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ISCB NEWSLETTER

Indian Society of Cell Biology (Regd.)

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Welcome Note by the President

Dear Colleagues, Fellow Cell Biologists, and Young Students,

It gives me immense pleasure to connect with you again through this newsletter. The past year has been truly rewarding. We are delighted to have received support from the Neer Tewari Foundation for an endowed award for student members of the Society, and to have renewed our membership with the Asian-Pacific Organisation for Cell Biology (APOCB). My Secreteriate colleagues Prof S. Ganesh and Prof Nitin Mohan and I have attended the APOCB Executive Committee meeting last month, and I am confident that this umbrella organisation will play a leading role in fostering collaborative research across the region.

IIT Kanpur hosted the 48th Annual Meeting of the Society in December 2025. It was an exceptionally well-organised event, with excellent sessions and speakers. With over 400 participants and 30 invited talks, the conference provided an ideal platform for discussing contemporary topics in cell biology and for students to learn from peers and experts. The student delegates showed remarkable enthusiasm in presenting their findings through posters and short talks, and their work was truly impressive. I would like to place on record my grateful appreciation for the organising committee, whose efforts in hospitality and planning ensured the success of this high-quality meeting.

I extend my congratulations to Prof. Sandhya Visweswariah for delivering the Professor Jyotirmoy Das Memorial Award Lecture. Her research journey is an inspiration to budding scientists. We are also grateful for her contribution of a review article in this issue, highlighting her celebrated findings on gut reactions and gut instincts. I sincerely thank all authors for their contributions to this newsletter and encourage members to share opinion pieces, commentaries, and reviews on contemporary topics for consideration in future issues. The newsletter I believe could be motivational to the student community and can serve as a valuable platform for meaningful dialogue amongst the membership.

The Society has also been active in outreach. Over the past year, we organised two hands-on workshops for students and four webinar series for the wider community. I would like to thank Cactus Communications for partnering with us in the webinars and Prof. Debdeep Dutta of IIT Kanpur for moderating the sessions. We are grateful to all the experts for their time and participation, and the feedback has been overwhelmingly positive. The Society now seeks fresh proposals for workshops and suggestions for upcoming webinar topics.

Looking ahead, the next Annual Meeting of the Society will be held in December 2026 at IISER Pune, details of which will be shared shortly. I thank our colleagues at IISER Pune for their enthusiasm, and I am confident the meeting will be a great success. I especially encourage student members to register and actively participate. We are also pleased to announce a new initiative—the ISCB Cell Biology Image Award. Details are included in this newsletter, and I urge student members to look out for the call.

I look forward to your comments and suggestions on the Society's activities and to working closely with all of you.

With warm regards,

Thelma BK

President, Indian Society of Cell Biology

Foreword by the Secretary

Dear Fellow Cell Biologists,

It gives me great pleasure to present the first issue of the Newsletter for 2026. This edition features the detailed report of the 48th All India Cell Biology Conference and Symposium, jointly organized by the Society and IIT Kanpur from 7–9 December 2025. The theme was "From Cell to Therapeutics."

The three-day event drew over 400 delegates, with 35 invited talks, 20 student speakers, and 260 posters. Poster sessions were lively, with 15 poster awards and 5 oral presentation awards offering young scientists a platform to showcase their work. A cultural evening added warmth to the scientific exchange. I thank all delegates, speakers, and the host institute for their support. Prof. Etsuko Kiyokawa from Kanazawa University penned a note on the conference from an outsider's perspective.

This issue also covers two workshops—Advanced Microscopy at IIT Kanpur and Cell Biology Methods at Lucknow University. We invite proposals for future workshops. An interview with Prof. Rajiva Raman, past President of the Society and my mentor, highlights his academic journey. It is a privilege to have his reflections in this issue. I thank him for his contribution.

Additionally, three research reviews explore intestinal homeostasis, geroscience, and lysosomal ion channels, alongside an article on hands-on lab training. I thank the authors for their contributions. I am sure members may find these articles informative, and we welcome submissions for the next issue. We also acknowledge our partnership with Cactus Communication in hosting a joint webinar series, moderated by Prof. Debdeep Dutta, that was well received by the community

Finally, I extend deep appreciation to Dr. Deepashree Seshadri for her editorial assistance, drafting the conference report, co-conducting the interview with Prof. Raman, and designing the newsletter layout.

Wishing everyone productive months ahead, filled with meaningful collaborations, and I look forward to meeting you all in Pune this December!

S.Ganesh
Secretary, Indian Society of Cell Biology

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48th All India Cell Biology Conference and Symposium 2025: From Cell to Therapeutics

Venue: Indian Institute of Technology Kanpur
Organizer: Prof. S. Ganesh
Date: December 7–9, 2025

Executive Summary: The 48th All India Cell Biology Conference and Symposium (AICBC 2025), hosted by the Indian Institute of Technology (IIT) Kanpur, stands as a premier forum for advancing the frontiers of cellular research in South Asia. This symposium serves a strategic institutional role, facilitating a high-level dialogue between the rigors of basic biological sciences and the exigencies of clinical translation. By bridging these domains, the conference underscores a commitment to interdisciplinary synergy as a prerequisite for addressing global health and agricultural challenges.

