Annexure-VII

Sectional Committee -VII

Molecular and Cellular Biology

Chair
Prof. Uday Bandyopadhyay, FNA

Prof. Uday Bandyopadhyay is Vice Chancellor of Kazi Nazrul University. He was a former director of Bose Institute, former Professor, Academy of Scientific and Innovative Research (AcSIR), former Senior Principal Scientist, Division of Infectious Diseases and Immunology, CSIR-Indian Institute of Chemical Biology. Prof. Uday Bandyopadhyay has made significant contributions in the field of Infectious Diseases (Malaria), Chemical Biology, Drug discovery, Biochemical Pharmacology and Cell Biology.

INSA Distinguished Lecture

The Glutathione cycle: A new cycle for an old molecule

Anand K. Bachhawat

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Glutathione is the most abundant sulfur-containing molecule in living cells. It carries out crucial functions in the cell that are important for health and disease. It is a tripeptide consisting of glutamate, cysteine and glycine with an unusual g-glutamyl linkage at its N-terminus. Glutathione was discovered over a century ago in 1888. Between 1920 to 1970, the structure, and metabolism (biosynthesis, degradation, transport) of glutathione were unravelled by many of the stalwarts of biochemistry of those years. And in 1969-70 Alton Meister who was at the forefront of glutathione research proposed the "g -glutamyl cycle" that was thought to capture the cycle of glutathione metabolism with a proposed role in amino acid transport. Ever since the cycle has been known in the field and in the literature. Thus, when we accidentally began work on glutathione in the late 1990s, it was thought that the biochemistry of glutathione, and its metabolism was completely known. We soon discovered that the 'degradation arc' of the cycle was wrong. We succeeded in identifying the first high affinity glutathione transporter as well as new enzymes in glutathione degradation. This eventually led us to propose a new cycle of glutathione metabolism, "The glutathione cycle" which we proposed should replace the previously known "g-glutamyl cycle" (proposed in 1969). A brief overview of our key findings, and a brief history into how such a wrong cycle of a key cellular metabolite has perpetuated will also be presented.

Speaker's Profile

Anand K Bachhawat is an Emeritus Professor at the Department of Biological sciences, IISER Mohali. He has completed his PhD in Biochemistry from Bose Institute, University of Calcutta, and post-doctoral research at the MGH Cancer Center- Harvard Medical School, Boston, USA and Carnegie Mellon University, Pittsburgh, USA before joining the Institute of Microbial Technology, Chandigarh. He moved to IISER Mohali in 2010. Dr Bachhawat's interests are largely in the area of metabolism with specific reference to sulphur, glutathione, redox and one-carbon metabolism

INSA Distinguished Lecture

Role of transcriptional enhancers in and genome organization and gene regulation

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Genes are regulated by distal regulatory elements known as enhancers that exert their function on target genes by establishing looping with the promoter. Although discovered over forty years ago, the molecular mechanisms underlying enhancer functions still remain poorly understood. Recently, another layer of complexity has been uncovered by the discovery that in addition to widespread transcription of long non-coding RNAs (lncRNAs) in mammalian cells, bidirectional ncRNAs are transcribed on enhancers, and are thus referred to as enhancer RNAs (eRNAs). However, it has remained unclear whether these eRNAs are functional or merely a reflection of enhancer activation. Different roles of eRNAs in gene regulation are just emerging.
Investigations using Hi-C/5C technologies has revealed highly organized topologically associated domains (TADs) in chromosomes. These megabase sized regions are characterized by increased frequency (~2 fold) of interaction between loci within the TADs when compared to their interaction to loci located outside the confines of boundary elements. However, the defining principle behind these ordered structure is unknown. I will talk about some evidences indicating, the role of transcriptional enhancers and their eRNAs in such hierarchical chromatin organization.

Speaker's Profile

Precise regulation of gene transcription is central to development and homeostasis. Distal regulatory elements known as enhancers play a crucial role in gene regulation. Understanding of such functional enhancers is of paramount interest, as their malfunction is often associated with developmental disorders and diseases. My lab uses cutting-edge tools such as genome-wide NGS-based assays at bulk and single cell level, to sophisticated high-resolution microscopy, to unravel the functions of enhancers in gene transcription and genome organization. We have identified "mother enhancers" in the genome that play a key role in generating reproducible transcriptional programs upon cyclic/rhythmic signaling such as growth hormones. Our findings suggest that "mother enhancers' are universally present and play a critical role in dictating the transcriptional programs in metazoans. Combining the series of contemporary approaches, we aim to uncover the precise "Mother enhancer-based architectural code" defined by specific proteome, RNA and 4D-nuclear position of a gene, which dictates diverse transcriptional programs in metazoans. The proposed study will thus have broad impact on transcriptional control mechanisms in development and disease.

