staining. Macrophage polarization was evaluated using M1-associated markers (IL-6 and TNF-α) and M2-associated markers (IL-10, PPAR-γ, and arginase-1), along with CD68 and EGR2 immunohistochemical markers. TLR4/NF-κB signaling was also evaluated.

Results: Curcumin pretreatment significantly reduced PQ-induced expression of the pro- inflammatory cytokines IL-6 and TNF-α while increasing IL-10, PPAR-γ, and arginase-1 expression. These findings indicate a shift from the pro-inflammatory M1 phenotype toward the regulatory M2 phenotype. Curcumin also suppressed PQ-induced TLR4/NF-κB signaling, suggesting its involvement in regulating macrophage polarization.

Conclusion: Curcumin attenuates PQ-induced ALI, potentially by promoting M2 macrophage polarization through inhibition of TLR4/NF-κB signaling. These findings highlight curcumin as a promising immunomodulatory strategy for PQ-induced pulmonary injury.

Flash Talk FT-30

Interplay between glutamylation and glycylation in regulating primary cilia functions

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Abstract: The tubulin code is a major fine regulator of microtubule functions. Among the diverse posttranslational modifications (PTMs), two key modifications, glutamylation and glycylation, are highly enriched in mammalian cilia and flagella. Our understanding of the roles of these modifications is limited to motile cilia, with their roles in primary cilia barely established. Our focus is on establishing their roles in primary cilia and how they regulate their structure and function. Here, our *in vitro* reconstitution assays with custom- modified tubulins, molecular motors and microtubule-associated proteins provide evidence that glycylation differentially regulates molecular motors and microtubule-associated protein activities and is antagonistic to glutamylation. This can, in turn, affect cilia stability and intraflagellar transport. At the cellular level, we establish that altering the balance of either PTM affects intraflagellar transport and ciliary signalling. We thus highlight a yin-yang relationship between these PTMs. To study clinical outcomes of altered tubulin code in human ciliopathies, we are investigating retinal ciliopathies caused by clinical mutations in a tubulin glutamylase, where we now show that loss of glutamylation delays ciliogenesis, disrupts intraflagellar transport and affects ciliary signalling. Overall, we have begun to establish that both glutamylation and glycylation affect specific molecular pathways that operate through the cilia.

Flash Talk FT-31

Deciphering the surface features and tubulin PTMs in human sperm

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Abstract: Spermatozoa possess a limited proteome and are believed to be transcriptionally and translationally silent following maturation. Therefore, post-translational modifications (PTMs) of existing proteins play a critical role in regulating sperm structure, motility, and function. Tubulin, undergoes diverse PTMs that influence microtubule dynamics and interactions with motor and regulatory proteins. Microtubule motor proteins have differential affinity towards different tubulin PTMs.Our study has characterised and compared the expression patterns of tubulin PTMs in spermatozoa from three groups: proven fertile controls, idiopathic infertile individuals, and couples experiencing recurrent pregnancy loss (RPL). Differential PTM profiles may provide insights into molecular alterations associated with impaired sperm function and adverse reproductive outcomes. In parallel, atomic force microscopy (AFM) is also used to characterise the biophysical properties and surface features of spermatozoa across the three groups. Pharmacological modulation enzymes involved in tubulin PTMs, may offer a novel approach to restore tubulin functionalization and improve sperm function. Thus, sperm tubulin PTMs may serve as potential biomarkers and therapeutic targets for male reproductive dysfunction.

Flash Talk FT-32

Decoding the structural and functional dynamics of a Kinetoplastid FEN1

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Abstract: Maintaining genome integrity during DNA replication relies on the replisome, a coordinated protein machinery that involves Flap endonuclease 1 (FEN1), a key enzyme that processes flap structures on Okazaki fragments during replication and during long-patch base excision repair. Although FEN1 has been characterized across organisms, its regulation and mechanism in *Leishmania donovani,* the causative agent of the Neglected Tropical Disease Leishmaniasis, remains unexplored. This study presents the structural and functional characterization of *Ld*FEN1. The C-terminal PIP motif, known to mediate PCNA interaction and support substrate delivery, was found to be dispensable for PCNA binding though, its deletion markedly compromises the structural stability of the protein and affects the activity. Metal-dependence studies showed that zinc competes with magnesium and abolishes its activity. Site-directed mutagenesis further revealed that the D183A substitution nearly abolishes flap endonuclease activity while conferring a pronounced gain of 3′ flap exonuclease activity, a catalytic switch not previously reported in any FEN1 homologs. These findings establish a mechanistic framework for FEN1 regulation in *L. donovani* and offer new structural insight relevant to FEN1 across organisms.

Flash Talk FT-33

ISGylation mechanism and cross-talk between ISGylation and Ubiquitination

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Abstract: ISG15 is a ubiquitin-like modifier that is upregulated in response to a wide range of pathogens, including viruses. Over the past several years, numerous studies have delineated the roles of ISG15 in host antiviral responses, both in its free (unconjugated) form and in its conjugated form, where ISG15 is attached to substrate lysine residues through ISGylation. To antagonize ISG15-mediated host immune responses, viruses have evolved specialized proteins that facilitate immune evasion. Furthermore, despite the structural and mechanistic similarities between ISG15 and ubiquitin, and between ISGylation and ubiquitination, no studies to date have reported cross-talk between these two pathways and their potential role in host defense. Here, we report that ISG15 itself can serve as a substrate for ubiquitination by multiple ubiquitin E3 ligases. We demonstrate that ubiquitination of ISG15 blocks its recognition by a viral protease, a key enzyme that counteracts host immunity. Although the viral protease fails to recognize ubiquitinated ISG15, the modified protein remains a substrate for a human deubiquitinase. Using crystal structures, together with supporting biochemical and biophysical analyses, we reveal an intriguing protective mechanism in which ubiquitin folds onto a critical interaction surface of ISG15 that is required for viral protease binding. Overall, our findings uncover a novel mechanism of ISG15 protection from viral proteases, with potential implications for therapeutic strategies against viral infections.

Abstracts of Poster Presentations

Poster P-001

Harnessing the Therapeutic Potential of Ion Channels and GPCRs in Cancer Immunotherapy

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Abstract: Cellular immunotherapy has emerged as a powerful tool in our fight against cancer. While CAR- T cells and NK cells are highly effective against haematological malignancies, the complexity of tumour microenvironment often makes immune cells dysfunctional against solid tumors. My research group harnesses the ion channel, GPCR, cytoskeletal and organellar dynamics of immune cells to make them more efficient against solid cancers like oral cancer, in complex environments like Hypoxia. We have recently demonstrated that genetic modulation of a lysosomal ion channel can metabolically rewire NK cells to glycolysis without compromising their anti-cancer activity. Further, we have demonstrated another calcium channel as a regulator of immune synapse formation, absence of which impairs NK cell activity against cancer cells. Activation of an adhesion GPCR by monoclonal antibody leads to increased migration of mature NK cells, opening up the possibility of improved NK cell infiltration into solid tumors. The Tissue Restoration Lab at IIT Kanpur is developing several strategies to genetically or pharmacologically modulate TRP channels and GPCRs to improve NK cell activity against solid tumours.

Poster P-002

Identification of E2F5-Associated sEV Signatures for Enhanced Graphene– MXene FET Biosensing toward Early and Minimally Invasive Detection of Prostate CancerP-002

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Abstract: Prostate-specific-antigen based detection of prostate cancer (PCa) is limited by suboptimal specificity, contributing to overdiagnosis/overtreatment. Minimally invasive discrimination of PCa from benign prostatic hyperplasia (BPH) remains a critical clinical need. Small extracellular vesicles (sEVs) provide a promising liquid-biopsy platform because they encapsulate disease-associated proteins amenable to antibody-based detection. We initially developed a graphene–MXene field-effect-transistor (FET) biosensor targeting E2F5, implicated in PCa through the p38/SMAD3–TFPI2/MMP-2/-9 axis. E2F5 in plasma sEVs from patients with BPH and PCa was evaluated by Western blot and E2F5-functionalized FET sensing, where sensor responses were analysed using a Random Forest classifier. The model efficiently discriminated healthy controls from PCa and BPH but showed limited resolution in differentiating BPH from low-grade PCa. To address this limitation, an integrative proteomic and bioinformatic workflow based on plasma sEVs from BPH and PCa samples identified additional E2F5- correlated biomarkers. Among prioritized candidates, KRT5 and ANXA2 showed significant differential expression. E2F5 overexpression in DU145 and PC3 cells, followed by qRT-PCR, further supported KRT5 and ANXA2 as potential downstream molecular determinants. Their diagnostic utility as complementary markers and incorporation into FET are being investigated to improve discrimination at the BPH/low-grade PCa interface to facilitate development of a multiplexed sEV-FET biosensing strategy.

Poster P-003

Genome-Wide Methylome Comparison of Gallbladder Tumor Tissue and cfDNA: Revealing Conserved Epigenetic Signatures

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Abstract: Gallbladder cancer is an aggressive disease often diagnosed at a late stage, and non-invasive markers for early detection are lacking. Because DNA methylation changes arise early in tumor development and can be detected in cell-free DNA (cfDNA), which may be an marker for early detection of GBC. To determine the concordance of genome-wide DNA methylation patterns between gallbladder cancer tissue and matched cfDNA, thereby identifying tumor-associated methylation alterations in cfDNA with potential utility as non-invasive biomarkers. We use the Illumina Infinium MethylationEPIC 850K array to analyze paired FFPE tumor tissue and matched serum cfDNA from 12 GBC patients (adenocarcinoma and intracystic papillary neoplasm with invasion) and 4 normal controls. Lumi and DMRforPairs were used to identify differentially methylated CpG sites and areas ($\Delta\beta > 0.2$, $p < 0.05$), and GO and KEGG enrichment was applied to shared genes. Global hypomethylation was present in both tissue and cfDNA, with promoter hypomethylation rising with advancement. PTPRN2, HDAC4, MAD1L1, RPTOR, and PRDM16 are among the 404 common differentially methylated overlap genes that we discovered to be connected to established cancer pathways. Tissue and cfDNA methylomes supports a robust, tumor-validated epigenetic signature and highlights cfDNA methylation profiling as a feasible strategy for early, non- invasive detection of gallbladder cancer.

Poster P-004

Understanding the oncogenic role of CD36 in Stromal Cell Protected Mantle Cell Lymphoma

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Abstract: Mantle cell lymphoma (MCL) is a clinically aggressive and incurable subtype of B-cell lymphoma, characterized by overexpression of CCND1 due to the translocation t(11;14)(q13;q32). The standard-of-care regimen for MCL includes R-CHOP, autologous stem cell transplantation, and targeted therapies. CD19-targeted CAR T-cell therapy is clinically effective, but despite standard treatment regimens, almost all MCL patients relapse and enters a vicious cycle of treatment followed by relapse. This is due to a resistant subset of tumor population preferably residing in the bone marrow which has lost the therapeutically targeted B-cell specific markers. Our work with patient-derived lymphoma samples has identified a subpopulation of tumor cells with low CD19. These CD19-low MCL cells shows elevated CD36 and cancer stemness associated gene signatures. From publicly available microarray-dataset, we inferred that high CD36-expressing cells had reduced expression of B-cell receptor signaling genes, and their high expression was associated with poor clinical outcomes in MCL. Increased CD36 expression is associated with stemness and resistance in multiple cancer types including MCL. Since, CD36 is a key fatty-acid transporter associated with metabolic reprogramming, immune suppression, and therapy resistance, understanding its enrichment in MCL-tumor initiating cell (TIC) populations may provide novel therapeutic opportunities to eliminate resistant lymphoma cells.

Poster P-005

Role of Guanylate Cyclase C Signalling in Basal Pancreatic Homeostasis and Cerulein Induced Acute Pancreatitis in Mice

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Abstract: Acute pancreatitis (AP) is initiated by pathological responses within pancreatic acinar cells following excessive secretagogue stimulation, resulting in intracellular calcium dysregulation, premature digestive enzyme activation, cellular stress, tissue injury, and subsequent inflammatory responses. Although the molecular mechanisms underlying cerulein induced AP are well characterized, the role of guanylate cyclase -C (GC-C), a membrane bound receptor that is expressed in the pancreas, and regulates cyclic GMP-dependent signalling and epithelial homeostasis, remains poorly defined. This study investigates whether loss of GC-C signalling alters basal pancreatic physiology and susceptibility to cerulean induced pancreatic injury. The pancreas from GC-C wild-type (WT; *Gucy2c*$^{+/+}$) and knockout (KO; *Gucy2c*$^{-/-}$) mice was evaluated histologically and serum biochemical parameters were assessed. Untreated mice reported optimal ranges of serum biochemical parameters, including lipase and amylase. Histology of the pancreatic head region exhibited well defined acinar cell morphology, filled with zymogens in WT mice. There were more centroacinar cells in GC-C$^{-/-}$ mice. Cerulein administration to mice revealed greater pancreatic damage in GC-C$^{-/-}$ mice and significant changes in acinar cell gene expression. Overall, this study suggests a previously underexplored link between GC-C/cGMP signalling and pancreatic stress adaptation and provides a framework for determining whether GC-C deficiency influences acinar cell homeostasis, susceptibility to acute injury, and subsequent tissue remodelling during AP.

Poster P-006

B3GNT5 as a Therapeutic Vulnerability in Triple-Negative Breast Cancer

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Abstract: Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype defined by the absence of estrogen receptor (ER), progesterone receptor (PR), and HER2 expression/amplification, resulting in limited targeted therapeutic options and an unfavourable prognosis. Glycosylation, an important post-translational modification, plays a critical role in tumour progression, invasion and metastasis. B3GNT5 (β-1,3-N- acetylglucosaminyltransferase 5) is an important enzyme involved in glycosphingolipid biosynthesis and has been implicated in cancer progression; however, its role in TNBC, particularly in the Indian population, remains poorly understood. In the present study, B3GNT5 was depleted in MDA-MB-231 and HCC1937 TNBC cell lines using lentiviral-mediated knockdown. B3GNT5 depletion markedly reduced cellular proliferation, migration and invasion, while increasing apoptosis and enhancing sensitivity to Adriamycin (doxorubicin), a commonly used neoadjuvant chemotherapeutic agent in breast cancer. Mechanistically, B3GNT5 knockdown increased p53 and PARP1 expression, enhanced intracellular ROS generation, and induced cell-cycle arrest. Furthermore, depletion of B3GNT5 resulted in the downregulation of key oncogenic signalling pathways, particularly STAT3 and ERK1/2, supporting its role in regulating tumour cell survival and proliferation. Further analysis of human breast cancer specimens using qRT-PCR and immunohistochemistry (IHC) demonstrated elevated B3GNT5 expression in tumour tissue, which was consistent with cell line data. Collectively, these findings indicate that B3GNT5 has a tumour-promoting role in TNBC, potentially through the modulation of glycosphingolipid-associated glycosylation and activation of STAT3 and ERK1/2 signalling. Its depletion suppresses TNBC cell proliferation and invasive behaviour, promotes apoptosis, and enhances chemotherapy sensitivity, suggesting that B3GNT5 may represent a potential therapeutic target and biomarker in TNBC.

Poster P-007

Role of Tumour Suppressor WT1 and its Interacting Protein RNA Helicase DDX5 in Regulating miRNA Expression in Kidney Mesenchyme

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Abstract: Wilms' Tumour (WT) is a paediatric kidney malignancy. WT1, a tumour suppressor, is mutated in the germline and soma in many WT cases, while somatic and germline mutations in microRNA-processing genes (MIRPG) independently cause WT, and both are associated with IGF2 upregulation. How these distinct genetic changes converge on a common tumorigenic mechanism remains unclear. WT1 is known to bind RNA and regulate mRNA stability. Here, we show that WT1 also interacts with microRNA let-7 and microRNA-processing proteins, among which DDX5 emerges as the central interacting node by protein-protein interaction (PPI) network analysis; this WT1-DDX5 interaction is RNA-independent, indicating a direct protein-protein interaction. To investigate this axis, we generated WT1-knockdown M15 cell lines and observed downregulation of mature let-7c, along with corresponding changes in primary and precursor let-7 levels. To dissect the contribution of DDX5, we are generating DDX5 knockdown and WT1/DDX5 double-knockdown lines, in which let-7 expression will be compared across single and double knockdowns. As let-7 targets Igf1r, we further plan to assess Igf1r expression to evaluate downstream effects on IGF signalling. This work aims to define the WT1-DDX5-let-7-Igf1r axis and provide mechanistic insight into how WT1 and MIRPG mutations converge to dysregulate IGF signalling in WT.

Poster P-008

Role of TGF-β-Induced miR-21-5p in Promoting Oral Squamous Cell Carcinoma Through Suppression of KLF5 and SPRY1

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Abstract: OSCC is a common and aggressive malignancy with a poor prognosis. Transforming growth factor-β plays a dual role in cancer, acting as both a tumor suppressor and a promoter in the early and late stages, respectively. miRNAs are small non-coding RNAs of ~22-23 nucleotides that regulate gene expression by binding mostly to the 3'UTR of target mRNA. This study investigates the role of TGF-β- induced miR-21-5p in OSCC progression. miRNA sequencing of SCC-25 OSCC cells treated with TGF-β identified several TGF-β-regulated miRNAs, with miR-21-5p being significantly upregulated. ChIP assay confirmed SMAD2/3 binding to the miR-21 promoter, while TGF-βRI inhibitor treatment verified SMAD- dependent regulation. An invasion assay using miR-21-5p mimics and inhibitors demonstrated its oncogenic role in OSCC cells. Dual-luciferase assays confirmed the interaction of miR-21-5p with the 3' UTR of KLF5 and SPRY1. siRNA-mediated knockdown of KLF5 and SPRY1, followed by pathophysiological assays such as cell proliferation, apoptosis, invasion, and colony formation assays, confirmed their roles as tumor suppressors in OSCC. Our findings thus indicate that TGF-β induces miR-21-5p via the SMAD2/3 pathway and promotes OSCC by targeting KLF5 and SPRY1. These findings suggest that targeting the TGF-β/miR-21-5p/KLF5 or SPRY1 axis could represent a novel therapeutic target in OSCC.

Poster **P-009**

Vitamin D: A dietary component to a marvel player regulating cell death in cancer

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Abstract: Cancer progression is closely associated with dysregulated cell survival, oxidative stress and resistance to programmed cell death. Vitamin D although a dietary compound, it has immense role in regulating cellular processes and have emerged as a promising candidate for cancer prevention but detailed underlying molecular mechanism is unveiled. Here, we probe for ways how possibly vitamin D can be used as anti -cancer therapeutic. It is quite convincing to use vitamin D as it is safe and non toxic, being a dietary component. The cytotoxic and anti proliferative effects were evaluated following treatment of lung cancer cells with different concentrations of the vitamin D. Treatment with the vitamin D resulted in loss of cancer cell viability in a concentration-dependent manner, accompanied by increased lipid peroxidation, reflected by elevated MDA levels, and depletion of cellular GSH. These alterations in turn disturbed cellular redox homeostasis and promoted oxidative damage through increased reactive oxygen species (ROS) and lipid ROSgeneration, thereby culminating in apoptotic and ferroptotic cell death. Collectively, the study provides evidence for the anti-cancer potential of vitamin D; as a modulator of apoptosis and ferroptosis in lung cancer and further encourages investigation of the underlying molecular mechanisms behind its therapeutic relevance.

Poster **P-010**

Role of SRT-1720 (a SIRT1 activator) and naturally occurring AMPK activators in reducing cancer cell aggressiveness

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Abstract: Lung and Colorectal cancer, are the two major leading causes of cancer related mortality worldwide. Differences in Genetic alterations, histological diversities and heterogeneity in gene expression are closely associated with varied therapeutic outcomes, frequently accompanied by resistance and differential drug response. AMPK is considered as a therapeutic target for cancer for its unique ability to directly recognize cellular energy status. The objective of this study is to identify and explore the role of different small molecules and bioactive compounds as AMPK activators in managing cancer cell aggressiveness and to understand the mechanistic details behind the process. Here, we demonstrated that SRT-1720, a SIRT1 activator, directly activates AMPK in LKB1 mutant A549 cells and HCT-116 cells resulting regulation of cancer cell aggressiveness by modulating p38 MAPK/ R1/MAO-A/ ROS signalling cascade. Additionally, we demonstrated that pomegranate peel extract contains different known AMPK activators which either alone or in combination with SRT-1720 can sensitize Cisplatin/ Doxorubicin resistant HCT-116 colorectal cancer cells. Altogether, this study demonstrates the importance of AMPK activation in the management of lung and colon cancer aggressiveness and identifies SRT-1720 as a potent repurposing agent for cancer treatment especially in NSCLC patients containing a point mutation in LKB1.

Poster **P-011**

Role of p38MAPK on iron sequestration components in glioblastoma cells

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Abstract: Glioblastoma multiforme (GBM) is an aggressive form of brain cancer in the central nervous system with a

high lethality rate. Glioblastoma exhibit an iron-seeking phenotype required for enhanced growth and proliferation. We earlier reported that endogenous Phosphoinositide-3-kinase activity of glioblastoma cells suppresses translation of the iron storage component ferritin to avail iron for proliferation. However, the role of other kinases in regulating iron homeostasis remains unexplored. To understand whether p38MAPK influences iron homeostasis, we treated glioblastoma cells with specific inhibitors and the regulation of iron homeostasis proteins was examined. Iron storage protein Ferritin (Ft-H and Ft-L) and iron export protein Ferroportin (Fpn) were upregulated at the transcriptional level. These regulations were observed only in glioblastoma cells but not in primary astrocytes. This may be due to elevated p38MAPK activity reported in glioblastoma cells and GBM patients. We found the role of the transcription factor Nrf-2 (Nuclear factor erythroid 2- related factor 2) in regulating Ft-H and Fpn. As a result, p38MAPK inhibitors can sequester the labile iron pool and thereby affect cell proliferation in these cells. Our results strongly suggest the role of p38MAPK in silencing iron sequestration components to utilize iron for proliferation of glioblastoma cells.

Poster P-012

Hesperetin and ZnO-NP loaded CMC-GG bio-polymeric nanocomposite for anticancer, antioxidant, anti-inflammatory properties and its biocompatibility studies in *Drosophila melanogaster*

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Abstract: Carboxymethyl Cellulose-Guargum based polymeric nanocomposite incorporated with biogenic synthesized ZnO-NP and hesperetin (CMC-GG/ZnO/Hsp) was synthesized to develop a phytochemical-based nanomaterial by following a simple synthetic procedure. In this study, hesperetin, a natural citrus flavonoid and green synthesized ZnO-NP was by entrapped within Carboxymethyl Cellulose-Guargum derived nanocomposite. CMC-GG/ZnO/Hsp were characterized using XRD, FTIR, SEM. High loading percentage of hesperetin in polymeric nanocomposites revealed excellent incorporation efficiency. In addition, pH responsive release behavior of hesperetin from nanocomposites exhibited sustained and faster release. IC 50 value of CMC-GG/ZnO/Hsp were used against SW-480 cell line. Synergistic effect of ZnO and hesperetin was observed in all the experiments. Experimental outcome confirmed excessive accumulation of reactive oxygen species (ROS) mediated cytotoxicity, mitochondrial depolarization and higher degree of nuclear damage followed by increased mortality of SW-480 cell after treatment with hesperetin and ZnO-loaded nanocomposite. Moreover, this composite resulted in enhanced antioxidant and anti-inflammatory properties. For *invivo* studies, *Drosophila melanogaster* was used to check the biocompatibility of this CMC- GG/ZnO/Hsp nanocomposite. Cytoxicity and genotoxicity studies in the tissue confirmed that it is safer for oral consumption for the flies. Further, the behavioral studies conducted had no significant effect on the flies.

Poster P-013

Single-cell transcriptomic profiling defines malignant cell plasticity and novel immune polarization in OSMF-Associated Oral Cancer

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Abstract: Oral submucous fibrosis (OSMF) is a highly prevalent premalignant disorder in India, with 7–13% risk of malignant transformation to oral squamous cell carcinoma (OSCC). Whether OSMF-associated OSCC is clinico-pathologically distinct remains poorly understood, thus limiting context-specific management. To study the effect of disease etiology on tumor microenvironment, we performed single-cell RNA sequencing of thirty OSCC patients with/without OSMF and validated significant findings in independent bulk and spatial transcriptomic datasets and by flow cytometry. Malignant cells showed the most transcriptional divergence between the two patient groups, resolving into

four distinct cellular states, ranging from a metabolically active, prognostically unfavorable population to states marked by partial epithelial-to-mesenchymal transition and oncofetal reprogramming. We identified context-dependent initiators of adhesion, migration pathways and defined a fibroblast-malignant signaling axis centered on *PLA2G2A-CXCL8* that promotes tumor-supportive stroma in OSMF. We also characterized a rare population of double-negative ($CD4^{-}CD8^{-}$) T cells, with a quiescent state enriched in non-OSMF tumors that associated with poor survival in TCGA-HNSC and ICGC-oral cancer cohorts. Thus, our study establishes OSMF-associated OSCC as transcriptionally distinct from non-OSMF OSCC, delineating subtype-specific malignant and T cell gene expression landscapes. These findings provide a mechanistic framework for developing context-specific biomarkers and therapeutic interventions in OSCC.

Poster P-014

The goldilocks relationship of nutrient and Wnt signalling pathway

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Abstract: The canonical Wnt signalling pathway, the primary contributor of colorectal cancer, operates via stabilization of the effector protein β-catenin, which translocates to the nucleus and regulates gene expression. There are multiple levels of regulations to manipulate the signalling, like at the ligand-receptor level, at the level of destruction complex of β-catenin and the translocation of β-catenin to the nucleus. In most of the colorectal cancers, APC (adenomatous polyposis coli) is found to be mutated, which is a component of β-catenin destruction complex. On the other hand, nutrient stress is a hallmark of the tumour microenvironment where depletion of glucose, lipids and amino acids induce homeostatic feedback pathways. We used three cell lines, HEK293T, CACO-2 and HCT116 expressing a luciferase based Wnt reporter system to study the starvation effect of these nutrients on Wnt output. While HEK293T shows an effect of NEAA starvation on Wnt output, each of them shows an altered Wnt output upon glucose stress regardless of their mutational differences. This indicates a cross talk between Nutrient and Wnt signalling. Whether this acts as a cue of metabolic rewiring in tumorigenesis is to be unfolded.

Poster P-015

Shikonin-mediated anticancer activity: Targeting mitochondrial dysfunction, DNA damage and EMT to suppress oral cancer

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Abstract: Phytotherapy has provided a new insight to the treatment of many cancers, including oral cancer, over conventional chemotherapeutic agents as it has lower side effects. Shikonin is a naturally biologically active naphthoquinone found in the roots of *Lithospermum erythrorhizon* plant exhibits strong cytotoxic effects against various cancers, including oral cancer. The present study assesses the anticancer effectiveness of Shikonin in SCC9 and H357 oral cancer cell lines, emphasising its antiproliferative, antimigratory, apoptosis-inducing mechanisms. We performed a series of assays, such as MTT, colony assay, wound healing, tumoroid assay, AO/EtBr, DAPI, comet assay, qRT-PCR, western blotting, and measurements of reactive oxygen species (ROS) and mitochondrial membrane potential (MMP). As a result, we found that Shikonin reduced the viability, proliferation, and tumorigenicity of SCC9 and H357 cells in a time and concentration-dependent manner. It promotes apoptosis via overexpressing proapoptotic Bax and caspase 3 via enhancing ROS that leads to MMP depletion. Moreover, Shikonin inhibited cell migration by regulating epithelial-mesenchymal transition (EMT) markers. In summary, our findings suggest that Shikonin possesses strong anticancer properties against oral cancer cells under both *in vitro* and *ex vivo* conditions, underscoring its promise as a potential therapeutic agent for treatment of oral cancer.

Poster **P-016**

Piperlongumine Targets BIRC5 to Suppress Oral Squamous Cell Carcinoma: An Integrated Computational and Experimental Study

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Abstract: Oral squamous cell carcinoma (OSCC) is still a major clinical problem and need an effective and selective therapeutic agent. Piperlongumine (PIP), a bioactive alkaloid of *Piper longum*, has been shown to have anticancer activity in OSCC, although molecular targets and mechanisms are still not known completely. In this study, an integrated bioinformatics, computational and experimental approaches were used to investigate the anti-cancer potential of PIP. Common OSCC-associated DEGs were detected from three OSCC gene expression datasets, and protein-protein interaction and functional enrichment analyses were subsequently performed. The PIP-related targets were prioritized using molecular docking, molecular dynamics simulation, MM/PBSA, free-energy landscape, and ADMET analyses. The findings were then confirmed with 2D and 3D culture of SCC9 and H357 tumor cells. Among the 444 OSCC-associated DEGs, BIRC5, CDK1, BUB1, BIRC5, and KIF23 were determined as hub genes of which all except MAD2L1 were linked to poor patient survival. MD simulation and MM/PBSA showed that BIRC5 has a stable free-energy landscape and favourable binding energy (-102.938 ± 5.488 kJ/mol). PIP selectively suppressed OSCC growth, enhanced ROS production, reduced MMP led to DNA damage, G2/M arrest and apoptosis, and down-regulated the expression of hub-gene, suggesting BIRC5 as a potential molecular target.

Poster **P-017**

Dietary Sirtuin Modulators as a Promising Natural Anti-Cancer Agent against Gastric Cancer through SIRT1 Activation

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Abstract: Gastric cancer remains a major global health concern, highlighting the need for safer and more effective therapeutic approaches. SIRT1, a NAD^+-dependent deacetylase, is an important regulator of cell proliferation, cellular metabolism, and apoptosis, and is well known to play a dual role in cancer. The present study investigates the protective effect of five dietary Sirtuin modulators (SM1–SM5) on gastric cancer and the underlying mechanisms involved. These compounds, structurally distinct and belonging to different chemical classes, were subjected to molecular docking studies against SIRT1, followed by in vitro validation of their anticancer potential. AGS (adenogastric carcinoma) cells were treated with different concentrations of the modulators, and MTT assay along with morphological analysis was performed to assess cell proliferation. SM5 exhibited the most favourable docking score and binding interactions with SIRT1. While SM1 and SM2 showed minimal toxicity even at higher concentrations (up to 200 μM), SM3, SM4, and SM5 significantly reduced cell viability and inhibited migration in the scratch assay. Based on docking and in vitro results, SM5 was selected for further study. Hoechst staining and Caspase-3 activity assay confirmed its apoptotic potential, while qPCR, western blot, and SIRT1 activity assay revealed significant upregulation of SIRT1 expression and activity. These findings establish SM5 as a promising natural SIRT1-activating anticancer agent against gastric cancer.

Poster P-018

To Assess the Effectiveness of Some Chemopreventive Agents in Various Cancer Cells

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Abstract:

Background: Chemoprevention means to find the ways to prevent cancer development by the use of potential chemical/natural compounds. In this study, we examined the potential of three chemopreventive agents Acumapimod, BAM15, and 7-Methoxyisoflavone (7-MIF). We also investigated the mechanistic details of their action inside the cells. We checked their efficacy in three different cancer cell lines: HCT116, MCF-7, and A549.

Methods: Cell proliferation and other assays were conducted to assess compound efficacy, specifically examining their effects on Monoamine Oxidase A (MAO-A) gene expression—a key marker of cancer aggressiveness—as well as on apoptotic and tumor-suppressor pathways.

Results: Acumapimod effectively controlled cancer progression by targeting MAO-A expression and activity. BAM 15 markedly inhibited cell proliferation across all three cell lines by upregulating the tumor suppressors p21 and p53, activating apoptotic pathways independently of MAO-A. In A549 and MCF-7 cells, 7-MIF exhibited robust antiproliferative activity accompanied by the upregulation of MAO-A, BAX, and p21, alongside the downregulation of the anti-apoptotic marker BCL2.

Conclusion: Acumapimod, BAM 15, and 7-MIF exert distinct anticancer effects by modulating divergent molecular pathways, including tumor suppressor activation, apoptotic regulation, and MAO-A inhibition. These findings identify several potential therapeutic targets for cancer chemoprevention.

Poster P-019

Chromatin remodeller MORC2 as a Novel Regulator of Ribosome Biogenesis in Breast Cancer Progression

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Abstract: MORC2 (Microrchidia Family CW-Type Zinc Finger 2) is an ATP-dependent chromatin remodeller and emerging oncogene that is overexpressed in multiple malignancies, including breast cancer. Although MORC2 promotes proliferation, invasion, epithelial–mesenchymal transition, and chemoresistance through its roles in chromatin compaction, DNA repair, and transcriptional regulation, its role in ribosome biogenesis, which is essential for cancer progression, remains elusive. Ribosome biogenesis is a highly coordinated process that supports the elevated protein synthesis demands of rapidly proliferating cancer cells, and its dysregulation is increasingly recognized as a hallmark of tumorigenesis. To investigate whether MORC2 contributes to this process, protein–protein interaction (PPI) network analysis carried out with data from MORC2 co-immunoprecipitation (Co-IP) and liquid chromatography–mass spectrometry (LC-MS) revealed that MORC2 interacts with several proteins involved in ribosome biogenesis. Furthermore, meta-analysis revealed that MORC2 positively correlates with genes involved in ribosome biogenesis. Validation of these results using RT -PCR and Western blot analysis identified several MORC2 target genes. Among these MORC2 target genes, RPS7 was identified as an ideal target gene, where MORC2 overexpression increased RPS7 mRNA and protein expression, whereas MORC2 knockdown reduced RPS7 protein expression in breast cancer cell lines. Further, Chromatin Immunoprecipitation (ChIP) assay demonstrated MORC2 enrichment at the RPS7 promoter, suggesting a potential transcriptional regulatory relationship. Based on these findings, we depict the role of MORC2 as a regulator of RPS7 expression and, in turn, its role in ribosome biogenesis and breast cancer progression.

Poster **P-020**

Elucidating the Role and Deciphering the olecular mechanism Associated with Fatty acid-mediated Cancer Progression

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Abstract: Alteration in fatty acid metabolism is a hallmark of cancer, and dysregulation of fatty acid synthesis, uptake, and oxidation has been implicated in various stages of tumorigenesis. Studies from our lab have already demonstrated the role of an oxidative enzyme Monoamine oxidase A (MAO-A) which is involved in the oxidative deamination of biogenic amines, leading to the production of hydrogen peroxide and aldehydes. The enhanced production of reactive oxygen species (ROS) resulting from MAO-A activity can cause oxidative stress, DNA damage, and cellular dysfunction, which may contribute to carcinogenesis. Our initial findings showed that various fatty acids (long, medium & short) induce MAO-A expression in A549 lung adenocarcinoma cells at both protein and mRNA level. We demonstrated the involvement of different PPARs in fatty acid-mediated upregulation of MAO-A gene expression. Additionally, we have also showed that Sp1 transcription factor plays a crucial role for oleic acid-induced MAO-A gene expression in A549 lung carcinoma cells. Currently we are exploring the involvement of the fatty acid receptors and fatty acid binding proteins in fatty acid-mediated MAO-A gene expression and cancer progression in different cancer cells. Altogether, our findings suggest that MAO-A inhibition can be employed as a therapeutic strategy for cancer prevention.

Poster **P-021**

Evaluation of Chenodeoxycholic acid (CDCA)-Butyrate(NaBu) Nanoformulation for Anti- inflammatory and Hepatoprotective Effects in Various Liver Cancer Models

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Abstract: CDCA-Butyrate polymeric nanoformulation is a novel strategy designed for targeting the gut dysbiosis and liver inflammation. The polymeric nanoformulation helps in more targeted delivery, small size, more bioavailability, controlled release and prevents premature drug release. Characterization of polymeric nanoformulation was performed by FTIR, NMR, for confirming the functional groups like aliphatic change of biotin, and the $–CH_2$ and -OCH_2 groups of PEG and ester linkage between Biotin-PEG, DLS for their size confirmation and TEM for the structural analysis. In-vitro analysis of polymers included the cell viability assay by MTT assay, oxidative stress is performed by DCFDA dye, and gene expression studies for inflammatory markers, apoptotic markers, TLRs, and MMPs levels. Male SD Rats were procured for the acute and sub-acute toxicity study. Efficacy study was performed in in-vivo models, where biochemical analysis, histopathological analysis for liver tissue, cytokines profile analysis for IL-1β, Il-6, IL-10 TNF- α, and gene expression studies for inflammatory markers, apoptotic markers, TLRs, and MMPs levels, and HPLC to estimate the SCFA levels. These polymeric nanoformulation proved to show better results when compared to the chemotherapeutic molecule, and provide proper targeted delivery, more bioavailability, controlled release and prevent premature drug release, and can act on the Gut-Liver axis.

Poster **P-022**

Integrative Bioinformatic and Experimental Analysis of POLQ Expression, Methylation and Survival in Head and Neck Squamous Cell Carcinoma

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Abstract: DNA polymerase theta (POLQ) plays a crucial role in error-prone microhomology mediated end joining DNA repair pathway that contributes to genomic instability and is aberrant in cancer. Here, using UALCAN database we have conducted bioinformatics analysis and report that POLQ is significantly upregulated in primary head neck tumors, has promoter hypermethylation compared to normal tissues immune infiltration and is associated with poor patient survival. The *insilico* findings are being evaluated experimentally for POLQ mRNA expression using qRT-PCR in HNC cell lines (AW13516, CAL27) and tumor tissues. POLQ mutations in sporadic HNC were analysed using COSMIC database and miR binding to POLQ was predicted using miRWalk database. There are several POLQ inhibitors being tested in clinical trials and target the polymerase and helicase domain of POLQ. However the impact of mutations in HNC on the activity of POLQ inhibitors remains to be tested. Collectively, these findings suggest that POLQ is dysregulated in HNSCC and is valuable therapeutic target in HNSCC.

Poster P-023

Unveiling the Therapeutic Potential of Bioactive Phytocompounds from *Ficus bengalensis* bark in the Epigenetic Regulation of OSCC

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Abstract: Ficus benghalensis (Banyan tree) is widely recognised for its rich phytochemistry and therapeutic potential. The present study explored the metabolite profile and anticancer efficacy of the methanolic extract of F. benghalensis bark (MEFB) and its key bioactive flavone in oral squamous cell carcinoma (OSCC). MEFB was prepared by maceration and subjected to qualitative and quantitative phytochemical screening, metabolite profiling by GC-MS and LC-MS (ESI positive and negative modes), and structural characterisation by ATR-FTIR and ^{1}H NMR spectroscopy. Molecular docking against epigenetic modifiers revealed strong interaction of the flavone subclass with DNMT1 and HDAC1. The extract showed significant antioxidant activity (DPPH IC_{50}, 22.95 µg/mL). In vitro, MEFB and the flavone markedly inhibited OSCC cell proliferation, migration and clonogenic potential. Mechanistically, flavone treatment caused dose-dependent downregulation of DNMT1 and HDAC1, reversal of epithelial-mesenchymal transition with increased CDH1 (E-cadherin) and decreased Vimentin expression, suppression of cancer stemness markers, and inhibition of RAS-MAPK signalling. Combination with the DNMT1 inhibitor azacytidine enhanced efficacy, producing more pronounced DNMT1 suppression and synergistic CDH1 upregulation than either agent alone. These findings identify the flavone as a key driver of the anticancer activity of MEFB and a promising multi-targeted candidate for oral cancer management.

Poster P-024

ANN model based Multi-Stage Virtual Screening Strategy for the Identification of Novel Poly(ADP-Ribose) Polymerase 14 (PARP14) Inhibitors

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Abstract: Poly(ADP-Ribose) Polymerase 14 (PARP14), a mono-ADP-ribosyl transferase, is a critical mediator of cell survival pathways and immune regulation, driving proliferation in severe malignancies like B-aggressive lymphomas. Due to its essential, non-redundant role, targeting the PARP14 catalytic domain is a high-value strategy for developing novel, selective small-molecule therapeutics. To overcome the immense challenge and cost of conventional high-throughput screening, we employed a highly stringent, integrative in silico approach to efficiently prioritize potent lead compounds from a large chemical space. Our multi-stage strategy began with the virtual screening of an in-house compound library using a high- throughput Artificial Neural Network (ANN)-based model, which rapidly filtered molecules with the highest predicted activity scores. This reduced set then underwent rigorous cheminformatics to

yield a refined, drug-like library. These compounds were subsequently screened using a ligand-based pharmacophore model to ensure the presence of critical features essential for binding. The resulting top hits were subjected to high-precision molecular docking (SBVS) into the PARP14 catalytic site to accurately model binding affinity. This four-tier pipeline successfully identified novel chemical scaffolds with optimal binding scores and favourable active-site interaction profiles. Having passed rigorous computational validation, these promising molecules are now prioritized for in vitro assay validation to confirm their inhibitory potency against PARP14.