The conference was formally inaugurated on December 7, 2025, with an opening ceremony featuring official welcome addresses and felicitations by the Secretary and President of the Indian Society of Cell Biology (ISCB), alongside the Director of IIT Kanpur and the Dean of Research and Development. A significant highlight of the inaugural proceedings was the official launch of the "Cell Biology Laboratory Manual," a comprehensive resource designed to standardize experimental protocols and enhance pedagogical quality in laboratory settings across the country.

The conference showcased the vibrancy of the Indian cell biology ecosystem, featuring 11 invited thematic sessions, the prestigious 13th Professor J. Das Memorial Lecture, a seminal Plenary Address, and an extensive engagement of 260 poster presentations. The impact of the three-day event is best defined by three Strategic Pillars:

KNOWLEDGE ADVANCEMENT: The conference deepened the collective understanding of cellular mechanisms, ranging from the noncanonical genomic imprinting that governs vertebrate development to the complex signalling pathways that maintain three strategic stasis states through cGMP regulation.

Inaugural Session (Day 1):
The conference was inaugurated by Prof. Manindra Agrawal, Director of IIT Kanpur, and Prof. Tarun Gupta, Dean of Research & Development, IIT kanpur. The Society was represented by President Prof. Thelma, Secretary and Conference Organiser Prof. Ganesh, and co-organisers Prof. Nitin Mohan and Prof. Rakesh Mahji. On this occasion, the Society launched its publication Laboratory Manual for Cell Biology.

TECHNOLOGICAL INTEGRATION (AI/MICROSCOPY): A significant focus was placed on the "Next Generation" of research tools. This included the adoption of "SMART" automated microscopy, super-resolution STORM imaging, and the strategic integration of Artificial Intelligence (AI) in both diagnostic thermodynamic modeling and academic writing ethics.

TALENT PIPELINE DEVELOPMENT: With 20 elite student oral presentations and 260 posters, the event functioned as a critical training ground, providing early-career researchers a high-stakes platform to interface with global experts in genome engineering and organelle dynamics. These outcomes directly fulfil the mission supported by our conference donors, fostering a collaborative environment in which basic science is translated into tangible societal progress and clinical applications.

Scientific Frontier: High-impact Thematic Sessions

The conference featured 11 invited sessions reflecting the interdisciplinary nature of modern cell biology. The various sessions of the 2025 conference covered a broad spectrum of research, ranging from fundamental plant and animal biology to advanced clinical applications and technological innovations. Below is a summary of the sessions based on the sources:.

DAY 1: GENOMIC SIGNATURES, PLANT MORPHOGENESIS, AND AI INTEGRATION

THE INAUGURAL FUNCTION

The 2025 Annual Conference of the Indian Society of Cell Biology was officially launched on the morning of December 7 with a formal Inaugural Function held in the Auditorium from 9:00 AM to 9:45 AM. The ceremony featured a series of welcome addresses from the leadership of the organizing bodies, including:

• Welcome Note by Prof. S Ganesh, Secretary of the ISCB.

• Felicitation to Prof. Tarun Gupta, Dean of R&D, IIT Kanpur

• Welcome note by Prof. B.K. Thelma, President of ISCB

• Welcome note by Prof. Tarun Gupta, Dean of R&D, IIT Kanpur

• Official launch of the Cell Biology Laboratory Manual by IIT Kanpur & ISCB Leadership

• Felicitation and Welcome note by Prof. Manindra Agrawal, Director, IIT Kanpur

• Concluding remarks by Prof. Nitin Mohan, Co-organizer of ISCB.

THE PRESIDENTIAL ADDRESS: GENOMIC FOUNDATIONS OF DISEASE MODIFICATION

The Presidential Address by **Prof. B.K. Thelma**, titled “From a GWAS finding to CIA Mice: Establishing ARL15 as a Disease Modifier in Rheumatoid Arthritis,” set a rigorous scientific trajectory for the proceedings. This session was chaired by **Prof. S Ganesh**. As a distinguished authority in human genetics and medical genomics, Prof. Thelma underscored the strategic necessity of transitioning from identifying genetic risk loci to their functional validation in complex human disorders.

Her address detailed a sophisticated methodology designed to bridge the gap between Genome-Wide Association Study (GWAS) data and therapeutic potential. By focusing on ARL15, a small GTPase identified as a non-HLA susceptibility gene, her team demonstrated how genetic risk factors influence the inflammatory landscape of Rheumatoid Arthritis (RA).