INSA New Fellow Lecture

Epigenetic reprogramming links extracellular matrix stiffness to immune signalling in cancer progression

Chandrima Das[1,2]

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The epigenome functions as a critical regulator of cellular physiology through dynamic, reversible modifications that govern gene expression. Our laboratory investigates chromatin readers/effectors, which recognize specific epigenetic landscapes and regulate gene expression programs. Our findings demonstrate these proteins' pivotal roles in regulating cancer hallmarks, offering insights into tumor heterogeneity. The tumor microenvironment significantly influences cancer progression through interactions between resident cells and the extracellular matrix (ECM). We show that epigenetic regulators program ECM gene expression, thereby altering ECM stiffness leading to cell free DNA release from the exosomes of the cancer cells. Further, immune signalling pathways are also deregulated by the epigenetic factors directly impacting the metastatic potential of the cancer cells. Our research illuminates how specific chromatin readers interpret the epigenetic code in cancer, emerging as promising therapeutic targets for future interventions.

Speaker's Profile

The research focus of Dr. Chandrima Das' laboratory is to understand the link between the epigenome and cancer. Further she has made contributions in understanding the role of matrix remodelling and immune signalling pathways that directly impact cancer metastasis. She is a recipient of several prestigious research fellowships and awards including Swarna Jayanti Fellowship, CDRI-Award for Excellence in Drug Research in Life Science category, S. Ramachandran National Bioscience Award for Career Development. She is an Elected Fellow of The National Academy of Sciences (FNASc.), India. She is an active member of Asian-Forum of Chromosome-and-Chromatin-Biology and Asian-Epigenomics initiative of six-Asian countries.

INSA New Fellow Lecture

Understanding the functions of annulate lamellae: An underexplored cell organelle

Jomon Joseph

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Annulate lamellae (AL) are specialized subdomains of the endoplasmic reticulum (ER) containing a distinct subset of nucleoporins (Nups). Although Nups are primarily known as components of nuclear pore complexes (NPCs), which mediate nucleo-cytoplasmic transport (NCT), the functional relevance of their presence at AL has remained largely unexplained. Our recent findings provide new insight into the biological roles of AL and the Nup358 nucleoporin that resides there. We show that AL physically associate with mRNP granules such as P-bodies. In this context, Nup358 acts as a scaffold that facilitates the pairing of microRNAs (miRNAs) with their target mRNAs, thereby influencing post-transcriptional gene regulation. In parallel, we have discovered that AL are positioned at ER-mitochondria contact sites (ERMCSs), which are essential for coordinating calcium signaling, mitochondrial metabolism, lipid exchange, and autophagy. We further demonstrate that Nup358 regulates ER–mitochondria connectivity through the mTORC2/Akt/GSK3β signaling axis, highlighting a functional link between NCT-associated proteins and organelle communication. Notably, disruptions in miRNA-mediated regulation, nucleo-cytoplasmic transport, and ERMCS function are all implicated in the development of neurodegenerative diseases and cancers. Therefore, our research reveals a previously unrecognized integration between RNA regulation and inter-organelle signaling mediated by AL and Nup358. These insights advance our understanding of fundamental cell biology and may inform new strategies for therapeutic intervention in disease contexts where these pathways are compromised.

Speaker's Profile

Dr. Jomon Joseph is a Scientist G at the National Centre for Cell Science (NCCS), Pune. He holds a Ph.D. in Biochemistry from the Indian Institute of Science and completed postdoctoral research at the NIH, USA. His research focuses on nucleoporins, annulate lamellae, ER–mitochondria contact sites, nucleo-cytoplasmic transport, and intercellular communication, particularly the roles of Nup358, Ran GTPase, and SUMOylation in mRNA regulation and signaling. His group has shown how annulate lamellae influence organelle interactions and cell metabolism. Dr. Joseph is an elected member of the Guha Research Conference and actively contributes to the Indian cell biology research community.