Poster P-025

Exploring Structure-guided Approach for Targeting *Mtb*ClpP1P2 Protease Machinery in Mycobacteria

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Abstract: MtbClpP1P2 is a barrel-shaped, heterotetradecameric serine protease comprising of two stacked seven-membered rings (ClpP1 and ClpP2) that together enclose a self-contained proteolytic chamber which is important for protein quality control in *Mycobacterium tuberculosis*. Each subunit carries a catalytic triad (Ser–His–Asp), and substrates enter the internal chamber through axial pores with help from unfoldases (ClpX/ClpC1) that are AAA+ ATPases. This key regulator of mycobacterial proteostasis was recently shown to be a viable drug target when cediranib was found to bind an unrecognized allosteric site within the equatorial handle domain of MtbClpP1P2 (PDB: 6IW7). This handle region, located at the ClpP1–ClpP2 interface holds the 14-mer together and allosterically links to the catalytic centers making it mechanistically distinct from both the internal active-site pocket and the surface acyldepsipeptide (ADEP)- binding groove. The newly identified pocket within the handle domain, now validated as druggable via cediranib, represents a potentially safer third target site apart from the catalytic and ADEP regions. In this work, structure-based virtual screening using an extended electron distribution (XED) field template derived from the bound cediranib structure was applied to this allosteric pocket. A pipeline combining tiered Glide docking (HTVS/SP/XP), Cresset Flare field- and shape-based alignment to the cediranib template, and LeadFinder rescoring narrowed roughly 50,000 Maybridge compounds down to 15 hits. Molecular dynamics simulations then ranked these by binding-pose stability, selecting eight for experimental testing. Fluorescence based MtbClpP1P2 protease assay identified three compounds with 25–30% protease inhibition at 25 μM, while Cediranib caused upto 40% inhibition of protease activity. The obtained MIC for Mtb culture was 50 μM. This approach has helped to indentify potential scaffolds for further SAR to improve the protease inhibition activity and cellular potency.

Poster P-026

Identification of JEV capsid-interacting domain(s) with host protein(s): Novel target for developing anti-JEV therapeutics

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Abstract: JEV infection. Virus–host protein interactions play critical roles throughout the viral life cycle and represent potential targets for antiviral intervention. In this study, we identified two functional domains of the JEV capsid protein, P2 and P7, using competitive peptide-binding assays. Pull-down assays followed by MALDI-TOF/TOF mass spectrometry demonstrated that the JEV capsid protein interacts with the host protein annexin A2 (ANXA2) through these domains. Treatment with P2 and P7 peptides disrupted the capsid–ANXA2 interaction in JEV-infected cells and significantly reduced viral growth. Furthermore, molecular docking of approximately 55,000 compounds from the Maybridge library identified 10 compounds with favourable binding to the P7 domain. Among these candidates,

SPB07257 exhibited potent anti-JEV activity, with an IC50 of 10 μM and a CC50 of >100 μM. Notably, SPB07257 also inhibited the capsid–ANXA2 interaction in JEV-infected cells. Overall, our findings demonstrate a novel antiviral strategy targeting functional domains of viral proteins involved in host–virus interactions and provide a potential approach for developing small molecules against JEV infection.

Poster P-027

Structure-Based Computational Screening of Phenazine and Fluorescein Derivatives Against KatG: An Integrated Multi-Parameter Approach

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Abstract: Tuberculosis (TB) remains a leading cause of infectious disease mortality worldwide, and multidrug-resistant strains make first-line treatment harder to sustain. Isoniazid resistance is frequently linked to dysfunction of the mycobacterial catalase-peroxidase KatG, which activates the prodrug within *Mycobacterium tuberculosis*. This study presents a structure-based computational screening pipeline targeting the KatG active site, using a focused library of phenazine and fluorescein derivatives — chemotypes often dismissed on legacy toxicity grounds despite established clinical precedents such as clofazimine and ophthalmic fluorescein. Virtual screening, combined with drug-likeness and ADMET filtering, narrowed the library to two lead candidates, one per chemotype, both showing favourable predicted binding affinity and drug-likeness. Notably, despite passing standard pharmacokinetic filters, one lead was flagged for predicted genotoxic risk, showing that drug-likeness and toxicity don't track together, so relying on one metric alone would have missed this. Quantum chemical analysis revealed markedly different electronic character between the leads, ranging from a reactive, low-stability profile to a stable, hard profile. Even so, MD simulations and binding free energy calculations showed both leads bind with similar overall stability, suggesting that shape complementarity within the pocket not electronic reactivity primarily governs affinity here. This suggests that combining multiple computational filters rather than any single one is important for prioritising chemically diverse inhibitor candidates against this drug-resistance-relevant target.

Poster P-028

Loop Dynamics and Disordered-core Interactions Tune the Stability of IscU: Studies on Apolar mutants of the Conserved -SSS- Region

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Abstract: IscU is a highly conserved scaffolding protein involved in iron–sulfur cluster biogenesis. Although IscUs are structurally well-characterized, the importance of three consecutive serine residues (-SSS-) that are conserved throughout mesophilic and psychrophilic IscUs is not known. Thermal denaturation of *E. coli* IscU monitored by circular dichroism spectroscopy indicates that S69A and S70A mutants increase the stability of the protein, whereas S71A has no effect. We further investigated the structural rearrangements upon mutation using molecular dynamics simulations. All three mutants enhance the dynamics of the loop regions. Particularly, the distance between loop-1 and loop-2 increases, but loop-2 to loop-3 distance decreases. Also, the helical interactions are reorientated, without altering their overall compactness. The additional interactions between the strands and disordered *N*-terminal region with helix-1 in S69A, and disordered *N*-terminal with loop-3 in S70A, might have contributed to the increased thermal stability of these mutants. However, the network of interactions between the β-strand and loops, and the helix-strand interactions could only enhance flexibility without altering the stability of S71A. Thus, we conclude that the mutants facilitating the interactions of the disordered region with helices/loop enhance the stability, while the additional interactions established by strands render no significant difference in stability.

Poster **P-029**

Integrated Functional and Structural Investigation of OR51X1: A Non- Canonical GPCR Implicated in Cardiovascular Disease

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Abstract: Cardiovascular diseases (CVDs) involve complex molecular mechanisms, and the contribution of several non-canonical G-protein-coupled receptors (GPCRs) remain poorly understood. OR51X1, an orphan olfactory receptor expressed outside the olfactory system, represents a poorly characterized GPCR with an unexplored role in cardiovascular pathophysiology. This study investigates the functional relevance and structural basis of OR51X1 in cardiovascular disease- associated conditions. OR51X1 expression was evaluated in H9c2 cardiomyoblasts and vascular smooth muscle cells (VSMCs) under normoxic and hypoxic conditions. Differential OR51X1 expression was observed following hypoxic stress. Furthermore, analysis of aortic tissue from normotensive, hypertensive, and enalapril-treated L-NAME induced hypertensive Wistar rats demonstrated down-regulation of OR51X1 under hypertensive conditions. To elucidate the molecular basis underlying OR51X1 function, structural characterization is being pursued. Determination of its three-dimensional structure may reveal receptor architecture, conformational states, ligand-binding determinants, and interactions with G-protein signaling partners. Collectively, this integrated functional and structural approach aims to define the molecular role of OR51X1 and establish its potential relevance in cardiovascular disease.

Poster **P-030**

Elucidating the role of amyloid prone regions (APRs) on the structure and function of pyroptotic executioner Gasdermin-D

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Abstract: Gasdermin-D (GSDMD) is a eukaryotic, pyroptotic executioner, pore-forming protein. Following inflammation, caspases cleave the full-length GSDMD. This leads to separation of its N-terminal domain (NTD) from the C-terminal domain (CTD). NTD, after cleavage from autoinhibitory CTD, oligomerizes on the membrane and forms functional pores, which allow release of inflammatory cytokines and cause cell death. Mechanism of pore-formation by GSDMD has been extensively studied. However, there exists knowledge gap regarding how various sequence elements could regulate pore-formation mechanism. Upon analysis of the protein sequence of GSDMD using different bioinformatics tools, we have noticed several APRs in its primary sequence. Recent study from our lab has shown that at least one of the APRs in GSDMD NTD plays crucial role in regulating pore-forming efficacy of GSDMD NTD. In our present study, we provide further insights into the implications of additional APRs for the structure-function mechanism of GSDMD. Our study provides crucial new insights into the regulation of the pore-forming mechanism and identify new targets for modulating the activity of GSDMD through its APRs.

Poster **P-031**

Characterization of Human Tyrosinase-catalyzed Eumelanin Nanostructures

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Abstract: Eumelanin is a biomacromolecule that imparts colour to our skin and provides photoprotection to our cells. The structure and kinetics of human tyrosinase, the key enzyme in the melanin biosynthetic pathway, differ significantly from bacterial and fungal tyrosinases. While mushroom tyrosinase has been extensively used to

synthesize and characterize melanin, the *in vitro* melanin synthesis by human tyrosinase remains uncharacterized. This highlights the need to study the properties of eumelanin produced by human tyrosinase and gain a better perspective into the pigmentation biology. In this study, the temporal evolution of the structure of eumelanin produced by recombinant human tyrosinase is probed by combining spectroscopy and electron microscopy. Imaging using SEM and TEM revealed that eumelanin evolves from nanoparticles to ordered sheet-like nanostructures. The electron diffraction recorded on eumelanin samples at different time points under TEM showed the progression from shorter intramolecular distances corresponding to indole systems to 3-4 Å distances, indicating π-bonding between the indole rings. The cyclic voltammetry shows the evolution of its redox behaviour with increasing structural ordering. Overall, this work presents experimental evidence of eumelanin's supramolecular structure and structure-function correlation at different eumelanin maturation stages, which advances the understanding of melanin biosynthesis mechanisms in humans.

Poster P-032

Epitope Mapping of a Pan-Flavivirus Neutralizing Antibody by Cryo- Electron Microscopy

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Abstract: Dengue virus (DENV) and Zika virus (ZIKV) are closely related flaviviruses that pose significant global health threats. Yet, the development of broadly protective antibodies and vaccines remains challenging due to antigenic variability and complex immune responses. Antibodies capable of neutralizing multiple DENV serotypes and ZIKV offer a unique opportunity to target conserved structural features of flaviviruses, but the molecular basis of such broad neutralization is not well understood. Here, we present cryo-electron microscopy (cryo-EM) studies of a broadly neutralizing antibody that potently neutralizes all four DENV serotypes as well as ZIKV. We have determined a 3.87 Å cryo-EM reconstruction of the DENV–D14.F25.S06 Fab complex, revealing the overall binding mode and spatial footprint of the antibody on the viral surface. The reconstruction suggests recognition of a conserved, likely quaternary epitope involving multiple envelope protein subunits, providing a structural rationale for the observed cross-flavivirus neutralization breadth. Ongoing efforts focus on improving data quality and resolution to enable high-resolution epitope mapping and precise analysis of antibody–virus interactions. These studies aim to elucidate conserved neutralization mechanisms across flaviviruses and to inform the rational design of broadly protective antibody-based therapeutics and next-generation vaccine immunogens.

Poster P-033

Structural Insights into Prokaryotic Translation Initiation

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Abstract: Translation initiation is the rate-limiting step of bacterial protein synthesis. Despite recent advances, the structural basis of the kinetically preferred pathway of 30S pre-initiation complex (PIC) assembly with full-length initiation factors and native mRNAs remains poorly understood. This study aims to determine the structures of bacterial 30S initiation complexes assembled with native mRNAs carrying canonical and near-cognate start codons to understand the molecular mechanism of translation initiation. 30S PIC reconstitution has been optimized by improving initiator tRNA preparation, mRNA selection, and complex stabilization. A native mRNA with stronger Shine–Dalgarno complementarity showed enhanced binding to 30S subunit compared with other mRNA constructs, leading to improved complex formation. BS3-mediated crosslinking further stabilized the complexes for cryo-EM analysis, and optimized data collection produced high-quality particle sets with preliminary 3D reconstructions showing densities at factor-binding sites. Lamotrigine, a recently identified IF2-binding antibiotic candidate, exhibited high- affinity binding to full-length IF2 and increased its occupancy on the 30S PIC, suggesting a potential

role in modulating translation initiation. In parallel, pull-down assays, AlphaFold3 modelling, and molecular dynamics simulations are being employed to complement the structural studies and investigate native initiation mechanisms.

Poster P-034

Decoding Molecular Architectures: The Strategic Role of SAIF, CSIR-CDRI in Accelerating Chemical and Pharmaceutical Innovations

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Abstract: The Sophisticated Analytical Instrument Facility (SAIF), hosted at the CSIR–Central Drug Research Institute (CSIR-CDRI), Lucknow, is a premier national analytical hub established in 1974–75. It is funded by the Department of Science & Technology (DST), Government of India, SAIF Lucknow provides advanced instrumentation access to researchers across academics, national laboratories, and R&D industries. The facility specializes in a robust, chemistry-centric suite of instruments including Nuclear Magnetic Resonance (NMR) spectroscopy, Mass Spectrometry (MS, HRMS), Liquid Chromatography-Mass Spectrometry (LC-MS/LC-HRMS), Fourier-Transform Infrared (FT-IR) spectroscopy and Elemental Analysis (CHNSO). These instruments are crucial for molecular structure elucidation, compound identification, qualitative and quantitative analysis and materials characterization. Annually serving approximately 350 researchers, more than 80% of SAIF's external users comprise university students pursuing MSc, MTech, and PhD research in organic, medicinal and natural-product chemistry. Sample submission processing is streamlined through an online workflow encompassing registration, slot booking, digital payment, and mail-in sample submission. Turnaround times range from 3–5 days for routine spectral analysis to 5–14 days for complex chromatographic and multi-dimensional structural characterization, significantly empowering decentralized scientific innovation. It transforms academic hypotheses into validated scientific discoveries, reinforcing the national framework for innovative drug discovery and materials science.

Poster P-035

Novel Cleavage Assay for Inhibitor Screening and Cleavage Motif Identification of PRSS55, a Slow-Kinetics Serine Protease

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Abstract: PRSS55 is a testis-specific serine protease essential for male fertility, making its inhibition a potential approach to non-hormonal contraception. However, no specific inhibitors of PRSS55 are currently known. Inhibitor screening is challenging due to its slow cleavage kinetics with the conventional serine protease substrate Boc-QAR-AMC. Furthermore, its preferred cleavage motif remains unknown, hindering the development of an efficient assay. Here, we aimed to establish a rapid, adaptable cleavage assay to identify the preferred cleavage motif of PRSS55 and facilitate inhibitor screening. We developed a nano-luciferase-based assay incorporating a protease cleavage motif (AQARIVGG), a flexible glycine-serine linker, and a C-terminal 6×His tag. Nano-luciferase was expressed, purified using Ni-NTA affinity chromatography, and immobilized on Ni-NTA magnetic beads. The beads were incubated with recombinant activated human PRSS55, magnetically separated, and the nano-luciferase released into the supernatant was quantified by luciferase assay. PRSS55 treatment produced a 10-20-fold increase in signal-to-noise ratio compared to the untreated control, whereas inactivated PRSS55 showed no detectable activity. This assay provides a rapid and adaptable platform for screening different cleavage motifs and identifying PRSS55 inhibitors, overcoming key limitations of conventional substrate-based assays.

Poster P-036

Diet Reversal in Western Diet Fed ApoE-/- Mice Restores Hepatic PUFA and Plasmalogens to Promote Atherosclerosis Regression

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Abstract: The progression of atherosclerosis is associated with extensive lipidome alteration. The present study investigates the effect of diet reversal on the lipidome of atherosclerotic mice and how it affects atherosclerosis regression. Atherosclerosis was induced in ApoE$^{-/-}$ mice by Western diet (WD) feeding for 20 weeks, regression was induced by diet reversal to chow for additional 90 days after 20 weeks of WD feeding. Plasma and hepatic lipid biochemistry along with histological analysis of aortic root and liver was performed by H&E and Oil Red O staining. The plasma, liver and adipose tissue were subjected to LC-MS/MS based lipidome analysis to identify alterations in the different lipid species. WD feeding resulted in increased circulating lipids and plaque development, hepatic steatosis and fibrosis. Diet reversal significantly reduced the circulating lipids, hepatic steatosis and atherosclerotic plaque. WD feeding resulted in accumulation of inflammatory lipids like lyso-phosphatidylcholines and ceramides, whereas a significant reduction in PUFA and plasmalogens is observed in the plasma and liver. Diet reversal showed reduction in the lyso-phosphatidylcholine and ceramide levels along with restoration in PUFA and plasmalogen levels. Therefore, present study identifies lipidome signature that can be associated with improved lipid profile and hepatic health and plaque regression.

Poster P-037

Cloning, Expression, and Purification of Pilus Adhesion LrpC fragments from and *Lactobacillus ruminis* for interaction studies with with ECM components

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Abstract: *Lactobacillus ruminis* is a gut autochthonous (indigenous) commensal and anaerobic probiotic strain. It relies on hair-like sortase-dependent pili, LrpCBA for adherence to the intestinal inner walls for colonization. The LrpCBA pilus consists of the tip LrpC, basal LrpB, and backbone LrpA pilin subunits. The LrpCBA pilus was shown to bind to intestinal surface components such as collagen and fibronectin, but it lacks affinity for mucus. The adherance property of LrpCBA pilus is attributed to the adhesive tip LrpC pilin subunit. To further understand binding mechanism and region involved in ECM binding, we have recombinantly produced various fragments of LrpC. These LrpC fragments are currently being used in interactions studies with different ECM components.

Poster P-038

Hyperglycaemia-Mediated Impairment of Diabetic Wound Healing in Oral Epithelial Cells

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Abstract: Diabetes, a major lifestyle-associated metabolic disorder, is accompanied by persistent hyperglycaemia that can impair tissue repair and delay wound healing. However, the cellular mechanisms linking metabolic stress to

defective wound repair remain incompletely understood. Histone deacetylase 6 (HDAC6), a cytoplasmic deacetylase involved in cytoskeletal dynamics and intracellular homeostasis, may serve as an important molecular link between hyperglycaemic stress and impaired cellular repair. In this study, we investigated the role of HDAC6 in hyperglycaemia -associated wound repair using oral squamous cell carcinoma cells as an in vitro model. Cells were exposed to normoglycaemic, borderline- hyperglycaemic, and hyperglycaemic conditions and treated with a specific HDAC6 inhibitor. Cellular homeostasis, cytoskeletal organisation, cell–cell interactions, and migratory responses were evaluated using complementary cellular, molecular, and nanoscale approaches. This study aims to elucidate the contribution of HDAC6 to hyperglycaemia-induced cellular dysfunction and explore its therapeutic potential in modulating impaired wound repair associated with diabetes.

Poster P-039

Mechanistic dissection of conformational dynamics of *E. coli* Pyruvate Dehydrogenase Regulator (PdhR) protein with implications in pyruvate sensor design

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Abstract: Protein function is modulated by allostery, a process involving binding of an effector molecule at a distant site (known as allosteric site) resulting in change of activity at the active site. Allosteric transcription factors (aTFs) are proteins that regulate gene expression in response to the availability of various small molecules. In bacteria, aTFs sense diverse stimuli in the environment and tune gene expression networks accordingly. Pyruvate Dehydrogenase Regulator (PdhR) is one such aTF, which belongs to the GntR family (FadR subfamily) of transcriptional regulators and comprises two distinct domains: An N-terminal helix-turn-helix (HTH) DNA-binding domain and a C-terminal effector-binding and oligomerization domain (E-O). Pyruvate binding at the C-terminal domain of PdhR leads to conformational changes in the protein that ultimately result in decreased binding to DNA at the N-terminal domain. Single fluorescence protein based as well as Fluorescence Resonance Energy Transfer (FRET) based sensors of pyruvate have been made using PdhR protein as a template. However, the mechanistic understanding of pyruvate mediated conformational changes is still lacking. Using Site Directed Mutagenesis, Hydrogen-Deuterium Exchange Mass spectrometry (HDX-MS) and Molecular Dynamics Simulations, we show that a network of amino acids comprising Tyr114-Arg118-His162 in the E-O domain are critical for the relay of pyruvate mediated conformational changes in PdhR. Interestingly, the double mutant Y114A/R118C showed complete loss of pyruvate mediated FRET changes while H162A mutant showed ~ 10 times increase in apparent *Kd* of pyruvate. Finally, the effect of these mutations on the pyruvate sensor performance was evaluated in living cells using ratiometric FRET imaging microscopy. Together this study elucidated the critical structural elements of PdhR protein that are pivotal for pyruvate mediated conformational changes that will aid in development of more effective genetically encoded fluorescence based sensors for pyruvate.

Poster P-040

Uncoupling of OXPHOS and Alteration of Mitochondrial Dynamics by a VDAC1 Inhibitor, DIDS

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Abstract: The voltage-dependent anion channel 1 (VDAC1) is a crucial regulator of mitochondrial activity and acts as a gatekeeper of transport, metabolism, and cellular death. However, the precise mechanism by which VDAC1 regulates mitochondrial oxidative phosphorylation (OXPHOS) remains unclear. To elucidate this mechanism, we examined how pharmacological inhibition of VDAC1 using the high-affinity inhibitor 4,4′-diisothiocyanatostilbene-2,2′-disulfonic acid (DIDS) affects cell viability and mitochondrial function. The IC_{50} value is 508 μM in U2OS cells. Also, 500 μM DIDS induced mitochondrial respiratory uncoupling, resembling the uncoupler CCCP. Additionally, exposure to 50–200 μM DIDS for 2h markedly disrupted the mitochondrial membrane potential, leading to mitochondrial depolarization. Furthermore, brief DIDS treatment increased the proportion of U2OS cells exhibiting hyperfused mitochondria and attenuated DRP1 recruitment to mitochondria. However, DIDS treatment did not alter the steady-state levels of OXPHOS complex I or complex V subunits. Consistent with findings in cell lines, DIDS significantly uncouples the isolated mitochondria from normal mouse muscle and liver and sarcoma tumor tissues. Finally, in silico analysis predicted that DIDS binds within the β-barrel structure of VDAC1. Collectively, these findings support a model in which DIDS interacts with the inner pocket of VDAC1, thereby contributing to mitochondrial respiratory uncoupling and mitochondrial hyperfusion.

Poster P-041

Integrated Functional and Structural Investigation of KCNX: A Non- Canonical Potassium Channel with Emerging Cardiovascular Relevance

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Abstract: Cardiovascular diseases (CVDs) involve complex alterations in vascular and cardiac signaling, while the contribution of non-canonical ion channels remains poorly understood. KCNX, a sodium-activated potassium channel, has emerged as a potential regulator of cardiovascular homeostasis; however, its functional significance and structural determinants remain underexplored. This study integrates functional and structural approaches to investigate the role of KCNX in atherosclerosis and hypertension to explore its therapeutic potential. Expression of KCNX and associated molecular alterations were investigated in Wistar rat models of high-fat-diet-induced atherosclerosis and L-NAME-induced hypertension. Cardiovascular phenotypes, histopathological changes, oxidative stress, and relevant signaling pathways were evaluated to determine KCNX-associated responses. An upregulation of expression of KCNX was observed under cardiovascular stress conditions, supporting its potential involvement in disease-associated remodeling. For structural characterization, domain-wise KCNX (transmembrane domain (TMD) and cytoplasmic C-terminal domain (CTD), respectively) constructs were expressed. Affinity purification using Strep-Tactin resin is being optimized for biochemical and structural studies, with single-particle cryo- electron microscopy being pursued to determine its three-dimensional architecture. Structural information will further support the identification of regulatory sites and structure-based drug design (SBDD) of activators of KCNX. Collectively, this integrated approach aims to establish KCNX as a potential druggable target in atherosclerosis and hypertension.

Poster P-042

Obesity Differentially Remodels Circadian Mitochondrial Lipid Rhythms in Liver and Brown Adipose Tissue

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Abstract: Mitochondrial membrane lipids are determinants of respiratory chain assembly, cristae architecture, and organelle bioenergetics. Their composition oscillates diurnally in coordination with metabolic demand. While diet-induced obesity (DIO) is established to disrupt circadian clock, whether DIO remodels the temporal organization of the

mitochondrial lipidome in a tissue-specific manner remains poorly understood. We performed shotgun lipidomics on mitochondria isolated from the liver and brown adipose tissue (BAT) of chow- and high-fat diet (HFD)-fed mice across six timepoints (ZT0–ZT20) and used JTK_Cycle analysis to define rhythmic lipid species. DIO disrupted hepatic mitochondrial lipid accumulation profile, reducing the fraction of oscillating phospholipid species from ~26% (Chow) to ~9% upon HFD, with homogenization of oscillation patterns across phospholipid classes. Rhythmicity of PE, PS, and ePE classes was lost, as was the oscillation of the PE/PC, ePE/PC, and PS/PC ratios. Strikingly, BAT mitochondria showed the opposite response. HFD nearly tripled the proportion of rhythmic lipid species (10.6% to 29% upon HFD), with new oscillations emerging predominantly among PC, ePC, and cardiolipins peaking at ZT14–16, and the PE/PC and CL/PC ratios acquiring rhythmicity. These results show that obesity does not uniformly suppress circadian lipid metabolism, but instead drives tissue-specific remodeling of mitochondrial membrane lipid rhythms.

Poster P-043

Therapeutic Repurposing of GRA for Chronic Kidney Disease: Protection against Renal Fibrosis and Mitochondrial Dysfunction

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Abstract: Chronic kidney disease (CKD) presents significant treatment challenge, as progressive renal fibrosis, oxidative stress, and mitochondiral dysfunction play roles in the advancement of the disease. Considering the therapeutic possibilities of the ghrelin receptor (GHSR) pathway beyond its known metabolic functions, we examined if the ghrelin receptor agonist, capromorelin (CM) could be redirected for treating kidney disease. In human proximal tubular epithelial cells, CM significantly diminished the profibrotic response triggered by TGF-β, as shown by decreased expression of collagen I, vimentin, and α-SMA at the transcript and protein levels. CM additionally maintained mitochondrial structure and membrane potential, decreased mitochondrial ROS production, and enhanced mitochondrial respiratory activity, while also lowering TGF-β-induced apoptosis. These results indicated that the antifibrotic effects of CM are linked to the maintenance of mitochondrial stability and reduction of oxidative stress. In line with the cellular observations, CM treatment in adenine-induced CKD significantly reduced renal structural damage and fibrotic remodelling, along with enhancements in molecular indicators related to renal injury and fibrosis. CM therapy also led to significant alterations in the renal metabolic profile, indicating a correction of metabolic issues related to CKD. Our results collectively highlight GRAs may be a potential therapeutic candidate in progressive renal disease due to their efficacy in ameliorating renal fibrosis by regulating mitochondrial ROS mediated profibrotic signaling.

Poster P-044

Deciphering the Role of YTH Domain-Containing m6A Readers in Podocyte Biology and Stress-Response Mechanisms in Diabetic Kidney Disease

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Abstract: N6-methyladenosine (m6A) is the most common modification of mRNA in eukaryotes which controls transcript stability, translation and splicing via a group of proteins known as the YTH domain family readers, e.g. YTHDF2 and YTHDC1. YTHDC1 is located in the nucleus while YTHDF2 is found in the cytoplasm. Although these proteins have well-defined functions in various cell types, their role in podocytes has not yet been elucidated. Podocytes are highly specialised, terminally differentiated cells of the glomerulus vital for maintaining the kidney's filtration barrier, and podocyte dysfunction is a major contributor to diabetic kidney disease (DKD), resulting in End-Stage Renal Disease (ESRD). In this study we examine the function of YTHDC1 and YTHDF2 by CRISPR mediated genome editing in temperature- sensitive SV-40-transfected conditionally immortalised mouse and human podocyte

cell lines. Our first objective is to find out if reader-deficient cells can carry out proper molecular and morphological differentiation when shifted to a non-permissive temperature (37°C), by looking at markers of differentiation and cytoskeletal reorganisation. Cells are then exposed to high glucose stress to simulate a diabetic environment. Our preliminary observation shows that high glucose exposure increases expression of both readers in podocytes, suggesting they may play a role in the cellular response to glucose-induced stress. Overall, this work aims to establish the physiological need for m6A readers in podocyte differentiation and their pathological role in glucose-induced podocyte injury, providing new mechanistic understanding of epitranscriptomic regulation in diabetic nephropathy.

Poster P-045

Investigating Anti-Fibrotic Interventions as Therapeutics Approach for the Management of Chronic Kidney Diseases

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Abstract: Chronic kidney disease (CKD) is a progressive disorder affecting more than 10% of the global population and is associated with limited effective therapeutic options. Renal fibrosis, characterized by excessive accumulation of extracellular matrix (ECM), represents a major pathological feature and a common final pathway of chronic kidney injury. Although pharmacological therapies are available for CKD management, their long-term use may be associated with adverse effects and may not adequately prevent renal fibrosis progression, highlighting the need for safer therapeutic alternatives. Natural therapies, particularly plant derived bioactive compounds, have emerged as promising candidates due to their nephroprotective and antifibrotic properties. *Myrica esculenta* (Kaiphal; family Myricaceae) is a medicinal plant traditionally used for various ailments and contains bioactive constituents, including diarylheptanoids, flavonoids, terpenes, tannins, and glycosides. Its polyphenolic compounds, including quercetin and epigallocatechin gallate, reported with antioxidant and Reno protective properties. Preliminary screening revealed that the water and methanol fractions of *M. esculenta* exhibited promising antifibrotic activity. Therefore, the present study aims to investigate the antifibrotic potential of *M. esculenta* using TGF-β1- induced NRK-52E cells and a folic acid-induced CKD rat model assessing renal function, histopathology, oxidative stress, and key fibrotic markers. The study is expected to provide insights into the therapeutic potential of *M. esculenta* as a natural antifibrotic intervention for attenuating renal fibrosis and slowing CKD progression.

Poster P-046

Protective Effects of Zinc Oxide Nanoparticles Against Alcohol-Induced Gut Barrier Dysfunction

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Abstract: Alcoholic liver disease (ALD) encompasses various liver disorders caused by chronic ethanol intake, with a prevalence of 3.5% overall, rising to 26% in hazardous drinkers and 55.1% in alcohol-use disorder patients. It starts with simple steatosis and can progress to hepatitis, fibrosis, and cirrhosis. A key factor in ALD is gut–liver axis disruption, where alcohol-induced dysbiosis lowers beneficial microbes and increases pro-inflammatory species, raising lipopolysaccharide (LPS) levels. Early on, alcohol damages intestinal barriers, increasing permeability and circulating endotoxins, causing endotoxemia. Ethanol metabolism produces acetaldehyde, a toxin harming tight junction proteins like claudins and ZO-1, weakening epithelial structure. Elevated MCP-1 and TNF-α signal inflammation and barrier breakdown. Zinc maintains epithelial integrity, oxidative balance, and inflammation regulation. Zinc oxide (ZnO) nanoparticles, with better bioavailability and cellular uptake, could enhance defenses against alcohol damage. In an experiment, Caco-2 cells exposed to ethanol with ZnO nanoparticles showed reduced cytotoxicity, oxidative stress, and preserved tight junctions, confirmed by molecular analysis. These results suggest ZnO nanoparticles may help maintain gut barrier health and prevent early ALD damage, but more research is needed.

Poster P-047

OSR1 Regulates Cardiac-Fibroblast to Myofibroblast Transition during Pathological Cardiac Hypertrophy

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Abstract: Persistent neurohormonal stress and mechanical forces drive the decompensation of the adult heart, transitioning from cardiomyocyte hypertrophy to excessive fibrosis and maladaptive remodelling, ultimately leading to heart failure. Transcriptomic analysis of the hypertrophied heart, followed by transcription factor binding site (TFBS) analysis of the top 200 differentially expressed genes (DEGs), identified OSR1 among the top 10 transcription factors predicted to bind to these genes' promoters. OSR1 is a zinc-finger transcription factor extensively studied in fetal cardiac development, with its knockout resulting in embryonic lethality; however, its role in adult cardiac hypertrophy remains unexplored. In a murine model of subcutaneous isoproterenol- induced cardiac hypertrophy, OSR1 expression was markedly elevated, concomitant with increased expression of hypertrophic and fibrotic markers. Knockdown of OSR1 in hypertrophied hearts using lenti-shOSR1 particles attenuated fibrosis and hypertrophy markers and reduced cardiomyocyte size. Interestingly, OSR1 was intrinsically more highly expressed in cardiac fibroblasts (NRCFs) than in cardiomyocytes. Consistent with the *in vivo* findings, OSR1 expression was significantly elevated in TGF-β-treated NRCFs. Moreover, OSR1 knockdown or overexpression in NRCFs attenuated or exacerbated, respectively, the expression of fibrotic markers in response to TGF-β, suggesting that OSR1 regulates myofibroblast transition during cardiac hypertrophy. Predominantly localized to the nucleus, OSR1 was found to interact with the RNA recognition motifs (RRMs) of three RNA-binding proteins (RBPs) through its three zinc- finger domains (ZFDs) in the hypertrophied heart, as revealed by endogenous IP/MS and Co-IP experiments. Future studies will investigate extracellular vesicle (EV)-mediated OSR1– transcription factor interactions as a potential novel regulatory axis underlying pathological cardiac hypertrophy and fibrosis.

Poster P-048

Spatio-Temporal Regulation of Acetate Metabolism Under Nutrient Stress

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Abstract: Acetyl-CoA Synthetase 2 (ACSS2) is a nucleocytosolic enzyme that converts acetate into acetyl-CoA in an ATP-dependent manner and this acetyl-CoA can be subsequently used in lipid synthesis and histone acetylation. Several studies observed an increase in ACSS2 expression and acetate utilization under hypoxia and nutrient stress. Interestingly, genetic depletion of this enzyme has little effect on normal physiology but can impair tumor growth in mice suggesting ACSS2 as a potential drug target in cancer. However, there are no studies that report on the biochemical characterization of human ACSS2. Further, it remains unclear whether ACSS2 is a chromatin-associated protein, how it is distributed within the nucleoplasm, and whether its primary role under nutrient-stress conditions is in the cytoplasm or nucleus. In addition, under nutrient stress, whether a nuclear pool of acetate can contribute to the cytoplasmic acetyl-CoA pool when extracellular lipid uptake is restricted remains unclear. To address these questions, we are trying to express human recombinant ACSS2 (hACSS2) protein by using the baculoviral expression system. Successful cloning of hACSS2 into the donor plasmid has been achieved and optimization of viral stock is done. Using the triple negative breast cancer cell line MDA- MB-468, we have generated several genetic modifications including deletion of Low-Density Lipoprotein Receptor (LDLR), deletion of hACSS2 and overexpression of activated form of Sterol Regulatory Element Binding Protein (SREBP-1c) and Carbohydrate Response element binding protein (chREBP) and have been characterized. Together, these studies may provide new insights into the role of ACSS2 in maintaining acetyl-CoA pool and its potential contribution to cancer-cell metabolic adaptation.

Poster P-049

Baicalein Protects Against DNA Damage Induced Ferroptosis in Diabetic *Drosophila melanogaster* by Restoring Malvolio–Ferritin–Mediated Iron Homeostasis

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Abstract: Among the diverse pathophysiological complications associated with diabetes, dysregulated iron metabolism remains a critical yet comparatively underexplored aspect. The present findings investigate the mechanism by which a high-sucrose diet induces iron overload in Drosophila, leading to ferroptosis, establishing a novel interrelationship between Type 2 diabetes (T2D) and ferroptosis. T2D flies had oxidative stress, which leads to persistent DNA damage in the gut and brain, activating the DNA damage response kinases *tefu* and *mei-41*, an upstream regulator of metal transcription factor (*mtf-1*). In T2D flies, downregulation of *mtf-1* inhibits ferritin. Concurrently, upregulation of the major iron importer protein malvolio further increased ferrous iron. Increased ferrous iron and oxidative stress generate toxic lipid radicals, which are the principal catalysts of ferroptosis. The study further reports baicalein as a potential modulator of diabetes-induced ferroptosis. Baicalein alleviates oxidative stress and reduces iron accumulation, potentially by regulating the mechanisms involved in iron uptake, intracellular trafficking, and storage. Molecular docking and simulation revealed that baicalein has a strong binding affinity with malvolio and ferritin. Binding of baicalein disrupts iron absorption by changing the functionality of malvolio, thereby restricting Fe^{2+} accumulation, and upregulates ferritin, promoting sequestration of iron in ferric form, thereby showing protection against ferroptosis.

Poster P-050

Unveiling the Anti-Fibrotic Potential of Genistein in Takayasu Arteritis: An *In Vitro* Study Combining Network Pharmacology and Molecular Docking Studies

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Abstract: Takayasu arteritis (TAK) causes arterial wall inflammation and fibrosis in large vessels. The pro-fibrotic M2 macrophages are dominant during resolution phase of arterial inflammation. Genistein possesses endothelial stabilizing properties that have not yet been explored in TAK.

PPI networks of proteins anticipated to be Genistein and TAK targets were formed by STRING. Genistein's interaction with target proteins were evaluated by AutoDock Vina. *In vitro* validation was done to know the effect of Genistein on THP-1 cells after M1/M2 polarization. Annexin V/PI staining was visualized by flow cytometry. TNF-α and IL-12 (M1 cytokines), along with CCL-17 and TGF-β (M2 cytokines) were analyzed after treatment with TAK/ healthy controls sera, genistein or tacrolimus with ELISA. Extracellular staining was also performed to check M1 and M2 polarization by Flow cytometry.

We identified 300 therapeutic targets, 20 of which were hub targets for Genistein. Amongst top 10 protein targets, TGF-β, MMP-9, MTOR (drivers of vascular fibrosis in TAK) had highest affinity for Genistein (binding energies of -8.4 kcal/mol, -8.3 kcal/mol and -9.4 kcal/mol, respectively). Further, *in vitro* studies showed that Genistein induces an increased in percentage of apoptotic cells in M2 polarized treatment group (IL-4+IL-13+TAK Sera+Genistein+Tacrolimus) and significantly reduced the TGF-β and CCL-17 and increased TNF-α and IL-12 levels in culture supernatant of M1 group.

Genistein inhibits the pro-fibrotic proteins (TGF-β, MMP9 & MTOR), by inhibiting M2 polarization of TAK patient's sera group and promotes M1 polarization as compared to Healthy control. Therefore, this *in vitro* effectiveness of Genistein might pave the way for future clinical trials in TAK.

Poster P-051

Dietary Advanced Lipoxidation End Products (ALEs) Shorten Lifespan and Induce Sarcopenic Obesity in *Drosophila melanogaster*

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Abstract: Advanced Lipoxidation End Products (ALEs) play a key role in the progression of neurodegenerative diseases, but their role in aging and other pathophysiological conditions is underexplored. The role of ALEs was checked in obesity and muscle degeneration. BSA and Oleic acid were mixed and stored at 37 °C for 42 days, with periodic UV exposure, to produce ALEs. Then it is fed to *D. melanogaster*, a well-known model organism used to decode muscle degeneration and obesity. A series of changes was observed in ALE-fed flies: they were obese, and their glucose concentration was comparatively higher. The belly was swollen, and the lipid droplets in the gut were higher. Climbing and jumping abilities were lower, whereas LDH activity was higher. In ALE-fed flies, the cell death in the muscle was higher, and the actin filaments and septate junctions were disrupted. The Reactive oxygen species (ROS), nitric acid Species (NOs), and Lipid peroxidation were higher in ALE-fed flies. The mRNA expression level of *Relish* and *InR* was upregulated, whereas the genes *Myosin Heavy Chain* (*Mhc), Act88F*, *Tm1* and *Sallimus* were downregulated. From the study, it was concluded that exogenous ALE ingestion leads to decreased lifespan and sarcopenic obesity.

Poster P-052

Mapping Protein Interactors of Cholesteryl Esters in Mammalian Cells *via* Metabolic Labelling

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Abstract: Cholesteryl esters (CEs) are widely regarded as inert storage forms of excess cholesterol, found in lipid droplets and circulating lipoproteins. Recent findings indicate that CEs might have more active roles in regulating cells by interacting with proteins. To explore this idea, we developed a metabolic labelling strategy that combines an alkyne-tagged cholesterol analogue with a diazirine-containing fatty acid to capture CE-interacting proteins. In-gel fluorescence profiling and fluorescence microscopy confirmed efficient probe uptake and intracellular localisation, while LC-MS-based lipidomics verified the formation of cholesteryl esters. Using quantitative LC–MS/MS proteomics, we identified a wide range of CE- interacting proteins. These include metabolic enzymes, transporters, chaperones and various known lipid and sterol-binding protein families. Functional annotation and database analyses revealed significant involvement of disease-associated proteins, linking CE interactions to pathways involved in metabolic, neurological, and cardiovascular disorders. Together, these findings challenge the traditional view of cholesteryl esters as being passive storage molecules and highlight their potential roles in mediating lipid– protein networks relevant to immune function and inflammatory diseases.

Poster P-053

Mapping Metabolic Pathways of Cholesteryl Esters during Oxidative Stress

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Abstract: Cholesterol is pivotal to mammalian lipid metabolism, and its dysregulation is associated with several human diseases. Physiologically, cholesterol is tightly regulated through the flux between cholesterol and cholesteryl esters (CEs). Under oxidative stress conditions, cholesterol and CEs are converted into potent immunogenic lipid

mediators such as oxysterols and oxidized cholesteryl esters (Ox-CEs). Despite significant knowledge on the conversion of cholesterol to CEs by the enzymes ACAT and LCAT, the identity of CE hydrolases that degrade CEs and Ox-CEs back to cholesterol has remained cryptic and unresolved. To address this, we attempt to identify CE hydrolases in mammals under physiological and oxidative stress conditions. We developed a facile LC-MS method to profile cholesterol and different CE and Ox-CE species. We found robust CE hydrolase activity in the membrane proteome of multiple tissues and circulation for CEs and Ox-CEs. Further, using substrate-based LC-MS assays, pharmacological screening, and competitive activity-based protein profiling, we identify two distinct enzymes from the metabolic serine hydrolase (mSH) superfamily governing CE and Ox-CE metabolism. Biochemical characterization of these enzymes demonstrates that they can metabolize CEs and Ox-CEs *in vitro*. Together, our findings help us move one step toward mechanistically understanding the in vivo regulation of CEs and Ox-CEs.