INVITED SESSION 1: DEVELOPMENT, DIFFERENTIATION, & DISEASE

Chaired by Prof. Jonaki Sen (IIT Kanpur), this session explored cross-species developmental mechanics:

- **Utpal Nath (IISc Bengaluru)**: Presented "Inter-cellular communications and epidermal control of organ growth in plants," demonstrating how miR319-regulated TCP transcription factors mediate inter-layer communications via direct protein movement.
- **Kalika Prasad (IISER Pune)**: Discussed "Self-organized morphogenesis in plant regeneration: Integrating mechanochemical and geometric cues," introducing a "stretch-compress" model to explain the re-establishment of the stem cell niche (SCN) through mechanical-biochemical integration
- **Subramaniam K (IIT Madras)**: Interrogated "PLP-1 / PURA: an RNA-granule component with roles in small RNA-mediated gene regulation," identifying PLP-1 as a P-granule component essential for germline gene silencing downstream of small RNA biogenesis.
- **Amitabha Bandyopadhyay (IIT Kanpur):** Detailed how "Articular cartilage can be regenerated in murine models of osteoarthritis," identifying that hyper-activation of BMP signaling drives OA pathology and that chondrocyte plasticity allows for the reversal of the disorder by modulating the joint microenvironment.

SPECIAL SESSION 2: AI IN ACADEMIC WRITING

A special session by Mr. Shashank Suri addressed the "double-edged sword" of AI in

Research include:

- Reliability: Verifying AI-generated data against primary sources to ensure scientific integrity.
- Data Privacy: Guarding proprietary or unpublished data against public AI models.
- Ethical Selection: Choosing tools based on transparency and alignment with academic standards.

ICMR-DHR SESSION 3: INNOVATION & THERAPEUTICS

Chaired by **Prof. Amitabha Bandyopadhyay**, this session highlighted academic publishing. Ethics Guidelines for AI in clinical advancements:

- **Kartik Sunagar (IISc Bengaluru):** Analyzed the "Evolutionary Ecology of Indian Snake Venoms," highlighting how regional venom variation severely impacts antivenom efficacy and necessitates pan-India therapeutic solutions.
- **Sivaprakash K. Ramalingam (IIT Kanpur):** Presented the preclinical validation of bi-specific CAR-T cells. He noted that CD19 antigen loss triggers relapse in more than 40% of patients, and his dual-targeting approach (CD19-CD22) showed superior anti-tumor

• **Ganesh P. Namasivayam (Kyoto University/IIT Roorkee):** Discussed "Programmable Epigenetic Switches," including the development of MITO-PIP—the first mitochondrial gene switch designed to eliminate mutated mitochondrial DNA.

DAY 2: CELL CYCLE CONTROL, TRANSLATIONAL SCIENCE, AND THE J. DAS MEMORIAL LECTURE

Day 2 shifted toward fundamental cellular mechanics and their translation into clinical paradigms, underscored by the conference's most prestigious endowed lecture.

INVITED SESSION 4: CELL CYCLE CONTROL, GROWTH & CANCER

Chaired by **Prof. Sathees C. Raghavan (IISc Bengaluru):**

• **Alok Krishna Sinha (NIPGR Delhi)**: Identified the MAPK cascade's role in regulating the rice cell cycle from G1 to S phase, significantly influencing plant architecture and yield.

• **Kaustuv Sanyal (Bose Institute):** Explored genome organization in *Cryptococcus neoformans*, noting that metazoan-like late-replicating centromeres likely favor the unclustered centromere state during S-phase.

• **Pradip Sinha (IIT Kanpur)**: Advocated for a host-centric perspective of cancer, using Drosophila models to show how host communication networks across distant organs collaborate to plunder host resources.

• **Shaida Andrabi (Univ. of Kashmir):** Utilized Polyoma virus small T antigen, which binds the phosphatase PP2A, to induce mitotic arrest and apoptosis via the upregulation of UNC5B and FOXO1/3.

THE 13TH PROFESSOR J. DAS MEMORIAL LECTURE: INTESTINAL HOMEOSTASIS AND SIGNALING

Professor J. Das Memorial Lecture commemorates the legacy of an eminent biophysicist who pioneered the study of the genetics of Vibrio cholerae. This year, the ISCB honored **Prof. Sandhya S. Visweswariah** for her pioneering work in cyclic nucleotide signaling, an area that epitomizes the integration of biochemistry and human pathology. In her lecture, "Fundamental 3Gs: Gut Reactions, Gut Instincts and cGMP," Prof. Visweswariah addressed the critical "So What?" of the GUCY2C gene. The gene encodes the receptor guanylyl cyclase C (GC-C), which maintains fluid-ion homeostasis in the gut. Utilizing mouse models and organoids harboring activating mutations, her lab identified novel pathways regulated by cGMP. This research offers a roadmap for therapeutic intervention by identifying molecular targets that can be modulated to treat severe secretory disorders, bridging structural biology with clinical gastroenterology.

INVITED SESSION 5: MICROBES, INFECTION & IMMUNITY

Chaired by **Dr. Rakesh K. Mahji (IIT Kanpur):**

• **Manoj Prasad (DUSC):** Detailed how SlATG8f interacts with viral TrAP proteins to mediate their degradation via autophagy, attenuating host RNA silencing suppression.

• **Indranil Banerjee (IISER Mohali)**: Discovered a noncanonical role for the WASH complex in lipid raft-mediated entry of Influenza A, regulated by a TRIM62-VPS35 mechanistic axis.

• **Santosh Chauhan (CCMB):** Positioned IRGM (the "Jesus Gene") as a central checkpoint that maintains immune homeostasis and restrains excessive interferon responses.