INSA New Fellow Lecture

Molecular drivers of mitotic chromosome segregation

Tapas K. Manna

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Abnormal chromosome content in cells, termed as aneuploidy, primarily arises due to mis-segregation of sister chromatids during mitotic division and is a leading cause of cancer, birth defects and various developmental disorders. Altered regulation of spindle microtubule attachment with kinetochore, the supra-molecular protein complex assembled on the centromeres of chromosomes promotes this process. Effective coupling of chromosome movement with the dynamic microtubules is critical for the sister chromatids to segregate faithfully. Our research has unveiled that specialized microtubule-associated proteins (MAPs) regulate this coupling both spatially and temporally via interaction with specific kinetochore proteins. We have shown that EB1, a microtubule protein aberrantly expressed in cancers, facilitates chromosome segregation in human metaphase cells by stabilizing microtubule attachment of kinetochore protein complex, Ska via formation of extended microtubule-bound structures. Some MAPs associate with both kinetochores and centrosomes suggesting of their co-regulation presumably via microtubules. Our work has revealed that as the cells progress from early mitosis to metaphase, centrosome protein, Cytoskeleton Associated 5 (CKAP5), also known as ch-TOG (colonic hepatic -Tumor Overexpressed Gene), that is loaded onto microtubules once they start emanating from the mitotic centrosomes, stabilizes kinetochore association of a centromere-specific kinesin motor, CENP-E, whose function is to move the chromosomes from the centrosomal areas to the spindle midzone and align them at metaphase plate. Loss of this function results in premature silencing of spindle checkpoint and chromosome mis-segregation. Mechanistic insights of these key mitosis-regulating proteins that we have uncovered, may foster newer therapeutic strategies to develop in the future.

Speaker's Profile

Prof. Tapas Manna accomplished his PhD in Biochemistry from Bose Institute, Kolkata in 2004 and carried out his postdoctoral research at the University of California, Santa Barbara and then at the Univ. of Massachusetts Medical school, USA, where he identified regulators and mechanisms that govern microtubule dynamics and mitotic checkpoint in human cells. Soon after a short attachment with the Cancer Institute of University of South Alabama, he joined IISER Thiruvananthapuram in 2009 and is currently a Professor at the School of Biology of IISER Thiruvananthapuram. His research has been primarily focused on unraveling mechanisms that control chromosome segregation errors and centrosome amplification and their links to human diseases. He is a recipient of National Bioscience Award by DBT and is a fellow of National Academy of Sciences (NASI) and Indian National Science Academy (INSA).

INSA New Fellow Lecture

Self-organized morphogenesis in plant regeneration

Kalika Prasad

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Our research group investigates the fundamental principles of self-organization in biological systems, using plant regeneration as a model to uncover how form and function re-emerge from disorder. We focus on the mechanics of morphogenesis—the process by which tissues and organs regenerate their structure. Morphogenesis unfolds through a delicate choreography of mechanical forces, cell geometry, and biochemical cues, including hormonal signals. Using *Arabidopsis thaliana* as a model, we examine both tissue culture–mediated and injury-induced regeneration to reveal how mechanical forces guide cellular self-organization. We discovered that shoot progenitors within undifferentiated callus tissues self-organize into functional meristems through a "stretch–compress" mechanism, where local compression and expansion reshape cell geometry and mechanical tension to sculpt the characteristic dome of the shoot meristem. Strikingly, a related "push–pull" mechanism operates during root tip regeneration, driving the convergence of cell files and reestablishment of the stem cell niche. Together, these findings illuminate how mechanochemical feedback and cell geometry orchestrate morphogenesis, offering a unified framework for understanding how plants rebuild themselves with exquisite precision.

Speaker's Profile

Kalika's group investigates the fundamental mechanisms underlying regeneration and developmental plasticity in plants. After earning his Ph.D. from the Indian Institute of Science, Bangalore, he pursued an EMBO postdoctoral fellowship at Utrecht University. His group at IISER Pune explores how mechanical, geometric and biochemical cues coordinate tissue regeneration. A Fellow of Indian Science Academies, INSA, IASc, and NASI, he serves on the Editorial Boards of Developmental Biology, Plant Communications and Journal of Genetics.