Poster P-054

Combination of Sodium Acetate and Butyrate Ameliorates Alcohol-Induced Liver Fibrosis in an *in vivo* Model

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Abstract: Chronic alcohol consumption drives hepatic fibrosis via stellate cell activation, extracellular matrix deposition, and gut–liver axis disruption. Gut-derived short-chain fatty acids (SCFAs) acetate and butyrate exert anti-inflammatory and anti-fibrotic effects through stellate cell modulation, HDAC inhibition, and SCFA-receptor signalling. This study evaluated combined sodium acetate–butyrate supplementation against alcohol-induced liver fibrosis in rats.

In methodology, male Sprague-Dawley rats (n = 6/group) were divided into control, pair-fed, disease, and treatment groups. Liver fibrosis was induced by chronic alcohol administration with weekly intraperitoneal CCl4 (1 mL/kg) over 4 weeks; the treatment group additionally received oral sodium acetate and butyrate. Hepatic injury and fibrosis were assessed via serum liver function markers, gross liver morphology, H&E histopathology, immunohistochemical staining for α-smooth muscle actin (α-SMA), qRT-PCR and ELISA of fibrosis-associated markers, and molecular docking of acetate and butyrate with target proteins.

Alcohol/CCl4 administration caused significant hepatic injury, marked by elevated serum liver enzymes and steatotic, fibrotic histology. Combined sodium acetate–butyrate treatment attenuated these changes by normalizing serum parameters, reducing α-SMA-positive staining and fibrosis-related gene/protein expression, and improving histoarchitecture; docking also showed favourable binding affinity of both compounds with [target protein(s)], supporting a plausible anti-fibrotic mechanism. These findings support sodium acetate–butyrate combination therapy as a promising translational strategy for alcohol-related liver fibrosis.

Poster P-055

Strengthening Innate Immunity of Uroepithelial Cells *via* Regulation of Mitochondrial-lysosomal Dynamics and Antimicrobial Peptides

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Abstract: Emergence of antimicrobial resistance among uropathogens has necessitated development of new strategies to strengthen host immunity. In this study, we have used human bladder epithelial cells and uropathogenic *E. coli* (UPEC) in presence of a FDA approved drug and demonstrated the antibacterial effect and mechanisms involved by q-RT-PCR, Microscopy, Flow-cytometry, functional assays. The FDA approved drug (BG01) led to mitochondrial fragmentation, increased mitochondrial ROS, Nitric Oxide without impacting cytosolic ROS. Additionally, BG01 led

to increased expression of several Antimicrobial Peptides and Matrix Metalloproteinases without affecting the Tight Junction Proteins. BG01 led to altered adhesion and invasion of UPEC concomitant with the expression profile of Mannose Receptor and Caveolin1. Interestingly, the intracellular survival of UPEC was severely compromised due to combined impact of Phago-Lysosomal formation, Reactive Oxygen Species generation and antibacterial activity of multiple AMPs. Killing of extracellular UPEC was augmented by secreted AMPs and pro-inflammatory cytokines. Live-cell imaging revealed the profound effect of BG01 on mitochondrial-lysosomal structure function and their correlation with microtubule post translational modifications. BG01 also resulted in expulsion of UPEC, limiting their ability to further execute another round of infection. Taken together, in this study, we present evidence demonstrating the effectiveness of strengthening host epithelial immunity in countering UTI.

Poster P-056

TRPV2 is a Key Regulator of Effector Functions and Cytoskeleton Remodelling of Neutrophils

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Abstract: Neutrophils are the most abundant circulating leukocytes and among the first responders to infection and inflammation. Recent literature has shown that different membrane receptors and ion channels play a crucial role in neutrophil activation through intracellular calcium signalling, downstream effector functions, and cytoskeleton remodelling. However, the role of TRPV2 ion channel in different neutrophil mediated pathophysiology remains largely unexplored. In this study, we put forward the comprehensive expression pattern and functional role of TRPV2 in human and murine neutrophils. TRPV2 is highly expressed in mature stages of human circulatory neutrophils, whereas its expression is enriched in tissue neutrophils derived from the spleen, lung, and liver and increased in bone marrow neutrophils following inflammatory stimulations. Activation of TRPV2 promoted cytoskeleton remodelling whereas its inhibition reduced neutrophil polarization and actin reorganization. Notably, TRPV2 inhibition also suppressed cytosolic and mitochondrial ROS generation, degranulation, and NET formation, and modulated cytokine release patterns. Cumulatively, our findings highlight endogenous TRPV2 activity as an important regulator of neutrophil dynamics and effector functions during inflammation.

Poster P-057

Rational Design of Epitope Focused Vaccine Candidate Targeting Humoral and Cellular Immune Response

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Abstract: Respiratory Syncytial Virus (RSV) represents the predominant etiology of respiratory tract infections in both pediatric and geriatric populations. Annually, RSV is responsible for approximately 13 million cases of acute lower respiratory infection (ALRI), resulting in 1 million hospitalizations and approximately 35.000 deaths. Currently approved RSV vaccines demonstrate limited population coverage and remain unavailable in India. Consequently, to mitigate disease burden, reduce hospitalization rates, and decrease mortality particularly among vulnerable populations, the development of an RSV vaccine constitutes an urgent clinical necessity. Our research work is to create an epitope-directed vaccine formulation by selecting neutralizing epitopes from critical protective regions of the prefusion F protein for scaffold construction, combined with a literature-supported T-cell epitope that promotes Th1-polarized immune responses. We present the development of a prefusion F (pre-F) protein-based vaccine candidate incorporating a CD8+ T-cell epitope. The candidate underwent comprehensive characterization including structural,

antigenic, immunogenic, and protective efficacy assessments. The formulation preserved trimeric architecture and demonstrated binding affinity to site-specific conformation-dependent antibodies comparable to native pre-F protein. Immunological and cellular response evaluations revealed induction of neutralizing antibodies and enhanced CD8+/IFNγ+ T-cell populations. Challenge studies and in vivo imaging demonstrated enhanced viral clearance in immunized subjects. These findings substantiate the incorporation of selected T-cell epitopes in epitope-directed RSV vaccine development. This investigation establishes a foundational framework for advancing epitope-focused vaccine candidate design.

Poster P-058

A Modular Protein-Scaffold Platform for Multivalent MPXV Vaccination and Protective Immunity

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Abstract: The development of next-generation orthopoxvirus vaccines requires strategies capable of targeting antigens expressed on both intracellular mature virions (IMV) and extracellular enveloped virions (EEV), thereby eliciting complementary humoral and cellular immune responses. Here, we developed a modular protein-scaffold platform for multivalent antigen presentation and evaluated its potential as an MPXV vaccine. An engineered MPXV protein scaffold was used to generate a bivalent scaffold-based protein (BSP) incorporating the MPXV antigens M1R and A35R. Following alum-adjuvanted immunization in mice, BSP-induced antigen-specific humoral and cellular immune responses were characterized, including $CD4^+$ and $CD8^+$ T-cell responses and virus-neutralizing activity. BSP immunization elicited high-titer MPXV antigen-specific antibodies together with balanced $CD4^+$ and $CD8^+$ T-cell responses. Immunized animals also developed VACV-neutralizing activity, demonstrating the induction of orthopoxvirus-directed humoral immunity. Following lethal respiratory challenge with neurotropic mouse-adapted vaccinia virus (VACV), BSP-immunized animals were protected from challenge, and no detectable infectious VACV was recovered from the brains of immunized animals. Collectively, these findings demonstrate the potential of a modular protein-scaffold platform for multivalent orthopoxvirus vaccination and provide a flexible strategy for incorporating additional antigens to promote coordinated humoral and cellular immunity.

Poster P-059

Mycobacterial PPE2 Inhibits Major Histocompatibility Complex Class I Antigen Presentation in Antigen Presenting Cells to Evade $CD8^+$ T-Cell Responses

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Abstract: Attenuation of host $CD8^+$ T-cell response is a major evasion strategy of *Mycobacterium tuberculosis* (M.tb) and the mechanism is not fully understood. Understanding factors that suppress $CD8^+$ T-cell responses may reveal new therapeutic targets against tuberculosis. M.tb proteins can access the cytosol through autophagosome-to-cytosol or endosome-to-cytosol pathways, where they contribute to Major Histocompatibility Complex (MHC) class I antigen presentation or modulate host immune effectors. Here, we investigate how the virulence factor PPE2 impairs MHC-I antigen presentation in APCs and consequently affects $CD8^+$ T-cell function. We previously showed that PPE2 localises to the nucleus and impairs macrophage nitric oxide production via its DNA-binding domain, while its SH3-like domain inhibits cytosolic ROS production. We have further observed that PPE2 suppress MHC class I recruitment in APC when infected with *M. smegmatis* expressing PPE2 or treated with recombinant PPE2 protein. This indicates that PPE2 may impede class I antigen presentation in APC and affects priming of $CD8^+$ T-cell, which eventually leads to bacterial survival within host. This poster highlights the role of PPE2 in the evasion of host immune response and the need for further research on the role of MHC class I and $CD8^+$ T- cells in TB pathogenesis.

Poster P-060

Hyperactivation of Receptor Guanylyl Cyclase C (GC-C) Remodels the Intestinal Intraepithelial Lymphocyte Compartment

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Abstract: Intestinal guanylyl cyclase C (GC-C) maintains mucosal homeostasis and fluid–ion balance through ligand-induced cyclic GMP (cGMP) signaling. cGMP activates protein kinase G II (PKGII), stimulating CFTR-mediated chloride secretion and inhibiting NHE3-dependent sodium absorption. Naturally occurring gain-of-function mutations in GC-C disrupt intestinal homeostasis and cause early- onset secretory diarrhea and chronic inflammation. The human S839I mutation and its orthologous mouse S839I mutation hyperactivate GC-C, but their effects on intestinal immune cells remain poorly defined. Using flow cytometry, RT-PCR, and ileal bulk RNA sequencing, we examined intraepithelial lymphocytes (IELs) in WT and S839I mice. S839I mice showed increased CD8αβ$^+$ and TCRαβ$^+$ T cells, with reduced CD8αα$^+$ and TCRγδ$^+$ populations. RNA sequencing revealed increased expression of *Cd8a*, *Cd8b1*, *Trac*, *Trbc1*, and *Trbc2*, consistent with enrichment of CD8αβ$^+$ TCRαβ$^+$ cells. Genes associated with T-cell activation and cytotoxicity (*Gzma, Gzmb, Cd69,* and *Runx3*) and recruitment (*Cxcl9, Cxcl10,* and *Cxcr3*) were also upregulated, together with tissue-retention genes including *Itgae, Itga4,* and *Itgb7*. Thus, GC-C hyperactivation \remodels the IEL compartment toward an activated, cytotoxic CD8αβ$^+$ TCRαβ$^+$ phenotype, potentially through altered recruitment and expansion rather than impaired IEL maintenance or survival.

Poster P-061

Understanding of Metabolic Adaptation and ROS Production under Glucose Restriction in Immature Neutrophils

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Abstract: Neutrophils are the most abundant innate immune cells that provide the first line of defence by performing functions including ROS generation. These functions are tightly regulated by their metabolic state. During prolonged inflammation, apart from mature neutrophils, the immature pool of neutrophils migrates into the circulation. Despite their presence in the circulation in chronic inflammatory conditions, how their metabolism adapt to the inflammatory milieu remains poorly understood. Neutrophils are historically considered as glycolytic cells. Glucose availability is one of the major nutrient factors regulating neutrophil responses. Here, we investigated how glucose availability is regulating their metabolic and functional outcome during inflammatory activation. Using murine bone marrow-derived immature neutrophils, we assessed the metabolic and functional state in glucose-restricted conditions. We found that, change in glucose availability alters neutrophil metabolic state. Remarkably, the inhibition of the glycolysis leads to enhanced extracellular ROS production in the glucose restricted conditions. Metabolic perturbations studies indicated the convergence of more than one pathway, with amino acid metabolism regulating the initial and fatty acid metabolism in the later phase. Together, our findings provide insights into how nutrient-limited inflammatory conditions may shape neutrophil-mediated immune response.

Poster **P-062**

Using Transgenic *Plasmodium berghei* Sporozoites to Assess the Protective Efficacy of *Plasmodium falciparum* SIMP and RON6 Antigens

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Abstract: *Plasmodium* sporozoite invasion of mammalian hepatocytes is a critical step for establishing malaria infection. Blocking this interaction is essential for vaccine development. We recently identified two sporozoite surface proteins, SIMP and RON6, which regulate parasite shape and infectivity. Immunofluorescence assays confirmed that both proteins possess C-terminal extracellular domains. In vivo treating *Pb*RON6-3XHA sporozoites with anti-HA antibodies delayed the onset of malaria infection in mice. Crucially, this protective delay was comparable to that achieved by targeting the major surface protein CSP with the potent monoclonal antibody 3d11. Because the C-terminal domain of SIMP is highly conserved among *Plasmodium* species and RON6 is vital for invasion, we aim to generate transgenic *P. berghei* sporozoites expressing either *PfSIMP* or *PfRON6.* This model will be utilized to evaluate the protective efficacy of *PfSIMP* and *Pf*RON6 specific antisera. These functional insights and models will aid the design of next-generation, sporozoite-inactivating malaria vaccines.

Poster **P-063**

Leishmania donovani Suppresses NLRP3 Expression by Exploiting IL-33/ST2 Signaling and Drives SOCS1-mediated p65 Degradation

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Abstract: Dynamic interplay between pro- and anti-inflammatory cytokines plays crucial role in regulating immune responses. Earlier study, showed *Leishmania donovani*-induced IL-33 destabilizes host cytokine dynamics by downregulating TNF-α and IL-12, aiding intramacrophage parasite survival. Another pertinent proinflammatory cytokine is IL-1β, whose maturation depends on activation of NLRP3 inflammasome-complex. Present study highlights, independent neutralization of IL-33 and its receptor ST2, results in elevated levels of NLRP3 both at mRNA and protein levels, with increased levels of mature IL-1β. Reduced NLRP3 expression, correlates with decreased protein levels of p65, the major subunit of NF-κB transcription factor complex. Unaltered transcript level of p65 in macrophages with reduced protein expression suggested post translational modification and ubiquitination mediated p65 degradation in presence of IL-33, was found to be driven by ubiquitin ligase SOCS1. Neutralizing IL-33 *in vivo*, enhanced expression of p65 and NLRP3, along with increased production of TNF-α, IL-12, IL-1β, suggesting IL-33 regulates these cytokines through a shared intermediary, p65. Neutralizing IL-33 led to reduced SOCS1 expression, and SOCS1 knockdown by targeted shRNA in mice restored p65 levels, reactivated inflammasome function, thus reducing parasite burden. This study highlights the IL-33/SOCS1 pathway as potential target for host- directed therapeutic strategies aimed at restoring immunity during chronic leishmaniasis.

Poster P-064

MOF-Based Multifunctional Nanoplatform for Sequential Immunomodulation and Cartilage Regeneration in Rheumatoid Arthritis

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Abstract: Rheumatoid arthritis, a chronic autoimmune disease results in painful joint swelling, morning stiffness, reduced mobility, and irreversible disability, significantly affecting their quality of life. Key indicator for tissue repair following inflammation, is the balance between pro-inflammatory M1 and anti-inflammatory M2 macrophages. In RA, however, this balance is disrupted. M1 macrophages become dominant and activate the NF-κB pathway, leading to excessive production of cytokines such as TNF-α, IL-1β, and IL-6, accelerating cartilage degradation, bone erosion, and chronic joint swelling, while preventing tissue regeneration. Current therapies are primarily focused on suppressing inflammation. Although these treatments can relieve symptoms, requiring long-term administration and associated with adverse effects and poor drug accumulation within inflamed joints. More importantly, they rarely restore immune balance or regenerate damaged cartilage. To overcome these limitations, we propose a multifunctional metal-organic framework (MOF)-based nanoplatform that sequentially targets the key stages of RA progression. First, a pH-responsive polymer rapidly releases methotrexate within the inflamed joint to suppress acute inflammation and reduce swelling. Next, macrophage-targeted siRNA silences the NF-κB pathway, reprogramming M1 into M2 macrophages and restoring immune homeostasis. Finally, controlled degradation of the MOF releases regenerative metal ions that stimulate chondrocyte activity, promote extracellular matrix synthesis, and facilitate cartilage and bone repair. By combining inflammation control, immune restoration, and tissue regeneration in a single platform, this strategy aims to move beyond symptom management toward long- term disease modification and functional joint recovery.

Poster P-065

Trophoblast-Driven Transcriptional Reprogramming of Vascular Smooth Muscle Cells Promotes a Proliferative and Pro-Survival Phenotype during Spiral Artery Remodelling

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Abstract: Successful placental development requires extensive remodelling of uterine spiral arteries, involving phenotypic plasticity of vascular smooth muscle cells (VSMCs). However, how trophoblasts regulate this process remains poorly understood. We investigated whether human trophoblasts induce VSMC de-differentiation, determine subsequent proliferative or apoptotic phenotypes and explored the molecular mediators involved. Co-culture of human trophoblast HTR-8/SVneo cells with hVSMCs led to decrease in contractile markers ACTA2 and CNN1 and increase in VIM, confirming VSMC dedifferentiation. Transcriptional profiling of co-cultured VSMCs revealed upregulation of ten transcription factors (TF) during de-differentiation. Functional interrogation using ASO-mediated downregulation of each of this TF, revealed EGR1, RELA, and MYC as key factors required for de- differentiation. Interestingly, trophoblast-induced de-differentiation of VSMCs was associated with enhanced a) proliferation, evidenced by increased Ki-67 and Cyclin D1 expression, b) survival signal evidenced by increase in BCL2. Furthermore, individual knockdown of EGR1, RELA and MYC in co- cultured VSMCs reduced proliferation and enhanced apoptotic responses, implicating these transcriptional regulators in maintaining the proliferative and pro-survival phenotype. To delineate trophoblast-derived signals to regulating the VSMC fate, secreted cytokine profiling of trophoblast cells was performed and of DKK1, Angiogenin and SERPINE1/PAI-1 were identified as prominent trophoblast-secreted cytokines. Treatment of hVSMCs with a cocktail of these three cytokines not only led to VSMC de-differentiation but also enhanced expression of EGR1, RELA, and MYC. In addition, inhibition of extracellular

vesicle (EV) secretion by trophoblast cells prohibited co-cultured hVSMC de-differentiation. Trophoblast-derived EVs were isolated, characterized and were shown to be internalized by VSMCs, indicating EV-mediated mode of communication between trophoblast and hVSMCs. Collectively, our findings demonstrate that trophoblast-derived signals transcriptionally reprogram VSMCs toward a dedifferentiated, proliferative and pro-survival state, revealing a potential mechanism underlying trophoblast-mediated vascular remodelling during pregnancy.

Poster P-066

Neutrophil Elastase Inhibitor from *Phaseolus coccineus* with Possible Role in Ulcerative Colitis

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Abstract: Ulcerative colitis (UC), an inflammatory bowel disease, distinguished by the chronic inflammation of the gastrointestinal tract. Neutrophil play a major role in the inflammation by forming neutrophil extracellular traps (NET) that releases neutrophil elastase (NE), which damage intestinal mucosal layer. NE is regulated by endogenous inhibitors mainly by elafin. Hyper expression of NE leads to an imbalance between the NE and elafin and causes tissue damage. Drugs available to treat UC have side effects and limited efficacy. Hence there is a need for alternative therapy with minimum or no side effects. Plants have been documented for the presence of anti-inflammatory molecules. In the present work based on *in-silico* studies, an elafin like inhibitory protein (ELIP) has been identified from *Phaseolus coccineus*. Molecular docking and interaction studies showed that ELIP and NE complex has better binding affinity than elafin and NE, suggesting ELIP may act as a potent inhibitor of NE. Further *in-vitro* inhibition with the total protein extracts of *Phaseolus coccineus* seeds showed 87% inhibition of NE at 10µg protein and IC50 was calculated to be 1.95µg, indicating the presence of neutrophil elastase inhibitor(s) in the seeds. These inhibitor(s) may be isolated, characterized and develop into an alternative safer therapy against UC.

Poster P-067

The Mitochondrial Calcium Uniporter Modulates Mitochondrial Dynamics in Fibroblast-like Synoviocytes, Promoting Invasive Behaviour Leading to Rheumatoid Arthritis Development

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Abstract: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by progressive joint damage and inflammation, with fibroblast-like synoviocytes (FLS) playing a crucial role in disease pathogenesis. RA-FLS exhibit metastatic properties including increased migration, invasiveness, resistance to apoptosis, and altered metabolism, contributing to joint destruction. Our study demonstrates the role of the mitochondrial calcium uniporter (MCU) in regulating this aggressive behaviour. We observed a correlation of high MCU expression with the metastatic behaviour of RA FLS which drives RA severity, alongside altered mitochondrial dynamics such as reduced size and peripheral localization in RA-FLS. Mechanistically MCU interacts with the transport protein Miro1 in a calcium dependent manner modulating mitochondrial dynamics and RA-FLS invasion. Inhibition of mitochondrial calcium uptake using the MCU-specific inhibitor Ruthenium-360 restored mitochondrial dynamics and reduced FLS invasiveness. Transcriptome analysis revealed that MCU-mediated calcium signaling activates actin cytoskeleton and focal adhesion pathways, promoting invasion, which is suppressible by MCU inhibition which makes MCU as a therapeutic target to prevent arthritic joint destruction.

Poster **P-068**

Treatment of Premature Ovarian Insufficiency Through BM-MSCs Regulate Downstream Hormonal Profiles

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Abstract: Premature ovarian insufficiency (POI) is characterized by the loss of ovarian endocrine function and reproductive potential before 40 years of age. Although several conventional treatments are available, their efficacy remains limited (5–10%). Mesenchymal stem cells (MSCs) have emerged as a promising therapeutic strategy for POI due to their availability, multilineage differentiation potential, in vitro expansion capacity, and immunomodulatory properties. In the present study, POI was induced through chemo-ablation in female Wistar rats, using a standardized dose of cisplatin. These infertile rats were treated by ovarian administration of bone marrow-derived MSCs (BM-MSCs). Following treatment, rats were mated and sacrificed at designated time points for collection of ovaries, uterus, and serum. Treated animals restored ovarian and uterine histoarchitecture toward normal within 4 weeks, while TGF-β-related gene expression (GDF9, BMP15, and AMH) and hormonal profiles of FSH, AMH, and LH approached normal levels from 6 weeks onward. Restoration of fertility was further confirmed by delivery of pups within 6 weeks of treatment whereas pups were not delivered in the chemo-ablated group up to 12 weeks of infertility induction. Overall, BM-MSCs promoted the recovery of ovarian function and fertility, potentially through regulating the reproductive hormone profiles and modulation of TGF-β superfamily members.

Poster **P-069**

From Inflammation to Fibrosis: Deciphering the Role of NOD2 in Skeletal Muscle Remodeling

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Abstract: Skeletal muscle fibrosis (SMF) is a pathological condition characterized by excessive extracellular matrix deposition, resulting in increased tissue stiffness, reduced elasticity, and compromised muscle strength. SMF is a major contributor to disbalance myogenesis, and functional decline in ageing, diabetes, muscular dystrophies, and chronic inflammatory disorders. Chronic low-grade inflammation is a key driver of SMF by promoting persistent immune activation, myo-fibroblast transition, and excessive extracellular matrix deposition. This study investigates specific role of NOD2, a cytoplasmic pattern recognition receptor (PRRs), in skeletal muscle fibrosis. NOD2 elevated TGF-beta/SMAD3- and WNT-mediated profibrotic signalling pathways. Activation of NOD2 promote myoblast to myo-fibroblast transition through α-SMA and fibronectin overexpression and excessive collagen deposition in L6 myoblast and rat skeletal muscle. NOD2 altered extracellular matrix dynamics through MMPs-TIMPs disbalance and growth factors (CTGF, PDGF) upregulation. Our findings demonstrate that NOD2-profibrotic signalling contribute to muscle fibrosis through chronic inflammation. This study will expand the pathological role of NOD2 beyond innate immunity and elucidating these inflammatory mechanisms may reveal novel therapeutic targets to prevent fibrosis and preserve skeletal muscle integrity

Poster **P-070**

Evaluation of an Osteoanabolic Dual AdipoR1 and AdipoR2 Agonist in Skeletal Muscle Atrophy

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Abstract: Skeletal muscle is a major protein reservoir of our body and comprises ~40% of the total body weight and is an important regulator of glucose and lipid homeostasis. Musculoskeletal disorders, including Skeletal muscle atrophy (SkMA) impact ~1.63 billion people globally making them the second leading cause of disability (WHO-GBD-2021). Skeletal Muscle Atrophy (SkMA) is reported in cancer, COPD, obesity, osteoporosis, and a host of metabolic disorders. Currently, there is no approved therapy for skeletal muscle atrophy. Adiponectin is an anti-inflammatory adipocytokine and myokine which is downregulated in various metabolic diseases. A decade of work from our lab and others has demonstrated that Adiponectin and its receptors play important roles in skeletal muscle function and integrity and can reverse skeletal muscle atrophy in preclinical setups. However, existing adiponectin receptor agonists require high (μM) concentrations for efficacy. Hence new scalable orally active small molecule AdipoR agonists are needed.

Poster P-071

Understanding the Structural-Functional Diversity of Sperm-specific Malate Dehydrogenase1B and its Role in Male Fertility

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Abstract: Malate dehydrogenase (MDH) catalyzes the reversible NADH/NAD^+ interconversion of malate and oxaloacetate. Well-characterized cytosolic and mitochondrial isoforms operate as homodimers using a glycine-rich NAD^+ interacting region and a substrate-binding catalytic triad comprising Histidine, Aspartate and Arginine. Conversely the sperm-specific isoform MDH1B has an extended N-terminus (1-120 aa), a catalytic middle domain (127-459 aa), and a disordered C-terminus (459-518 aa). Though, MDH1B retains the Rossmann-fold but it lacks the conserved Arginine, possessing only a His-Asp dyad. To evaluate the biochemical activity of MDH1B activity, recombinant ΔC and ΔNΔC constructs were recombinantly expressed and purified using affinity chromatography and size-exclusion chromatography (SEC). SEC and transmission electron microscopy (TEM) revealed that ΔC MDH1B forms higher-order multimeric assemblies ranging from tetramers to dodecamers, contrasting sharply with canonical MDH homodimers. Luminescence & absorbance-based assays demonstrated that unlike bi-directional canonical MDHs activity, MDH1B performed very slow unidirectional L-Malate to oxaloacetate conversion. Immunofluorescence experiment showed that MDH1B is localized mainly in tail region of human sperm. Genetic studies in Indian infertile men identified MDH1B mutation in a normozoospermic infertile patient. The heterozygous substitution, c. c.237G>C, resulted in L79F change in the protein. The absence of this substitution in 600 fertile controls and extremely low frequency in public databases suggests its pathogenic nature; subsequent functional analysis is planned to evaluate its effect. The slow enzymatic activity of MDH1B, unique multimerization, and associated sperm deformations indicate MDH1B encompasses both specialized metabolic and essential structural roles in sperm.

Poster P-072

The Epigenetic Role of PRMTs in Osteoclast Differentiation and Bone Resorption

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Abstract: Osteoporosis is a prevalent metabolic bone disorder characterized by low bone mass and micro-architectural deterioration due to excessive osteoclast-mediated bone resorption. Current therapies present severe long- term side effects, necessitating novel therapeutic targets. Receptor activator of NF-κB ligand drives osteoclast differentiation by inducing key transcription factors such as NFATc1. Although Protein Arginine Methyltransferases (PRMTs) are well-established post-translational modifiers with documented roles in diverse inflammatory and metabolic pathologies, their specific epigenetic contribution to osteoclastogenesis remains poorly understood. By expression profiling of all PRMTs, our study revealed a significant upregulation of PRMT1 and robust upregulation of PRMT5 at both mRNA and protein levels during osteoclastogenesis. Unlike PRMT1, the role of PRMT5 in the context of osteoclast differentiation is poorly understood. Pharmacological inhibition of PRMT5 markedly suppressed mature osteoclast formation and disrupted F-actin ring formation. Mechanistically, PRMT5 regulates expression of NFATc1 by depositing activatory H3R2me2s mark at its promoter. Additionally, PRMT5 inhibition significantly downregulated core osteoclast-specific markers including TRAP, CtsK, etc at both transcript and protein levels. Collectively, our results suggested that PRMT5 activity is essential for osteoclastogenesis, osteoclast specific gene expression, and cytoskeletal reorganization. Further *in vivo* validation by targeting & inhibiting PRMT5 may represents a promising epigenetic strategy for mitigating pathological bone loss.

Poster P-073

Multi-Omic Investigation Reveals EGLN3 as a Candidate Regulator of Placental Dysfunction in Spontaneous Preterm Birth

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Abstract: Preterm birth (PTB) remains a leading cause of neonatal morbidity and mortality, yet the biological pathways underlying risk remain unclear. Using the GARBH-Ini pregnancy cohort from India, we integrated genetic, epigenetic, single-cell, and functional data to investigate PTB mechanisms. Genome- wide association analysis identified genetic variants associated with PTB risk, including population- specific and trans-ethnic signals. To determine how these variants may influence risk, we profiled maternal blood DNA methylation across three pregnancy stages and assessed genetic effects on methylation. This analysis implicated *EGLN3*, a key regulator of cellular responses to hypoxia. A PTB- associated variant was linked to reduced methylation at an *EGLN3* promoter CpG, potentially altering regulatory protein binding and increasing *EGLN3* expression. Single-cell placental analysis further demonstrated elevated *EGLN3* expression in trophoblasts from preterm deliveries. Functional experiments indicated that *EGLN3* disruption affects pathways involved in oxygen sensing, vascular development, tissue remodeling, and trophoblast invasion. Together, these findings suggest that genetic variation influencing *EGLN3* regulation may contribute to placental dysfunction and PTB susceptibility. This integrated multi-omics framework provides mechanistic insight into PTB biology and highlights *EGLN3* as a potential molecular target for understanding and identifying women at increased risk of preterm birth and may ultimately support early clinical risk stratification approaches.

Poster P-074

Identification of Lysophosphatidyl-Serine Lipases in Mammalian Spleen, Lungs and Heart

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Abstract: Lysophosphatidylserine (Lyso-PS) is a bioactive lipid playing a crucial role in cell signaling, membrane dynamics, and inflammatory processes. Dysregulation of lyso-PS has been implicated in the pathogenesis of autoimmune diseases and neurodegenerative disorders. Although it plays an important role in physiological processes, lyso-PS metabolism is poorly explored in mammalian tissues other than the brain. ABHD12 is well studied lyso-PS lipase found in the brain. When tissues of ABHD12 knockout mice were profiled for lyso-PS lipase activity, the activity was similar to those of their wild type counterparts, except for the brain. Hence, in order to identify possible lyso-PS lipase candidates in peripheral tissues, an *in vitro* inhibitor screen was performed previously and ABHD6 was found to be the lyso-PS lipase in liver and kidney. The present study aims to identify novel lyso-PS lipases in spleen, lung, and heart tissues, using a combination of pharmacological inhibitor screening and LC-MS/MS-based proteomics using serine hydrolase-directed probe fluorophosphonate-biotin (FP-biotin). Candidate enzymes identified through this approach will be cloned and overexpressed in HEK-293T cells, and their ability to hydrolyze lyso-PS will be evaluated using substrate hydrolysis assays. Thus, identification of additional lyso-PS lipases will help us elucidate the molecular basis of tissue-specific lyso-PS metabolism.

Poster P-075

Understanding the mechanism of substrate processing in SPATA5, a AAA+ chaperone

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Abstract: The maturation of the pre-60S ribosomal subunit in the cytoplasm requires extraction of the placeholder protein RLP24, a rate-limiting and an essential step towards the downstream assembly events. In *S. cerevisiae*, this task is accomplished by a single AAA+ ATPase, Drg1, which unfolds and removes Rlp24 from the pre-60S particles. In humans, the homologous function is instead carried out by 55LCC, a multi- subunit complex containing two distinct AAA+ ATPases, SPATA5 and SPATA5L1. Why the human system requires additional complexity and how the two AAA+ subunits divide labor during substrate extraction and unfolding events remains unresolved. To address this, we combine ATPase activity assays, size-exclusion chromatography, crosslinking mass spectrometry, and hydrogen-deuterium exchange mass spectrometry to dissect the architecture and mechanochemical cycle of the reconstituted 55LCC complex. These approaches will define how SPATA5 and SPATA5L1 coordinate ATP hydrolysis and how RLP24 is engaged, unfolded and released during processing. As mutations in SPATA5 and SPATA5L1 are associated with ribosomopathies and neurodevelopmental disorders, this work will provide mechanistic insight into how disruption of AAA+-mediated RLP24 extraction contributes to disease and may clarify the evolutionary expansion of this essential ribosome maturation step. Few of the preliminary experiments and results of the study are presented here.

Poster P-076

Functional Characterization of ABHD16A: A Phosphatidylserine Lipase Associated with Hereditary Spastic Paraplegia

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Abstract: ABHD16A (α/β-hydrolase domain-containing protein 16A) is functionally annotated as the principal phosphatidylserine (PS) lipase in the mammalian brain. It catalyzes the conversion of PS to lysophosphatidylserine (Lyso-PS), a bioactive lipid implicated in immune regulation, glucose metabolism, and cancer. Previous work by

Kamat et al. (2015) proposed that *Abhd16a*$^{-/-}$ mice might exhibit partial embryonic lethality, suggesting its role in development. Recent genetic studies have further linked biallelic ABHD16A mutations to a complex form of hereditary spastic paraplegia (HSP). However, the basis of the observed partial lethality and the role of ABHD16A in HSP pathophysiology remain unexplored. Here, we establish that *Abhd16a*$^{-/-}$ mice exhibit early postnatal lethality, with the majority of knockout pups dying within 48 hours after birth. Blood glucose profiling revealed no significant genotype-dependent differences, indicating that altered glucose homeostasis is unlikely to be a major contributor to lethality. We further characterized HSP-associated ABHD16A variants and found reduced enzymatic activity in the mutants relative to wild-type ABHD16A, suggesting that impaired ABHD16A function might contribute to HSP pathophysiology. Complementing these studies, we are further investigating whether loss of ABHD16A recapitulates HSP-associated phenotypes in *Abhd16a*$^{-/-}$ mice and thereby assessing the potential of *Abhd16a*$^{-/-}$ mice as an *in vivo* model of HSP.

Poster P-077

Gut Microbiota Sets the Tempo of Postnatal T-cell Development through Progenitor-Intrinsic Interleukin-1-Responsiveness

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Abstract: Background: In recent years, the gut microbiota has emerged as critical regulators of the postnatal immune system development and activities. However, whether and how the microbiota influences the earliest window of postnatal T-cell development, encompassing progenitor expansion and T-lineage specification under the influence of microenvironmental signals such as Notch, remains unexplored. Methods: A publicly available transcriptome dataset was reanalyzed to identify gene-expression signatures unique to postnatal T-cell progenitors. Broad-spectrum antibiotics-based microbiota depletion and fecal microbiota transplantation were carried out in perinatal as well as adult mice, and their impact on early thymopoiesis was examined by in vivo label-tracking experiments. Mechanistic experiments were performed on sort- purified T-cell progenitors to dissect the regulation of Notch1 expression downstream of IL-1 signaling. Results: Postnatal T-cell progenitors exhibited a developmental stage-specific and gut microbiota- dependent expression of IL1R1. Pharmacological or shRNA-mediated inhibition of IL-1 signaling decelerated postnatal T-cell development, with pronounced changes in progenitor differentiation and proliferation kinetics. Mechanistically, IL-1-responsiveness contributed to the stabilization of Notch1 transcripts by Elavl1, resulting in an increased Notch1 expression and signaling. Conclusion: Collectively, our findings identify a hitherto uncharacterised microbiota-dependent host immune adaptation that allows the calibration of postnatal T-cell development with the gut microbiota.

Poster P-078

Short-chain Fatty Acid Production by Gut Microbiota is a Determinant of Host T Cell Development

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Abstract: Background: Gut microbiota acts as a major source of short-chain fatty acids (SCFA) in mammals. The

ability of the microbiota to produce SCFAs has been associated with different aspects of T cell function and dysfunction in the periphery. However, its influence on the intrathymic development of T cells has not received much attention. Methods: Pregnant mice were maintained on broad-spectrum antibiotics till 15 days post-partum to generate microbiota-depleted (ABX) offspring. These offspring were maintained on sterile drinking water with/without Sucrose or SCFAs. The ackA gene, encoding a rate-limiting enzyme for acetate production, was deleted from a commensal E. coli strain. ABX mice were mono-colonized with wild-type and ackA-knocked-out (ΔackA) bacteria, and T cell development was monitored. Results: ABX mice showed signs of slower T cell development and reduced thymic productivity, along with reduced serum SCFA levels. These defects could be partly rescued by SCFA, but not Sucrose. Mono-colonization with wild-type, but not the ΔackA strain, rescued T cell development and thymic output in ABX mice. Conclusion: These findings connect the SCFA-productivity of the gut microbial consortium to T cell development and thymic productivity, and argue against its general role in meeting the caloric needs of the host.

Poster P-079

Metabolic Rewiring Exacerbates *Acinetobacter baumannii* Infection in Obesity

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Abstract: Chronic metabolic diseases are associated with increased susceptibility to bacterial infections. We propose that metabolic rewiring represents a higher-order determinant of infection outcome by simultaneously altering host immunity, bacterial physiology, and antibiotic response. Using a murine model of obesity, we investigated how disease-associated metabolic alterations influence host–pathogen interactions during infection with the nosocomial pathogen *Acinetobacter baumannii*. In obesity, altered host metabolism was associated with increased bacterial burden in infected organs, impaired immune-mediated bacterial clearance, and reduced antibiotic efficacy. Obesity was also associated with gut microbiota dysbiosis, characterized by a shift toward non- fermentative taxa and depletion of short-chain fatty acids (SCFAs). SCFA depletion was associated with increased susceptibility to infection and reduced antibiotic effectiveness. SCFA supplementation in combination with antibiotic treatment improved bacterial clearance of both *A. baumannii* and clinical *Pseudomonas aeruginosa* isolates, while partially restoring the gut microbiota. Together, our findings support a model in which chronic metabolic rewiring creates a permissive host state that reshapes immune function, bacterial physiology, and therapeutic response, thereby increasing susceptibility to bacterial infection. These findings identify host metabolic state as a potential target for metabolite-based strategies to improve infection outcomes.

Poster P-080

Proteome-Wide Identification and Biophysical Characterization of Novel Secretory Effectors of *Orientia tsutsugamushi* in Scrub Typhus Pathogenesis

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Abstract: Scrub typhus, caused by the obligate intracellular bacterium *Orientia tsutsugamushi* (*Ot.*), is a major neglected disease with poorly understood molecular pathogenesis. Secretory effectors are critical virulence determinants that subvert host immunity, apoptosis, and organelle homeostasis.

In methodology, an integrated *in-silico* pipeline was applied to the *Ot.* UT76 proteome. Effector and secretion system predictions were conducted using DeepSecEDb; virulence potential via VirulentPred 2.0 and VFDB; signal peptides and localization using SignalP 6.0 and PSORTb; and intrinsically disordered regions (IDRs) via PONDR. Functional pathways were annotated using BLAST/KOALA and KEGG. AlphaFold2-generated 3D models were validated by Ramachandran plot analysis (EMBL-EBI) and binding-pocket prediction. Host-effector interactions were evaluated

using protein-protein interaction (PPI) networking.

The pipeline prioritized 22 novel effectors spanning Type I–IV secretion systems, including ankyrin-repeat proteins, conjugative transfer proteins, peptidoglycan-associated proteins, transporters, amidases, and uncharacterized proteins. All 22 effectors contained IDRs, indicating structural plasticity. AlphaFold2 models demonstrated high stereochemical accuracy (>91% residues in favored Ramachandran regions). PPI networking linked these effectors to host protein trafficking, apoptosis, microtubule assembly, and inflammasome pathways.

This study provides a validated panel of *Ot.* candidate effectors and interaction networks, establishing structural targets to accelerate biomarker and therapeutic discovery in scrub typhus.