• **Dhiraj Kumar (ICGEB):** Interrogated the regulation of host alternative RNA splicing by Mycobacterium tuberculosis, proposing that the evolution of virulence in Mtb coincided with its ability to establish a stranglehold on host splicing machinery.

INVITED SESSION 6: TRANSLATIONAL SCIENCE

Chaired by **Dr. Debasmita Pankaj Alone (NISER):**

• **Rita Mulherkar (BKL Walawalkar Hospital):** Discussed an ongoing Phase 1 trial for back pain using IVD cells cultured with non-xenogenic supplements such as autologous serum (AuS) and autologous platelet lysate (AuPL).

• **Mathivanan Jothi (NIMHANS)**: Identified PAX3 as a molecular "gatekeeper" and presented potential small-molecule PAX3 activators to inhibit pediatric malignancies like neuroblastoma.

CULTURAL INTERLUDE: "SCIENCE MEETS RHYTHM“

In a spectacular conclusion to the second day, the conference celebrated the harmony between scientific precision and artistic expression. The evening featured a Kathak dance drama titled “Nritya Rang”, presented by the Padmaja Kala Sansthan. This performance underscored the theme of "Science meets rhythm," offering attendees a moment of creative reflection amid the rigorous scientific schedule.

DAY 3: NEUROSCIENCE, SIGNALING, AND THE FUTURE OF MICROSCOPY

The final day focused on high-resolution imaging and the molecular orchestration of the nervous system.

JAY PULLUR SESSION (SESSION 7: NEUROSCIENCE)

Chaired by **Prof. S. C. Lakhotia (BHU):**

• **Manish Jaiswal (TIFR Hyderabad):** Revealed that targeted depletion of polyphosphate (polyP) in neuronal mitochondria leads to progressive neuronal dysfunction and shortened lifespan.

• **Nihar R. Jana (IIT Kharagpur)**: Investigated the maternal-specific expression of UBE3A, noting that its loss causes Angelman syndrome while gain-of-function is associated with autism.

• **Samir K. Maji (IIT Bombay):** Discussed how phase separation and the subsequent solidification of alpha-synuclein result in amyloid fibril formation in Parkinson’s disease.

INVITED SESSION 8: CELLULAR SIGNALING

Chaired by **Prof. Arun Shukla and Prof. Sai Paydi (IIT Kanpur):**

• **Jyothilakshmi Vadassery (NIPGR):** Identified JACE1 as a plasma membrane-localized ABC transporter that functions as a JA-Ile efflux transporter with Ca2+-conducting abilities.

• **Jomon Joseph (NCCS):** Revealed that Nup358 restricts ER-mitochondria contact sites (ERMCSs) by regulating the mTORC2/Akt/GSK3β axis.

• **Prem N. Yadav (CDRI):** Explored TGR5 signaling in neural stem cell homeostasis, demonstrating its role in rescuing "inflammageing" via the p53-p16 pathway.

• **Murty Srinivasula (IISER TVM):** Examined the role of endosomal and lysosomal ubiquitin ligases in regulating inter-organelle dynamics and homeostasis.

INVITED SESSION 9: TOOLS & METHODS

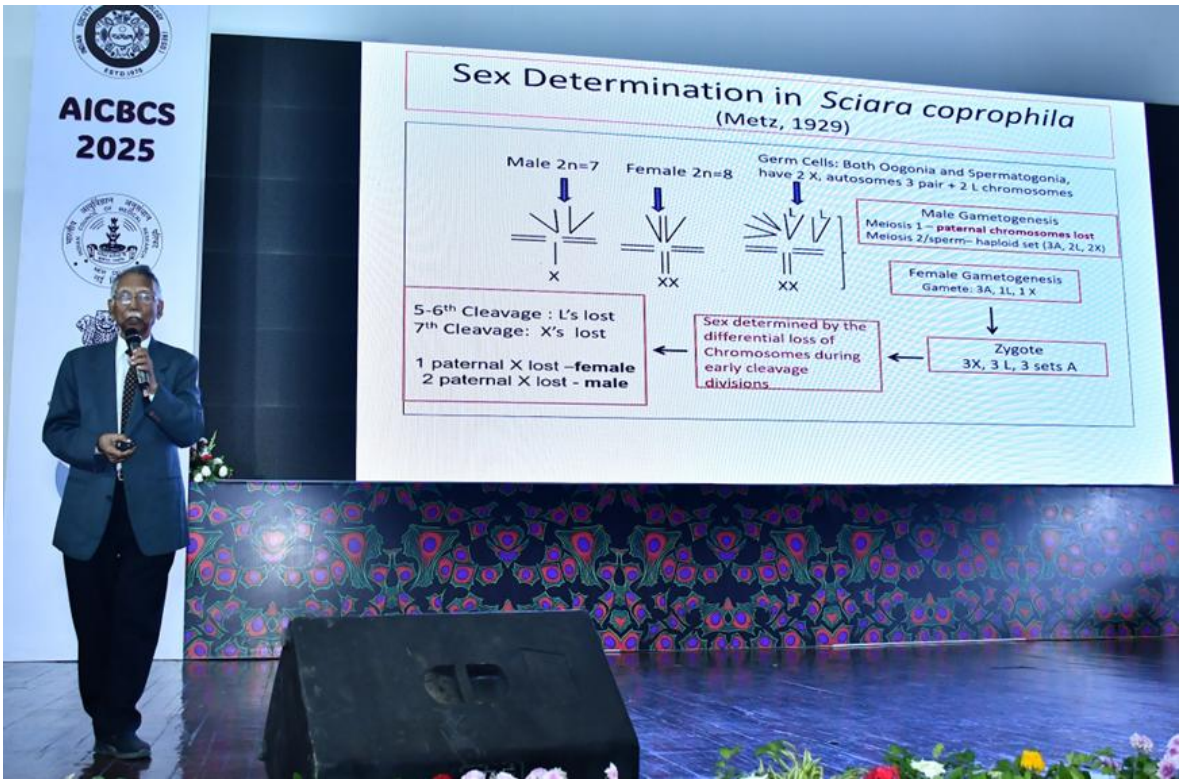
Chaired by **Dr. Nitin Mohan (IIT Kanpur):**