INSA Associate Fellow Lecture

HDACs regulate immune cell dynamics and ECM remodelling during appendage regeneration in zebrafish and axolotl

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Vertebrates, such as zebrafish (*Danio rerio*) and axolotl (*Ambystoma mexicanum*), possess a remarkable tissue regenerative capacity that enables them to restore complex tissues, including the retina, spinal cord, tail, and limb. Deep injuries to their appendages induce epimorphic regeneration, resulting in the scar-free restoration of damaged organs. Zebrafish and axolotls regenerate appendages through cellular reprogramming, driven by a diverse range of genetic, epigenetic, and extracellular matrix (ECM) cues. Histone deacetylases (HDACs) regulate the chromatin state, thereby affecting the activation or suppression of gene programs during reprogramming. We examined the pre-amputation role of HDACs in appendage regeneration in zebrafish and axolotl. Pharmacological HDAC inhibition with Trichostatin A (TSA) led to excessive ECM deposition and altered the immune microenvironment, thereby impairing tissue regeneration. RNA-seq revealed a pro-inflammatory transcriptional milieu, which was phenocopied by bacterial lipopolysaccharide (LPS). Combined LPS/TSA treatment increased infiltration of pro-inflammatory $CD11b^{+}$ myeloid cells, promoted $CD4^{+}$ T-cell recruitment, and drove TGF-β-dependent collagen deposition. The LPS/TSA-induced regeneration block was rescued by the free-radical scavenger N-acetylcysteine. Conversely, blocking lymphocyte egress with FTY720 prevented regeneration, whereas Collagenase D rescued the TSA-mediated block. Collectively, our findings demonstrate that stringent HDAC-mediated control of immune cell trafficking and collagen deposition is crucial for the successful regeneration of appendages.

Speaker's Profile

Prof. Rajesh Ramachandran has been working on tissue regeneration since 2007, beginning with postdoctoral research at the University of Michigan in Ann Arbor. He joined IISER Mohali in 2012, where he continues to study retinal regeneration in zebrafish and established the axolotl as a model for limb and tissue regeneration. His group investigates how genetic and epigenetic regulators, as well as systemic conditions such as diabetes, shape regenerative outcomes. A central focus is identifying conserved cellular reprogramming signatures across species and tissues to form curative strategies for mammalian retinal blindness. He has published several peer-reviewed articles on regeneration.

INSA Young Associate Lecture

Harnessing the unconventional molecules in parasitic signalling pathways for drug development in protozoan parasite E*ntamoeba histolytica*

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Protozoan parasite *Entamoeba histolytica* causes amebiasis in humans through a coordinated role of motility, adhesion, cytolysis, and multiple endocytic processes leading to symptoms ranging from diarrhoea, dysentery to invasive forms. Pathogenesis begins when the parasite degrades host tissues via phagocytosis (ingestion of dead cells or debris) and trogocytosis ("nibbling/eating" live host cells) to ingest host material, leading to tissue damage and eventual ulceration. Although there have been overlap of molecules participating in phagocytosis and trogocytosis yet only an AGC family kinase is known to be involved in the trogocytosis exclusively. Along with other signalling events, Ca^{2+} dependent signalling has been shown to be important for the endocytic processes and pathogenesis as well. We are currently looking at unconventional CDPK Related Kinases (CRKs) expressed in the parasite which has not been investigated so far. These kinases present sequentially diverged CaM and Ca^{2+} binding sites in sequences, which were not reported before and indicate existence of a divergent signalling system present in the parasite which can be harnessed for drug development. It is also noteworthy, apart from phosphorylation events, membrane undergoes lots of remodelling during endocytic events by membrane remodelling proteins. We are currently focussed on putative I BAR class of protein which is sequentially diverged from proteins of other system yet displays biochemical characters typical of I BAR class of proteins. Overall, our research is trying to orchestrate the endocytic events that lead to pathogenesis and identify the druggable targets for developing anti amoebic agents.

Speaker's Profile

Dr. Somlata has completed her education from University of Delhi and Jawaharlal Nehru University. She has been working on understanding signalling pathway of protozoan parasite since 2005. Her lab is trying to build the signalling orchestra which leads to endocytosis by parasite involving kinases, actin remodelling and membrane remodelling. Her PhD work led to identification of a C2 domain kinase involved in initiation of phagocytosis by parasite E. histolytica and its detailed biochemical characterisation. Further, in post doctoral research she identified a kinase exclusively involved in trogocytosis by the parasite, which is first report of a kinase to be involved in trogocytosis. She is currently focussing on identifying inhibitors for kinases important in pathogenesis along with membrane remodelling. Her work has so far led to 5 grants by UGC, DBT and SERB along with DST Inspire faculty award in 2012 and INSA young scientist in 2016.