Poster P-081

Unravelling the Menistic Roles of Cholesterol-Binding Motifs in Host Membrane Interactions of Listeriolysin O, a Virulence Factor of *Listeria monocytogenes*

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Abstract: Listeriolysin O (LLO) is a β-barrel pore-forming toxin. It is a key virulence factor of *Listeria monocytogenes*, a Gram-positive bacterium that causes listeriosis, particularly in immunocompromised individuals and pregnant women. LLO belongs to the family of cholesterol-dependent cytolysins (CDCs) and contributes to *Listeria* pathogenesis by forming large pores in the phagolysosomal membrane, enabling bacterial escape, survival in the host, and spread to neighbouring cells. Cholesterol plays an important role in modulating LLO binding to the host cell membrane. Recently, it has been reported that motifs other than the established cholesterol-recognition motif (CRM) of LLO may contribute to cholesterol-binding by the toxin. In this direction, we have identified six potential CRAC (cholesterol recognition amino acid consensus) motifs in LLO. Alteration of one such motif has shown compromised pore-forming activity and impaired oligomerization. These findings suggest that at least one of the potential CRAC motifs may play a crucial role in LLO function. Our result may help identify additional residues/motifs involved in cholesterol recognition and membrane interaction by LLO.

Poster P-082

Elucidating the Functional Implications of the Pore-Forming Motif of *Staphylococcus aureus* α-Hemolysin

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Abstract: *Staphylococcus aureus* α-Hemolysin (Hla) is an archetypical β-barrel pore-forming toxin (β-PFT). It is secreted by the bacteria as soluble monomeric molecule, in which the specialized pore-forming motif (PFM) remains stacked against the toxin's core 'cytolysin' domain. Upon exposur e to the membrane environment, Hla forms heptameric transmembrane β-barrel pores, and in this process PFM of the toxin protomers detaches from the cytolysin domain, inserts into the lipid bilayer to create the β-barrel scaffold. The most baffling questions here are: how the PFM rearrangement remains arrested in the soluble monomeric state, and how it gets triggered specifically in the membrane environment. Our study has uncovered a critical molecular switch, a conserved amino acid residue, located in the hinge region of the Hla PFM that seems to regulate oligomerization of the toxin in the course of the pore-formation process. Mutation of this residue allows premature oligomerization of Hla in solution, even in the absence of membrane lipid bilayer. Such oligomeric forms of the Hla mutant formed in solution seem to represent pre-pore-like states of the β-PFTs that are otherwise form in the process of membrane pore-formation. Taken together, our results provide novel insights into the Hla pore-formation mechanism.

Poster **P-083**

DIP2-Dependent Diacylglycerol Regulation Governs Virulence in Pathogenic Fungi

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Abstract: Fungal pathogenicity is a multifaceted process involving the concerted interplay of diverse biomolecules. Although several studies have elucidated mechanisms that regulate fungal virulence, the contribution of lipid metabolism remains underexplored. In this study, we identify DISCO-Interacting Protein 2 (Dip2) as a critical regulator of fungal virulence by maintaining diacylglycerol (DAG) lipid homeostasis in *Candida albicans*. Loss of Dip2 leads to accumulation of specific DAG species, while genetic complementation with *DIP2* restores the DAG levels. Deletion of *DIP2* also disrupts mitochondrial morphology, reduces mitochondrial membrane potential and increases susceptibility to oxidative stress, indicating broader mitochondrial dysfunction. In a murine infection model, *ΔΔdip2* strain exhibited markedly attenuated virulence compared to the wild type. Furthermore, mice previously exposed to *ΔΔdip2* strain were protected against a subsequent lethal challenge, highlighting its potential as a live-attenuated vaccine candidate. Collectively, these findings connect lipid regulation to fungal pathogenicity and shed light on the role of Dip2 in virulence in pathogenic fungi.

Poster **P-084**

Understanding the Molecular Basis of CDC48.3 and AIR2 Interaction

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Abstract: The ubiquitous AAA+ (**A**TPases **A**ssociated with diverse cellular **A**ctivities) protein superfamily is a large family of P-loop ATPases members that control a diverse array of cellular processes. *Caenorhabditis elegans* CDC48.3 is a Type II AAA+ ATPase that interacts with AIR2, the *C. elegans* homolog of human Aurora kinase B and inhibit its downstream processes. AIR2 is an essential protein vital for cell division fidelity whereas CDC48.3 is a homolog of human SPATA5, a AAA+ chaperone essential for replication and ribosome biogenesis. The SPATA5 in complex with three different proteins extracts RLP24 from the pre-60S ribosomal particle like its *S. cerevisiae* functional homolog, DRG1 during ribosome biogenesis. Does CDC48.3 have a similar role in RLP24 extraction in ribosome biogenesis and does it follow the same mechanism during AIR2 inhibition is still unknown. Our work focuses on unravelling this mechanism by using different biochemical and mass spectrometry approaches. Through our findings, we anticipate to gain detailed insights into the mechanics of CDC48.3 interactions. Preliminary experimental data of the study are presented here.

Poster **P-085**

Characterizing the Interaction Specificity of Histone-fold Domain Containing Heterodimers in *Candida albicans*

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Abstract: *Candida albicans* is a human fungal pathogen that ordinarily colonises skin and other mucosal surfaces as a

harmless commensal but turns pathogenic in immune-compromised people. The cellular plasticity and increasing tolerance to antifungals, makes it to the critical fungal pathogen list released by the World Health Organization (2022). Hence, along with the advancement of antifungals, understanding and identifying new targets is also vital for treating candidiasis. Our interest has been on two TAF12 paralogous genes, *TAF12* and *TAF12L* encoded by *C. albicans*. Taf12 and Taf12L proteins contain highly related H2B-like histone fold domains (HFD). Genetic and biochemical analysis showed that Taf12 is a subunit of TFIID and Taf12L is a subunit of the SAGA chromatin modifying complex in *C. albicans.* Recombinant expression in *E.coli* and pull-down experiments showed that full-length Taf12 and Taf12L specifically interact with the H2A-like HFDs of Taf4 and Ada1, respectively. To further understand the molecular details of these interactions, we carried out computational analysis involving molecular modelling studies using HFD sequences and found that, surprisingly, Taf12 and Taf12L HFDs form energetically stable heterodimers with both Taf4 and Ada1 HFDs. Unlike the full-length constructs, pull-down assay using histone fold domain regions revealed not only that HFD is sufficient for the heterodimer interaction between Taf12HFD-Taf4HFD and Taf12LHFD-Ada1HFD, but heterodimeric interactions between non-cognate partners i.e., Taf12HFD-Ada1HFD and Taf12LHFD-Taf4HFD were identified indicating that regions outside the HFD are required for specificity of interactions of the dimers. To identify amino acid residues conferring interaction specificity between the HFD sequences, we are carrying out genetic and biochemical experiments using mutants of the Taf12 and Taf12L HFDs guided by the structural models. This study will uncover the molecular details of protein-protein interactions in the heterodimeric histone-fold domain containing non-histone proteins.

Poster P-086

Understanding the Role of TORC1 and Bxi1 in Cellular Homeostasis and Apoptosis in *Fission Yeast (S. pombe)*

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Abstract: Eukaryotic organisms evolved mechanisms to modulate cellular metabolism in response to environmental changes and mitochondria is the key organelle to mitigate these alterations. The target of rapamycin (TOR) is a member of the phosphoinositide-3 kinase-related protein kinase family that regulate various cellular processes such as cell growth and cell proliferation is conserved from yeast to humans. Pop3/*wat1*, a mammalian *Lst8* ortholog is an important component of both TOR complexes and has been implicated in the oxidative stress response pathway. We showed that the absence of *wat1* or mutation in *tor2* gene (tor2-287) lead to mitochondrial dis-function resulting in mitochondrial ROS accumulation, apoptosis and autophagy. The interaction studies of Tor2 and Mmm1 proteins revealed a cross-talk between mitochondria and endoplasmic reticulum through the Mitochondria-associated membranes (MAM) and endoplasmic reticulum-mitochondria encounter structure (ERMES) complex indicating its role in calcium ion homeostasis maintenance and fatty acid beta oxidation. The fission yeast Bxi1 is a BAX inhibitor family protein that contains BCL-2 homology domain 3 (BH3) has been implicated in Endoplasmic reticulum calcium ion homeostasis. The overexpression analysis of *bxi1* gene in *S. pombe* cells revealed apoptotic like cell death and DNA fragmentation suggesting its role in apoptotic cell death. Overall, the present study provides an insight mechanism involving the TOR complex and *bxi1* induced mitochondrial dysfunctioning as well as cell death respectively in fission yeast.

Poster P-087

LdZIP3 Regulates the Autophagy-to-Apoptosis Switch in *Leishmania donovani* Under Zinc induced Stress

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Abstract: Visceral leishmaniasis (VL), caused by the intracellular protozoan *Leishmania donovani (Ld)*, remains a major global health challenge, with no efficacious vaccine and increasing drug resistance necessitating the identification of novel therapeutic targets. Zinc is essential for *Ld* survival and cellular homeostasis. This study investigates the role of the zinc transporter *LdZIP3* in maintaining zinc homeostasis and parasite survival. Chelation of intracellular zinc using TPEN significantly reduced parasite viability by 72 h, while partial viability was retained at 48 h, indicating a biphasic response to zinc stress. FluoZin -3 AM fluorescence imaging and partial rescue by exogenous zinc supplementation further confirmed the essential role of zinc. FACS analysis showed no significant apoptosis at 48 h, whereas apoptotic cells increased at 72 h. Semi-quantitative PCR demonstrated time-dependent upregulation of *LdZIP3,* autophagic markers *ATG8*, and *SIR2* up to 48 h following TPEN exposure, suggesting an early adaptive response involving enhanced zinc uptake and autophagy-associated survival. Sustained zinc deprivation may subsequently shift this pro-survival response toward apoptosis-like death. To determine the functional role of *LdZIP3*, knockout parasites were generated to assess whether transporter loss disrupts zinc homeostasis, compromises parasite survival, and alters the autophagy-to-apoptosis response. Thus, establishing the *LdZIP3*-regulated autophagy–apoptosis pathway may identify *LdZIP3* as a novel therapeutic target.

Poster P-088

Ubc12-mediated Neddylation is Essential for Ookinete Maturation and Malaria Parasite Transmission

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Abstract: Post-translational modifications are essential regulators of eukaryotic cell-cycle progression and developmental transitions. NEDD8 conjugation activates Cullin-RING ubiquitin ligases and is mediated by a conserved enzymatic cascade, yet its role in malaria parasite development remains poorly understood. Here, we investigate the function of the NEDD8-conjugating enzyme Ubc12 in the rodent malaria parasite *Plasmodium berghei*. Phylogenetic and biochemical analyses demonstrate that Ubc12 is an evolutionarily conserved and functional NEDD8 E2 enzyme capable of forming a covalent NEDD8-Ubc12 conjugate. PbUbc12 is expressed throughout multiple parasite life-cycle stages and localizes predominantly to the cytosol. Targeted deletion of Ubc12 revealed that the gene is dispensable for asexual blood-stage growth and gametocyte formation. However, Ubc12-deficient parasites fail to complete mosquito-stage development, exhibiting a complete block in oocyst formation. Detailed phenotypic analysis shows that loss of Ubc12 does not impair gametocyte activation or fertilization but results in arrest during the retort- to-ookinete transition, preventing parasite transmission to the mosquito vector. Conditional deletion of Ubc12 in sporozoites further demonstrates that the enzyme is not required for sporozoite transmission from midgut to salivary galnd, liver-stage development, or initiation of blood-stage infection. Together, these findings identify Ubc12-mediated neddylation as a critical regulator of ookinete maturation and reveal a stage-specific vulnerability in malaria parasite transmission that may be exploited for transmission- blocking interventions.

Poster P-089

Drug-Resistant *Leishmania donovani* Evades Host Ubiquitin-Mediated Cell-Autonomous Immunity through Upregulation of Parasite Deubiquitinating Enzymes (Ld-DUBs)

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Abstract: Ubiquitination and deubiquitination are essential processes regulating host and microbial cell biology and physiology. Deubiquitinating enzymes (DUBs) remove ubiquitin from target proteins, edit ubiquitin chains, and process ubiquitin precursors. Ubiquitin-mediated recognition of intracellular pathogens is an important cell-autonomous host defense mechanism that promotes pathogen targeting and degradation. Although this pathway is well established against *Toxoplasma gondii*, its role against other vacuolar protozoan pathogens, including *Leishmania*, remains poorly understood. We investigated whether Leishmania-containing vacuoles (LCVs) are targeted by the host ubiquitin system and delivered to lysosomal/autolysosomal compartments to restrict parasite growth. We further investigated whether parasite deubiquitinating enzymes (DUBs) counteract this host defense mechanism to promote intracellular survival.

We found that LCVs are ubiquitinated and targeted to lysosomal/autolysosomal compartments, resulting in restricted intracellular parasite growth. Compared with antimony- sensitive *L. donovani* (SbS-Ld), antimony-resistant parasites (SbR-Ld) exhibited reduced LCV ubiquitination and lysosomal targeting, suggesting enhanced evasion of host cell-autonomous immunity. This was accompanied by differential expression of specific Ld-DUBs in SbR-Ld. CRISPR-Cas9-mediated disruption of selected Ld-DUBs in SbR-Ld enhanced LCV ubiquitination and lysosomal fusion, resulting in significantly reduced intracellular parasite growth compared with wild-type SbR-Ld.

Our findings identify *Ld*-DUBs as important regulators of *L. donovani* immune evasion. These parasite enzymes appear to counteract host ubiquitin-mediated recognition and lysosomal targeting of LCVs, thereby promoting intracellular parasite survival and proliferation. Targeting *Ld*-DUBs may therefore represent a potential strategy for restoring host cell-autonomous immunity against *L. donovani* and developing novel antileishmanial interventions.

Poster P-090

Diagnostic Potential of *Leishmanial* SPV-22 Protein for the Detection of VL, PKDL, and VL-HIV Co-Infection Patients

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Abstract: Visceral Leishmaniasis (VL) is a life-threatening protozoan disease caused by parasite *Leishmania donovani*. VL-coinfection has been identified as one of the major emerging challenges for VL control. Available diagnostic facility for VL, rk39 strip test has less sensitivity and specificity to detect VL- coinfected cases, which limits its use in detecting VL-coinfected cases. However, the sensitivity of gold standard parasitological test for PKDL in case of macular lesion is also very less. In this direction, our lab has identified SPV-22 protein from *L. donovani* was expressed and purified by affinity chromatography. ELISA was performed for the assessment of 425 samples sensitivity and specificity of SPV-22 using the sera samples of disease groups VL (75), PKDL (75), VL-HIV (75) and control HIV (50), TB (50), Healthy endemic & nonendemic (50 each). Titer of antibodies against SPV22 was approximately 1.5 to 2.0-fold increase in patients' sera samples as compared to healthy or positive diseases controls. Immunoblotting of 90 sera samples were performed against SPV -22 for VL (15), PKDL (15), VL-HIV (30) and control group HIV (10), TB (10), Healthy Endemic (10). This result clearly depicts that SPV-22 have a better diagnostic potential for the detection of VL, PKDL and VL Co-infected patients.

Poster P-091

Exploring the Role of Vector Salivary Proteins (VSPs) in Host Immunomodulation and Protection against Experimental Lymphatic Filariasis

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Abstract: Lymphatic filariasis**,** a debilitating vector-borne disease-causing chronic disability, lacks adulticidal drugs or vaccines, highlighting the need for novel interventions. As early infection is asymptomatic and chronic stages incurable, transmission-blocking vaccines are ideal. VSPs modulate host immunity and recently emerged as vaccine candidates and biomarkers. Therefore, we evaluated *Aedes aegypti* VSPs induced immunomodulation and vaccine efficacy against *Brugia malayi* infection.

Ae. aegypti VSPs were isolated and characterized via proteomic and molecular analyses, confirming their diversity and structural integrity. Co-infection with L3 larvae and VSPs, mimicking natural transmission, did not confer significant protection as expected. However, VSP pre-immunization in Balb/c mice reduced L3 burden by ~69%, and whereas in *Mastomys* ~74% and ~57% protection was observed against microfilariae and adult worms, respectively. filarial proteins, respectively, together with negligible antibody-dependent cellular cytotoxicity (ADCC), suggested a minimal contribution of humoral immunity. In contrast, ex vivo sensitization of peritoneal macrophages (PMØs) with VSPs elicited robust innate immune activation, characterized by enhanced macrophage proliferation, phagocytic activity, PRRs upregulation, antigen presentation, and MHC-II expression. Co-culture of VSP-primed PMØs with T cells further induced a balanced Th1/Th2/Th17 immune response, supported by activation of NF-κB signaling and increased expression of lineage-specific transcription factors and cytokines. Moreover, VSP immunization elicited a strong delayed-type hypersensitivity response accompanied by infiltration of activated macrophages and effector/memory $CD4^+$ T cells. Collectively, these findings indicate that VSP-mediated protection is driven by DTH-associated cellular immunity and coordinated Th1/Th2/Th17 responses and findings warranting cDNA library-based screening to identify the most ideal individual candidate in future.

Poster P-092

Plasmodium DERA Supports Stress Adaptation during Blood-stage Growth Despite Life-cycle Dispensability

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Abstract: Plasmodium remains a global health challenge with an estimated 282 million malaria cases and 610,000 malaria deaths across 80 endemic countries (world Malaria Report 2025, WHO). Plasmodium parasites undergo ample metabolic and environmental fluctuations throughout their complex life cycle and must adapt to diverse stress conditions to maintain successful propagation. Deoxyribose-phosphate aldolase (DERA), an enzyme involved in deoxyribose-phosphate metabolism, has been identified in Plasmodium, but its role in parasite biology remains unknown. Here, we investigated the role of DERA during parasite life cycle. DERA-deficient parasites were viable and grew similarly to wild-type parasites, indicating that DERA is not required for blood-stage development. Furthermore, DERA knockout parasites developed normally through the mosquito and liver stages. Bioinformatic analysis suggested that DERA may be involved in the parasite's stress response. Next, we exposed the parasites to different stress conditions and found that DERA-deficient parasites showed delayed propagation under lactic acid-induced stress and after UV radiation exposure. In vivo serial passage further revealed a progressive delay in parasite

propagation compared with wild-type parasites. These findings indicate that although DERA is not required for parasite survival or propagation under normal conditions, it contributes to the parasite's capacity to withstand and adapt to metabolic/chemical, physical, and physiological stress during blood-stage growth.

Poster P-093

Role of SPV55 Protein as Potential Diagnostic Biomarker for the Detection of VL, PKDL, and VL Co-Infection Patients

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Abstract: Visceral leishmaniasis (VL) is a life threatening disease caused by *Leishmania donovani*. An estimated 2-7% of VL cases are co-infected with HIV. Both HIV and VL are endemic in Bihar, and thus HIV-VL has been identified as one of the emerging challenge for the VL elimination. The current biomarker rK39 is used to detect VL, PKDL, and VL-co-infected cases (VL-HIV, VL-TB); however, it shows false positive result in malaria, TB, and pregnant cases and false negative in VL co-infection. Parasite identified by skin slit smear of PKDL patients has very low sensitivity (58%). To overcome this diagnosis issues associated with PKDL and VL co-infection, we are working to develop the novel biomarker with significant specificity and sensitivity for the detection of PKDL and VL co-infected cases. In the present study, a SPV55 protein was expressed and purified. This protein was used for immunoblotting and ELISA for the detection of VL, PKDL, and VL-coinfected cases, which showed high antibodies titer in diseases sera samples than control groups. IgG isotypes in pre and post treated patient's sera were also evaluated by ELISA. This result suggested that SPV-55 protein has better diagnostic potential for the detection of VL, PKDL, and VL co- infected cases.

Poster P-094

Secretary Leishmanial protein as a Novel Biomarker for Detecting VL, PKDL, and Co-Infected Cases

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Abstract: Visceral Leishmaniasis (VL) is a life threatening disease caused by *Leishmania donovani*. Bihar is the most endemic state for VL in India; an estimated 2-7% of VL cases are co-infected with HIV. For diagnosis of leishmaniasis the rk39 strip test frequently used but in case of VL-HIV the sensitivity of rK39 decreased. In case of PKDL, mostly in macular lesion the sensitivity of gold standard test is decreased. To overcome this diagnosis related issues, we are working on to develop the novel biomarker with significant sensitivity and specificity for the detection of PKDL and VL co-infected cases. In this study, we have identified SPV16 protein and analyzed its potential as biomarker by immunoblot and ELISA for the diagnosis of VL, PKDL, VL-HIV, VL-HIV-TB and VL-TB patient's sera with HIV, TB, Malaria and Typhoid as control groups. IgG- isotyping was also done in pre- and post-treatment. Thus, our protein is recognized antibodies in VL, PKDL and VL-HIV patient's sera samples as compared to control, suggested that our antigen have showed better response than rK39 test to detect PKDL and VL co-infected cases.

Poster P-095

Investigating the Role of Bm-CALU1 in Maintaining Cuticular Integrity of *Brugia malayi*

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Abstract: Lymphatic filariasis (LF) affects approximately 41 million people worldwide and continues to impose a substantial socioeconomic burden. Current mass drug administration programs primarily target microfilariae, but their limited efficacy against adult worms highlights the urgent need for novel macrofilaricidal therapeutics. Targeting proteins involved in parasite cuticle biogenesis may provide a promising strategy to compromise the structural integrity of adult filarial parasites. In this study, we investigated *Brugia malayi* calumenin (Bm-CALU1), an endoplasmic reticulum-localised calcium- binding protein implicated in collagen processing and cuticle formation. Bm-CALU1 showed substantial structural divergence from human calumenin, suggesting the potential for parasite-selective targeting. The protein was detected across multiple developmental stages and in excretory-secretory products of the parasite. Recombinant Bm-CALU1 was successfully expressed, purified, and characterised using circular dichroism spectroscopy. Functional assessment through RNA interference resulted in a marked reduction of Bm-CALU1 protein levels, which was confirmed by Western blot analysis. Importantly, scanning electron microscopy revealed pronounced disruption of cuticular architecture and surface organisation in Bm-CALU1-silenced parasites compared with controls. Together, these findings demonstrate that Bm-CALU1 plays an important role in maintaining cuticular integrity in *B. malayi*, highlighting its potential as a molecular target for the development of novel macrofilaricidal interventions.

Poster P-096

Unravelling the Role of LdHSK in Oxidative Stress Regulation and Parasite Survival in *Leishmania donovani*

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Abstract: Visceral leishmaniasis (VL), caused by *Leishmania donovani*, is a life-threatening neglected tropical disease in 73 countries with limited therapeutic options and increasing drug resistance. *Leishmania* amastigotes survive within macrophage phagolysosomes by counteracting host-derived ROS/RNS through the thiol-based antioxidant system. Homoserine kinase (HSK) contributes to oxidative-stress adaptation and parasite survival. In the present study, we investigated the functional role of HSK in oxidative stress management and parasite survival in *Leishmania donovani*. The expression of HSK and key thiol-metabolic enzymes, including trypanothione synthetase (TryS), trypanothione reductase (TR), cytosolic tryparedoxin (cTXN), and cytosolic tryparedoxin peroxidase (CTP), was evaluated in promastigotes exposed to H_2O_2 and menadione using semi-quantitative PCR and real-time PCR. Intracellular ROS levels were quantified by H_2DCFDA-based assays, revealing oxidative-stress- induced changes in ROS accumulation. Increased expression of HSK and thiol-metabolic enzymes suggested their association with the parasite antioxidant response. Recombinant LdHSK was cloned, expressed, and purified by affinity chromatography, followed by biophysical characterization. Polyclonal anti-LdHSK antibodies were validated by immunoblotting and immunolocalization, confirming predominantly cytosolic localization. Functional studies using LdHSK knockout and overexpressing parasites demonstrated alterations in growth, oxidative-stress response, ROS levels, and survival. Overall, these findings establish LdHSK as a functionally relevant component of the Leishmania parasite's stress biology response.

Poster P-097

Metabolic Reprogramming as a Driver of Immune Modulation and Parasite Survival during *Leishmania donovani* Infection

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Abstract: Early-phase *L. donovani* infection upregulates glycolysis, enabling faster ATP production through lactate production pathway than oxidative phosphorylation (OXPHOS). Excess ATP is exported extracellularly and converted to adenosine, which activates the A2AR, a GPCR. A2AR activation suppresses pro-inflammatory cytokines in infected macrophages, thereby promoting parasite survival. We showed that A2AR blockade reduces Heme oxygenase-1 (HO-1), an antioxidant enzyme that reduces pro-inflammatory cytokine production. Infection-mediated A2AR activation increases intracellular cAMP, activates PKA, and subsequently activates the transcription factors CREB and NRF2, which regulate HO-1 expression. During late-stage infection, increased energy demand may induce a metabolic shift toward OXPHOS, potentially reducing adenosine availability and A2AR signaling. This raises the question of how a parasite-favorable environment is maintained. Such metabolic reprogramming is reflected by changes in the NAD+/NADH ratio. Our preliminary findings show an increased NAD+/NADH ratio during late-stage infection, indicating a shift toward OXPHOS. NAD+ is a cofactor for sirtuin deacetylases that regulate metabolism and stress responses. NQO1, an antioxidant enzyme, generates NAD+ and directly interacts with and activates SIRT1. We hypothesize that *L. donovani* induces the NQO1-NAD+-SIRT1 axis, promoting NRF2 deacetylation, enhanced activity and HO-1 binding, thereby establishing a positive-feedback loop that sustains parasite survival.

Poster P-098

Leishmania donovani Exploits Host PKA and A-kinase–Anchoring Protein (AKAP) Interactions to Modulate ROS and Apoptosis for Disease Propagation

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Abstract: In Visceral leishmaniasis (VL), manipulation of host signaling pathways is critical for parasite sustenance. Among these, cAMP-dependent PKA, comprising of regulatory subunits RI and RII, plays differential roles to inhibit macrophage ROS and apoptosis, leading to infection propagation. In vitro and in vivo experiments documented that while PKARI inhibition enhanced ROS and reduced IL-10 expression, PKARII inhibition augmented TNF-α. production. PKARI-mediated ROS inhibition resulted from reduced expression of the antioxidant transcription factor NRF2 and although inhibition of either PKARI or PKARII increased caspase-3 activity, PKARII inhibition predominantly reduced the anti-apoptotic protein MCL1, supporting parasite survival. Substrate targeting of PKA is achieved by binding of RI and RII with scaffold proteins AKAP and disrupting this association by inhibitor peptides augmented both ROS and apoptosis. PKARI inhibition reduced GSK-3β phosphorylation, increasing its inhibitory grip on NRF2 signaling axis regulating redox homeostasis. On the other hand, MCL1 expression in VL depends on CREB, a downstream PKA effecter, uncovering a PKARII– AKAP–CREB–MCL1 pathway. Interestingly, despite the dominant role of PKARII in CREB-mediated MCL1 expression, PKARI dependent GSK-3β phosphorylation appears important for maintaining MCL1 stability, highlighting crosstalk between the two PKA compartments and establishing AKAP- organized PKA signaling as a determinant of parasite persistence.

Poster **P-099**

Elucidating the Functional Interaction Between PfGCN5 and PfCDPK1

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Abstract: Malaria is a parasitic disease caused by Plasmodium species. In Plasmodium, epigenetic regulation broadly controls parasite gene expression. GCN5 is a histone acetyltransferase that regulates diverse cellular processes, including acetylation of histone and non-histone proteins. PfGCN5 is a ~171 kDa protein containing a conserved bromodomain, a HAT domain, a coenzyme-A binding pocket, and an ADA2-interacting domain. LC-MS/MS analysis identified that GCN5 interacts with non-histone protein CDPK1, among others. CDPK1 is a serine/threonine kinase essential for the Plasmodium life cycle and is not expressed in humans. From phosphoproteomics data, we identified phosphorylated residues in PfGCN5, suggesting that PfCDPK1 may phosphorylate PfGCN5. To validate this, we expressed and purified His- PfCDPK1 and performed an in vitro pulldown assay. His-PfCDPK1 interacted specifically with the mid region of PfGST-GCN5, but not with the CTD region. Furthermore, a 3D7 cell line expressing episomal GFP-CDPK1 was used to validate the in vivo interaction of GFP-CDPK1 with GCN5 via co- immunoprecipitation. Subcellular fractionation was performed to confirme the localization of PfCDPK1, and a kinase assay checked phosphorylation of PfGCN5 by PfCDPK1. Phosphorylation of PfGCN5 may act as a molecular switch regulating its activity. The main features of these experiments will be discussed accordingly.

Poster **P-100**

Leishmania donovani Dipeptidylcarboxypeptidase (*Ld*DCP): A Crucial Zn++ Metalloprotease for Parasite Survival, Proliferation and Infectivity

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Abstract: Proteases play crucial roles in parasite metabolism, making them attractive targets for drug development. Dipeptidyl carboxypeptidase of *Leishmania donovani* (*Ld*DCP), a zinc-dependent metalloprotease of the M3 family, has previously been identified as a potential therapeutic target for visceral leishmaniasis. In the present study, the biological significance and essentiality of *Ld*DCP were investigated through genetic modulation of its expression. Single-allele replacement, *Ld*DCP-overexpression, and complemented parasites were generated and validated. Single-allele deletion resulted in approximately 0.5-fold reduction in *Ld*DCP expression, whereas overexpression resulted in increased protein levels by approximately 2.2- fold. Repeated attempts to generate double-allele replacement mutants were unsuccessful, proving the essentiality of *Ld*DCP for parasite survival. Overexpression of *Ld*DCP resulted in reduced proliferation of promastigote while enhanced growth rate of amastigote was observed. Though the underexpression of *Ld*DCP did not affect promastigote growth but significantly reduced its infectivity. Similar trend was observed under *in vivo* condition in the *Leishmania donovani*/golden hamster model. *Ld*DCP modulation also significantly influenced susceptibility to captopril, an ACE (mammalian DCP) inhibitor, while responses to standard antileishmanial drugs remained largely unchanged. Collectively, these findings establish *Ld*DCP as an essential determinant of *L. donovani* survival, infectivity, and intracellular proliferation, supporting its potential as a promising therapeutic target against visceral leishmaniasis.

Poster P-101

Functional Characterization of *Pf*Nbp35 and *Pf*HCF101 in the Cytosolic Iron- Sulfur Assembly Pathway of *Plasmodium falciparum*

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Abstract: [Fe-S] clusters have critical roles in catalysis by many enzymes, and are assembled through three pathways in *Plasmodium* spp.-ISC, SUF and CIA. The cytosolic CIA depends on mitochondrial ISC. We previously identified *Pf*ATM1 in the mitochondrial membrane as an essential transporter of cluster intermediates to the cytosol. The present study investigated the interaction between *Pf*ATM1 and early CIA components *Pf*Nbp35 & *Pf*HCF101. IFAs for *Pf*Nbp35 showed mitochondrial overlap, and the N-terminal extension of *Pf*ATM1 interacted with *Pf*NBP35 in pull-down assays. Both recombinant *Pf*Nbp35 and *Pf*HCF101 bound [4Fe-4S] and were functional ATPases, an activity required for [Fe-S] transfer to downstream CIA carriers. *Pf*Nbp35 could pull down *Pf*HCF101 from parasite lysate indicating their interaction. MD simulations confirmed the structural stability of the *Pf*Nbp35-*Pf*HCF101 heterotetramer. Since ATM1 knockdown/upregulation in *Toxoplasma gondii* alters levels of NEET proteins CDGSH1 and CDGSH2, we tested whether these might interact with ATM1 in *P. falciparum.* Although *Pf*CDGSH1 localized in proximity to mitochondria, pull-down experiments revealed no direct interaction between *Pf*ATM1 and *Pf*CDGSH1/*Pf*CDGSH2, suggesting that *Pf*ATM1 transfers clusters directly only to CIA components. Our findings indicate that *Pf*Nbp35 and *Pf*HCF101 are components of the *P. falciparum* CIA pathway, and *Pf*Nbp35 interacts with *Pf*ATM1 to receive [Fe-S].

Poster P-102

Excluded by Design: Role of Vesicular Trafficking in the Development of Amphotericin B Unresponsiveness in Leishmania-Infected Hosts

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Abstract : Visceral leishmaniasis, caused by *Leishmania donovani(*Ld*)*, continues to pose a major global health burden, especially in India. Antimonial resistance has made Amphotericin B (Amp- B) a principal treatment. However, increasing treatment failure and reduced drug responsiveness threaten its efficacy. Our previous study showed that amastigotes of antimony-resistant(Ld-R), unlike their antimony-sensitive counterparts(Ld-S), accumulate significantly more lipid droplets (LDs) around their parasitophorous vacuoles. This enhanced lipid accumulation not only promotes rapid proliferation of the Ld-R but may increase their tolerance to Amp-B, possibly by reducing local concentration of the lipophilic Amp-B around Ld-R-amastigotes. Scanning electron microscopy revealed increased extracellular-vesicle (EV) release from Ld-R-infected macrophages compared to Ld-S. We hypothesize that Ld-R-induced enhanced lipid accumulation promotes vesicular secretion, facilitating expulsion of sequestered Amp-B and contributing to treatment failure in host. To investigate this, we plan to track intracellular fate of florescent labelled Amp-B using advanced imaging and cell-biology approaches. This study aims to elucidate mechanism of selective Amp-B expulsion from Ld-R-infected macrophages and determine whether sequestration of Amp-B in LDs play a role in its release. These findings may reveal novel strategies to enhance Amp-B efficacy and combat drug resistance not only in VL, but for other infections caused by lipid-auxotrophic pathogens.

Poster P-103

Structural Characterization of *L. donovani* Peroxins Involved in PTS1- Dependent Protein Translocation

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Abstract: Glycosomes are peroxisome-like organelles that host key metabolic processes in kinetoplastids. Their function depends on PEX-mediated import of cytosolic enzymes bearing either a PTS1 or PTS2 signal recognized by PEX5 or PEX7, respectively, through the WxxxY/F motif. The receptor-cargo then interact with the membrane translocon PEX14/13, enabling translocation into the organelle. Here, we investigate the structural basis of PTS1 cargo recognition and translocon assembly in *Leishmania donovani,* focusing on the distinctive mechanism by which *Ld*PEX5 associates with *Ld*PEX14. We cloned, expressed, and purified recombinant *Ld*PEX5, *Ld*PEX14, and selected PTS1-tagged cargo proteins for structural and biochemical characterization. Individually, these constructs are predicted to adopt higher-order assemblies, as reported in homologs. To characterize the reconstituted complex, we performed single-particle cryo-electron microscopy (cryo-EM), followed by a standard image processing pipeline that yielded particle populations suitable for 3D reconstruction and structural analysis, which are currently underway. To resolve individual constructs, complementary X-ray crystallography was employed, with subsequent crystallization trials and optimization of crystal hits. Size-exclusion chromatography and native PAGE indicated an apparent ~150 kDa ternary complex, consistent with a 1:1:1 assembly of *Ld*PEX5, *Ld*PEX14 and cargo, suggesting a stoichiometry distinct from the reported homologous system. These findings would provide initial structural and biochemical insights into the unique organization of the *L. donovani* glycosomal import machinery, aiding the identification of novel molecular targets for therapeutic intervention.

Poster P-104

Understanding the Differences in the Conformational Dynamics of Plasmodial and Human HSP70-HSP110

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Abstract: The human malaria parasite *Plasmodium falciparum* (*Pf)* has a metastable proteome that encodes low-complexity regions which are vulnerable to misfolding and aggregation. It is interesting that despite the environmental fluctuations and immune threats, the parasite is able to maintain its proteome in functional state. Our previous work has shown that parasite has evolved a highly diverged proteostasis machinery which may have given a competitive survival edge to the parasite over human host. The HSP70-HSP110 forms the central node coordinating with the folding and degradation machinery. Using computational approaches (microscale-MD simulation), we have probed conformational dynamics of HSP70 and HSP110 with respect to their human respective human orthologs. Within the conserved NBD domain of HSP70, we observed distinct differences in the dynamics of the subdomains in the ATP and ADP states of human and parasite HSP70, which is also correlating with the limited proteolysis assay and thermal stability curve. Similarly, a comparison of the conformational ensembles of the human and parasite HSP110 proteins in the ATP state revealed that the *Pf* HSP110 protein is more flexible across all domains than its human orthologue. Docking analysis showed that the HSP70–HSP110 NBD interaction interface is partially conserved, 45% Of the interacting residues are the same between the *Pf* and human complexes. This level of conservation hints at a shared

mechanism for how these chaperones interact. Still the residues that are not conserved could be responsible for differences in how the interaction works in each species. Ongoing molecular dynamics simulations will further assess the stability and conformational dynamics of these complexes, providing insight into the conserved and parasite-specific determinants of HSP70–HSP110 interaction.

Poster P-105

Correlation of Human Hormones with Malaria Progression: A Role for Insulin in *Plasmodium falciparum* Growth

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Abstract: Malaria, caused by *Plasmodium falciparum*, begins with an asymptomatic hepatic stage before merozoites invade red blood cells, where cytoadherence and sequestration of infected RBCs drive severe pathology like cerebral malaria (capillary occlusion, seizures, coma), hemolytic anemia and jaundice, blackwater-fever-associated acute kidney injury, and placental sequestration causing miscarriage, low birth weight or preterm delivery. The liver, beyond filtering infected cells and enlarging (hepatosplenomegaly) during infection, is metabolically central and produces insulin-like growth factor-1 (IGF-1). It clears circulating insulin secreted by the pancreas, so hepatic dysfunction during malaria can directly disturb insulin homeostasis and glucose metabolism. This hepatic-insulin disturbance falls within a broader pattern of endocrine imbalance during malaria and is most evident in pregnancy. Pregnancy-associated hormonal shifts and reduced immunity heighten susceptibility to infection, and malaria-induced hypoglycemia (from parasite glucose consumption and antimalarial treatment) is common in pregnant women, worsening maternal anemia, spontaneous abortion, stillbirth, and low birth weight, particularly in sub-Saharan Africa. Since host hormone levels fluctuate with pregnancy, stress, and metabolic disease, we asked whether these hormones directly modulate parasite growth. Synchronized *P. falciparum* cultures were exposed to insulin, thyroid hormone, steroid, estrogen, and progesterone across a wide concentration range and parasitemia was measured after 48 hr. Insulin produced the strongest, most consistent dose-dependent effect, enhancing parasite growth by nearly 40% at the highest concentration, while the other hormones showed modest or non-monotonic responses, several becoming inhibitory at high doses. To determine whether the growth-promoting effect was dependent on biologically active insulin, synchronized *P. falciparum* cultures were treated with heat-inactivated insulin. Heat inactivation abolished the insulin-mediated increase in parasite growth, indicating that the observed effect required biologically active insulin and was not attributable to a nonspecific effect of the insulin preparation. This selective insulin-growth link connects malaria directly to diabetes, a chronic hyperinsulinemic state epidemiologically associated with nearly 46% higher risk of *P. falciparum* infection. Insulin-treated infected RBCs showed elevated intracellular reactive oxygen species (ROS) and altered phosphorylation of membrane-cytoskeleton proteins, linking insulin signalling to oxidative stress and structural remodeling of the host cell.

Poster P-106

Evolutionary Insights into Leishmania Cyclase-Associated Proteins Reveal Conserved Regulators of cAMP Signaling and Candidate Antileishmanial Targets

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Abstract: Cyclic adenosine monophosphate (cAMP) signaling governs essential processes in kinetoplastid parasites, including proliferation, differentiation, stress adaptation, and host survival. Despite its importance, the roles of several cAMP-associated proteins in *Leishmania* remain poorly defined. Cyclase-associated proteins (CAPs) are

evolutionarily conserved regulators that link actin cytoskeletal dynamics to cAMP signaling. Notably, *Leishmania* encodes two CAP homologs, a conventional CAP1 and an atypical CAP2, suggesting possible functional specialisation. In this study, we characterised the evolutionary, structural, and functional features of *Leishmania* CAPs. Phylogenetic and structural analyses revealed that the CAP-C domains of CAP1 and CAP2 represent early-diverging lineages under strong purifying selection, indicating conserved biological relevance. Both genes were expressed throughout the parasite life cycle and across pathogenic *Leishmania* species. Overexpression of CAPs enhanced metacyclogenesis and increased parasite infectivity in macrophages, whereas CAP deletion impaired infectivity, reduced intracellular cAMP levels, and elevated oxidative stress. Together, these findings establish CAPs as key regulators within the *Leishmania* cAMP signaling network, with critical roles in parasite differentiation and infectivity. This work advances our understanding of cAMP signaling in *Leishmania* and identifies CAPs as promising candidates for antileishmanial targeting.

Poster P-107

Sparsely Phosphorylable Residues, Tuned by Agonist Chemotype, Shapes GPCR Signaling

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Abstract: GPCR signaling diversity is often attributed to an intracellular phosphorylation "barcode," in which ligand-dependent modification of multiple receptor phosphoresidues encodes selective engagement of downstream transducers. However, whether such an extensive phosphorylation of the receptor is universally required remains unclear. Here, we show that the melanocortin-4 receptor (MC4R), a central regulator of energy homeostasis, achieves remarkably diverse and pathway-selective signaling through a sparse set of strategically positioned regulatory phosphoresidues. Systematic study of these phosphoresidues within helix 8 and the C-terminal tail revealed distinct, spatially segregated contributions to receptor function. Substitution of helix 8 residues S306 disrupted β-arrestin2 recruitment, early endosomal trafficking, and ERK1/2 activation, while visibly altering Gαs- cAMP signaling in all the receptor variants. In contrast, distal C-terminal substitutions had little effect on β-arrestin2 coupling and trafficking, revealing that these regions are not functionally redundant. Surprisingly, signaling through Gαq/11- and Gα12/13-linked pathways remained largely constrained across receptor variants, further demonstrating pathway-specific control by these phosphoresidues. Notably, ligand chemotype reshaped the functional consequences of these substitutions: setmelanotide selectively restored or enhanced signaling through pathways that were compromised by specific receptor mutations. Together, our findings argue that GPCR signaling diversity does not necessarily require an extensive phosphorylation barcode. Instead, MC4R uses a minimal number of spatially organized phosphoresidue that can differentially control transducer engagement and downstream signaling, while ligand chemistry determines how this regulatory landscape is accessed.