• **Gaurav Ahuja (IIIT Delhi):** Introduced "Inertrope," an AI-guided liquid biopsy that diagnoses cancer with over 90% AUC-ROC using thermodynamic "ping-pong" in plasma.

• **Chayan Kanti Nandi (IIT Mandi):** Discussed the rational design of fluorescent nanomaterials, such as carbon nanodots, for multimodal organelle imaging.

PLENARY SESSION 10: GENOMIC IMPRINTING

Prof. Rajiva Raman's Plenary Address, "Genomic Imprinting – A hundred years of Enigma," synthesized a century of research from the *Sciara coprophila* model to the Igf2/H19 gene cluster on mouse chromosome 7. This session was chaired by Prof. Madhu Tapadia, BH U Varanasi. He distinguished between Canonical imprinting (governed by DNA methylation) and Noncanonical imprinting (governed by diverse epigenetic factors, such as histone modifications). Prof. Rajiva Raman provided an expert overview of genomic imprinting, discussing the epigenetic mechanisms (such as DNA methylation and histone modifications) that govern gene expression based on parental origin. He addressed the long-standing mysteries of imprinting and its implications .



SPECIAL SESSION 11: EVOLUTION OF MICROSCOPY

Dr. Rishi Kant (Carl Zeiss) evaluated "SMART" microscopy, which uses AI for automatic sample recognition and auto-calibration for various sample carriers. This session was chaired by Prof. Sujit K Bhutia, NIT Rourkela.

NURTURING THE FUTURE: STUDENT ORAL AND POSTER PRESENTATIONS

The student research showcases were a cornerstone of the conference, featuring three dedicated oral sessions and extensive poster presentations. These sessions highlighted the next generation of scientists' contributions to cell biology, ranging from molecular mechanisms to innovative therapeutic applications. With 20 elite student oral presentations and 260 posters, the event functioned as a critical training ground, providing early-career researchers a high-stakes platform to interface with global experts in genome engineering and organelle dynamics.

The conference's quantitative metrics reflect a significant shift in Indian cell biology toward computational integration and mechanobiology. The robust representation of student speakers and a heavy emphasis on AI-driven diagnostics and integrated omics suggest a maturing scientific ecosystem increasingly focused on high-throughput, high-resolution data.

STUDENT ORAL PRESENTATIONS

1. **Sumanta Kar**: Is there a molecular brake for endosomal chloride/proton exchangers? The answer may lie with TMEM9

2. **Deepak M. Khushalani**: Many Make Mighty: LC3 forms functional nanoclusters on autophagic vesicles

3. **Saurabh Chand Sagar**: RhoGTPase and CDC42 disruption in the absence of Caspase-3 activity affects actin homeostasis through Rok, Arp2/3 and Gelsolin in Drosophila Malpighian tubules

4. **Priya Chouhan**: Arl8b promotes LAMP1 sorting to endolysosomes by inactivating Rab11-mediated endocytic recycling pathway

5. **Bhawna:** Understanding the effect of antidepressant Paroxetine on hepatic lipid metabolism: Implications in fatty liver disease

6. **Shreetama Banerjee:** Basic FGF downstream ZIC3 at the fulcrum of Neurons and Astrocytes fate specification

7. **Ankita Das**: The CRISPR-Cas System Distinctly Regulates Acid Tolerance, Bile Resistance, and AMP Susceptibility in Salmonella serovars

8. **Kavikumar A. Karuppusamy**: Cardiac Dysfunction in Lafora Disease: Evidence of Peripheral Organ Involvement in a Neurodegenerative Disorder.

10. **Dharitri Chaudhuri**: Hyperactivation of receptor Guanylyl cyclase C (GC-C) increases susceptibility to infection with an entero-pathogen

11. **Rakesh Kumar Kar**: Autophagic degradation of PAX9 maintain stemness and its reactivation drives cellular senescence in oral cancer stem cells.