Poster P-108

RAMP-ing Up: Decoding Functional Diversity within RAMP-GPCR Complexes

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Abstract: Receptor Activity-Modifying Proteins (RAMPs) act as accessory subunits of G protein-coupled receptors (GPCRs), shaping receptor trafficking, ligand recognition, pharmacology, and downstream signal transduction. Although their role at a small number of receptors is explored, the breadth of RAMP influence across Class B GPCRs remains largely undefined. We therefore profiled all RAMP isoforms against a panel of eight Class B receptors- CALCRL, CALCR, CRF1, GCGR, GIPR, PTH1, PTH2, and VPAC1- quantifying cAMP accumulation, β-arrestin recruitment, and SRE-based ERK activation. RAMPs did not act as uniform modulators. Each receptor: RAMP pairing

produced a distinct functional signature: cAMP responses were altered in a receptor-specific manner, selected pairings markedly enhanced β-arrestin recruitment, and ERK activation was enhanced, reduced, or unchanged depending on the combination. Notably, a given RAMP could influence pathways unequally at the same receptor, indicating that RAMPs redistribute signaling rather than simply scale it. These findings establish RAMPs as a combinatorial regulatory layer that expands a panel of eight receptors into a substantially larger repertoire of functionally distinct signaling units. Because several of these receptors are established drug targets, Receptor: RAMP- specific signaling profiles offer a mechanistic framework for GPCR functional selectivity and a tractable route to therapeutics that discriminate between receptor populations on the basis of their RAMP partners.

Poster P-109

Deciphering the Structural Determinants of Ca^{2+}-Induced Folding in Calumenin

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Abstract: Ca^{2+} is a classic second messenger that regulates several signaling pathways and cellular processes. Ca^{2+}-binding proteins (CaBPs) tightly regulate the intracellular concentration and spatio-temporal dynamics of Ca^{2+} by sensing, buffering, and relaying the signal. Calumenin is an ER-resident protein that binds to Ca^{2+} through seven EF-hand motifs. Within the endoplasmic reticulum, calumenin interacts with Ca^{2+}-handling proteins, including SERCA and RyR. In addition, calumenin works as a molecular chaperone for several proteins, including CFTR, vimentin, and fibulin. Calumenin exist in an intrinsically disordered state in its Ca^{2+} free (apo) form, undergoes a substantial conformational change upon binding to Ca^{2+}. Interestingly, a single amino acid substitution in the 4^{th}EF-hand (L150G) enables calumenin to adopt a structured conformation in the absence of Ca^{2+}. Given its conformational flexibility, understanding the molecular basis of Ca^{2+} binding and its influence on structure is essential to decipher its functional mechanism. In this study we aim to investigate the intrinsic dynamics of the protein and identify the region involved in Ca^{2+}-sensing. Our biophysical studies shows that the 4^{th} EF-hand has a major role in initiating Ca^{2+} binding. The findings also reveal a possible cross-talk between N-terminal and C-terminal region during $_{Ca}{}^{2+}$ binding.

Poster P-110

Functional Interaction Surfaces of the Bacterial Transcription Terminator Rho are Required for the Interactions with the Elongation Factor NusG

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Abstract: Transcription terminator Rho interacts with the elongation factor NusG to induce efficient termination. By employing random mutagenesis, structure-guided site-directed mutagenesis, and phenotypic re-evaluations of our laboratory mutants, we identified several mutations in the Rho-linker region (~135-155) and the hydrophobic pocket (200-230), in addition to those observed in the CTD region (>250). These mutants exhibited synthetic growth defects and *in vivo* termination defects in the presence of the NusG-CTD mutant G146D, which is defective for Rho binding. Mutants from the Rho-CTD (I382A/N) were the most defective for NusG binding; however, mutants from the linker (E148R) and hydrophobic pocket (P167L) were also significantly impaired. These mutants did not respond properly to NusG in the *in vitro* transcription reactions. Fluorescence quenching assays showed that in presence of NusG, single-cysteine derivatives at 166C (near the linker), 202C (hydrophobic pocket) and at 325C (Rho-CTD) were buried from the surface, whereas that at 80C remained exposed to the solvent. A unique mutation of Rho, H256Y, defined the pathway of Rho-CTD to its NTD conformational changes upon binding to NusG. We propose that NusG-CTD - Rho-CTD induces a conformational change pathway to the latter's NTD to accelerate Rho-close complex formation upon binding to the *rut* sites.

Poster P-111

Understanding the Role of Primary Cilia and its Tubulin Posttranslational Modifications in Regulating Skin Tissue Repair

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Abstract: Microtubules in eukaryotes have functional diversity, which is influenced by the tubulin code, which encompasses various tubulin isotypes and posttranslational modifications on both α- and β-tubulin. Among these, glutamylation and glycylation being highly enriched in axonemes the core microtubule- based structures of cilia and flagella. They play crucial roles in motile cilia but their role in primary cilia and its function in tissue homeostasis and repair is barely understood. We aim to understand how these modifications regulate homeostasis, repair and remodelling using the skin as a model organ as it is a key barrier tissue prone to homeostatic changes and repair post injury that harbors several ciliated cells. Using fibroblasts that overexpress the tubulin glycylase only in the cilia, we have established that perturbing the balance of glycylation in fibroblasts varies polyglutamylation levels, impairs intraflagellar transport, and disrupts signalling receptor localization to primary cilia. Functionally, these cells appear to have disrupted migration in a 2D wounding assay, suggesting that cilia-dependent migration can be impaired upon altered glycylation. We have isolated fibroblasts from mice lacking glycylases and are investigating the effect of loss of tubulin glycylation on levels of glutamylation and intraflagellar transport. The interplay between these modifications and the functional implications of this on regulating homeostasis in vivo is also being investigated in mice knocked out for one or both glycylases. Overall, we provide initial evidences that suggest that glycylation in cilia is tightly balanced and this appears to regulate key molecular processes that regulate structure and function in skin.

Poster P-112

Investigating the Role of Tubulin Glutamylation in Mammalian Primary Cilia

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Abstract: Tubulin glutamylation is a prominent post-translational modification enriched in primary cilia and is recognized as an important regulator of their assembly and function. However, the mechanisms by which defective glutamylation contribute to TTLL5-associated retinal ciliopathies remain poorly understood. To investigate the role of TTLL5, we generated a CRISPR/Cas9-mediated TTLL5 knockout in hTERT RPE-1 cells. Loss of TTLL5 enzyme activity markedly reduced axonemal glutamylation and delayed primary ciliogenesis under conditions of serum starvation. Although prolonged starvation eventually restored cilium formation, newly formed cilia remained hypoglutamylated, while subsequent ciliary elongation proceeded comparably to wildtype cells. These findings suggest that TTLL5-mediated glutamylation is particularly important during early ciliogenesis and is also required for proper intraflagellar transport organization and distribution. Together, our results provide insight into how impaired tubulin glutamylation may contribute to ciliary dysfunction in TTLL5-associated retinal ciliopathies. To extend these findings to a retinal context, we have established a human iPSC-derived RPE model and are currently working toward introducing TTLL5 clinical mutations to examine their effects on ciliary biology and thus RPE maturation. Future studies will further examine altered TTLL5 activity and glutamylation of non-tubulin ciliary substrates, like RPGR protein, to elucidate mechanisms underlying TTLL5 deficiency and disease-associated variants.

Poster P-113

Microtubule Glycylation Fine Tunes Motor and MAP Function, Ciliary Stability and IFT

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Abstract: Primary cilia are essential sensory organelles whose dysfunction leads to a spectrum of disorders collectively termed ciliopathies, including retinal degenerative diseases. Photoreceptor outer segments are highly specialized primary cilia, and disruption of ciliary transport is a well- established cause of progressive retinal degeneration. Emerging functional evidence indicates that loss of TTLL3-mediated tubulin glycylation results in photoreceptor degeneration in adult mice, highlighting glycylation as a critical but understudied regulator of photoreceptor health. Our research investigates how tubulin glycylation governs mammalian primary cilia architecture and transport dynamics, with direct implications for ciliopathies. Using an *in-vitro* biochemical reconstitution system with custom-modified tubulin and purified motors, we demonstrate that glycylation suppresses microtubule-severing and depolymerizing enzymes while differentially modulating kinesin-1 and kinesin-2 motility. These findings establish glycylation as a stabilizing tubulin modification that fine-tunes motor–microtubule interactions—processes fundamental to intraflagellar transport (IFT). To model disease-relevant perturbations, we generated CRISPR/Cas9-mediated TTLL3 knockout and glycylation-elevated RPE1 cell lines. Strikingly, both depletion and excess glycylation disrupt IFT, causing particle accumulation at the ciliary base. Similar defects in fibroblast-derived ciliated cells suggest a conserved mechanism. Our findings provide a mechanistic link between TTLL3 loss, impaired axonemal stability, and ciliary transport failure which might play a key role in the disease progression. By integrating biochemical and cellular disease models, our work positions tubulin glycylation imbalance as a potential molecular trigger in retinal degeneration and broader ciliopathies. Understanding how TTLL3-dependent glycylation safeguards ciliary transport may uncover new therapeutic avenues for cilia-associated retinal disorders.

Poster P-114

Species-specific Difference in Venom Composition of *Trimeresurus erythrurus* and *T. popeiorum* that Result in Difference in Severity of Toxicity in Snake Envenomation

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Abstract: Snakebite remains a major public health problem in tropical regions, particularly in Northeast India, where green pit vipers (*Trimeresurus* spp.) are important yet neglected causes of envenomation. *Trimeresurus erythrurus* and *T. popeiorum* are closely related species that produce distinct clinical manifestations, suggesting species-specific differences in venom composition and toxicity. This study compared the proteomic profiles, biochemical activities, and toxicological effects of venoms from both species to elucidate the molecular basis of their differential pathophysiology. The proteomic analysis revealed marked variation in the abundance of major toxin families. T. erythrurus venom was enriched in thrombin-like snake venom serine proteases, K49 phospholipase A_2 isoforms, and other proteins, compared to *T. popeiorum* venom. These compositional differences were reflected in their biological activities, with *T. erythrurus* exhibiting greater lethality, stronger procoagulant and defibrinogenating activities, more severe myotoxicity, and extensive tissue and organ damage than *T. popeiorum*. Histopathological and biochemical analyses further confirmed species-dependent differences in envenomation severity. These findings demonstrate that species-specific venom composition determines the clinical manifestations and severity of pit viper envenomation and

underscore the need for species-specific therapeutic strategies and improved antivenoms for effective snakebite management in Northeast India.

Poster P-115

Identification of Atg1/ULK1 as a Novel RNA Polymerase II Associated Kinase and Understanding its Role in Regulating Autophagy Mediated Gene Expression

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Abstract: Autophagy is a system of self-degradation and a prevalent element of drug resistance in tumors. ULK1/Atg1 is the only serine/threonine kinase in the core autophagy pathway and represents an excellent drug target. The enzyme plays a significant role in the occurrence and progress of autophagy in various types of cancers. However, direct inhibition of the enzyme has limited success and also drugs that are in use to inhibit autophagy show resistance in breast and other cancers. ULK1/Atg1 has been identified as RNA polymerase II associated kinases during autophagy and it is likely that the enzyme also plays a role in gene expression during autophagy linked cancer. Atg1 can mimic ULKs and its inhibition is likely to provide a comprehensive view of cellular processes and disease mechanisms in cancer. We are using analog-sensitive functional variant of ULK1/Atg1 to facilitate the screening of compound libraries and identification of appropriate inhibitors. The analog-sensitive mutants have been created and the impact of inhibition of ULK1/Atg1 on the underlying molecular mechanisms during autophagy will be assessed by biochemistry, genetics and omics approaches.

Poster P-116

The Identification of Atypical RNA Polymerase II CTD Phosphatases and their Role in mRNA Transcription

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Abstract: The C-terminal domain (CTD) of the largest subunit of RNA polymerase II (RNAPII) comprises of repeated Tyr1Ser2Pro3Thr4Ser5Pro6Ser7 motif, copy number which generally increases with the complexity of the organism. The pioneering studies including genome-wide profiles of RNAPII and its phosphoisoforms showed that CTD undergoes sequential post-translational modifications during the transcription cycle. The dynamic phosphorylation and de-phosphorylation of CTD, plays critical role at every stage of transcription and coordinate the stage-specific association and release of cellular machines. Where the placement of phosphorylation marks in transcription cycle is well explored, the genome-wide engagements of phosphatases that remove these marks are not only poorly understood but remain controversial. We have identified PPH3, a serine/threonine-protein phosphatase to be specifically dephosphorylating Ser2 of CTD. The deletion of PPH3 affects the global CTD phosphorylation. Since the Ser2 phosphorylation mark is present during major part of elongation, and no dedicated phosphatase is known for this process, the identification is very important in terms of understanding the transcription elongation process. The identified phosphatase shall further be looked for its binding partners and effect on the change in global CTD phosphorylation and gene expression analysis.

Poster P-117

Unravelling the Novel Interplay of Ubiquitination in the Regulation of Gene Expression

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Abstract: The essential components of cell survival include the ubiquitin-proteasome system and gene regulation. The carboxy terminal domain (CTD) of the catalytic subunit of RNA Polymerase II is composed of tandem heptad sequences of Tyr1Ser2Pro3Thr4Ser5Pro6Ser7. The dynamic phosphorylation and dephosphorylation of CTD helps coordinate the stage-specific association and release of regulatory proteins, required for mRNA biogenesis and export. We observed overexpression of HECT-E3 ubiquitin ligases due to mutation in the CTD, where cells are also highly sensitive to UV irradiation. Given that the interaction occurs with the stalled RNA Polymerase II during transcription elongation, the possibility of combinatorial phosphorylation of CTD residues cannot be ruled out. In contrast to all previous findings where Ser phosphorylation is desired for the recruitment of proteins, our findings suggest that its dephosphorylation is essential not only for the upregulation and recruitment of HECT E3 ligases but also sets an example where the abnormal expression of an E3 ligase is directly regulated by CTD. Given that both overexpression of E3 ligases and cellular DNA damage are associated with the promotion of cancer cell proliferation, it would be beneficial to identify the associated signature proteins in order to gain valuable insights into the novel gene regulation.

Poster P-118

Molecular Characteristics of Modular-UVR8 Photoreceptors from Green Algae Suggests their Novel Optobiotehnological Applications

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Abstract: UVR8 (UV resistance locus 8) is a photoreceptor responsible for photoprotection, plant-pathogen resistance, photomorphogenesis, plant immunity, disease resistance, and stress adaptation. In its inactive state, canonical UVR8 forms a homodimer; UV-B exposure induces monomerization, allowing activated UVR8 to promote light-mediated physiological responses. This can be achieved either by directly binding to transcription factors (WRKY 36 and MYB77) or through stabilizing them (HYH and HY5), while RUP catalyzes the re-dimerization. Despite the characterisation of UVR8 among green species, the existence of novel modular UVR8 among Chlorophyceae is still unexplored. This study identifies modular UVR8 homologues from Chlorophyceae, which showed conserved UV-B-responsive motifs alongside lineage- specific diversions. Unique UVR8-coupled module structural features may influence intracellular protein- protein interactions and signalling specificity. UVR8 coupled to HETC (catalytic protein) can be used to transfer ubiquitin to the substrate, maintaining protein homeostasis upon functional expression in a suitable host, including mammalian system, simply by UV-B illumination. UVR8-PLC holds potential as a light- controlled DAG/IP3 production and linked to associated signaling pathways. The molecular features, cellular signaling, photodynamic properties, and putative functional output associated with these identified modular-UVR8 photoreceptors, and their optobiotechnological applications, including green biomanufacturing of biomaterials simply by illumination, will be presented in detail.

Poster P-119

Role of Light Signaling Genes in Regulating Root Responses to Elevated Temperature

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Abstract: Climate change is a major challenge for global food production so, it is important to understand how plants adjust their growth and development. Although shoot system responses to elevated temperature are well studied, root responses remain less understood. In Arabidopsis it was shown recently that any increase in ambient temperature beyond the root thermomorphogenesis range (elevated temperature or ET) causes drastic changes in root architecture, including reduced primary root length. In the shoot system, the *phytochrome interacting factors (PIFs*), particularly *PIF4*, play an important role in shoot thermomorphogenesis and responses to rising temperature through auxin. However, its role in root growth under ET remains unclear. Thus, I decided to investigate the involvement of light-signalling PIF family members in root growth regulation under ET and their possible connection with auxin response and root meristem activity. So far my results suggest that many *PIF* gene mutants including single mutants, double mutants and higher order mutants are involved in regulating root growth under ET conditions. Interestingly, it appears that PIF genes involvement in root growth regulation is ET-specific. Furthermore, *pif4pif5* showed reduced sensitivity to exogenous auxin under ET. In conclusion, my results suggest that the PIF family of genes are involved in coordinating root growth responses to ET.

Poster P-120

Deciphering Root Adaptation Under Combined Stress

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Abstract: Plants are constantly exposed to changing environmental conditions, often experiencing multiple stresses simultaneously. Although plants have well-established responses to individual stresses, how different stress-signalling pathways work together to regulate root growth under combined stress is still not fully understood. In this study, we investigate the general stress-response mechanisms involved in root adaptation to combined elevated temperature and water-deficit stress in *Arabidopsis thaliana*. Our initial observations revealed distinct changes in primary-root growth under combined stress, suggesting that multiple signalling pathways contribute to this response. To explore these mechanisms, we are examining key components of Ca^{2+}, ROS and ABA signalling, together with downstream stress-responsive regulators including DREBs and HSFs, using genetic and phenotypic approaches. Analysis of different mutants is being used to identify components that influence root growth under individual and combined stress conditions. We are further exploring the possible interactions between these signalling pathways to understand how environmental stress signals are perceived, integrated and translated into changes in root growth. Overall, this work aims to develop a better understanding of the general stress-signalling network that enables roots to adapt to combined environmental stresses.

Poster P-121

Neuroprotective Action of Nanonized Quercetin against Parkinson's Disease

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Abstract: Quercetin, naturally occurring flavonoid, exhibits neuroprotective role in several neurodegenerative disorders. Nano-form of quercetin (CPQN) was synthesized and found to have more antioxidant potential than free quercetin. Here, neuroprotective role of CPQN against Parkinson's disease (PD), generated in mice by treatment with 'paraquat (PQ)'is reported. Anti-Parkinson efficacy of CPQN on PQ-exposed mice was investigated through

behavioural, biochemical, histological, immunohistochemical and western blot analyses of the mice brain. Behavioural results demonstrate significant protective effect of CPQN (4 mg/kg body weight) treatment on PQ (10 mg/kg body weight)-exposed mice. Biochemical analyses of the change in levels of reduced glutathione, mitochondrial superoxide dismutase and lipid peroxidation in brains of mice by PQ-exposure, get considerably reversed by CPQN treatment. Histological analysis showed deterrence of Lewy body formation in PQ-exposed mice brain by CPQN treatment. Immunohistochemical analysis of alpha-synuclein and tyrosine-hydroxylase, together with western blot analysis of alpha- synuclein depict high anti-PD efficacy of CPQN. Moreover, anti-PD potency of CPQN is higher than that of free quercetin and among pre-, co- and post-treatment of CPQN with respect to PQ exposure, the pr e- treatment condition has the maximum anti-PD efficacy. These findings suggest further accomplishment of pharmacological and clinical studies for establishing CPQN as an effective anti-PD medicine.

Poster P-122

Two Mechanistically Distinct Modes for Body Wide UV Sensing in Headless Planarians at the Interface of Extraocular Photoreception and Nociception

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Abstract: Light is a fundamental cue significantly impacting survival, behaviour and physiology of most organisms. Animals with eyes rely on their eye brain coordination to generate light-influenced behaviours. However, it remains largely unclear how organisms with decentralized nervous systems perceive adjacent wavelengths into distinct sensory modalities. In this study, we dissect the dichotomy of decentralized system (headless planaria) at different level including sensory modalities, molecular pathway, neural subsets and behavioral response. We show, even without brain these organisms can sense distinct wavelength and activate unique sensory system. We demonstrate that headless planarians use two parallel, spectrally tuned extraocular modalities—a novel, noncanonical opsin–Gαq–PLC mediated slower UVA phototransduction and a ROS–TRPA mediated faster UVB nociception. This distinction is translated to behavioural locomotion and neural population. UVA exhibiting default cilia driven gliding mediated via serotonergic neural population, whereas UVB shows muscle driver scrunching response mediated via cholinergic neural subsets. Discovery of novel opsin signalling provides new opportunities for optogenetic tools, while the distinct UVA and UVB responses and processing reveal the evolutionary divergence of extraocular photoreception and nociception. Developmentally, headless hatchlings lack UVA but retain UVB sensitivity revealing a developmentally segregated emergence of opsin-mediated UVA phototaxis and conserved UVB nociception.

Poster P-123

Nobiletin and Tangeretin Ameliorate Tau Acetylation-induced Autophagy and Mitochondrial Dysfunction through the SIRT1 Pathway

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Abstract: Tau undergoes extensive post-translational modifications (PTMs) that alter its physiological function and promote pathological aggregation. Among these modifications, lysine acetylation has emerged as a key regulatory mechanism influencing tau stability, clearance, and propensity to aggregate. Our findings indicate that the site-specific acetylation of tau at lysine 174 (K174) is associated with dysregulation of key autophagic markers, such as Beclin1. Additionally, treatment with NOB (40 μM) and TNG (30 μM) significantly restored autophagic flux and reduced mitochondrial dysfunction. This was evidenced by increased levels of LAMP1 and Beclin1, along with decreased phosphorylation at pSer202/Thr205 (AT8) and acetyl 174 tau. Furthermore, molecular docking and simulation analyses reveal favourable binding interactions between NOB and TNG and SIRT1. These results underscore the crucial role of tau acetylation in regulating neuronal proteostasis and suggest that targeting the SIRT1-tau acetylation axis may offer a promising therapeutic strategy to mitigate tau pathology.

Poster P-124

Peripheral Oxidative DNA Damage, Cell-Death Profiles and Autophagy in Drug-Resistant Temporal Lobe Epilepsy: An Exploratory Cross-Sectional Study

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Abstract: Drug-resistant temporal lobe epilepsy (DR-TLE) is associated with recurrent seizures and may involve systemic oxidative and cellular stress. We compared peripheral oxidative stress, oxidative DNA damage, cell- death profiles, autophagy, mitophagy, cellular-aging measures, and circulating neurodegeneration-associated proteins in 48 adults with temporal lobe epilepsy: 24 antiseizure medication-responsive participants and 24 with DR-TLE. Plasma reactive oxygen species (ROS) and 8-hydroxy-2′-deoxyguanosine were measured by fluorometric assay and ELISA, respectively; neurodegeneration-associated proteins by bead-based multiplex immunoassay; relative telomere length and mitochondrial DNA copy number by quantitative PCR; and apoptosis, autophagy, and mitophagy in peripheral blood mononuclear cells by flow cytometry. At the nominal raw-P level, DR-TLE participants showed higher ROS and 8-hydroxy-2′-deoxyguanosine, shorter relative telomere length, lower total tau, lower early apoptosis, higher late apoptosis, and lower autophagy-positive cells. However, none of 15 between-group biomarker comparisons remained significant after Benjamini-Hochberg false-discovery-rate correction (all adjusted $P \geq 0.071$). These findings are exploratory and hypothesis-generating rather than validated biomarkers or evidence of causal mechanisms. Larger, prospectively powered cohorts are required for independent validation.

Poster P-125

Mechanism of Gating in GABA Transporter 1 (GAT1) at the Neural Synapse

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Abstract: The plasma membrane neurotransmitter transporters GAT1 and GAT3 clear the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) from the synaptic space using sodium and chloride driven electrochemical gradients. Targeting GABA reuptake by inhibiting GATs and thus prolonging GABAergic signalling is a leading strategy to treat disorders arising due to an imbalance in inhibitory neurotransmission, such as epilepsy, anxiety and neurodegenerative disorders. We aim to understand the transport cycle of GAT1 and its modes of inhibition through high-resolution structural studies using cryo- EM. We present the structures of GAT1 from *Rattus norvegicus* captured in two stages of the transport cycle. We trapped the transporter in the cytosol-facing conformation, bound to its substrate GABA, representing a conformation preceding substrate release. We determined the structure of the occluded conformation of rGAT1, an intermediate state in the transport cycle, bound to inhibitor nipecotic acid. We also report the structure of a gating mutant of rGAT1, Q291N, which highlights crucial interactions required for the formation of the extracellular gate of the transporter. Our studies also provide an insight into the chloride dependence of GAT1 through substitutions of chloride coordinating residues. We have additionally designed and validated a series of *de novo* nanobody binders for GAT1 for neuronal imaging studies and for use as a potential fiducial marker in cryo-EM samples.

Poster P-126

Neuroprotective and Neuritogenic Effects of *Albizia julibrissin* Durazz. against Paraquat-induced Neurotoxicity in PC-12 Cells and *Caenorhabditis elegans*

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Abstract: Neurodegenerative disorders (NDs), including cognitive decline, motor dysfunction, and severe disability, result from the degeneration of CNS neurons, with herbicides like paraquat (PQ) contributing to these NDs. The Ayurvedic *Charaka Samhita* describes mixing equal portions of *Albizia julibrissin* Durazz tree fruits, roots, bark, blossoms, and leaves as a powerful remedy; however, this mixture was never tested for antidote efficacy. Therefore, this study investigated the neuroprotective potency and mechanism of *A. julibrissin* against PQ-induced toxicity in PC-12 cells and *Caenorhabditis elegans*. The aqueous extract of *A. julibrissin* promotes neuritogenesis and reduces PQ-induced toxicity in PC-12 cells. In *C. elegans*, it mitigated PQ-induced toxicity by decreasing the production of ROS, mitochondrial membrane depolarization, lipid peroxidation, and chemosensory dysfunction. The extract prevented dopaminergic neuron degeneration and α-synuclein aggregation in transgenic strains of *C. elegans*, associated with Parkinson's disease (PD). qRT-PCR analysis in *C. elegans* revealed that the extract reversed PQ-induced oxidative stress, apoptosis, and neuronal damage by downregulating genes in the pmk-1 downstream pathway. GC-MS and LC-MS/MS profiling identified neuroactive constituents in the extract. Acute oral toxicity evaluation in Swiss albino mice at 2 g/kg revealed no adverse effects, supporting a favourable safety profile. These findings highlight the neuroprotective potential of *A. julibrissin* as a promising natural therapeutic candidate for PD.

Poster P-127

Neuroprotective Potential of *Marsilea minuta* L. against Herbicide-induced Oxidative Stress and Sleep-Regulatory Associated Pathways

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Abstract: The widespread use of pesticides, such as paraquat (PQ), has become a major global health concern associated with neurodegeneration and stress-related sleep disorders (SDs). SDs are among the most prevalent non-motor symptoms of Parkinson's disease (PD). As current therapies primarily provide symptomatic relief and are often accompanied by adverse effects, there is a need for safer and more effective alternatives. The leaves of *Marsilea minuta* L., an edible medicinal plant traditionally used to treat insomnia, anxiety, and mental ailments, have not been investigated for its neuroprotective potential. We investigated the aqueous extract of *Marsilea minuta* L. (AEMM) for its antioxidant, neuroprotective, and sleep-regulatory potential in PQ-induced *Caenorhabditis elegans* models, along with its safety profile. AEMM promoted neuritogenesis in PC-12 cells and significantly attenuated PQ-induced oxidative stress by reducing ROS, nitrite production, mitochondrial depolarization, lipid peroxidation, dopaminergic neurodegeneration, and α-synuclein aggregation. These protective effects improved chemotaxis behaviour,

normalized conserved sleep- and stress-regulatory genes, and enhanced autophagy-related genes in *C. elegans*. Furthermore, findings from the CAM-1 (functional homolog of mammalian TrkA receptor) mutant strain suggest that the neuroprotective activity of AEMM in *C. elegans* is predominantly mediated through the CAM-1 signaling pathway. The AEMM demonstrated preclinical safety via oral routes in rats.

Poster P-128

Investigating the Molecular role of AIMP2 in *Drosophila* Central Nervous System Development

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Abstract: Aminoacyl t-RNA synthetase complex-interacting multifunctional protein 2 (AIMP2) is a non-catalytic scaffold protein in the MSC complex. In eukaryotes, a subunit of nine cytosolic Aminoacyl t-RNA synthetases (ARSs), along with three scaffold proteins AIMP1, AIMP2, and AIMP3, are present in the macromolecular multi t-RNA synthetase (MSC) complex. AIMP2 is the core member of the complex and stabilizes the MSC complex. Pathogenic mutations in MSC complex components have been implicated in various neurological disorders. Recently, a homozygous pathogenic variant (Tyr35Ter) in AIMP2 was identified in two children from unrelated consanguineous families. Clinical features in the children include microcephaly, intellectual disability, and spastic quadriplegia. MRI changes in the patient include atrophy in the cerebrum, cerebellum, and spinal cord. The pathophysiological mechanism of the disease is not well understood yet. We hypothesise that the AIMP2 gene might affect the integrity of the complex. In this study, we are using *Drosophila* as our model organism to study the AIMP2-related disease.

Poster P-129

Structural Determinants of Calcium Potentiation in α7 Nicotinic Acetylcholine Receptors

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Abstract: α7 nAChR is a homopentameric ligand-gated ion channel highly permeable to calcium upon binding of acetylcholine, and has a low affinity for classical agonists like nicotine. Studies show that α7 nAChR is regulated through calcium-binding sites. Acetylcholine (Ach) produced by nerves diffuses rather slowly before reaching its receptor, and is mostly degraded by acetylcholine-esterases. Extracellular and ECD-TMD coupling region binding sites of calcium in α7 nAChR has been identified, that can modulate the activity of the receptor in the perisynaptic space where [Ach] is low. Our MD simulations of α7 nAChR in the presence of calcium also identified calcium binding sites in both extracellular (ECD) and region coupling ECD and transmembrane (TMD) domains (coupling site), suggesting multisite regulation of calcium potentiation of neuronal nicotinic acetylcholine receptors. Calcium screening was performed for WT, ECD mutants, and ECD-TMD mutants using Fluo 4-AM calcium sensors, in the presence of Ach and calcium. Among the ECD residues mutated, D163S showed the highest reduction in calcium flow compared to WT. Among the coupling site mutants, E172Q and E44G showed the highest reduction in calcium flow. We further investigated concentration dependent agonist response of D163, E44 and E172 residues. The investigation showed and all these residues are individually regulating calcium activity. In this research, we aim to understand the receptor kinetics and molecular mechanisms behind α7 nAChR-mediated calcium signaling and its role in neuronal growth, synaptic plasticity, and degeneration in relation to normal and pathological conditions.

Poster P-130

Biochemical, Biophysical and Structural Characterization of NDM-1 from *K. pneumoniae*

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Abstract: New Delhi metallo-β-lactamase-1 (NDM-1) exhibits broad hydrolytic activity towards β-lactam antibiotics. To develop novel NDM-1 inhibitors, the protein was expressed in *E. coli* and purified to > 95% purity. The biochemical enzyme kinetics of NDM-1 were characterized by using nitrocefin as a substrate. The assay is being used for screening of rationally designed inhibitors. Thermal shift assay of NDM-1 showed that zinc binding significantly enhanced its thermal stability. ^{1}H-^{15}N HSQC NMR of apo and zinc-bound NDM-1 showed sharpening of peaks upon zinc binding. NDM-1 crystals were generated using the sitting drop method by screening the Jena Bioscience crystallization screens. Crystals diffracting up to 2.5 Å were obtained and diffraction data was collected at the BRIC-NII X-ray diffraction facility on a Rigaku FR-E + superbright using R-AXIS IV ++ detector. The structure was solved in P1 space group with four protein molecules in the asymmetric unit. Each protein molecule was bound to two zinc ions with Zn1 complexed by His120, His122, His189, and Zn2 complexed by Asp124, Cys208 and His250. The crystallography work is being extended to determine the structures of NDM-1 bound to potential inhibitors to aid in the development of therapeutics that can counter NDM-1 mediated antimicrobial resistance.

Poster P-131

Understanding the role of Fibril and MreBs of *Spiroplasma citri* in shape determination and motility

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Abstract: *Fibril* is a unique species-specific protein of *Spiroplasma* which forms the central component of the cytoskeletal ribbon and believed to be required for force generation. It contains an N-terminal domain (NTD), homologous to MTAN, and a novel C-terminal domain (CTD). MTANs are obligate dimers and none were shown to polymerize. Our phylogenetic analysis shows that the NTD is a non-functional MTAN that is closely related to Mollicutes. Inconsistencies in gene tree-species tree topology and shared gene neighbourhood between canonical MTAN and Fibril collectively support a probable HGT of the Fibril NTD from an unknown mollicute donor. Structural similarity searches combined with structural phylogenetics reveal that the CTD adopts a restriction endonuclease-like fold. Moreover, we improved the purification of Fibril protein from *E. coli* heterologous expression system using sucrose density-gradient ultracentrifugation. Bead-based sonication followed by TEM imaging revealed well-distributed filaments with intact "donut-shaped" morphology and minimal bundling. We show that an interface mutant of Fibril fails to form filaments and remains soluble when co-expressed with MreB5. This protocol gives us a starting point for high resolution structure determination of fibril as well as Fibril-MreB5 complex using Cryo-EM and also provides a framework for studying filament-filament interactions.

Poster **P-132**

Characterisation of a minimal machinery for bacterial cell division

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Abstract: FtsZ, a tubulin homolog, plays a crucial role in bacterial cell division. FtsZ polymerises into filaments that assemble into a Z-ring whose constriction, ultimately leads to cell division. Along with its membrane anchors, FtsZ recruit's machinery for cell wall synthesis, while treadmilling of FtsZ filaments guides the cell wall synthesis process. The GTPase activity of FtsZ determines the rate of FtsZ treadmilling. Investigating a cell-wall less system can provide valuable insights into the role of a minimal components in bacterial cell division. FtsA and SepF are the only two other components in a cell wall-less bacterial divisome. Here we characterise *Spiroplasma melliferum* SepF and investigate its interaction with SmFtsZ using biochemical and structural approaches. We found out that SmSepF enhances the GTPase activity of SmFtsZ, indicating its role in regulating FtsZ dynamics. Furthermore in-vitro reconstitution experiments demonstrate that SmFtsZ and SmSepF together can induce change in membrane curvature. These findings suggest a regulatory role of SmSepF in modulating SmFtsZ dynamics beyond its established function as a FtsZ membrane anchor.

Poster **P-133**

Structural and Functional Insights into the DNA-Binding Function of the Single-stranded DNA-binding Protein from *Pseudomonas aeruginosa*

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Abstract: DNA replication is the process by which a cell duplicates its genome to maintain constant genetic material across generations. During DNA replication, DnaB helicase unwinds the dsDNA, and the SSB protein stabilizes the single-stranded state. While standard prokaryotic SSBs binds ssDNA using all four subunits, *Pseudomonas aeruginosa* SSB (*Pa*SSB) forms a stable homotetramer that binds ssDNA through a unique (SSB)3:1 mode, leaving one subunit unoccupied. This suggests that *Pa*SSB likely adopts a distinct binding mode, possibly due to differences in their C-terminal domains. Thus, our study aims to structurally and biochemically characterize *Pa*SSB. We will explore how the unique properties of *Pa*SSB, particularly its C-terminal domain, influence its interactions with ssDNA, with the goal of shedding light on the molecular mechanisms of DNA replication in *P. aeruginosa*. Our study has shown that the CD thermal profile of *Pa*SSB does not show a canonical two-state unfolding transition rather it shows temperature-dependent conformational rearrangement. However, chemical denaturation profile of *Pa*SSB shows two-state unfolding transition with Cm at 1.50M for urea and 4.36M for guanidinium chloride. Furthermore, salt concentration has minimal effect on secondary structure, but a significant change in the DNA-binding activity was observed. Therefore, *Pa*SSB exhibits temperature- and salt-dependent DNA-binding activity.

Poster **P-134**

Surface-exposed bacterial Lipoproteins: Supramolecular Structural assembly and multipronged activity

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Abstract: Bacterial lipoproteins in the cell envelope are involved in a wide range of vital processes. Surface-exposed lipoproteins mediate interactions with their environment and are accessible to the host immune system. The pathogenic

Leptospira, which causes zoonotic disease, is a spiral-shaped spirochete that produces numerous outer-surface lipoproteins. Their roles in host–pathogen interactions, immune evasion, and virulence are emerging. However, comprehensive identification, structural, and functional investigations of many are still lacking. Our study reports a comprehensive identification of surface-exposed lipoproteins in the *Leptospira interrogans* proteome and the atomic structure of one of them, Leptospiral lipoprotein 41 (LipL41). Proteome analysis revealed 236 predicted lipoproteins containing a conserved lipobox motif. Among those, 69 lipobox-containing proteins were predicted to be localized to the extracellular or outer membrane. These proteins are mostly conserved in pathogenic Leptospiral strains. LipL41 exclusively expressed in pathogenic strains, exhibited DNA cleavage activity. Moreover, it also demonstrated the ability to bind hemin. The cryo-EM structure provided insights into its three-dimensional architecture, molecular organization, and basis of Supramolecular assembly. The structure revealed that 18-mer LipL41 forms a ring-like structure. Our analyses provide an integrated view of *Leptospira* lipoproteins and establish a structural framework for understanding the organization and multipronged activity of LipL41.

Poster P-135

Effect of amino acids on temperature-dependent phase separation of a globular protein

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Abstract: Proteins and bio-macromolecules form condensates within cells through liquid-liquid phase separation (LLPS). The cellular environment contains various amino acids and metabolites whose concentrations are dynamically regulated. Changes in these components might influence protein–protein interactions and consequently LLPS. However, the molecular basis by which amino acids regulate LLPS of proteins is yet to be understood. Here, we investigate the effect of amino acids on the phase separation of a model protein, lysozyme. LLPS was characterised by turbidity and phase diagrams were constructed under different amino acid concentrations, ionic strength, and temperature. Further, changes in surface charge by zeta potential and the morphology of condensates by microscopy were analyzed. We correlate the factors, amino acid concentration, surface charge, ionic strength and temperature on formation and stability of the condensates. These findings can provide a framework for understanding how changes in cellular amino acid levels and temperature could influence protein condensation.

Poster P-136

Domain-Specific Determinants of G-Quadruplex Recognition and Protein Self-Assembly in Nucleolin

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Abstract: Nucleolin (NCL) is a non-ribosomal protein of the nucleolus comprising of three domains: N- terminal domain, a central domain having four RNA recognition motifs (RRMs) which recognize structured nucleic acids such as G-quadruplexes, and a C-terminal (RGG-rich) domain. G-quadruplexes are non- canonical secondary structures formed by guanine-rich DNA or RNA sequences through stacking of guanine tetrads, enriched at telomeres and regulatory regions of the genome. Human telomeric DNA have G-rich repeats (TTAGGG) at the end which is capable of forming DNA G-quadruplexes and transcribing these repeats form telomeric repeat-containing RNA (TERRA), that folds into RNA G-quadruplexes. Although NCL–G4 recognition is primarily mediated by its RRM domains, individual RRMs display distinct binding preferences, with RRM3 and RRM4 showing stronger recognition of RNA G4s. Here, we aim to investigate the domain-specific determinants of NCL–G4 recognition by mutating identified

residues that may contribute to differential binding. In addition to its structured nucleic acid recognition, NCL possesses molecular features commonly associated with proteins that undergo phase separation through multivalent and transient interactions, often mediated by intrinsically disordered regions. However, the domain specific contribution in higher-order assembly remains poorly understood. Taken together, NCL emerges as a multifunctional protein whose modular domain architecture underlies both its selective recognition of G-quadruplex structures and its propensity to undergo self-assembly. Addressing how individual NCL domains regulate nucleic acid binding and phase separation will provide a unified framework for understanding how NCL integrates molecular recognition with emergent biophysical behaviour.

Poster P-137

Biochemical Investigation of PumG, a Key Pyridoxal 5′-Phosphate (PLP)-Dependent Aminotransferase Involved in Pseudouridimycin Biosynthesis

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Abstract: Pyridoxal 5′-phosphate (PLP)-dependent aminotransferases are central to nucleoside antibiotic biosynthesis, introducing amino functionality into ribose-derived intermediates to generate structurally diverse aminonucleosides. However, the molecular basis underlying substrate recognition and catalytic promiscuity of these enzymes remains poorly understood. Here, we present an integrated biochemical, structural, and computational investigation of PumG from *Streptomyces rimosus* (SrPumG), a key aminotransferase in the biosynthesis of pseudouridimycin (PUM), a potent bacterial RNA polymerase inhibitor. In vitro reconstitution, biochemical characterization, spectroscopy, molecular modeling, molecular dynamics simulations, and mutagenesis establish SrPumG as a stable homodimer PLP-dependent enzyme that converts pseudouridine aldehyde (PUA) to amino pseudouridine (APU) using L-arginine as an amino donor. Structural and MD analyses reveal that Lys289 and residues from both protomers coordinate the PLP/PMP cofactor and PUA through electrostatic, hydrogen-bonding, and aromatic interactions. Mutational analysis further identifies residues contributing to dimer-interface stability. Notably, SrPumG displays limited discrimination between C- and N-nucleoside substrates, supporting a gatekeeper role for the upstream oxidoreductase PumI in pathway specificity. Together, these findings define the structural determinants governing SrPumG catalysis and provide a framework for understanding and engineering aminotransferases in nucleoside antibiotic biosynthesis.

Poster P-138

Biochemical characterization of biosynthetic pathway of Arginomycin

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Abstract: The study of enzymes bridges the fields of chemistry and biology, offering profound insights into the catalytic processes that sustain life. Among the natural catalysts, biocatalysts play a crucial role in unraveling the mechanisms underlying various biological transformations. Organic chemistry serves as the foundation for understanding natural products, which have immense significance in drug discovery, agricultural chemistry, and biotechnology. One such intriguing natural product is arginomycin, a rare arginine-derived peptidyl nucleoside isolated from *Streptomyces arginensis* NRRL 15941. Arginomycin comprises a nucleoside moiety linked with a β-methylated arginine residue, a nonproteinogenic amino acid that distinguishes it from other nucleoside antibiotics. It exhibits potent antimicrobial activity against Gram- positive bacteria and fungi while maintaining relatively low toxicity compared to its structural analogs. The biosynthetic pathway of arginomycin involves unique enzymatic tailoring steps, including hydroxylation, methylation, and amidation, which collectively define its structural and functional specificity. We are currently focusing on four enzmes at first that is ArgD,ArgE,ArgM,ArgN which is a

glycosidase, cytosly glucuronic acid synthase, PLP dependent aminotransferase and SAM dependent methyltransferase respectively.Understanding the enzymatic mechanisms underlying its biosynthesis could enable pathway optimization and the design of novel hybrid molecules with enhanced pharmacological properties for biotechnological applications.

Poster P-139

Structural basis of inhibition and activation of K^+:H^+ antiport through YcgO, from *Escherichia coli*

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Abstract: Ionic homeostasis inside a cell control vital processes to maintain homeostasis. Cation:Proton Antiporters(CPA) are central to maintaining cellular ionic balance, as they selectively transport cations in exchange of protons across the cell, yet their regulatory mechanisms remain poorly understood. In this study, we characterize YcgO, a K^+/H^+ antiporter present in *E.coli*. a member of the CPA1 family, and understand how its activity is modulated by the phosphorelay protein PtsN. Using biochemical and mutational analyses, we establish YcgO primarily as a proton-coupled K^+ efflux transporter. Binding assays reveals that unphosphorylated PtsN interacts with YcgO, forming a stable complex via its cytoplasmic domain. Cryo-EM analysis yields high-resolution structures of apo YcgO (3.4 Å) and the YcgO–PtsN complex (3.2 Å), showing both adopt an identical occluded conformation. Unphosphorylated PtsN interacts with the cytosolic RCK and CorC domains and restricts the transport helices of YcgO. A phosho-mimic substitution of PtsN at H73 releases PtsN from interacting with YcgO thereby activating K^+ efflux in YcgO. The study provides an insight into phosphorylation-dependent inhibitory mechanism for activation of K^+ efflux through YcgO and delivers the first integrated structural and mechanistic framework for YcgO regulation through allosteric control within the CPA1 transporter family.

Poster P-140

Mechanistic Studies of Bifunctional AmiM in Amicetin Biosynthesis

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Abstract: Amicetin is a promising disaccharide nucleoside antibiotic exhibiting broad-spectrum antibacterial activity against Gram-positive and Gram-negative bacteria, with notable potency against *Mycobacterium tuberculosis*. It inhibits bacterial protein synthesis by targeting the peptidyl transferase center of the ribosome. Its selective inhibition of prokaryotic translation, low cytotoxicity, and potent antimycobacterial activity make amicetin an attractive lead for antitubercular drug development. Structurally, amicetin contains a characteristic C–N glycosidic bond comprising a cytosine base, disaccharide framework, *p*- aminobenzoic acid (PABA), and α-methylserine. PABA biosynthesis in the amicetin pathway is catalyzed by AmiM, a bifunctional aminodeoxychorismate synthase that uniquely fuses glutamine amidotransferase (PabA) and aminodeoxychorismate synthase (PabB) domains within a single polypeptide. This architecture provides an opportunity to investigate catalytic coordination and interdomain communication during aminodeoxychorismate formation. In this study, AmiM was heterologously expressed and purified for biochemical and mechanistic characterization. Enzymatic activity was evaluated using chorismate and glutamine, with product formation monitored by HPLC and confirmed by LC–MS. Conserved catalytic residues were identified through sequence analysis and investigated using site-directed mutagenesis. Comparative biochemical analysis of wild-type and mutant enzymes provided insights into substrate binding, catalysis, and domain function. These findings advance understanding of AmiM-mediated PABA biosynthesis and provide a foundation for future mechanistic and structural studies.

Poster P-141

A Novel Organosulphur Compound with a Sulfur Linkage Disrupts FtsZ Polymerization and Exhibits Broad-Spectrum Antibacterial Activity

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Abstract: The bacterial cell division protein FtsZ is a known target for antimicrobial development. The PC190723-derived TXA709 has reached phase 1 clinical trials; however, its activity remains limited to *Bacillus subtilis* and *Staphylococcus aureus*. In this study, we combined structural features of PC190723, TXA707, and IP-01 to develop novel organosulphur-based FtsZ inhibitors with broader antibacterial spectrum. Six hundred derivatives were rationally designed and virtually screened, and the top 25 compounds were synthesized. The lead compound demonstrated broad-spectrum bactericidal activity against clinically relevant bacteria, including *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Vibrio cholerae*, with minimum inhibitory concentrations (MICs) of 5–8 μM. Microscopy revealed cell elongation and Z-ring disruption without affecting DNA segregation or membrane disruption, indicating FtsZ as the main target. Surface plasmon resonance confirmed direct FtsZ binding with the compound ($K_d = 5.26 \pm 1$ μM). Sedimentation, light scattering, TEM, and AFM demonstrated inhibition of FtsZ polymerization and filament formation. The compound also inhibited biofilm formation, was largely non-toxic to mammalian cells, and caused negligible hemolysis. Our findings show that rational structural modification can extend the antibacterial spectrum of FtsZ inhibitors, enabling them to target clinically relevant pathogens.

Poster P-142

Structure-Guided Identification and Quantification of Accessible N^6- Methyladenosine Motifs in mRNA Transcripts

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Abstract: Accurate identification of functionally accessible m⁶A sites remains challenging, as sequence based and machine-learning tools often overpredict inaccessible motifs, while transcriptome-wide sequencing approaches require substantial RNA input, specialized infrastructure and high cost. To address these constraints, we developed a lightweight structure- aware computational pipeline, m^6A Functional Index in Transcription (m^6A-FINDIT), that reconstructs full-length transcripts, predicts minimum free-energy secondary structures and calls only DRACH motifs located in unpaired regions. In parallel, we established a simple probe-based enzyme-linked immunosorbent assay, Methylation6A Quantification for Genes (MAQ-G), which uses complementary capture oligonucleotides for sensitive, motif-specific m^6A quantification without the need for next-generation sequencing. Application of these two newly developed methods to selected transcripts, including *IRF8*, *RB1* and *TP53*, identified accessible motifs. Inhibition of the demethylase FTO elevated methylation at the predicted sites and altered transcript abundance. Together, m⁶A-FINDIT and MAQ-G provide a practical biochemical framework that advances the study of post-transcriptional regulation and holds translational potential for investigating RNA modifications in health and disease.

Poster **P-143**

Cryo-EM studies of Entamoeba histolytica translational machinery

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Abstract: *Entamoeba histolytica* causes amoebiasis, characterized by bloody diarrhoea and liver abscesses in humans. Amoebiasis is prevalent in tropical regions with poor sanitation, including India. Protein synthesis is a vital cellular process that occurs on the ribosome in all cells. The ribosome structure of *Entamoeba* has been recently published from our laboratory. However, the translational complexes involved in the process, other than P-tRNA, are yet to be elucidated. Also, the mechanism by which ribonucleases degrade the ribosome remains poorly understood. To examine the various translational complexes, we collected cryo-EM data from the cell lysate of *Entamoeba* trophozoites. Upon data processing, we have identified a ribosomal complex that may be attributed to eukaryotic elongation factor 2 (eEF2). For studying ribosome degradation, we have identified putative ribonucleases from the genome of *E. histolytica*, and three of the ribonucleases- EhRrp42, EhRrp44 and EhT2.2 have been purified on a large scale. The activity of EhRrp42 in degrading the 30S subunit of the ribosome and ribosomal RNAs has been carried out. In the future, we aim to identify additional translation complexes from the lysate and determine a high-resolution cryo-EM structure of the *Entamoeba* ribosome ribonuclease complex to decipher its molecular mechanism of action.

Poster **P-144**

Decoding Rare NAA15 Variants: Structural and Dynamic Insights into NatA Dysfunction

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Abstract: N-terminal acetylation (NTA) is a prevalent co-translational modification regulating protein stability, localization and function. The NatA complex, comprising catalytic *NAA10* and auxiliary *NAA15*, acetylates nascent proteins following initiator methionine removal. Although *NAA15* variants are associated with neurodevelopmental disorders and cardiomyopathies, their impact on NatA function and underlying disease mechanisms remains unclear.This study investigates how *NAA15* variants perturb the structural and dynamic properties of *NAA15,* alter its association with *NAA10*, and potentially disrupt the cellular landscape of NatA-mediated protein acetylation.We integrated structure-based analysis, molecular dynamics simulations and cellular imaging to assess variant induced changes in *NAA15* stability, conformational dynamics and its spatial association with *NAA10*. We also performed proteome-wide analysis of N-terminal motifs and tissue-specific expression to identify protein populations vulnerable to altered NatA activity.*NAA15* variants displayed distinct conformational and dynamic properties versus wildtype, with perturbations in functionally critical regions. Cellular imaging revealed reduced co- localization of selected variants with *NAA10*. Proteome analysis identified >2,000 proteins bearing N- terminal motifs compatible with NatA acetylation, including neuronal and cardiac enriched candidates. Our findings indicate that *NAA15* variants disrupt NatA's structural and cellular organization, providing a molecular link between impaired NTA and disease phenotypes.This work highlights how broad co- translational modification pathways can selectively affect specific cellular proteomes.

Poster **P-145**

Ustilago maydis SWR1 Regulates Bioactive Melanin (UstiMel) Biosynthesis – A Photoprotective Biomaterial for UV-protective Hydrogels

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Abstract: The phytopathogenic fungus *Ustilago maydis,* which causes smut disease in maize plants, can produce an array of bioactive molecules. These molecules are vital for coping with stress and serve defensive and communicative roles, affecting the fungi's survival and infectivity. The production of such molecules is condition-specific, and chromatin remodelers modulate the chromatin landscape to facilitate specific gene expression patterns for their production. Here we studied the role of SWR1, the catalytic subunit of the SWR1 chromatin remodeling complex, in *U. maydis.* Transcriptomic profiling upon disruption of SWR1 highlighted its role as a key transcriptional regulator, whose deletion led to misregulation of numerous transcription factors, impaired stress adaptation, and upregulation of genes in the melanin biosynthetic pathway. With microbes emerging as a sustainable source for the production of bioactive molecules, we explored the ability of *the U. maydis Δswr1* mutant to overproduce melanin (UstiMel) for biomedical applications as a UV filter. UstiMel, characterized with UV–Vis, FTIR, NMR, and mass spectrometry, showed similarity to *Sepia* melanin. UstiMel incorporated in a hydrogel (UstiMela-gel) showed efficient photoprotection against UV irradiation due to its superior free-radical scavenging, antioxidant and UV- shielding properties. Further, the *in vivo* testing in UV-irradiated Sprague Dawley model rats demonstrated reduced erythema, lower epidermal thickening, and diminished inflammatory responses, establishing UstiMel a valuable biomedical product.

Poster P-146

Development of Genetically Encoded Fluorescent Protein based Sensor for S -Adenosyl Methionine

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Abstract: S -Adenosyl Methionine (SAM), is not merely the universal methyl donor for Methyltransferases but also takes part in Polyamine metabolism, Nucleotide biosynthesis, Transsulfuration pathway, Glutathione synthesis etc. SAM is widely synthesized in the cytosol, though there are some reports of local SAM synthesis in nucleus and mitochondria. This spatio-temporal distribution of SAM is of great importance in shaping the Epigenetic landscape. Advanced techniques like NMR and Mass spectrometry require cell lysis where we lose the spatiotemporal information. There are some RNA and Genetic switch-based SAM sensors, however, stable expression and sub-cellular targeting is limited. As genetically encoded Fluorescent Protein based sensors meet these requirements, we have screened five SAM binding proteins cloned between two FRET pairs (mturquoise and cp173venusd). Out of these, MetJ (Methionine repressor of *E. coli*) showed change in FRET upon 5mM SAM addition but a thorough analysis showed that the change was due to drop in pH upon SAM addition and not due to any conformational change. MetJ structure remains almost unaltered except in two loop regions (14 to 20 and 79 to 84) as per the alignment of unliganded and liganded crystal structures already available in PDB. After introduction of circular permutation in the loop regions (cp17MetJ and cp81MetJ), cp17 MetJ FRET protein showed slight increase in FRET ratio in comparison to wild type and cp81MetJ FRET protein in unliganded condition. To probe it further, we introduced a circularly permutated fluorescent protein (cp173venusd) in the loop (14 to 20) of MetJ but this protein also showed comparable decrease in fluorescence intensity as the cp173venusd control upon SAM addition indicating the drop in fluorescence is not due to interaction of SAM with MetJ. The other two proteins dSAMTOR and delN dSAMTOR FRET proteins showed degradation in *E. coli* but remained intact when expressed in HEK293T and we could see slight increase in FRET upon SAM addition. We introduced double mutation in the linker region between NTD and CTD of dSAMTOR as mentioned in literature and could express a comparatively stable protein in *E. coli* and purified the intact protein through Gel filtration Chromatography. In the initial experiment, the purified intact dSAMTOR V66W E67P FRET protein showed a dose dependent decrease upon SAM addition although further studies are required.

Poster P-147

Enzyme kinetics, substrate optimization, and identification of inhibitors of PRSS55

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Abstract: PRSS55 is a testis-specific serine protease essential for sperm motility and male fertility. Native PRSS55 bears a signal sequence, a pre-protease domain (Res. 19-67), a protease domain (Res. 68-300), and a post-protease domain that is cleaved by transamidase with attachment of a GPI anchor at residue S325. For biochemical studies, recombinant PRSS55 (Res. 19-320) bearing an enterokinase activation site was expressed in HEK293T cells as a secretory protein and was purified from the media. The enzyme kinetics of PRSS55 were characterised using the trypsin substrate Boc-QAR-AMC. It exhibited slow enzyme kinetics with K_m = 254.04 μM and max = 43.66 RFU/min. The activity of PRSS55 was inhibited by nafamostat with an IC50 of 0.89 μM. To optimize the substrate of PRSS55, asystematic approach was undertaken. Firstly, twenty dipeptides (Boc-XR-AMC) were screened. Next, twenty-three tripeptides were tested. Tripeptide substrates Boc-DCR-AMC and Boc-DPR-AMC displayed significantly higher catalytic turnover than Boc-QAR-AMC. Further, tetrapeptides based on DCR and DPR tripeptides will be tested to discern the substrate specificity of PRSS55. In a screen of non-covalent serine protease inhibitors, only the Factor Xa inhibitor apixaban inhibited PRSS55 with an IC50 of 7.6 μM. Apixaban SAR is being explored to develop a more potent and selective inhibitor of PRSS55.

Poster P-148

Molecular Characterization of Barnyard Millet Bioactive Peptides Targeting DPP-4 and GLP-1-Associated Metabolic Signalling

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Abstract: Barnyard millet-derived bioactive peptides (mBAPs) were investigated for their potential anti-prediabetic activity through DPP-4 inhibitory and GLP-1-mediated mechanisms. Yeast-assisted fermentation using *Kluyveromyces marxianus* and *Saccharomycopsis fibuligera* was optimised, followed by ultrafiltration, RP-HPLC fractionation, and LC-MS/MS-based peptide profiling. Over 200 unique peptides sequences below 3 kDa were identified, with 42 candidates exhibiting predicted DPP-4 inhibitory potential. Five lead peptides were then selected

through in-silico screening and molecular docking studies. In vitro validation demonstrated cell viability more than 85% up to 60 µM and cell-free DPP-4 inhibitory IC_{50} values of 3.35-15.61 µM for PEP1 to PEP5 respectively. Enzyme kinetic analyses were performed to characterise the mode of DPP-4 inhibition, providing insights into peptide-mediated modulation of enzymatic activity. Molecular dynamics simulation studies supported stable peptide-DPP-4 interactions, while antioxidant assays indicated cytoprotective potential against oxidative stress. GLP-1-related mechanistic investigations incorporated MTT-based viability assessment in NCI-H716 cells, alongside completed GLP-1 receptor docking and molecular dynamics simulations. GLP-1 secretion analysis remains to establish the functional incretin response. This integrated approach provides a mechanistic framework for investigating mBAPs in DPP-4 regulation and GLP-1-associated metabolic signalling, supporting their potential application in prevention and early management of prediabetes.

Poster P-149

Development of Peptide-based Fusion Inhibitors as an Antiviral Strategy

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Abstract: Enveloped viruses transfer their genome into host cells via membrane fusion, making viral fusion an attractive target for developing broad-spectrum antiviral strategies (Purohit et al., 2025; Haldar, 2022). Our current work aims to develop peptide-based fusion inhibitors that prevent membrane fusion by altering membrane properties without directly targeting a specific viral or host protein. This approach would allow the inhibitor to be effective against a broad spectrum of viruses. With this overarching goa l, we have carefully designed tryptophan-aspartic acid (WD)-containing peptides from Coronin 1, a phagosomal protein (Panda et al., 2024; Pandia et al., 2025). Coronin 1 has been implicated in preventing the fusion of phagosomes containing live mycobacteria with lysosomes (Ferrari et al., 1999). Our results show that mTG- 23, a WD peptide from Coronin 1, inhibits Influenza A Virus (IAV) infection in cells. Furthermore, mTG- 21 inhibits influenza hemagglutinin-mediated membrane fusion and viral genome transfer to the nucleus of the IAV-infected cell. Interestingly, mTG-23 also inhibits JEV infection in cells. We surmise that mTG-23 interacts with the viral envelope and cellular membranes, akin to model membranes, and orders the acyl chains (prevents splaying) in a way that stabilizes hemifusion structures and prevents fusion pore formation. We envisage that the proposed antiviral strategy can be extended to other viruses that employ a similar modus operandi, providing a novel pan-antiviral approach.

Poster P-150

Novel synthetic compounds for inhibiting neutrophil extracellular traps for the amelioration of pulmonary fibrosis

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Abstract: Neutrophil extracellular traps (NETs) are decondensed DNA, decorated with granule proteases that traps and kills pathogens and are critical for host defense. However, dysregulated NET formation can damage tissues and prolong inflammation and are linked to pathologies like RA, SLE, ARDS and also mediate interstitial lung diseases like pulmonary fibrosis. NET markers are upregulated in lungs of non-surviving Idiopathic pulmonary fibrosis (IPF) patients and NETs greatly correlates with the disease. FDA approved drugs like pirfenidone and nintedanib slow down fibrosis progression but demonstrate hepatotoxicity. New drug candidates are the need of the hour and targeting NET formation represents an attractive strategy for the management of IPF. PAD4, a deaminating enzyme causes chromatin

decondensation and is indispensable for NET formation. We performed docking studies to identify important PAD4 inhibiting interactions and screened multiple libraries to identify novel candidates. >80 candidates were then screened against recombinant PAD4 and ionomycin stimulated neutrophil extracellular traps to find hits. Lead compounds inhibiting both PAD4 activity and NET formation were further derivatized and SAR analysis was performed. These compounds are likely to provide in-vivo efficacy in bleomycin induced fibrosis mice model. Collectively, this work identifies novel PAD4 inhibitors with potential to ameliorate pulmonary fibrosis.

Poster P-151

Chemical chaperones enhance IgG1 production in CHO-S cultures

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Abstract: Chinese Hamster Ovary (CHO) cells are the predominant host for monoclonal antibody production in the biopharmaceutical industry. Chemical chaperones, small molecules that facilitate protein folding, were explored as potential enhancers of protein secretion. Eight chemical chaperones were individually screened across a range of concentrations for their effect on IgG1 production by CHO-S cells. Positively performing chaperones were subsequently combined and optimized to develop a supplementation strategy for enhanced productivity. The optimized chaperone combination increased absolute IgG1 titre by ~70% and cell-specific productivity by ~90% in shake-flask batch cultures. Product quality assessment, including aggregate content and charge heterogeneity, showed no significant adverse effects on critical quality attributes. Metabolic profiling revealed reduced glucose uptake during the growth phase followed by increased uptake during production, alongside reduced lactate accumulation, suggesting more efficient glucose utilization. PI–Annexin V analysis indicated no detrimental effect on cell viability. Thioflavin T staining suggested reduced protein-folding stress, while endoplasmic reticulum staining indicated expansion of the ER network, consistent with enhanced protein-folding capacity. The optimized supplementation strategy was further evaluated in a conventional fed-batch bioreactor, demonstrating comparable improvements in IgG1 titre. Overall, strategic chemical chaperone supplementation enhanced antibody productivity while maintaining product quality and cellular health.

Poster P-152

Herbal Phyto-therapeutics to Target Malignant Cancer Cells

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Abstract: Shukramatrika bati (SB) is a complex mixture of herbal and functionalized metal preparations. The SEM and DLS analysis indicate presence of irregular nanoparticles. The IR spectrum of SB indicates that the particles are enriched with bioactive compounds. HPLC analysis of SB is giving peaks belonging to polyphenols, alkaloids, tannins. SB is giving anti-cancer activity IC50 from 14.7-26.5µg/ml against series of cancer cells with an excellent therapeutic index. SBAE-treated cancer cells show cell-cycle disruption, with reduced cells in S-phase and increased ROS. Oxidative stress in cancer cells induces apoptosis via the mitochondrial pathway. Cancer cells treated with SBAE and stained with JC-1 show disrupted mitochondrial membrane potential, as evidenced by no accumulation of JC-1 dye aggregates inside the mitochondria. Cytochrome c release results from disruption of mitochondrial membrane potential during apoptosis. Caspase-3 activation leads to downstream events in apoptosis. Cells treated with Shukramatrika show DNA fragments in a characteristic laddering pattern. A cheminformatics approach revealed that 214 protein targets from phytochemicals were present in an extensive network within the cell, with 214 nodes and 402 edges. The cross-talk of protein targets governing different cellular pathways of cancer cells. The KEGG pathway analysis revealed 320 key pathways. Hence, in the current manuscript, we explored the potential of Shukramatrika Bati as a source of anti-cancer agents and the underlying mechanism by which it exerts its therapeutic effect to kill cancer cells.

Poster P-153

Energy and Contact Features Identify Crystal-Like PROTAC-mediated Ternary Complex Models

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Abstract: PROteolysis TArgeting Chimeras (PROTACs) are bivalent molecules that recruit an E3 ligase to the target protein to form a ternary complex. While targeted protein degradation has emerged as a novel therapeutic modality, rational design of proximity inducers is not widely practiced. This is due to the challenges involved in identifying plausible ternary complexes among hundreds of generated decoy models. To address this ranking challenge, we developed a computational pipeline that generates and ranks models of PROTAC-mediated ternary complexes. The ranking is achieved using a combination of energy terms, geometric-based, knowledge-based frameworks and contact features. This method was benchmarked on a set of 39 VHL-based PROTAC-mediated ternary complex structures available in the PDB. For 80% of this set, the best complexes (within 5Å RMSD) identified by our method were ranked among the top 15 models out of several hundred solutions. Furthermore, supervised tree-based ML classifiers were trained using contact and energy features. The classifiers ranked the near-native structural models in the top 10 with a success rate of 75%. By addressing the ranking challenge, our method takes an important step towards prospective structure-guided design of novel VHL-based PROTACs for the degradation of any protein of interest. This pipeline can be extended to other E3 ligases as their ternary complex structural space expands.

Poster P-154

Development of Recombinant Constructs for CRISPR-Cas13 and Cas12 Mediated FGFR2 Fusion genes Targeting

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Abstract: Fibroblast growth factor receptors (FGFRs) are a family of receptor tyrosine kinases that regulate diverse biological events, including cell proliferation, differentiation, migration and survival. Deregulated FGFR signalling plays a vital role in cancer development and progression. Among the genomic aberrations affecting FGFRs, chromosomal rearrangements that generate FGFR fusion genes are of particular interest, as fusion-driven tumours have been shown to respond to targeted therapy. Efficient and accurate identification of such fusions is therefore essential for determining treatment strategies and prognosis. The present study was undertaken to design and develop CRISPR/Cas13d and CRISPR/Cas12a based systems for the targeting and detection of FGFR2 fusion genes. Guide RNA constructs specific to FGFR2 fusion transcripts were designed and cloned for Cas13d mediated oncogenic RNA targeting, with cloning carried out using standard molecular cloning techniques. In parallel, guide RNA primers spanning the FGFR2 fusion region were designed for Cas12a based detection of the fusion genes. The study successfully generated cloned Cas13d gRNA constructs and fusion-specific guide RNA primers for Cas12a mediated detection. Together, these findings demonstrate the feasibility of employing CRISPR based platforms for both therapeutic RNA targeting and molecular diagnostics of FGFR2 fusion genes.

Poster P-155

Deconstructing Viral Immune Evasion: Functional Coupling of SARS-CoV-2 ADPRP with NSP15 and Structure-Guided Inactivation of NSP15 Endoribonuclease Activity

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Abstract: SARS-CoV-2 NSP15 (NendoU) requires tight regulation within the replication-transcription complex (RTC), but its viral regulators remained unknown. Here, we demonstrate that NSP15 activation depends on oligomerization, identifying the hexamer as the catalytically competent state, functional metal ion regulation, and quantitative stability. Furthermore, we identify NSP3 ADP-ribose phosphatase (ADPRP/Mac1) as the first viral protein that directly binds and stimulates NSP15 endoribonuclease activity. Surface plasmon resonance confirmed moderate-affinity binding (KD = 1.59 ± 0.4 µM), which Mn^{2+} significantly enhanced over metal-free conditions. FRET assays demonstrated close molecular proximity, and pull-down assays confirmed stable complex formation (~51% ADPRP retention). Functionally, ADPRP enhanced NSP15-mediated RNA cleavage from 51–52% to 90–98%, with Mn^{2+} further potentiating maximal efficiency. Kinetic analysis showed increased kcat with unchanged Km, indicating enhanced catalytic turnover rather than altered substrate affinity. EMSA and denaturing PAGE verified that ADPRP neither binds nor cleaves RNA, supporting an indirect regulatory mechanism. AlphaFold modeling placed the interaction binding site near the N-terminal oligomerization domain, while Normal Mode Analysis revealed a dominant low-frequency motion reflecting functional conformational flexibility. Finally, molecular docking studies using SYBYL-X v2.1 Surflex-Dock identified three hits validated through molecular dynamics simulation, biophysical, and in vitro studies. Overall, we establish NSP15- ADPRP as a novel regulatory pathway for direct therapeutic exploitation.

Poster P-156

Evolutionary Origins and Structural Sensing Mechanisms Governing Nidoviral RNA Proofreading Fidelity

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Abstract: Large RNA genomes operate under the stringent constraints of Eigen's error threshold, where high mutation rates risk lethal mutagenesis. Coronaviruses uniquely circumvent this barrier by encoding a proofreading exoribonuclease, NSP14. Central to NSP14 are two N-terminal zinc-coordinating motifs whose functional and evolutionary contributions have remained largely obscure beyond presumed structural roles. Here, we identify a previously unrecognized role for these motifs in regulating the viral proofreading machinery activity and provide evidence that NSP14 function is responsive to features of RNA structure. Our findings further reveal that viral proofreading is regulated rather than a constitutive biochemical activity. Using phylogenomic and sequence-homology analyses, we trace the evolutionary ancestry of this viral domain to a host RNA-surveillance protein, challenging models proposing an independent de novo origin within Nidovirales. Our analyses suggest that a conserved host RNA-surveillance architecture was co-opted during viral evolution and subsequently incorporated into the proofreading machinery. Together, these findings uncover an unexpected evolutionary link between host RNA surveillance and viral genome fidelity and provide a framework for understanding how ancestral RNA viruses overcame replication error constraints, facilitating the emergence of complex RNA genomes. The structural and molecular basis underlying these regulatory and evolutionary relationships will be presented.

Poster P-157

Mitochondrial ROS-dependent higher-order assembly of HBx attenuates MAVS-dependent antiviral immunity during HBV infection

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Abstract: Attenuation of antiviral RLR signalling, a characteristic of hepatitis B virus (HBV) infection, underpins the chronicity of HBV. While emerging evidence shows multifaceted importance of mitochondria in the pathophysiology of HBV, whether this organelle influences the virus' ability to attenuate RLR signalling remains unexplored. A publicly available transcriptome dataset was reanalyzed to identify gene-expression programmes associated with different levels of type-III interferon gene expression in HBV-infected patient liver. HBV infection and genome-transfection experiments in hepatoma cell-lines and primary hepatocytes were performed alongside mitochondrial ROS (mROS)-targeted pharmacological interventions. Mechanistic investigations were carried out using sequential co-immunoprecipitation and ubiquitination experiments, along with SDD-AGE and detergent-solubility fractionation. Type-III interferon gene expression signatures were inversely related to mitochondrial gene expression programmes in HBV-infected patient livers. In HBV-infected cells, mitochondrial ROS suppressed the signatures of RLR signalling by primarily destabilizing the mitochondria-localized detergent-insoluble TBK1-MAVS complexes. Mechanistically, mROS potentiated the higher-order assembly of HBx, which facilitated its association with the TBK1-MAVS complexes and contributed to their K48-linked polyubiquitination and proteasomal degradation. Collectively, our findings identify the importance of mROS in suppressing MAVS-mediated innate immunity in presence of HBx, highlighting this mechanism as a potential therapeutic vulnerability in HBV infection.

Poster P-158

Synthesis of Staining Fluorescent Dyes and Quenchers for RT-PCR based Detection kit for Arboviruses

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Abstract: Mosquito-borne viral infections, such as dengue (DENV), Zika (ZIKV), and chikungunya (CHIKV), are major global health concerns. Since these infections often show similar and non-specific symptoms, accurate diagnosis can be challenging. Although real-time RT–PCR is one of the most reliable methods for detecting these viruses. The high cost and limited availability of imported TaqMan probes can restrict large-scale testing. To address this challenge under the "Self-Reliant India" initiative, our research group is developing an efficient and cost-effective method for the in-house preparation of TaqMan-like probes. We are using click chemistry as an alternative to conventional phosphoramidite chemistry, which can simplify probe preparation and reduce costs.We have successfully synthesized commonly used fluorophore dyes and developed a novel class of fluorescence quenchers, including a universal quencher suitable for multiplex detection. Our overall aim is to develop reliable, affordable, and easily accessible fluorophore–quencher probes for the rapid molecular detection of Arboviral infections.

Poster P-159

SARS-CoV-2 pore-dilation stage involves membrane-tension and actin- cytoskeleton activity

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Abstract: SARS-CoV-2 Spike (S) protein-mediated cell–cell fusion is a key determinant of syncytium formation and viral pathogenesis. In this study, we developed a fusion model capturing an intermediate cold-arrested stage (CAS) to investigate temperature as a physicochemical regulator of S-mediated membrane fusion. Fusion was markedly inhibited at 4°C, allowing protein engagement while restricting downstream fusion. Subsequent temperature elevation from CAS to 37°C resulted in enhanced fusion compared with conventional fusion at 37°C, highlighting the role of temperature- dependent molecular dynamics in fusion progression. Using two-color cell-tracker and membrane-dye assays, we further resolved distinct fusion kinetics among SARS-CoV-2 variants. Membrane tension was modulated using osmotic shock to investigate its contribution to fusion-peptide-mediated pore expansion. Application of fusion-inhibitory peptide at CAS-to-37°C transition prevented six-helix bundle (6HB) formation, suggesting that pore expansion stage is preceded by bundle formation. These perturbations revealed variant-specific differences in lateral membrane tension, with Delta S exhibiting enhanced progression toward pore expansion and syncytium formation. Pharmacological modulation of actin dynamics produced concentration-dependent inhibition of fusion for S-variants, demonstrating the contribution of dynamic actin regulation to efficient syncytium formation. Overall, our CAS temperature-shift model identifies lateral membrane tension and actin remodeling as interconnected determinants of variant-specific SARS-CoV-2 fusion.

Poster P-160

SARS-CoV-2-Induced Antibody Responses and Their Cross-Reactivity with Dengue Virus

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Abstract: The COVID-19 pandemic raised concerns about interactions between SARS-CoV-2 and other viral infections, including dengue virus (DENV), particularly whether SARS-CoV-2- induced antibodies influence DENV infection. The SARS-CoV-2 immune response targets multiple viral proteins, antibodies against the receptor-binding domain (RBD) are associated with neutralizing activity, whereas nucleocapsid (N) antibodies are predominantly non-neutralizing and indicative of prior infection. To investigate their heterologous reactivity with DENV, recombinant SARS-CoV-2 N and RBD proteins were expressed in Escherichia coli and Pichia pastoris, respectively, purified, and characterized. BALB/c mice were immunized to generate antigen- specific immune sera. Anti-N and anti-RBD sera were evaluated for reactivity with DENV envelope (E) and envelope domain III (EDIII) proteins by ELISA, and functional activity was assessed using a flow cytometry-based virus neutralization test (FNT). Anti-RBD sera showed very low reactivity toward DENV E proteins, whereas anti-N sera demonstrated detectable reactivity with E proteins from all four DENV serotypes. Both sera showed only basal binding to EDIII. Anti-N sera exhibited moderate neutralization against DENV3, low activity against DENV2 and DENV4, and negligible activity against DENV1, while anti-RBD sera showed limited activity, primarily against DENV3. Overall, anti-N sera demonstrated greater heterologous DENV reactivity and neutralizing activity than anti-RBD sera, highlighting differential cross-reactivity between SARS-CoV-2 antigens and DENV.

Poster P-161

Identification of Novel Inhibitors of JEV RdRp as Potent Antiviral Drugs: Targeting NS5-NS3 Protein Interaction

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Abstract: JEV belongs to the Flavivirus family, where the RdRp domain at the C-terminus of NS5 regulates de novo genome synthesis via a conserved priming loop in thumb domain. Viral replication initiates with interaction between NS5 and NS3, and inhibiting this interaction directly inhibits replication. However, the exact function of the priming loop in the context of the NS5-NS3 interaction was previously unknown. In this study, we analysed the priming loop function in the NS5-NS3 interaction and viral replication. Using a structure-based drug design approach, we screened the Maybridge library against the RdRp priming loop and identified 15 compounds based on binding energy. Among these, DSHS00151 showed significant inhibition of the NS5-NS3 interaction with IC50 of 3.5 μM in the mammalian two-hybrid assay, inhibited viral infectivity with IC50 of 2.54 μM, and reduced viral load with IC50 of 2.9 μM, outperforming CD10712. Molecular Dynamics simulations revealed that DSHS00151 exhibits stronger binding with the priming loop residues (790–812) compared to CD10712. Docking analyses indicated that the priming loop normally rotates towards NS3 to stabilize the complex, whereas compound binding restricts this rotation, compromising stability and replication. These findings validate the priming loop as a functional allosteric site and identify DSHS00151 as a promising non-nucleoside inhibitor for anti-JEV therapeutic development.

Poster P-162

Development of a Recombinant Virus-Like Particle (VLP)-Based Subunit Vaccine Candidate Against Japanese Encephalitis Virus

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Abstract: Japanese encephalitis virus (JEV) is a mosquito-borne flavivirus and an important cause of viral encephalitis in Asia. Although licensed JEV vaccines are available, the continuing disease burden warrants investigating alternative platforms, as well as characterising vaccine-induced cross-reactive antibodies where JEV and dengue virus (DENV) co-circulate. Here, we developed and evaluated a recombinant JEV envelope (E) ectodomain-based vaccine candidate using Pichia pastoris. The JEV E ectodomain (55.8 kDa) was expressed via pPICZA and purified using affinity chromatography. Following stepwise refolding, the protein assembled into ~64 nm virus-like particles (VLPs), confirmed by dynamic light scattering and transmission electron microscopy. Immunisation of BALB/c mice with alum-adjuvanted VLPs elicited favourable JEV E-specific antibody responses in > 90% of animals two weeks post-booster. Pooled day-56 sera demonstrated cross-reactive binding against JEV-E, JEV envelope domain III (EDIII), and E and EDIII proteins across all four DENV serotypes. In flow cytometry-based neutralisation tests, antisera neutralised JEV (FNT50 titre 1:799) and showed cross-neutralising activity against DENV-3 and DENV-4, with minimal neutralisation of DENV-1 and DENV-2. These findings support yeast-derived JEV E particulate assemblies as a vaccine candidate. Further JEV challenge studies and DENV antibody-dependent enhancement (ADE) assays are needed to establish protective efficacy and biological relevance.

Poster **P-163**

A Novel Method to Monitor Viral Fusion

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Absract: Membrane fusion is a crucial, tightly regulated step that allows enveloped viruses to enter host cells and initiate infection, but studying this process in live cells is challenging due to biosafety and cellular complexity. To address these limitations, we developed a method to study influenza and other viral fusion events without using the whole virus. We generated plasma membrane-derived vesicles (PMVs) (Levental et al., 2015) from NIH 3T3 cells stably expressing influenza HA (Hemagglutinin) (Clone 15) (Wilson et al., 2015) to mimic the viral envelope. Human RBCs (Red blood cells) containing sialic acids were then incubated with these HA-PMVs to simulate virus–host binding. In our study, we found some interesting structures. At higher concentrations, RBCs encircled the vesicles and formed rosette-like structures, as reported previously (Long et al. 2006). PMVs from influenza-infected cells showed similar patterns, while uninfected PMVs did not, confirming specificity. This system provides a safe, quantitative platform for monitoring HA-mediated fusion and screening antiviral agents without cellular complexities.

Poster **P-164**

A Novel Indole-Based Inhibitor Targeting the RNA-Dependent RNA Polymerase of Japanese Encephalitis Virus

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Abstract: Japanese encephalitis virus (JEV), a mosquito-borne flavivirus, remains a leading cause of viral encephalitis across Asia, and despite vaccination efforts, breakthrough infections persist with no approved antiviral therapy, current management relying solely on supportive care. The viral RNA-dependent RNA polymerase (RdRp) harbors a conserved prime-loop region (residues 790-812) essential for de novo genome synthesis, offering an attractive, largely unexploited druggable target. Employing a structure-based drug discovery strategy directed at this region, we performed iterative hit-to-lead optimization of an initial screening hit, generating a novel series of indole-based analogs. The optimized indole-based inhibitor exhibited potent anti-JEV activity (IC50 < 1 μM) in a flow cytometry-based infectivity assay in Vero cells, with dose-dependent suppression of viral RNA confirmed by RT-qPCR, alongside a favorable cytotoxicity profile (CC50 > 100 μM), yielding a selectivity index exceeding 100. Pharmacokinetic evaluation further confirmed the compound's suitability for in vivo testing. Together, these findings identify this indole-based scaffold as a promising direct-acting antiviral chemotype, warranting advancement into in vivo efficacy testing in a murine JEV challenge model as a critical next step toward a targeted therapeutic for a disease currently managed only symptomatically.

Poster **P-165**

Translation of a Universal Vaccine Candidate of Influenza to a Viral Vector system; targeting pandemic preparedness

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Abstract: Influenza viruses undergo continuous antigenic shift, drift and reassortment mechanism, limiting the effectiveness of strain-specific seasonal vaccines and highlighting the need for broadly protective influenza vaccines. Hemagglutinin (HA) is a highly dynamic trimeric glycoprotein that undergoes conformational transition between open and close, commonly referred as "HA breathing," which transiently exposes the cryptic conserved epitopes, ideal for universal influenza vaccine candidate development. In this study, we characterized a recombinant HA antigen designed to maintain a native-like transient open-closed trimeric conformation and evaluated its conformational dynamics, immunogenic and protective efficacy. Immunization studies in mice demonstrated that our candidates elicited robust humoral and cellular immune responses. Immunization induced antibodies showed significant hemagglutination inhibition (HAI) titre and serum neutralizing activity against multiple influenza subtypes, including, H1N1, H3N2 and H5N1 indicating broad neutralization potential. Cellular responses lead to efficient upregulation of IFNγ secreting CD8+ T cells. Following viral challenge, immunized animals showed reduced viral load and improved protection compared with control animals. Structural studies further highlight the unique conformational feature of the recombinant HA antigen. Building on these findings, we aim to develop and express the vaccine candidate using a viral vector platform to achieve durable, broad and robust protective immunity, supporting future pandemic preparedness.