12. **Rudranarayan Sahoo**: Caspase-1 Dependent Pyroptosis and DPP8 Downregulation in Fuchs' Endothelial Corneal Dystrophy

13. **Anjali Kumari**: Non-canonical Acinetobacter baumannii GapA enables iron acquisition via hemin, human iron transport proteins

14. **Sougata Das**: Vibrio cholerae Outer Membrane Vesicles deliver OmpU to mitochondria via lysosomal trafficking to alter epithelial cell homeostasis

15. **Aditya Ramdas Iyer**: CD19-CD22 Coregulation Shapes Antigen Selection in Multi-Target CAR T-cell Strategies for B-cell Malignancies

16. **Nitin Agnihotri**: Spatially resolved transcriptomic profiling identifies BMP signaling-dependent gene regulatory network controlling neuronal migration and polarity during cerebral cortex development

17. **Upasana Bhattacharyya**: Development of ex vivo hematopoietic stem cell maturation-based assay system using peripheral blood mononuclear cells and testing of druggable compound for Thalassemia treatment

18. **Janvi Patel:** Adaptive signaling rewiring drives Tucatinib resistance in HER2-positive Breast Cancer

19. **Somnath Jan:** Engineered Bio-inspired Peptide Based Total Wound Care

20. **Sreyashi Nath**: Characterisation of a novel peptide binder isolated by Phage display peptide screening for Platinum-resistant Ovarian Cancer






POSTER SESSIONS

The poster sessions of the conference, held on Day 1 and Day 2 for two hours each, proved to be a highlight of the meeting. With over 130 posters presented on each day, the sessions showcased the breadth and depth of research being carried out by young scientists. Nearly two-thirds of the posters were in competition for awards, judged by a distinguished panel of 20 experts. As is well recognised in the Society's meetings, the poster sessions remained the most vibrant and engaging part of the programme. Delegates thronged the poster area, interacting enthusiastically with the presenters, exchanging ideas, and offering constructive feedback. This dynamic environment not only encouraged scientific dialogue but also greatly benefitted the student community, giving them exposure, confidence, and valuable networking opportunities. The high quality of presentations this year was particularly noteworthy. In recognition of the outstanding work displayed, the organisers decided to increase the number of awards to 15, ensuring that more deserving contributions were acknowledged. This decision further motivated the participants and underscored the importance of poster sessions as a platform for nurturing young talent. Overall, the poster sessions went exceedingly well, reinforcing their reputation as the most lively and impactful component of the conference.

VALEDICTORY FUNCTION AND RECOGNITION OF EXCELLENCE

The closing ceremony celebrated academic merit and institutional support. We extend our deepest gratitude to our esteemed sponsors who made this vibrant scientific gathering possible. Your support fosters innovation and provides a platform for the next generation of cell biologists.

The distribution of honors at AICBC 2025 is organized around three structural pillars, each representing a unique form of endorsement within the academic hierarchy.

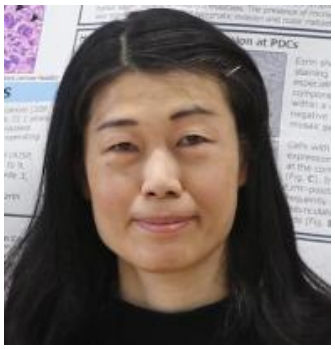
Congratulations to AICBCS-2025 Awardees!

	Name of the award	Awardee	Affiliation
Oral Awards	Neer Tewari Foundation Award	Upasana Bhattacharyya	Univ. of Burdwan, Burdwan
	Dr B R Sheshachar Memorial	Aditya Ramdas Iyer	IIT Kanpur
	Cactus Prize	Somnath Jan	IISER Kolkata
	J K Cement Prize	Rudranarayan Sahoo	NISER Bhubaneswar
	Development Dynamics Award	Priya Chouhan	CSIR-IMTECH, Chandigarh
Poster Award	Neer Tewari Foundation Award	Sweta Kushwaha	IIT Kanpur
	Dr C M S Das Prize	Shreyasi Dey Sarkar	SINP, Kolkata
	Dr S R V Rao prize	Muqtada Ali Khan	CSIR-CDRI, Lucknow
	Dr V C Shah Prize	Sayeda Fauzia Iqbal	IIT Kanpur
	Dr A S Mukherjee Memorial Prize	Sampurna Pal	IISER Mohali
	Dr A N Bhishey Prize	Omkar Dhurat	ACTREC-TMC, Navi Mumbai
	Dr Mansi Ram Memorial	Sudhamani Ramakrishnan	IIT Kanpur
	J K Cement Prize	Srayasi Majee	IIT Kanpur
	ISCB Prize	Shefali Tripathi	IIT Kanpur
	Cactus Prize	Divya Bindra	IISER Bhopal
	Organizers Award	Deepa Ajnar	IIT Kanpur
		Diksha Joshi	ACTREC-TMC, Navi Mumbai
		Aranya Pal	NISER Bhubaneswar
		Pratyashaa Paul	IISER Berhampur
		Agimanailiu Khapuinamai	LVPEI, Hederabad
		Biswaheree Mahananda	IISER Mohali
		Mohankumar B SenthilKumar	IIT Kanpur
		Lekha Yadav	IISER Mohali
	Development Dynamics	Oeshi Sarkar	IIT Kanpur
		Saptadipa Basak	UM-DAE-CEBS, Mumbai