Poster P-166

Characterisation of the non-canonical Role of Arp8 in Ribosome Biogenesis: Role beyond chromatin remodeling

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Abstract: Actin-related proteins (Arps) are essential components of chromatin remodelling complexes (CRCs). In yeast, the INO80 CRC utilises its Arp8 module (composed of Arp8, Actin, and Arp4) for linker DNA sensing, DNA binding, and ATPase activities required for histone eviction. Deletion of Arp8 attenuates the overall ATPase activity of the INO80 complex and mimics an INO80 null mutant. Our biophysical characterisation of yArp8 using molecular docking, EMSA, and in *vitro* real-time kinetic assays demonstrated that the 100 kDa yArp8 protein selectively binds 5.8S rRNA through its 75 kDa C- terminal domain (CTD). In contrast, its unique N-terminal domain (NTD) mediates nonspecific interactions with total RNA. Consistent with these RNA-binding characteristics, the co-localisation study of yArp8 suggested its specific compartmentalisation within the nucleolus, a site for ribosome biogenesis. Furthermore, the Arp8 null mutant displays an altered ribosome profile compared to wild-type yeast. To map the molecular network driving this phenotype, we coupled the Arp8 pull-down with liquid chromatography-tandem mass spectrometry (LC-MS/MS). The resulting MS proteomic dataset revealed enrichment for ribosome biogenesis factors co-precipitated by the Arp8 pull-down, suggesting a probable physical link to the pre-ribosomal processing machinery. Collectively, our findings uncover a novel, non-canonical function of yeast Arp8 in ribosome biogenesis, expanding the functional repertoire of Arp family proteins beyond traditional chromatin remodelling.

Poster P-167

Understanding the role of Telomerase-RNP complex in telomere homeostasis in the human malaria parasite

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Abstract: In order to ensure successful rounds of infection, the malaria parasite must maintain its AT -rich genome and its GC-rich telomeres spanning across 14 chromosomes. Amongst the malaria causing species *Plasmodium falciparum,* exhibits an intriguing telomere-telomerase dynamics. It has an unusually large telomerase (TERT, 304 kDa), which is 2.5 times larger than in humans, as well as a structural RNA (2,148 nt.), which is five times larger. While studies have reported the essentiality and expression of *Pf* TERT across both sexual and asexual stages, there are currently no studies on the telomerase-RNP complex or on its non-coding telomerase structural RNA. The RNP comprises a dimeric heterotetramer (GAR1, NOP10, NHP2 and dyskerin) and a monomer (TCAB1). A series of experiments were conducted to determine the expression and cellular partitioning of telomerase-RNP proteins. Using STORM microscopy, we observed distinct perinuclear Pf TERT localisation in the ring, trophozoite, and schizont stages of *P. falciparum*. We also introduced small perturbations like MMS, FCCP, Quercetin, and 17-AAG, and observed reduction in telomere. Our results suggest that the dynamics of the telomerase RNP complex could enable it to perform both canonical and non-canonical functions that aid the survival of intracellular parasites in evolutionarily divergent hosts.

Poster P-168

Characterization of Boronic Acid Derivative B3 as a Lead Antibacterial and Antibiofilm Agent Targeting Gram-Positive Bacteria

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Abstract: Antimicrobial resistance (AMR) is a growing global health concern, with bacterial biofilm formation contributing significantly, leading to treatment failure. ~80% of all chronic infections are caused by biofilm-forming pathogens. Chemicals capable of preventing or disrupting biofilm formation and associated phenotypes may offer a promising approach to addressing AMR. In this study, we screened an array of boronic acid derivatives and identified B3 as an antibacterial and antibiofilm compound active against *B. subtilis* strains at an MIC as low as 0.8 µg/mL. Further, B3 showed antibacterial activity against seven different *Bacillus* species and Gram-positive clinical isolates, including methicillin-resistant *S. aureus, E. faecium,* and *E. faecalis*, with MICs ranging from 12.5 to 50 µg/mL. B3 inhibited biofilm formation in *B. subtilis*, *S. aureus*, and *M. smegmatis*. In *B. subtilis*, B3 treatment downregulated the genes essential for biofilm formation and maturation. B3 also affected EPS production and altered the characteristic wrinkled colony morphology in a concentration-dependent manner. Overall, these results showed that B3 exhibited multifaceted antibacterial and antibiofilm activity affecting bacterial growth, biofilm-associated gene regulation, EPS production, and colony architecture. We present B3 as a lead compound, based on which SAR studies can be done to develop antibacterial and antibiofilm agents.

Poster P-169

Deciphering the Molecular Mechanism of Pt(II) NHC Complex Mediated Growth and Biofilm Inhibition in *Mycobacterium tuberculosis*

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Abstract: Tuberculosis (TB) is one of the major global health concern and Antimicrobial Resistance (AMR) is making it worse. Antimicrobial Resistance (AMR) occurs when microbes develop resistance against antibiotics to which they were once susceptible, contributing to increased morbidity and mortality rates of bacterial infections. Biofilms act as a protective barrier, enhancing tolerance to most antibiotics and host defences. Canonical SOS response regulated by LexA, RecA and non-canonical PafBC pathway contributing to stress tolerance in *Mycobacterium tuberculosis*. Differential expression of certain stress-response genes under the SOS promoter aids rapid adaptation to drugs and biofilm formation. Metals have long been known for their antimicrobial activities and have been shown to treat mycobacterial infections in their unique mode of action. A recently characterized Pt(II) based compound, 'Pt(II) NHC Complex', specifically inhibits Gram-positive bacteria. The MIC and biofilm suppression at nanomolar potency in WT, *ΔrecA*, and *ΔpafBC* strains, indicating its therapeutic potential as an antimycobacterial compound. Based on these preliminary findings, we hypothesize that it may directly interact with DNA to halt *Mycobacterial* growth however, the precise mode of action is yet to be deciphered.

Poster P-170

Volatile ammonia acts as a multicellular infochemical regulating biofilm architecture, territoriality, and cell fate in *Bacillus subtilis*

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Abstract: In bacterial biofilms and structured microbiomes, complex intercellular signalling networks coordinate collective behaviours, regulate spatial territoriality, and respond to microenvironmental dynamics. Canonical quorum sensing relies on aqueous diffusion, whereas volatile infochemicals enable rapid, long- range communication across phase boundaries. Here, we identify volatile ammonia, produced endogenously via urease (UreA)-catalysed nitrogen catabolism, as a master infochemical regulating multicellular development and biofilm architecture in *Bacillus subtilis*. We show the use of multi-well spatial exposure systems and buffered media paradigms to separate ammonia-specific signalling cascades from non-specific alkaline-pH artefacts. Airborne ammonia induces a strong motile-to-sessile transition, with wrinkling of the macrocolony surface, accumulation of pellicle biomass, multicellular chaining, and inhibition of flagellar gene expression. In addition, volatile ammonia gradients induce local cell death, stimulate the production of pulcherrimin, which sequesters iron in a distance-dependent manner, and stimulate

endospore differentiation through the Spo0A and SlrR pathways. Importantly, although 3D structural remodelling is driven by extracellular matrix components (EpsE, TapA) and urease activity, matrix integrity is not required for sibling colony self-recognition and territorial boundary demarcation. Collectively, our results indicate that volatile ammonia is a critical determinant of biofilm morphogenesis, territorial boundaries and developmental cell-fate decisions in surface-associated microbial communities.

Poster P-171

Structural and Biochemical Characterization of *Pseudomonas aeruginosa* DnaB Helicase: Insights into Its Dynamics and Macromolecular Assembly

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Abstract: DNA replication is a fundamental biological process that enables a cell to duplicate its genetic material. Helicase unwinds double stranded DNA into ssDNA during DNA replication. Replicative helicases exhibit profound structural diversity and divergent loading mechanisms across prokaryotic phyla. Among most bacterial species, loading of DnaB helicase on the replication fork site required DnaC or DnaI protein. *Pseudomonas aeruginosa* lacks these loading proteins and instead has DciA which is not an ATPase like *E.coli's* DnaC, thereby follows a distinct loading strategy. The current understanding of the function of *Pa*DnaB helicases is not clear due to a lack of biochemical and structural information about this protein. To understand the domain-specific structure and function, we report the biochemical characterization of *Pa*DnaB, including full-length and various deletion mutants of *Pa*DnaB. Our Cryo- EM structures of *Pa*DnaB reveal distinct 3D conformational states associated with its functional cycle, showing that apo-DnaB is conformationally dynamic and that holo-DnaB can undergo ring opening to facilitate self-loading and accommodate ssDNA within its central chamber.These studies will elucidate the role of DnaB structural dynamics and oligomeric assembly in its biochemical function during DNA replication.

Poster P-172

Investigating the Role of "SOS" Response Regulated VapBC40 Toxin- Antitoxin Module in Stress Tolerance and Survival of *Mycobacterium tuberculosis*

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Abstract: Tuberculosis is an infectious disease caused by a single infectious agent, *Mycobacterium tuberculosis* (Mtb). Due to the high mortality it causes, it was believed to be an incurable disease. After the advent of revolutionary anti-TB drugs such as streptomycin, isoniazid, pyrazinamide, ethambutol and rifampicin, the disease was widely under control. However, due to the widespread and unsupervised use of anti-TB drugs, the emergence of resistant strains led to the treatment of TB very difficult. Several studies have been conducted to comprehend the strategy behind the success of Mtb in the emergence of drug-resistant strains. The major mechanisms adapted by Mtb to promote its survival under unfavouring conditions is the formation of non-replicating persisters. One of the major contributors of this survival strategy is toxin- antitoxin (TA) modules. Mtb encodes a huge repertoire of TA systems that are crucial for bacterial survival, antibiotic resistance, stress tolerance, and persistence. Out of 93 reported TA systems in Mtb, a staggering 50 belong to virulence-associated protein, VapBC family. However, VapBC40 is unique to Mtb as the sole system putatively regulated by the SOS response, though this regulatory link awaits experimental confirmation. "SOS" response refers to the cellular response in the presence of DNA damage which is controlled by two master regulators, LexA (repressor) and RecA(inducer). T*vapBC40* operon harbors a "SOS" box consensus nucleotide sequence in its promoter region, which has been investigated in this study. Functional analyses have shown that deletion of *vapBC40* showed compromised growth towards various stress conditions and drug tolerance,

corroborating with the finding of other TA systems studied so far. Taken together, this study will help us to uncover the role of this unique TA module of Mtb in its survival and pathogenicity.

Poster P-173

Combating Antimicrobial resistance in *Mycobacterium tuberculosis* by employing the "SOS" inhibitor 3-nitrophenyl boronic acid

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Abstract: Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), kills ~1.5 people annually. AMR has worsened the problem, especially in India, the global leader of TB burden. Since Mtb is an intracellular infection, the host immune system and antibiotics constantly impair its DNA and cell. Mtb deploys numerous stress mechanisms to survive in such a hostile environment. The "Save Our Soul (SOS)" stress response system helps Mtb repair DNA and cellular damage. Targeting such pathways could weaken the pathogen's ability to withstand the host's immune system and TB regimen. Based on this notion, we identified 3-nitrophenylboronic acid, a novel inhibitor of the mycobacterial "SOS" response. Our biochemical and cell-based reporter experiments showed that 3nPBA inhibits the "SOS" response by binding to the LexA repressor's autoproteolytic residues (the primary regulator of the "SOS" response). Through a whole-cell transcriptomics approach to explore how 3nPBA affects Mtb's physiology, we found that crucial physiological pathways such as translation and cell division were downregulated. Critical survival pathways of Mtb, such as acidic pH survival, DNA damage response, and "SOS" response, were drastically downregulated, which have been validated orthogonally by qRT-PCR. Finally, 3nPBA exhibited antibacterial efficacy against drug-resistant Mtb strains, suggesting its untapped potential as a therapeutic adjuvant.

Poster P-174

Characterization of YtnP Lactonase as a Quorum-Quenching Enzyme Targeting *Pseudomonas aeruginosa* Virulence

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Abstract: *Pseudomonas aeruginosa* is an opportunistic human pathogen responsible for acute and chronic infections, with multidrug resistance increasing due to extensive antibiotic misuse. This highlights the need for anti-virulence strategies that attenuate bacterial pathogenicity without directly affecting bacterial viability. Quorum sensing (QS), a bacterial communication system regulating virulence, motility, and biofilm formation, is a promising target for controlling *P. aeruginosa* pathogenicity. In this context, quorum quenching (QQ) enzymes have emerged as anti-virulence molecules that disrupt QS by targeting QS signalling molecules, i.e., N-acyl homoserine lactones (AHLs). QQ enzymes are classified as lactonases, acylases, and oxidoreductases. In this study, we heterologously

expressed and purified the *Bacillus subtilis*- derived YtnP lactonase. In silico analysis identified a conserved HXHXDH motif and an αβ/βα fold characteristic of the metallo-β-lactamase superfamily. AHL degradation assays using biosensor strains demonstrated higher activity toward substituted AHLs than unsubstituted AHLs. YtnP exhibited optimum activity at pH 6 and at temperatures of 50–60 °C, and kinetic analysis confirmed its catalytic activity. Moreover, YtnP treatment attenuated biofilm formation and multiple virulence-associated phenotypes of *Pseudomonas aeruginosa*. Collectively, these findings support YtnP as a promising quorum quenching enzyme with potential for anti-virulence applications.

Poster P-175

Functional significance of different putative diguanylate cyclases of *Mycobacterium abscessus*

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Abstract: *Mycobacterium abscessus,* is a rapidly growing mycobacterial species that causes skin and soft tissue infections and severe respiratory infections, particularly in patients with underlying lung diseases. Due to its intrinsic and acquired resistance to multiple antibiotics, *M. abscessus* is an emerging public health concern. Evidences suggest the formation of biofilms by *M. abscessus* in infected lungs. Cyclic diguanylate (c-di-GMP) is a universally conserved bacterial second messenger that regulates critical physiological processes, including biofilm morphogenesis, cell motility, and virulence phenotypes. Intracellular c-di-GMP homeostasis is tightly controlled through the opposing actions of diguanylate cyclases (DGCs)—characterized by canonical GGDEF domains—and phosphodiesterases (PDEs) possessing either EAL or HD-GYP catalytic domains. Although the *Mycobacterium abscessus* genome encodes multiple GGDEF- and EAL-domain-containing proteins, the specific contributions of these enzymes to c-di-GMP turnover and bacterial physiology remain uncharacterized. To address this knowledge gap, we systematically generated gene knockdown (downregulation) mutants targeting four such genes and evaluated their resulting phenotypes. Downregulation of every gene altered core physiological functions, including growth rate, biofilm formation, motility, oxidative stress response, and active efflux activity. The results suggest that all the four GGDEF genes in *M. abscessus* are functional and influence important phenotypes.

Poster P-176

Characterization of GlVps2 and GlVps24 Reveals Possible Unique ESCRT- III Adaptations in *Giardia lamblia*

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Abstract: *Giardia lamblia*, the causative agent of the diarrheal disease giardiasis, acquires nutrients from the host intestine through peripheral vesicles (PVs). These specialized organelles perform both endocytic and endo-lysosomal functions due to the absence of distinct endosomes and lysosomes in *Giardia*. Maintenance of PV architecture is therefore critical for parasite survival. PVs exhibit diverse morphologies, including spherical, tubular, and polymorphic forms, suggesting active membrane remodeling by the ESCRT (Endosomal Sorting Complex Required for Transport) machinery. However, unlike canonical eukaryotic systems, *Giardia* possesses a highly reduced ESCRT complement and lacks Snf7, the principal membrane-deforming ESCRT-III component. This raises the possibility that the remaining ESCRT-III proteins, especially GlVps2 and GlVps24, play expanded roles in membrane organization. We have characterized these two proteins and show that GlVps2 directly interacts with GlVps24. GlVps2 localizes not only to PVs but also to flagellar tips, implicating it in generating membrane curvature required for maintenance of parasitic appendages. In addition, GlVps24 interacts with multiple paralogues of a microtubule motor protein, a feature not reported for other Vps24 orthologues. Together, these findings reveal unique adaptations of the giardial ESCRT machinery that support membrane remodeling, compartment homeostasis, and cytoskeletal coordination in this evolutionarily divergent parasite.

Poster P-177

Mapping the Secretory Effector Repertoire of *Orientia tsutsugamushi*: An Omics-Based Approach to Potential Therapeutic Target Discovery

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Abstract: Scrub typhus, caused by *Orientia tsutsugamushi*, is a neglected tropical disease responsible for significant morbidity and mortality in endemic regions. The absence of effective targeted therapeutics and the limited understanding of pathogen-specific virulence mechanisms continue to challenge disease management. In alignment with the theme of omics-driven innovations for human disease management, our study focuses on identifying key molecular determinants that can serve as potential therapeutic targets in scrub typhus. Through integrative proteome wide analysis of the UT76 strain, we identified 22 high-confidence secretory effector proteins potentially involved in host–pathogen interactions. These include cell wall associated enzymes, magnesium transporters, ubiquinone biosynthesis proteins, and a notable enrichment of conjugal transfer proteins (TraN, TraH) and ankyrin repeat containing proteins. The predominance of ankyrin containing effectors suggests a strategic role in modulating host cellular pathways and immune responses. Importantly, several candidate proteins exhibited significant intrinsically disordered regions, indicating structural adaptability that may enhance host interaction, immune evasion, and intracellular survival. In addition, multiple previously uncharacterized secretory proteins were prioritized, expanding the repertoire of unexplored drug targets in *O. tsutsugamushi*. Collectively, our findings provide a curated effector signature landscape of scrub typhus, offering novel insights into its molecular pathogenesis. This work establishes a foundation for downstream functional validation and rational drug target development, demonstrating how omics-guided strategies can accelerate precision therapeutic approaches in neglected infectious diseases.

Poster P-178

Production, Purification and Characterization of Antimicrobial peptide from *Bifidobacterium breve* NCIM 5671

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Abstract: Antimicrobial peptides are a unique and diverse group of molecules and are potent, and demonstrate broad spectrum. Ribosomally synthesized and post-translationally modified peptides (RiPPs) are a promising source of new antimicrobials in the face of rising antibiotic resistance. *Bifidobacterium breve* NCIM 5671 is a native probiotic bacterium isolated from infant feces and well- studied for its probiotic and functional attributes. Previous studies on this bacteria revealed the presence of class II lasso peptide which seems to have the antimicrobial activity. Lasso peptides are natural products present in bacteria. They belong to a specific family of ribosomal-synthesized and post translationally modified peptides with a unique lasso structure. These peptides have robust thermal and proteolytic stability and various biological activities. They have promising potential therapeutic effects on gastrointestinal diseases, tuberculosis, and are highly stable. The peptide was purified from cellular extracts by RP-HPLC, with a major peak detected at a retention time of approximately 11 min. The corresponding fraction showed thermostable activity, and its identity was confirmed by LC-MS. However, the peptide yield from the native source was low (approximately 0.2 mg/L), restricting further characterization. So, the peptide-encoding genes were cloned into the pRSF-Duet vector for heterologous expression, followed by purification of the recombinant product using RP-HPLC.

Poster **P-179**

Targeting Hydrogen Sulfide-Producing Enzymes to Combat Antimicrobial Resistance in *Enterococcus faecalis*

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Abstract: Antimicrobial resistance (AMR) is a major global health challenge, highlighting the need for novel therapeutic targets. Endogenously produced hydrogen sulfide (H_2S) contributes to bacterial defense against oxidative and antibiotic stress, making H_2S-producing enzymes promising targets for antimicrobial intervention. In this study, H_2S-producing enzymes from *Enterococcus faecalis* were investigated for their potential as therapeutic targets. O-acetylserine sulfhydrylase (EfOASS) was overexpressed, purified, and biochemically characterized. Size-exclusion chromatography suggested that EfOASS exists as a homodimer. Kinetic analysis yielded a Km of 43.43 ± 9.26 μM and Vmax of 1.289 ± 0.103 μM/min. The previously reported OASS inhibitor F3226-1387 inhibited EfOASS with an IC_{50} of 50 μM and demonstrated dose-dependent growth inhibition against both wild-type and resistant *E. faecalis* strains. Preliminary antibiotic combination studies were also performed. These findings highlight H_2S -producing enzymes as potential targets for developing alternative strategies to combat AMR in *E. faecalis*.

Poster **P-180**

Molecular and Immunoinformatic Characterization of the *Mycobacterium tuberculosis* ESX-1 Secretory Protein EspE (Rv3864): Implications for Host-Directed Interventions in Tuberculosis

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Abstract:

Background: Tuberculosis remains the leading cause of death from a single infectious agent, underscoring the need for host-directed therapies. The ESX-1 type VII secretion system encodes virulence factors critical for immune evasion and phagosomal rupture, representing a promising therapeutic target. Among its components, EspE (Rv3864) is notable for its dual role in transcriptional regulation and membranolytic activity, warranting further characterization.

Methods: EspE was computationally evaluated for physicochemical stability, virulence potential, and antigenicity, with B-cell and T-cell (MHC-I/MHC-II) epitope prediction identifying HLA alleles with high binding affinity. The codon-optimized *EspE* gene was cloned into pET28a (+), transformed into *E. coli* DH5α, and expressed in BL21(DE3), Rosetta, and Rosetta (DE3) pLysS strains. Recombinant protein was purified via Ni-NTA affinity chromatography, and THP-1 macrophages were stimulated with purified EspE to assess cytokine production and inflammatory marker expression.

Results: In silico analysis confirmed the structural stability and virulence potential of EspE protein with strong predicted binding to HLA-B*53:01, HLA-DRB1*15:01, and HLA-DRB5*01:01, indicating substantial immunogenicity. Expression optimization among different expression strains, induction temperatures, and IPTG concentrations identified 37˚C with 0.1mM IPTG as the optimal condition for EspE overexpression. Recombinant EspE significantly altered the macrophage cytokine and inflammatory marker profiles.

Conclusion: EspE was successfully cloned, expressed, and purified, with immunoinformatic analyses supporting its antigenicity and capacity to modulate macrophage innate responses, positioning it as a promising target for host-directed tuberculosis interventions.

Poster P-181

Identification and Characterization of Potential Druggable Targets of *Mycobacterium tuberculosis*

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Abstract: Tuberculosis is a recurrent and progressive bacterial disease caused by *Mycobacterium tuberculosis* posing a significant challenge globally due to its antimicrobial drug resistance, makes the treatment critically challenging. To combat the prevailing situation, it is important to explore new anti- TB drugs which target essential bacterial pathways. In this study, FDA – approved drugs were virtually screened against Rv3644c and RV3441c to identify potential inhibitors. For both gene, selected drugs showed high molecular docking scores. Further, molecular dynamics simulations analysis of protein complex reported stable interactions. The anti – TB activity of drugs was further evaluated under in vitro and ex vivo condition. In vitro analysis revealed that the selected drugs had MIC value of 3.15 ug/ml , 25 ug/ml and 2.5 ug/ml , whereas cell cytotoxicity evaluation on THP1 cells revealed no toxicity even at higher concentration demonstrating excellent biocompatibility. This preliminary data suggests potential antimycobacterial activity of selected drugs targeting these essential gene in Mtb.

Poster P-182

Design and Evaluation of a Novel Antimicrobial Peptide against WHO Priority Pathogens

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Abstract: Antimicrobial resistance (AMR) is one of the growing global health crises, severely compromising the effectiveness of conventional antibiotics, which leads to extended illness, higher mortality, and higher healthcare expenses. The emergence of multidrug-resistant pathogens has intensified the demand for alternative strategies that can bypass classical resistance mechanisms. In this regard, antimicrobial peptides (AMPs) have attracted researchers in recent years because of their effectiveness as a first line of defense against multidrug-resistant pathogens. Antimicrobial peptides are considered potential novel biopharmaceutical agents against AMR. In this regard, antimicrobial peptides (AMPs) have attracted researchers in recent years because of their effectiveness as a first line of defence against multidrug-resistant pathogens. In this study, we found that the antimicrobial peptides GLL-1 and GLL-2 exhibited strong antimicrobial activity against *K. pneumoniae* ATCC 27736, *E.coli* ATCC 25922, *S. aureus* ATCC 29213, and their clinical isolates (Minimum Inhibitory Concentrations of 3.13–12.5 μM/ml). In addition, these peptides were stable in salt and 20% citrate plasma, showed low toxicity toward mammalian cell lines, and caused minimal hemolysis of RBCs. The secondary structure and membrane-damaging potential of peptides were evaluated using circular dichroism and scanning electron microscopy, respectively. In addition, the peptides showed promising in vivo activity in a lung infection model.

Poster P-183

A novel gene from Marine bacteria *Bhargavaea indica* encoding imipenem specific degrading enzyme: A Potential Threat to Antibiotic Therapy

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Abstract: Marine bacteria can survive harsh, unstable, high-salinity, and extreme environments largely because of their highly adaptable, plastic genomes. Microbial genomes often contain cryptic or silent genes; however, their role in the evolution of antimicrobial resistance remains poorly understood. Metallo-β-lactamases (MBLs) are zinc-dependent enzymes that hydrolyse a broad range of β-lactam antibiotics, including carbapenems. Although clinically important MBLs have been extensively characterised, MBLs from environmental and marine sources remain comparatively unexplored. In this study, we identified and characterised a metallo-β-lactamase gene, designated *Bi*MBL244, from the marine-derived bacterium *Bhargavaea indica* isolated from the Gulf of Mannar, India. In silico, *in vitro*, and *in vivo* analyses were carried out to investigate its structural and functional characteristics. Sequence and structural analyses revealed the characteristic H-X-H-X-D-H metal-binding motif and an MBL-like fold, supporting the classification of BiMBL244 as a B3 subclass MBL. Recombinant *Bi*MBL244 exhibited metal-dependent β-lactamase activity and efficiently hydrolysed imipenem and the chromogenic β-lactamase substrate nitrocefin. These findings show that the *Bi*MBL244 gene of *B. indica* encodes a functional MBL capable of imipenem hydrolysis, highlighting marine bacteria as potential reservoirs of β-lactamase diversity and giving insights into the environmental significance of B3 MBLs.

Poster P-184

Linkage between an activated Cpx response and potassium metabolism in *E. coli*

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Abstract: The Cpx pathway in *E. coli* comprises the sensor kinase CpxA, the response regulator CpxR and the CpxA negative regulator CpxP. The inducible Cpx system constitutes one of the five envelope stress response systems that maintain envelope integrity and homeostasis. In this study we report an unexpected linkage between an activated Cpx response and potassium (K^+) metabolism. We report the identification and characterization of transpositions in *cpxA* (*cpxA** alleles) that lead to elevated expression of member genes of the Cpx regulon. CpxA* mediated Cpx activation is dependent of CpxR and acetyl phosphate whereas that mediated by wild type CpxA is dependent on CpxR. Activation by CpxA* or by a natural Cpx inducing signal, leads to impaired growth in media with high external K^+ concentration, that paradoxically is associated with K^+ limitation. CpxA* mediated K^+ limitation is alleviated by elevated cytoplasmic K^+uptake. To elucidate the underlying mechanism of this metabolic constraint, an analysis of its genetic suppressors is presented. Overall, these studies are compatible with a physiological scenario wherein adaptation to envelope stress via the Cpx system may induce K^+ limited bacteriostasis as a survival mechanism to tolerate cell envelope damage.

Poster P-185

Modulating Motility and Biofilm Dynamics in *Bacillus subtilis* via Tetrahydrofuran (THF) Exposure

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Abstract: Tetrahydrofuran (THF) is a pervasive industrial solvent and environmental pollutant[1], making the study of its impact on biofilm behaviour critical for understanding microbial stress adaptation and bioremediation in contaminated ecosystems. The transition between sessile biofilm formation and flagellar-driven motile lifestyles is a critical adaptive mechanism in bacteria[2,3,4]. Here, we investigated how sub-inhibitory THF exposure modulates the surface motility and biofilm dynamics of *Bacillus subtilis* IITKSM1. Supplementation of THF (0.01%–0.04%) significantly accelerated surface spreading and swarming kinetics in wild-type (WT) strains on LB agar. Microscopic examination of the colony margin revealed pronounced cellular dispersal and altered boundary architecture upon THF treatment compared to untreated controls. To identify the genetic pathways mediating this phenotype, deletion mutants associated with extracellular matrix formation (Δ*epsE*, Δ*tapA*) and motility/surfactant synthesis (Δ*sigD*, Δ*srfAC*) were evaluated. While matrix-deficient mutants (Δ*epsE*, Δ*tapA*) retained THF-stimulated spreading, the enhanced motility was completely abolished in *sigD* and *srfAC* mutants. These results demonstrate that THF-mediated surface colonisation and biofilm dispersal strictly rely on functional flagellar machinery and surfactin biosynthesis. This study provides fundamental insights into xenobiotic-driven biofilm remodelling and bacterial survival strategies under chemical stress.

Poster P-186

Structural and Mechanistic Insights into Transcription Regulation of Motility and Biofilm Genes by SbrI and SbrR in *Pseudomonas aeruginosa*

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Abstract: *Pseudomonas aeruginosa* is a rod-shaped gram-negative bacterium which causes nosocomial infections in patients in ICU, and with open wounds and burns. Its ability to transition between motile and sessile lifestyles is crucial for host colonization, biofilm formation, and persistence during infection. This transition from motile to sessile form is regulated at the level of transcription where extracytoplasmic sigma factor (ECF) play a central role. They enable RNA polymerase (RNAP) to recognize distinct promoter classes in response to environmental cues. The SbrI–SbrR pair, comprising an ECF sigma factor SbrI and its cognate anti-sigma factor SbrR, has been implicated in the regulation of swarming motility and biofilm-associated processes in P. aeruginosa. However, the molecular basis underlying SbrR-mediated inhibition of SbrI and SbrI-dependent transcription remains poorly understood. We aim to elucidate the structural and mechanistic basis of SbrIR-mediated transcriptional regulation. For that, we aim to determine the high-resolution structure of the SbrI–SbrR complex to define the interaction interface and identify the molecular determinants responsible for anti-sigma activity. In the present study, the complex of sigma factor SbrI and anti-sigma factor SbrR is cloned, overexpressed and purified to homogeneity and crystallized in 0.1M citrate pH 6.0, 25% v/v PEG smear medium.

Poster P-187

Molecular studies on cell division regulatory proteins MinC and MinD in a coccus-shaped bacterium *Deinococcus radiodurans*

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Abstract: In bacterial cells, division is achieved through the coordinated action of the divisome, a multiprotein complex that synthesizes the new cell wall at the division plane. This process is precisely controlled by the MinCDE and Nucleoid Occlusion systems in rod-shaped bacteria. However, spatial regulation of division plane positioning remains less understood in cocci, which lack inherent polarity. *Deinococcus radiodurans* is a spherical, multipartite bacterium renowned for extreme stress resistance, whose genome encodes MinC, MinD, and DivIVA—the functional replacement for MinE in some Gram-positive species. Here, we investigated the physiological roles and spatiotemporal dynamics of the *D. radiodurans* Min system. For these studies, we constructed *ΔminC* and *ΔminD* knockout strains and fluorescently tagged protein-expressing strains. Our results from microscopic and cell survival studies revealed that the mutant cells showed abnormal cellular morphologies and sensitivity to various DNA-damaging agents compared to wild-type cells. In *ΔminC* cells, the FtsZ-GFP ring formation was also affected. Further, the time-lapse microscopic studies revealed that MinD-GFP shows an oscillatory pattern in this coccus bacterium and MinC-GFP localizes to cellular membranes. Together, these findings demonstrate that precise Min system regulation is essential for correct septal placement, morphology maintenance, and cellular survival under environmental stress in *D. radiodurans*.

Poster P-188

Multi-level Characterization of Vitiligo-Derived Lymphoblastoid Cell Lines: Cellular Phenotype, Doxorubicin Response and DNA Repair Gene Expression

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Abstract:

Introduction: Vitiligo is a systemic idiopathic autoimmune skin depigmentation disorder often associated with exaggerated oxidative stress. Patient-derived lymphoblastoid cell lines (LCLs) provide a sustainable and personalized model to study oxidative stress in vitiligo.

Method: Twelve novel LCLs derived from vitiligo patients (n=6) and healthy controls (n=6) were generated from peripheral blood lymphocytes and extensively characterized for cell surface markers and ploidy. Functional response to genotoxic stress was tested by MTT assay. Expression analysis of DNA repair genes and proteins was analyzed by qRT-PCR and western blotting. Drug-response data were analysed using two-way ANOVA.

Result: LCLs showed typical rosette morphology on phase-contrast microscopy. Flow cytometric analysis confirmed B-lymphoid phenotype, with 97% cells positive for $CD45^{+}CD56^{-}$ and 92% for $CD3^{-}CD19^{+}$ in the LCLs. DNA content analysis revealed diploid status and the genotype matched the genomic DNA from blood for each LCL. Doxorubicin treatment produced dose-dependent reduction in viability demonstrating inter-individual variation among LCLs. The LCLs showed RNA and protein expression of XRCC1, PARP1 and TP53.

Conclusion: The novel vitiligo LCLs will serve as a useful model to investigate oxidative stress induced mechanisms in vitiligo.

Poster **P-189**

Systematic epigenetic screening identifies PRMT1 as a regulator of *TNF-α* transcription and a therapeutic target in Acute Lung Injury

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Abstract: TNF-α is a central driver of pathological inflammation and a clinically validated therapeutic target. Although TNF-α-neutralizing biologics are widely used, small-molecule strategies that directly suppress *TNF-α* production at the transcriptional level remain limited. We therefore used pharmacological epigenetic screening to uncover the chromatin-regulatory mechanisms controlling inflammation-induced *TNF-α* transcription and identify key epigenetic targets for suppressing inflammatory responses. Screening 152 epigenetic inhibitors in LPS-stimulated THP-1 macrophages identified 20 compounds spanning six regulatory classes including HATs, bromodomain proteins, HDACs, histone demethylases, PRMT1, and PLK1indicating that multiple distinct epigenetic regulators converge on inflammatory *TNF-α* expression. Selected inhibitors also suppressed broader inflammatory cytokine responses and NF-κB activity. Among these, the PRMT1 inhibitor TC-E 5003 was prioritized for mechanistic and *in vivo* validation. PRMT1 inhibition reduced inflammatory mediators and oxidative stress in RAW 264.7 macrophages and decreased PRMT1, NF-κB p65, and p300 occupancy at the *Tnf* promoter, together with H4R3me2a, H3K27ac, and H4K8ac. In LPS-induced murine acute lung injury, PRMT1 inhibition attenuated inflammatory infiltration, cytokine burden, oxidative stress, mucin accumulation, and NF-κB/p38 MAPK activation while preserving lung architecture. Collectively, these findings identify PRMT1 as a key epigenetic regulator of inflammatory transcription and support transcriptional targeting of TNF-α as a potential small-molecule strategy for acute inflammatory lung injury.

Poster **P-190**

Ensemble Machine Learning and Graph Neural Network-based Virtual Screening Pipeline for the Discovery of Novel MMP-12 Inhibitors for Cardiovascular Diseases

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Abstract: Matrix metalloproteinase-12 (MMP-12) has emerged as a critical therapeutic target for cardiovascular diseases, including atherosclerosis and abdominal aortic aneurysm. We present an integrated computational framework combining ligand-based and structure-based approaches for MMP-12 inhibitor discovery. Machine learning (ML) and deep learning models were developed, featuring a Graph Isomorphism Network with Edge features (GINE), a Graph Neural Network architecture achieving exceptional predictive performance (GNN: 0.997) alongside Random Forest (RF: 0.998), Support Vector Machine (SVM: 0.999), and k-Nearest Neighbors (kNN: 0.995). The validated predictive models screened the Maybridge chemical library to prioritize promising hits, which were subsequently subjected to molecular docking against MMP-12. Top-ranked docked complexes underwent all-atom 100 ns molecular dynamics simulations to evaluate structural stability and binding interactions, followed by MM-PBSA calculations to quantify binding free energies. Additionally, comprehensive scaffold decomposition demonstrated high chemical diversity, prioritizing novel scaffolds with distinct chemotypes. Furthermore, applicability domain assessment confirmed that 95% of predictions fall within reliable chemical space. This hierarchical workflow combining GNN and machine learning prioritization, molecular docking, molecular dynamics, and MM-PBSA validation provides a robust platform for cardiovascular drug discovery, identifying novel MMP-12 inhibitor scaffolds with strong binding affinities as promising leads for further experimental optimization.

Poster **P-191**

Molecular Basis of CMTX1: Atomistic Simulations Reveal Divergent Gating Dysregulation in Cx32 Mutants

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Abstract: Charcot-Marie-Tooth disease X-linked 1 (CMTX1) is an inherited peripheral neuropathy caused by point mutations in the Connexin32 (Cx32) hexameric hemichannel. Due to the complex dynamics of Cx32, the domain-specific impact of various mutations remains poorly understood and the associated fast and slow gating transitions. We investigated pre-gating dynamics using 100 ns membrane-bound atomistic molecular dynamics simulations of a trRosetta-modeled Cx32 wild- type (WT) and five distinct mutants: M34T, A39V, I127F, R142Q, and D178Y. Our structural and energetic analyses reveal that all mutations disrupt vital hexameric cooperativity and allostery, lipid occupancy, forcing channels into asymmetric functional states distinct from the WT. Transmembrane (TM1) mutations restrict motion: M34T disrupts N-terminal voltage-sensing contacts to create a highly rigid structure with altered permeability, while A39V introduces a valine-rich hydrophobic stretch that disrupts helix flexibility and proper membrane positioning. The novel cytoplasmic loop mutation I127F paralyzes loop mobility, severely constraining overall channel dynamics. The TM3 mutation R142Q destroys critical inner-pore stabilizing anchors, driving staggered protomer motions often associated with sensorineural deafness. Conversely, the EL2 mutation D178Y obliterates critical inter-protomer extracellular networks responsible for calcium sensing, stabilizing a highly dynamic and pathologically leaky conformation. Ultimately, these distinct structural divergences converge on a single conformational pathway of symmetry breaking.

Poster P-192

Integrated structure-based and ensemble machine learning framework for identification and validation of novel scaffolds against PARP1 in Triple Negative Breast Cancer

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Abstract: Triple-negative breast cancer (TNBC) lacks estrogen receptor, progesterone receptor, and HER2 expression, which leaves patients with few targeted therapeutic options. Poly(ADP-ribose) polymerase 1 (PARP1) is a clinically validated target in this setting, yet there is still a need for structurally novel inhibitors with improved potency. In this study, we combined machine learning-based ligand screening with structure- guided computational validation to discover new PARP1-directed chemotypes. Classification models were trained on a curated set of 4,103 labelled active and inactive PARP1 compounds, using several complementary fingerprint encodings. The best-performing models were merged through a consensus voting scheme spanning the different fingerprint types, and this ensemble was used to screen a commercial small-molecule library. The compounds selected by consensus were then filtered through molecular docking, molecular dynamics simulations, MM/PBSA binding free-energy estimation, and in silico ADME assessment. This workflow narrowed the pool to 30 structurally diverse hits, of which 13 displayed stable binding behaviour and favourable energetics. Biochemical testing of a subset of these hits confirmed PARP1 inhibition: one compound achieved roughly 70% inhibition at 10 μM, and four others showed moderate inhibitory activity. Together, these results show that pairing ensemble ligand-based prediction with structure-based evaluation is an effective route to identifying diverse PARP1 inhibitor scaffolds worthy of further development for TNBC.

Poster **P-193**

From Molecular Features to Experimental Validation: An Integrated Machine Learning and Structure-Based Approach for Identification of Novel PPARγ Agonist

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Abstract: Peroxisome proliferator activated receptor γ (PPARγ) is a ligand activated nuclear transcription factor predominantly expressed in adipose tissue. It modulates insulin sensitivity and regulates glucose metabolism. Despite extensive research on PPARγ only two FDA approved drugs, rosiglitazone and pioglitazone with same scaffold are found with major side effects like weight gain, fluid retention etc. In this study we employed integrated machine learning and structure-based drug discovery approaches to identify novel PPARγ agonists for treatment of Type-2 diabetes. Extensive feature identification and selection were performed with molecular descriptors and molecular fingerprints using multiple feature selection process and Machine learning models. Consensus hits predicted by four best performing models were subsequentially selected for structure-based analysis. Molecular docking and dynamics simulations are performed to check the binding and to track and analyze the physical movement of molecule overtime. Perform binding free energy calculations using MM-GBSA method for further prioritizing the compounds. Finally, 14 compounds are shortlisted for the experimental evaluations for their PPARγ agonist activity.

Poster **P-194**

An Ensemble Machine-Learning Workflow with Structure-Based Validation for Novel DOT1L Inhibitor Discovery

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Abstract: DOT1L, the sole methyltransferase responsible for H3K79 methylation, is a validated epigenetic target in MLL-rearranged leukaemia, yet computational ligand discovery against it is limited by the scarcity and redundancy of available bioactivity data, in which a small number of congeneric series dominate the chemical space and allow models to achieve apparently high performance by recognising familiar scaffolds rather than genuine activity determinants. To address this, bioactivity data compiled from ChEMBL, BindingDB and PubChem were pre-processed, and all partitioning was performed at the Bemis–Murcko scaffold level so that no congeneric series was shared between training and test sets. Compounds were represented by Morgan fingerprints together with physicochemical descriptors, and three algorithmically distinct classifiers — Random Forest, gradient boosting and a dimensionality-reduced Gaussian process — were tuned under scaffold-grouped cross-validation. Rather than refitting a single model, all fold-level models were retained, their outputs corrected by isotonic calibration on held-out data. Application of this calibrated ensemble to the Maybridge library yielded potential hits that, on docking into the DOT1L SAM- binding site, achieved more favourable scores than the reference probe SGC0946 while reproducing its conserved interactions; the highest-ranking complexes were subsequently subjected to molecular dynamics simulations.

Poster **P-195**

Machine Learning-Guided Identification of Dietary Monoterpenoids as Potential mTOR-Targeting Candidates for Neurodegenerative Diseases

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Abstract: The mechanistic target of rapamycin (mTOR) is a key regulator of cellular processes including autophagy, neuronal survival, and proteostasis and has been implicated in the pathophysiology of several neurodegenerative disorders. In this study, a machine learning-guided computational workflow was developed to prioritize dietary phytochemicals as potential mTOR-targeting candidates with predicted blood–brain barrier (BBB) permeability.

Bioactivity data curated from the BindingDB database were used to develop and compare eight machine learning models for mTOR activity prediction, with the Random Forest Regressor showing the best predictive performance (R^2 = 0.82) A total of 1,560 food-derived phytochemicals were obtained from the PhytoHub database, and since BBB permeability was a key requirement, compounds were subsequently screened based on predicted BBB permeability, yielding 429 candidate compounds. Structural clustering of these compounds identified a predominant cluster comprising 83 monoterpenoids, which were further evaluated for predicted mTOR inhibitory activity. Machine learning-based IC50 prediction prioritized 54 compounds, which were subsequently subjected to molecular docking, molecular dynamics simulations, and density functional theory calculations. Integration of predicted binding scores, molecular dynamics stability, and electronic properties resulted in the prioritization of nine monoterpenoid candidates for further investigation. Overall, the study demonstrates a machine learning-assisted virtual screening strategy for prioritizing BBB-permeable dietary phytochemicals as potential mTOR-targeting candidates, providing a computational basis for their further evaluation in the context of neurodegenerative diseases.

Poster P-196

Machine Learning-Guided Identification of Flavonoid-Based VEGFR2 Inhibitors for Anti-Angiogenic Applications

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Abstract: Vascular endothelial growth factor receptor 2 (VEGFR2) is a critical regulator of angiogenesis and a validated target for therapeutic intervention. Flavonoids represent a promising class of naturally occurring polyphenolic compounds with significant anti-angiogenic potential. This study employed an integrated computational framework combining machine learning and structure-based methods to identify novel VEGFR2 inhibitors. A curated dataset of known VEGFR2 inhibitors was used to train machine learning models for activity prediction, which were then applied to screen a flavonoid-based molecular library. Candidates were systematically filtered for human intestinal absorption permeability and favorable pharmacokinetic properties, followed by molecular docking studies to evaluate kinase domain binding interactions. Molecular dynamics simulations validated the stability of predicted protein–ligand complexes, while off-target analysis assessed selectivity and safety profiles. This comprehensive assessment prioritized nine lead molecules for further development. The results underscore the efficacy of flavonoid-based scaffolds in anti-angiogenic development and validate the integrated computational strategy as a powerful approach for rational drug discovery and lead-molecule prioritization.

Poster P-197

Unravelling the Therapeutic Potential of *T. cordifolia*-derived N-trans- Feruloyltyramine in Type 2 Diabetes through Network Pharmacology and Molecular Simulation

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Abstract: Type 2 Diabetes Mellitus (T2DM) remains a major global health burden, and conventional pharmacological treatments often fail to address its complex, multifactorial pathophysiology. *Tinospora cordifolia* (*T. cordifolia*), a widely used Ayurvedic herb, offers a promising multi-target alternative. This study applied an integrated network pharmacology and molecular simulation framework to elucidate its anti-diabetic mechanism. Systematic screening of *T. cordifolia* identified 14 bioactive constituents, whose predicted targets overlapped with 110 T2DM-associated genes. Protein-protein interaction network analysis further narrowed these to six core targets, namely AKT1, TNF, HSP90AA1, STAT3, BCL2, and JUN, linked to eight key phytoconstituents, including Makisterone A, N-trans-feruloyltyramine, Ecdysterone, Palmatine, Polypodine B 20,22-acetonide, Magnoflorine, Tembetarine, and Jatrorrhizine. Pharmacokinetic evaluation highlighted N-trans-feruloyltyramine as the most favorable candidate, showing good intestinal absorption and P-glycoprotein non-substrate behavior. Molecular docking demonstrated stable binding for several compound-target pairs, while 250 ns molecular dynamics simulations confirmed that only

the HSP90AA1-N-trans-feruloyltyramine complex retained consistent structural stability throughout the trajectory. These results underscore the multi-target therapeutic potential of *T. cordifolia* and identify N- trans-feruloyltyramine as a promising lead molecule capable of modulating HSP90AA1-associated pathways implicated in insulin resistance and inflammation. The findings provide a computational foundation for future experimental validation and development of standardized, HSP90AA1-targeted phytotherapeutic strategies for T2DM management.

Poster P-198

AI-Guided De Novo Design of Nanobodies Targeting DENV-2 E Fusion Loop

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Abstract: Dengue virus infects an estimated 390 million individuals annually, with India accounting for approximately one-third of the global burden. The WHO reports an 11-fold increase in dengue cases over the last decade, driven by expanding vector range and climate change, imposing a substantial economic burden on healthcare systems. Despite this, no approved antiviral therapeutics exist, and current monoclonal antibody discovery methods remain slow and resource-intensive. Antibody-dependent enhancement (ADE) further complicates conventional IgG-based approaches for dengue. Here we demonstrate de novo computational design of VHH nanobodies i.e., a single-domain antibodies lacking an Fc region, inherently avoiding classical ADE mechanisms against the DENV-2 envelope protein fusion loop using a generative AI pipeline. We implemented diffusion-based structural hallucination followed by AbMPNN sequence redesign targeting hotspot residues Trp101, Leu107, and Phe108 on the DENV-2 E protein (PDB I'd1OAN). Fifty-two trajectories were generated across two epitope campaigns using NVIDIA A100 and L40S GPUs. From the fusion loop campaign, three high-confidence candidates were identified based on structural confidence (pLDDT) and interface prediction metrics (i_pTM). The top-ranked candidate (s660901) achieved pLDDT = 0.849 and i_pTM = 0.718 followed by independent structural validation using Chai-1. These results establish the feasibility of AI-driven VHH design against a clinically important dengue epitope.

Poster P-199

Characterization of Non-Canonical PX Domains of *Giardia lamblia*

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Abstract: Phosphoinositides act as molecular landmarks on organelle membranes, recruiting the effector proteins that govern membrane trafficking. Many effectors recognise these lipids through the PX (Phox homology) domain, whose ligand-binding pocket is defined by a conserved, positively charged motif. We previously identified six PX domain-containing proteins in the early-diverging parasite *Giardia lamblia*. While four of these carry the canonical motif, two possess unusual sulfur- containing residues within their binding pockets—a feature not reported in PX domains of model organisms. Since *Giardia* is an oxygen-sensitive microaerophile, these redox-sensitive residues may represent a unique adaptation. Using complementary *in vitro*, *in vivo* and *in silico* approaches, we investigated whether these non-canonical domains retain phosphoinositide-binding activity and how the atypical residues influence ligand specificity. Site-directed mutagenesis, protein-lipid overlay assays and fluorescence localization studies together showed that the sulfur-containing residues are key determinants of binding specificity. Molecular dynamics simulations further revealed that these residues help maintain the ligand specificity of the binding pocket, restricting its accessibility to larger ligands. Overall, the study advances our understanding of phosphoinositide recognition by PX domains and reveals a novel structural adaptation of membrane-trafficking proteins in *Giardia lamblia*.

Poster **P-200**

AI-Guided Design of Sesquiterpenoids Targeting GPX4 as Potential Ferroptosis Inducers in Triple-Negative Breast Cancer

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Abstract: Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype with limited targeted therapeutic options and a high propensity for treatment resistance. Targeting glutathione peroxidase 4 (GPX4), a key regulator of lipid peroxide detoxification, represents a promising strategy for inducing ferroptosis in resistant cancer cells. Here, we developed an AI-guided computational framework to discover novel sesquiterpenoid-based GPX4-targeting compounds with potential ferroptosis-inducing activity. Ferroptosis-associated chemical and molecular information from FerrDb was integrated with 1,347 sesquiterpenoids from the TPCN database to identify relevant structural features. An AttentiveFP-based fragment-scoring approach coupled with a scaffold-conditioned Graph Isomorphism Network-Variational Autoencoder (GIN-VAE) was employed to generate novel candidates. From 927 generated structures, sequential drug-likeness, medicinal chemistry, 3D pharmacophore, and ADME-based filtering prioritized 14 candidates. Molecular docking against GPX4 (PDB: 6HKQ) identified promising binding profiles, with the lead molecule showing a predicted binding affinity of -6.30 kcal/mol, compared with -5.65 kcal/mol for the reference inhibitor ML162 under non-covalent docking. Following 500 ns molecular dynamics simulations, six lead molecules were prioritized based on their binding characteristics and conformational stability. These candidates provide a focused set of GPX4-targeted sesquiterpenoid leads for further experimental investigation as potential ferroptosis-inducing agents against TNBC.

Poster **P-201**

Alphacrossxl-2.0: An Integrated Computational Framework For Resolving Multimeric Protein Architecture Using Cross-Linking Mass Spectrometry

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Abstract: Mapping structural features of proteins and protein complexes using mass spectrometry dates to the 1990s, and the field of cross-linking mass spectrometry (XL-MS) has since undergone transformative advancement in experimental workflows and computational strategies. The XL-MS pipeline, comprising biochemical cross-linking, proteolytic digestion, and mass spectrometry, provides distance constraints that reflect the maximal separations between cross-linked amino acids. While advances in mass spectrometers have enabled proteome-scale XL-MS studies, major analytical challenges persist with the endpoint structural inferences. Existing visualization and analysis tools, including Xlink Analyzer, XVis, and ChimeraX plug- ins, provide valuable capabilities but face key limitations. These include reliance on simple Cα–Cα distance measurements without accounting for protein dynamics, limited scalability, time-intensive setup, and challenges in mapping cross-links across multimeric assemblies. To this end, we developed AlphaCrossXL- 2.0, an improved version of AlphaCross-XL that combines XL-MS data with structural biology approaches, enabling more reliable modelling of proteins and protein complexes while accounting for the dynamic conformational states of these systems. This platform enables distance interpretation, supports large-scale analyses, and generates biologically meaningful structural hypotheses. As proof of concept, yeast expression cassettes have been designed for overexpression of RPL25 and other genes of interest (non- toxin), tagged with immuno-epitopes (e.g., FLAG) to facilitate downstream analysis and further to capture native protein conformations in real time within biological systems, and address complex biological questions at a proteome-wide scale. By bridging experimental XL-MS with computational structure analysis, AlphaCrossXL-2.0 can significantly enhance the resolution and interpretability of protein architectures, thereby deepening our understanding of complex cellular processes.

Poster **P-202**

Substrate Selectivity in Formate/Nitrite Transporters (FNT): Role of Histidine protonation in substrate transport

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Abstract: Identifying new drug targets is crucial for fighting infections. During anaerobic respiration in enteric microbes, mixed acid fermentation produces weak acids like formate, lactate, and acetate from pyruvate. Formate/nitrite transporters (FNTs), found in prokaryotes and lower eukaryotes, selectively transport monovalent anions and support bacterial growth while countering host defences. As FNTs are absent in higher animals, they are attractive targets for diseases including malaria, amoebiasis, typhoid, amoebic meningoencephalitis, and other related infections worldwide. The central His residue forms one of two constriction regions, and analysis of over 2000 FNTs shows more than 95% conservation of this highly conserved residue. However, in the amoebiasis-causing *Entamoeba histolytica* (EhFNT), His is replaced by Asn. The role of His and its protonation state in substrate transport and selectivity remains unresolved. In this study, we performed molecular dynamics simulations and umbrella sampling on EhFNT (eukaryotic FNT) and *Vibrio cholerae* (prokaryotic FNT). We have also carried out in silico mutations of other specific residues. Our results indicate that a neutral substrate passes easily through the transporter, while an anionic substrate faces a net energy barrier in wildtypes, suggesting temporary neutralization while crossing the membrane. Based on these results, we speculate the likely protonation state of the conserved central His.

Poster **P-203**

Deciphering the Molecular Basis of CETP inhibition and discovering novel inhibitors through Integrated Computational Approaches

Akshaya K.T., Avishek Chowdhury, Shivangee Yadav, Gaurava Srivastava, Mohammad Imran Siddiqi*
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Abstract: Cholesteryl Ester Transfer Protein (CETP) facilitates the exchange of cholesteryl esters and triglycerides among plasma lipoproteins, making it an important regulator of lipid transport and a potential therapeutic target beyond cardiovascular disease. To understand the molecular mechanism of CETP inhibition, the conformational dynamics of the wildtype CETP and four experimentally validated mutants were comparatively investigated using molecular dynamics simulations. Residual energy decomposition and principal component analysis identified key residues involved in ligand stabilization and revealed their influence on the flexibility of Helix-X and the central tunnel associated with lipid transfer. To extend these mechanistic insights toward inhibitor discovery, machine-learning based prediction was integrated with pharmacophore screening of the MayBridge chemical library. Their consensus resulted 9,969 compounds, which were reduced to 5,782 structurally diverse molecules through similarity-based clustering. Subsequent molecular docking, molecular dynamics simulations and binding free-energy calculations identified compounds with stable tunnel engagement and restricted Helix-X mobility. Compounds 2 and 4 exhibited favorable interaction profiles throughout the simulations supporting their potential as lead candidates for further experimental studies. This integrated computational approach provides a systematic framework for the identification and prioritization of novel CETP inhibitor candidates, supporting their experimental evaluation and structure-guided optimization.

Poster **P-204**

Network Pharmacology and Molecular Docking of Phytochemicals Against *Fusobacterium nucleatum* Targets in Colorectal Cancer

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Dolphin PG Institute of Biomedical and Natural Sciences, Dehradun
Amity University, Lucknow

Dolphin PG Institute of Biomedical and Natural Sciences, Dehradun
BIOINFOCORE Solution, Lucknow

Abstract:

Background: Colorectal cancer (CRC) is a major cause of cancer-related mortality, and Fusobacterium nucleatum is increasingly associated with CRC progression, immune evasion, and chemoresistance. Identifying bacterial targets and potential plant-derived inhibitors may provide new therapeutic insights.

Objective: To identify hub proteins in F. nucleatum ATCC 25586 using protein-protein interaction (PPI) analysis and screen CRC-related phytochemicals against the hub target.

Methods: Protein-coding genes were retrieved from NCBI, and selected gene symbols were analyzed using STRING and Cytoscape. cytoHubba ranked hub genes using 12 topological algorithms. Twenty phytochemicals were evaluated for ADME, toxicity, and molecular docking against the identified hub protein.

Results: Of 2,068 retrieved genes, 1,963 were protein-coding, and 517 gene symbols were used for network construction. The STRING network contained 57 nodes and 1,567 edges and was enriched in ribosomal and translation-related proteins. rpsJ was the only gene ranked among the top 20 by all 12 algorithms. Apigenin showed a docking score of −9.256 kcal/mol and genistein
−7.963 kcal/mol. Both showed favourable ADME profiles and predicted low toxicity.

Conclusion: rpsJ was identified as a consensus hub, while apigenin and genistein emerged as promising candidates requiring experimental validation.

Poster P-205

In silico insights into pathogenicity and structural consequences caused by missense variants of KATNAL2

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Abstract: KATNAL2 is a katanin-family of AAA-ATPases that works on microtubule-associated processes to control cytokinesis, ciliogenesis, sperm differentiation, and neuronal morphogenesis. Katnal2 pathogenic variants link ciliary dysfunction to hydrocephalus, male infertility, and autism spectrum disorders across multiple model systems and human patients. The missense mutation in katnal2 proteins may alter nucleotide binding and ATP hydrolysis, potentially affecting protein oligomerization and subunit assembly. This study aimed to identify and analyse deleterious nonsynonymous single nucleotide polymorphisms (nsSNPs) in Katnal2 that may affect protein function. An integrated in silico approach combining multiple predictive tools (SIFT, PolyPhen-2, PhD-SNP, PANTHER, Meta-SNP, FATHMM, I-Mutant 2.0, INPS-MD, Medusa, MutPred2, DynaMut2, ConSurf, NetSurfP-2.0, STRING) were used to identify pathogenic nonsynonymous SNPs in Katnal2 and analyse their structural and functional effects. A total of 5 pathogenic nsSNPs were found at R32, R57, L230, A236, T241 and were uniformly identified as harmful across all predictive models. L230S, A236D, and T241K pathogenic variants leading to the gain or loss of catalytic and allosteric sites, alteration in the metal-binding site, as well as gain or loss of PTMs, methylation at different residues within the active sites of mutated Katnal2 enzymes. As the majority of variants fall in the NBD, they likely lead to protein misfolding or interfere with its ability to bind ATP and induce significant changes in protein stability, flexibility, and interaction potential, leading to compromised Katnal2 function and contributing to microtubule dysfunction underlying disease mechanisms.

Poster P-206

Proteome-Wide Mining of MHC Class I, Class II, Cryptic and B Cell Epitopes of *Leishmania donovani*: An Integrated *In Silico* Approach towards Vaccine

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Abstract: Visceral leishmaniasis, caused by *Leishmania donovani*, affects millions of people in India and Africa, and no effective vaccine is available to date. We employed an integrated immunoinformatics approach to screen the *L. donovani* proteome (7960 proteins) for vaccine candidates. Subtractive proteomics, signal peptide, GPI anchor and antigenicity predictions shortlisted 21 antigenic proteins, from which 11 MHC class I restricted epitopes were obtained from 9 proteins. Separately, 130 MHC class II binding epitopes were identified and evaluated for hydrophobicity and IFN-γ and IL-10 inducing potential, and 24 peptides were selected for modelling. Docking and molecular dynamics (MD) simulation with GROMACS showed that four class I epitopes (YPAFAALVF, VAVAATVAY, AAAPTEAAL, MYPLVAVVF) and three class II epitopes (TQVLLALQGSSTILQ, TTQFLIVSATPIHPE and TTTQFLIVSATPIHP) bound stably to their respective HLA alleles in the binding cleft, comparable to reference peptides. Cryptic epitope analysis showed that tyrosine modification lowered IC50 values for five peptides, with two to three modified peptides (cryptic epitopes) showing better docking scores. Linear and conformational B cell epitopes were also predicted to support humoral responses. These epitopes could be promising vaccine candidates against *L. donovani* and require experimental validation.

Poster P-207

Design and Synthesis of New Fluorescent Probe for Selective Staining of DNA/RNA G-Quadruplex

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Abstract: G-quadruplexes (G4s) are non-canonical DNA/RNA secondary structures involved in diverse cellular processes and associated with several diseases. Their precise visualization is essential for understanding their biological significance. In this context, we have rationally designed a G4-selective near-infrared (NIR) fluorescent turn-on probe with a large Stokes shift, low toxicity, and high selectivity over single- and double-stranded nucleic acids. Additionally, our research group developed GreenR, an indigenous cyanine-based DNA staining dye under the Self-Reliant India Campaign. GreenR exhibits fluorescence upon binding to nucleic acids, with high sensitivity and selectivity toward double-stranded DNA (dsDNA). Commercially available through the Government e-Marketplace (GeM), GreenR offers a cost-effective alternative to imported DNA stains, with the advantages of non-mutagenicity and easy disposal. Together, these fluorescent probes highlight advances in selective nucleic acid imaging and the development of accessible, indigenous tools for biomedical research.

Poster P-208

Mesenchymal Stem Cell-Mediated Restoration of Testicular Function in a Chemoablated Rat Model

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Abstract: Chemotherapy-induced testicular dysfunction is a significant cause of male infertility, primarily due to the loss of spermatogonial stem cells (SSCs) and the disruption of spermatogenesis. In this study, the efficacy of Bone Marrow (BM)-derived MSCs was evaluated for restoring testicular function in an infertile rat model induced by

chemoablation. Chemoablated male rats received two doses of 15 mg Busulfan with a two-week interval between doses. BM-MSCs were assessed for purity by FACS analysis of specific cell-surface markers and injected into the testes of chemoablated rats; their gradual restoration was evaluated at 2, 4, 6, 8, and 10 weeks. Testicular restoration was assessed through histological and mating analyses. The control group had a normal litter size of 10-12 pups, but the induced infertile group had no pups delivered, whereas the MSC-treated group delivered a litter of 8 pups after 8 weeks. BM-MSC transplantation promoted progressive recovery of testicular morphology and reproductive parameters; also enhanced the expression of stem cell and sperm maturation markers. Transcriptomic analysis further revealed that MSC treatment modulated genes associated with stress responses, inflammation, and spermatogenesis, shifting the molecular profile toward control testes. Overall, BM-MSC transplantation restored reproductive function and fertility, demonstrating its potential as a regenerative approach for male infertility.

Poster **P-209**

SAS1B Regulates Cervical Cancer Cell Proliferation through Aurora A Kinase

Akanksha Vyas[1,3], Saurabh K Agnihotri[4], Ankita Jain[1], Niranjan Kumar[1,3], Rashmi Rani Sahu[1,3], Abdul Basit Khan[2,3], Prerona Das[1,3], Deependra Singh[1], Vaishali Tyagi[1], Rajnikant Mishra[1,2], Madanlal B Bhatt[4], Kirti Srivastava[4], Rajeev Gupta[4], Rekha Sachan[4], J Venkatesh Pratap[2,3] and Monika Sachdev[1,3]

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Abstract: Cervical cancer (CaCx) is a major cause of cancer-related mortality among women worldwide, including India. Persistent high-risk human papillomavirus (HPV) infection is a key etiological factor, while additional molecular alterations also contribute to cervical carcinogenesis. Cancer Oocyte Antigen (COA)- SAS1B (Sperm Acrosomal SLLP1 Binding Protein) has been reported in a few cancers, but its role in CaCx remains unexplored. The present study investigated SAS1B expression and its functional significance in CaCx. Prominent expression of SAS1B was found in different CaCx cell lines. The lentiviral shRNA-mediated knockdown of SAS1B in CaSki (HPV-positive) and C-33A (HPV-negative) CaCx cells significantly reduced cell proliferation and stemness potential. SAS1B silencing also altered proteins involved in epithelial–mesenchymal transition, cell-cycle regulation, and apoptosis.

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Vision

I ➡ INSPIRING
Next generation scientists/ technologists

D ➡ DELIVERING
To the Nation

E ➡ ENGAGING
With key stakeholders

A ➡ ADMINISTRATION
Facilitating Excellence in Science, Technology and Innovation

Alignment with Sustainable Development Goals



SDG-17:PARTNERSHIP FOR THE GOALS
- Collaborative R&D/ CSIR Mission Projects

SDG-3:GOOD HEALTH AND WELL-BEING
- Antibacterial bioactive glass
- Acetone Breath Sensors
- Rare-earth doped lasers

SDG-11: CLIMATE ACTION
- Anti-reflective coatings on glass

SDG-4: QUALITY EDUCATION
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SDG-10:REDUCED INEQUALITIES
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SDG-6:CLEAN WATER & SANITATION
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SDG-7:AFFORDABLE & CLEAN ENERGY
- Anode supported SOFC
- Paper based ceramic separators

SDG-8:DECENT WORK & ECONOMIC GROWTH

SDG-9:INDUSTRY, INNOVATION & INFRASTRUCTURE
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- Yb doped fibre lasers
- Superior ramming mass refractory
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- Optical fibre lasers
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- Ceramic radomes

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Skill India

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National Hydrogen Mission - to make India a global hub for the production and export of green hydrogen

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Membrane separation technologies for water purification

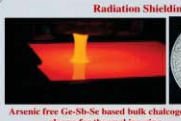
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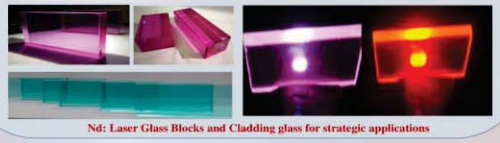


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Silicon Nitride Radomes





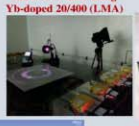
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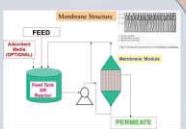
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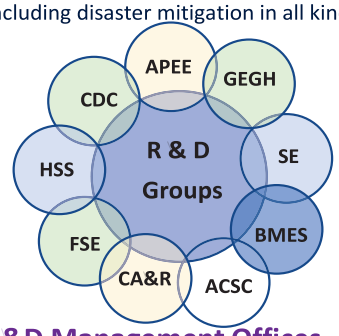
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- डीएसआईआर–आईआईटीआर–सीआरटीडीएच पर्यावरण निगरानी और हस्तक्षेप हब

सेवाएं दी गईं

- जीएलपी प्रमाणित पूर्व–नैदानिक विषाक्तता अध्ययन
- एनएबीएल (आईएसओ/आईईसी 17025:2017) मान्यता प्राप्त एनसीई की सुरक्षा/विषाक्तता मूल्यांकन
- जल गुणवत्ता मूल्यांकन और निगरानी
- विश्लेषणात्मक सेवाएं
- पर्यावरण निगरानी और प्रभाव मूल्यांकन
- रसायनों/उत्पादों के बारे में जानकारी
- कम्प्यूटेशनल भविष्य कहनेवाला विषाक्तता मूल्यांकन

मान्यताएं

- वैज्ञानिक और औद्योगिक अनुसंधान संगठन (एसआईआरओ)
- यूपी प्रदूषण नियंत्रण बोर्ड (जल और वायु)
- भारतीय कारखाना अधिनियम (पीने का पानी)
- भारतीय मानक ब्यूरो (सिंथेटिक डिटर्जेंट)
- भारतीय खाद्य सुरक्षा और मानक प्राधिकरण (FSSAI)

विकसित/उपलब्ध प्रौद्योगिकियां

- ओनीर– सुरक्षित पेयजल के लिए एक नया समाधान
- पोर्टेबल जल विश्लेषण किट
- पर्यावरण और मानव स्वास्थ्य के लिए मोबाइल प्रयोगशाला
- सरसों के तेल में आर्जीमोन की त्वरित जांच के लिए एओ किट
- मक्खन पीले रंग का पता लगाने के लिए एमओ जांच, एक मिलावटी, खाद्य तेलों में

R & D Divisions

- Food, Drug, Environment & Systems Toxicology (FEST)
- Analytical Sciences & Services and Industrial Support through Technological Solutions (ASSIST)
- Regulatory and Computational Toxicology (ReaCT)

Research Areas

- Food, Drug & Chemical Toxicology
- Environmental Toxicology
- Regulatory Toxicology
- Toxicoinformatics & Industrial Research
- Systems Toxicology & Health Risk Assessment

R & D Partnership for Industries & Startup

- Centre for Innovation and Transnational Research (CITAR-BIRAC-BioNEST)
- DSIR-IITR-CRTDH Environmental Monitoring and Intervention Hub

Services Offered

- GLP certified pre-clinical toxicity studies
- NABL (ISO/IEC 17025:2017) accredited Safety/ toxicity evaluation of NCEs
- Water quality assessment and monitoring
- Analytical services
- Environmental monitoring and impact assessment
- Information on chemicals/ products
- Computational predictive toxicity assessment

Recognitions

- Scientific & Industrial Research Organizations (SIROs)
- UP Pollution Control Board (Water & Air)
- Indian Factories Act (Drinking water)
- Bureau of Indian Standards (Synthetic detergents)
- Food Safety & Standards Authority of India (FSSAI)

Technologies Developed/ Available

- Oneer- A novel solution for safe drinking water
- Portable Water Analysis Kit
- Mobile Laboratory for environment and human health
- AO Kit for rapid screening of Argemone in mustard oil
- MO Check for detection of Butter Yellow, an adulterant, in edible oils

#startupindia

विषविज्ञान भवन, 31, महात्मा गाँधी मार्ग
लखनऊ-226001, उ.प्र., भारत
फोन/Phone:+91-522-2627586, 2614118, 2628228 फैक्स/

VISHVIGYAN BHAWAN, 31, MAHATMA GANDHI MARG
LUCKNOW-226001, U.P., INDIA
director@iitrindia.org www.iitr.res.in

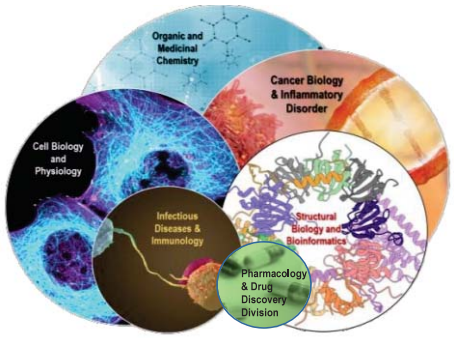
सीएसआईआर-भारतीय रासायनिक जीवविज्ञान संस्थान

4, राजा एस सी मल्लिक रोड, कोलकाता - 700 032



सीएसआईआर-भारतीय रासायनिक जीवविज्ञान संस्थान (आईआईसीबी), जिसकी स्थापना मूल रूप से 1935 में भारतीय आयुर्विज्ञान अनुसंधान संस्थान के रूप में हुई थी, बाद में वैज्ञानिक एवं औद्योगिक अनुसंधान परिषद (सीएसआईआर) का एक अंग बन गया। इस संस्थान की स्थापना हैजा उन्मूलन के महान लक्ष्य के साथ की गई थी, जिसकी परिणति मौखिक हैजा के टीके के विकास के रूप में हुई। यह संस्थान छह अनुसंधान प्रभागों के माध्यम से संचालित होता है और कोलकाता के यादवपुर और साल्ट लेक स्थित दो परिसरों में फैला हुआ है, जहाँ अग्रणी अनुसंधान और नवाचार के लिए उत्कृष्ट बुनियादी ढाँचा उपलब्ध है।

प्रमुख प्रभाग और प्रमुख क्षेत्र:

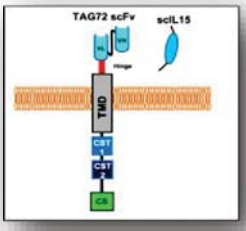


वैश्विक स्तर पर ज्ञान का सृजन:

- औसत प्रकाशित पेपर / वर्ष > 170
- एच-इंडेक्स : 112
- कुल उद्धरण: 1,05,217 (स्व-उद्धरण के बिना)
- औसत प्रभाव कारक > 5.3

ज्ञान को धन में बदलना (आईपी):

- पेटेंट दायर / वर्ष > 4
- पेटेंट प्रदान किया गया / वर्ष > 4



डिम्बग्रंथि के कैंसर को लक्षित करने वाले CAR-T संरचनाओं का विकास और पूर्व-नैदानिक सत्यापन

प्रस्तावित पीएच.डी. कार्यक्रम:

सीएसआईआर-भारतीय रासायनिक जीवविज्ञान संस्थान, कोलकाता एसीएसआईआर , यादवपुर विश्वविद्यालय और कलकत्ता विश्वविद्यालयों के माध्यम से निम्नलिखित क्षेत्रों में पीएचडी कार्यक्रम प्रदान करता है:

- कैंसर जीवविज्ञान और चिकित्सा विज्ञान (रक्तविज्ञान और ठोस कैंसर)
- दवा खोज और विकास , एपीआई और केएसएम
- इम्युनोलोगि
- चयापचय संबंधी विकार (हृदय रोग, मधुमेह, फेफड़ों के रोग)
- न्यूरोडीजेनेरेटिव रोग और न्यूरोजेनेसिस
- कार्बनिक एवं औषधीय रसायन विज्ञान
- फाइटोफार्मास्युटिकल्स
- ट्रांसक्रिप्शनल गलत विनियमन मानव रोगों में
- वायरल और परजीवी रोग (लीशमैनिया , मलेरिया)

आउटरीच गतिविधियाँ:

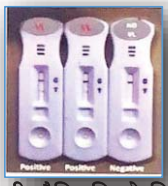
सीएसआईआर-आईआईसीबी अपनी प्रमुख आउटरीच पहलों - सीएसआईआर-जिज्ञासा कार्यक्रम और सीएसआईआर-एकीकृत कौशल पहल कार्यक्रम के माध्यम से समाज से जुड़ता है।





हाल ही में विकसित संभावित प्रौद्योगिकियां:

- नावेल थर्मोस्टेबल इंसुलिन सूत्रीकरण
- स्वप्रतिरक्षी रोगों के लिए शक्तिशाली TLR9-चयनात्मक और TLR9 और 7 दोहरे प्रतिपक्षी
- लीशमैनिया और कवक के
- ट्रॉपिसेट्रॉन के निर्माण की नवीन प्रक्रिया
- लीशमैनियासिस (वीएल) और पोस्ट कालाजार डर्मल लीशमैनियासिस (पीकेडीएल)
- डेंगू के आरएनए-आधारित पता लगाने के लिए उपयोग में आसान पॉइंट-ऑफ-केयर प्रणाली
- के लिए डायग्नोस्टिक किट आमवाती हृदय रोग का पता लगाना
- मैंने टिलोरोन और उसके लवणों
- लीशमैनिया के विरुद्ध
- 'इंडियन मिस्टलटो' थेरेपी
- प्रोस्टेट हाइपरप्लासिया/मूत्र विकारों का प्रबंधन (प्रोस्टालिन[R] का व्यावसायीकरण किया जा रहा है)
- जीवित कोशिका इमेजिंग के लिए ऑर्गेनेल विशिष्ट फ्लोरोसेंट जांच



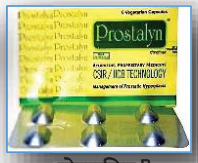
लीशमैनियासिस के लिए रैपिड डायग्नोस्टिक किट



आरएचडी के लिए रैपिड डायग्नोस्टिक किट



तेजी से रक्त का थक्का जमाने के लिए हेमोस्टेटिक पैड



प्रोस्टालिन[R]



मेधा प्लस

संपर्क : निदेशक, सीएसआईआर-आईआईसीबी, कोलकाता,
फ़ोन: 033-24995700 (पायलट संख्या), 033-24995701 (निदेशक), ईमेल : director@iicb.res.in ,
वेबसाइट: https://iicb.res.in

Lady Tata Memorial Trust invites applications for the below Fellowships and Grants for 2027–28

1) Junior Research Fellowship (JRF) (2027–28)

Purpose: To support scientific investigations having a bearing directly or indirectly on the alleviation of human suffering from disease.

Eligibility:

- Indian Nationals from Universities/Institutes/Labs.
- First-class academics (60%+) from Class X onwards.
- Completed M.B.B.S./M.Sc./M.Pharm/M.Tech in 2025 or 2026.
- Age limit: below 27 years (as on 31 March 2027).

2) Young Researcher Award (YRA) 2026

Purpose: To recognise and reward young Indian scientists, with outstanding track record in biological sciences, a strong commitment to finding innovative solutions to major health challenges related to human diseases and potential for high-quality research.

Eligibility:

- Indian nationals, below 40 years (as on 31 March 2027).
- Ph.D. in Life Sciences OR Master's in Medical Sciences/related Biotech fields with over 4 years professional experience post-degree.
- Regular position in an Indian institute; independent research publications in reputed journals.

3) Teacher's Training Program (TTP)

Purpose: To equip teachers in colleges offering B.Sc./M.Sc. in biological sciences on new scientific topics and experimental techniques for effective teaching.

Eligibility :

- 2–3 day lecture with hand of training /workshops.
  Evidence of quality teaching & student performance, Infrastructure for workshop, Program details & budget to be provided by the college.
- Minimum 30 teachers with ≥5 years before retirement and proven teaching achievements have to be trained.

4) LTMT Research Project Grant 2027-28

This grant advertisement invites proposals for the Biology and Management of
A) Leukemia and blood disorder (for details on area of proposal, plz check on website)
B) Alleviation of human suffering (for details on area of proposal, plz check on website)

Applications are invited from Scientists/Clinicians/Clinical researchers, from public and private Academic Institutions/Universities/ R&D centers, engaged in scientific research work in the advertised areas. Please note that IEC/IAEC approval is mandatory for submission.

Applications will be open from the month of November 2026. Please visit **http://www.ladytatatrusts.org** or write to **ltmt@tatatrusts.org** for more information.

CSIR-Indian Institute of Integrative Medicine, Jammu J&K, India-180001

CSIR-Indian Institute of Integrative Medicine (CSIR-IIIM) is a premier national research institution under the aegis of the Council of Scientific & Industrial Research (CSIR), located in Jammu, with branch lab in Srinagar and four field research stations across different locations in the Union Territory of Jammu and Kashmir. CSIR-IIIM is actively involved in the discovery of new drugs and therapeutic approaches from natural products of both plant and microbial origin, leveraging biotechnology to develop high-value technologies, drugs, and products for national and international markets.



Over the years, CSIR-IIIM has pioneered several innovative technologies, processes, and models that have greatly contributed to national goals. The institute has played a crucial role in fulfilling the nation's mandate to double farmers' income, driving the Purple Revolution through the introduction of lavender farming and promoting various aromatic and medicinal plants in the J&K region. With its formidable research infrastructure and expert manpower, CSIR-IIIM has consistently addressed emerging challenges and offered sustainable solutions to pressing problems.

Thus, CSIR-IIIM is engaged in multidisciplinary R&D programs that encompass both basic and applied research across scientific disciplines, focusing on economic, environmental, and societal benefits for the people of India. With a vision to emerge as a globally recognized R&D institute trusted by industries and valued by society, CSIR-IIIM continues to make strides in drug discovery and allied sciences. The institute is already involved in technology transfer partnerships with various industries and has established an extensive client network both nationally and internationally.

Another vital aspect of CSIR-IIIM's mission is its significant contribution to employment oriented skill development initiatives, empowering youth with sustainable skills for future growth.

CSIR-IIIM provides expertise in its core competencies, which include NABL-GLP compliant lab standards, which are meant for animal testing, analysis, quality control, CMC drugs and drug leads. The institute offers lab to pilot scale chemical and fermentation process development, as well as standardization, cGMP extraction, and formulation capabilities for botanical drugs. Additionally, CSIR-IIIM undertakes R&D and extension projects through consultancy, collaboration, sponsorship, and Public-Private Partnership (PPP) arrangements.

Contact: Director, CSIR-Indian Institute of Integrative Medicine (IIIM)
Canal Road, Jammu-180 001, J&K (INDIA). Tel No.:0191-2584999, 2585222.
Email: director@iiim.res.in
Website: www.iiim.res.in

CSIR – Central Drug Research Institute, Lucknow

A Centre for Integrated Drug Discovery and Development

CSIR-CDRI is a premier biomedical research institute focused on the discovery and development of drugs, affordable technologies and diagnostics for diseases of relevance to India. Since its inception in 1951, the Institute has played a key role in the growth of the Indian Pharmaceutical Industry. Institute has end-to-end drug discovery and development research capabilities which include structure-guided drug design, medicinal chemistry, in vitro screening, pharmacology, pharmacokinetics, formulation development and toxicology.

Therapeutic Research Areas

- Microbial Infections
- Viral Infections
- Parasitic Infections
- Neurological Disorders
- Metabolic Disorders
- Musculoskeletal Health Disorders
- Cancer
- Reproductive Health

Vision

To drive discovery and development of cutting edge and affordable healthcare technologies

Mission

Discovery and development of therapeutics for nationally important diseases with global impact, understanding fundamental disease biology and training future drug researchers



Achievement Since Inception

- 13 New Drugs Discovered and Developed
- 6 Diagnostics
- > 80 Process Technologies
- > 12,000 Research Publications
- > 456 Patents Filed Abroad
- > 586 Patents filed in India
- > 2,000 Ph.D.'s
- > 2,000 Sponsored Trainings
- > 7000 Post Graduate Trainings

Licensing / Co-development Opportunities

Small Molecules
- S011-1793 (Anti-malarial)
- S016-1348 (Anti-cancer) Smac mimetic
- SB-CDRI4-105 (Neuropathic pain)

Phytopharmaceuticals
- NMITLI-118 AF1 (Anti-stroke)
- 1703F003 4-HIL (Anti PCOS)

Cost effective Generics
- Olaparib
- Nintedanib
- Nitazoxanide
- Centhaquin
- Niclosamide
- Centbucridine

Business Model

Co-development | Out-licensing | Contract R&D | Consultancy

For more details: please visit https://www.cdri.res.in
Or contact: director.cdri@csir.res.in, head.bdu.cdri@csir.res.in

CSIR-Central Drug Research Institute

Sector 10, jankipuram Extension, Sitapur Road, Lucknow-226031, India; Phone:+91-522-2771940 Fax: +91-522-2771941