Conference Evening:
Kathak dance drama "*Nirya Rang*", presented by *Padmaja Kala Sansthan*

Conference report was prepared by
Dr Deepashree Sheshadri (IIT Kanpur)

Experiencing the 48th All India Cell Biology Conference: A Perspective from Japan



Professor Etsuko Kiyokawa is a prominent pathologist, professor and chair of the Department of Oncologic Pathology at Kanazawa Medical University, Japan. She is an active member of the *Japan Society for Cell Biology (JSCB),* currently serving as an Editor for its official journal, ***Cell Structure and Function***. Her research specializes in biosensors and molecular pathology, bridging advanced cell imaging with clinical diagnostics.

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First of all, my sincere greetings to all members of the Indian Society for Cell Biology (ISCB). I am Etsuko Kiyokawa, a professor of the Department of Oncologic Pathology at Kanazawa Medical University, Japan. I recently attended the 48th All India Cell Biology Conference and Symposium and Prof. S Ganesh kindly gave me an opportunity to contribute to the newsletter. In this article, I would like to share my impressions of the conference, introduce myself, the Japanese Society for Cell Biology and its journal, CSF.

On arrival

On December 5th, I arrived in Delhi in the evening after a roughly 10-hour flight from Tokyo. At a hotel near the airport, I ate chicken biryani, took a shower, and drifted off to sleep. When I woke up in the middle of the night and opened my laptop, I found an email from IndiGo informing me that the next day's flight, Delhi to Kanpur, had been cancelled. I remember that Prof. S. Ganesh had previously advised me to fly from Delhi to Lucknow. I went to Air India website and managed to book a flight: By that time, there were only four seats left. Despite the sudden change, the conference office arranged for a taxi. I enjoyed a comfortable drive along the highway in the hazy dim light. It was so calm that I could see in the rearview mirror that the driver was trying to stay awake, but the only thing rising were his eyebrows. That might have been the most dangerous moment of the entire trip. Entering Kanpur, the hustle and bustle of cars, people, and motorcycles started to surround us. Silence returned again upon entering the IIT campus. With its green lawns and brick buildings, it was as if I had traveled back as a graduate student arriving at the Oncogene Meeting at the university outside Washington, USA.

After the lecture on conference Day 0 evening, I enjoyed a dinner under the moonlight. This was my second visit to India (the first time was a 10-day sightseeing trip about 25 years ago), and it was my first time in an academic meeting in India. I felt the same unique Indian tolerance and floating sensation reminiscent of Tabucchi's novels as before. The auditorium filled with flowers, outdoor poster sessions and exhibits with dogs, a break for chai and pakoras, and classical Indian music and dancing. The conference had a very refreshing atmosphere, unlike anything I had experienced in other countries, including Japan.

Introduction of myself

Society members attending the conference must have wondered, "Who is she?" I was born and raised in Hamamatsu City, Shizuoka Prefecture, Japan. I graduated from a local medical school and obtained my medical license. I entered graduate school, majoring in pathology. In my third year of graduate school, I joined the Department of Infectious Disease Pathology at the National Institute of Infectious Diseases in Tokyo. I moved to Dr. Didier Trono's Lab (Geneva, Switzerland). I then worked at RIKEN (Wako, Japan), Osaka University, and Kyoto University. In 2011 I had the opportunity to have my own lab in Kanazawa. As I have worked in various places and my research interests are diverse: Basic cell biology to clinical medicine; cell polarity in cell migration and organoids, HIV-1 infection, inflammation, cancer cell invasion and metastasis; small G proteins and lipids; FRET live imaging in mice. I have pursued what I found interesting at those moments. My long-term mentorship with Dr. Michiyuki Matsuda in Tokyo, Osaka and Kyoto, led to my participation in this conference in India.

I am currently serving as a part-time researcher at the Japan Society for the Promotion of Science (2024-2026) to investigate trends in academic journals, and as one of the editors (2023-2026) of CSF.

Impression of the conference

At the conference, I received a strong intention to encourage and support junior researchers. The committee members sat in the front row among the audience and asked many questions. I found it is helpful for young researchers that the chairpersons' career paths were presented, including their experiences studying abroad. Although the presentations were filled with endless questions (I would expect more questions from students), which went well over time, it was magic that the conference ended on time. The large number of disease-related issues, such as cancer and infectious diseases. In JSCB meeting, we are more focusing on basic research. It is similar between ISCB and JSCB meetings that they cover a wide range of subjects and methods, from cultured cells to model organisms such as mice and *Drosophila*. I also found many posters on chemical biology and engineering. We have another societies, Japanese Society for Developmental Biology and Japanese Society for Chemical Biology. JSCB shares the annual meeting with them once in several years.

During the poster session, it was dazzling to see the students understand the significance of their research and explain clearly the key points in their own words. Many presentations showcased innovative experimental systems and thorough quantitative analyses, which truly represent the essence of cell biology. It seemed that they were aiming for top journals. I was also very impressed by the large number of female researchers among the president and committee members, as well as by the fact that most of the award recipients were women. JSCB is a little behind in this regard.

About JSCB and CSF Promotion

JSCB was established in 1950 with the aim of contributing to life science research and education in Japan. JSCB has maintained a membership of up to 1,000. CSF is a long-established journal that will reach its 50th volume in 2025 and has published over 2,000 papers. Its IF is 2.2 (we support DORA, but in Japan IF is sometimes important when applying for jobs, so it cannot be completely ignored). CSF is listed on PubMed, and papers are fully open on J-Stage and PMC. It receives approximately 600,000 hits per year from around the world, mainly from the United States, Europe, and China.

The editorial team of CSF for 2025-2026 consists of Editor-in-Chief Michiyuki Matsuda, and four editors; Hiderou Yoshida, Junichi Ikenouchi, Tomohiko Taguchi, and myself, as well as 42 Associate editors, a 16-member of Editorial board, and 19 International editors. The entire editorial team, including associate editors and editorial board members, reviews all papers

published in CSF and selects the best papers of the year. To be more international, we have made many improvements to meet international standards, including registering with COPE, transferring data from bioRxiv, and transparent peer review contents.

A problem with CSF is that most of the papers it publishes originate in Japan. These years, we have been taking steps to enhance its recognition abroad. In December 2024, we set up a booth at Cel lBio 2024 (the joint annual meeting of the American Society for Cell Biology and EMBO). After the meeting, we got dramatically increasing website accession. Although we watch and focus on the United States and Europe, we should work more on attracting submissions from Asia, since Japan is a member of Asian countries. In September 2025, we set up a booth at the annual meeting of the Korean Society for Molecular and Cell Biology (KSMCB). After that, the web access from Korea increased. Since KSMCB has its own journal (Molecules and Cells), we are afraid that the Korean researchers may not choose CSF to submit their results.

Why India?

In other Asian countries, it is difficult to find on line information about cell biology societies, and it is difficult to know whether they even exist. In contrast, I easily found the well-established website of the ISCB. I also read the newsletters with solid scientific contents, including mini-review articles. Furthermore, there is no academic journal (although I later discovered that there is the Proceedings of the Indian National Science Academy).

I could see from the newsletter that the ISCB is quite active. Many of my high school classmates work for Suzuki Motor Corporation (headquartered in Hamamatsu) and frequently travel to India on business. I also had a personal desire to observe the state of research in India, as I have invested my trust funds in India related projects with confidence in the country's future. However, I hesitated for a while, unsure whether participation from outside India was possible. I had been busy for a while, and by the time I checked the website again, the deadline had already passed.

Suddenly, I felt anxious, realizing that if I missed this year's event, there might not be another one! So I decided to take the plunge and emailed the office, which immediately replied with a positive message. It turned out that Prof. S. Ganesh, who gave me messages, and I were at the same time in RIKEN and Kyoto University. What a coincidence!

It was good to know that the predatory journals have not invaded to ISCB yet. You may have experiences of misguided or overly weighty peer review comments, when you submitted to open-access journals affiliated with major publishers. CSF is committed to respecting authors' findings and offering constructive feedback. We strive to provide a fast response, with a median first response of 17 days (the median) for accepted papers in 2025 and a median period from submission to acceptance of 43 days. We aim to support particularly young researchers, by providing graduate students, post-docs, and assistant professors with the opportunity to experience the publishing process.

When we looked into submissions from India, one paper was submitted each in 2012, 2016, 2020, 2023, and 2024, but unfortunately, they were all rejected. In 2025, one paper was submitted and rejected. After coming back from the conference, I am happy to announce that the first paper from India was accepted in 2026! CSF is looking forward to having many good papers from India. Not only original research papers, we encourage to submit review articles, too. Papers submitted from India in 2026 will incur no publication charges. If you have any questions before submitting, please feel free to contact us by email at csf@nacos.com (CSF Editorial Team).

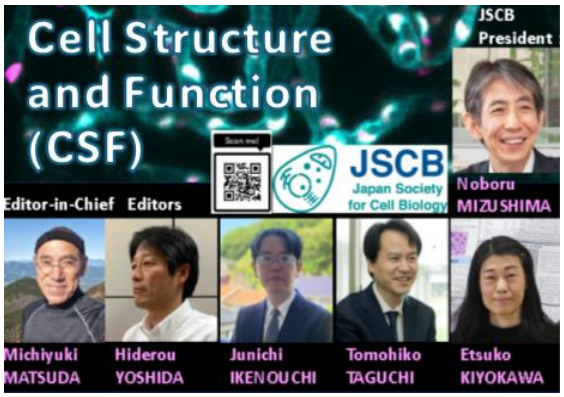
See you again!

Finally, I would like to express my gratitude to Prof. S. Ganesh and his team for their attentive and kind support. They consistently looked after me, often checking whether everything was okay, and even called me while I was in the taxi back to Delhi from Kanpur.

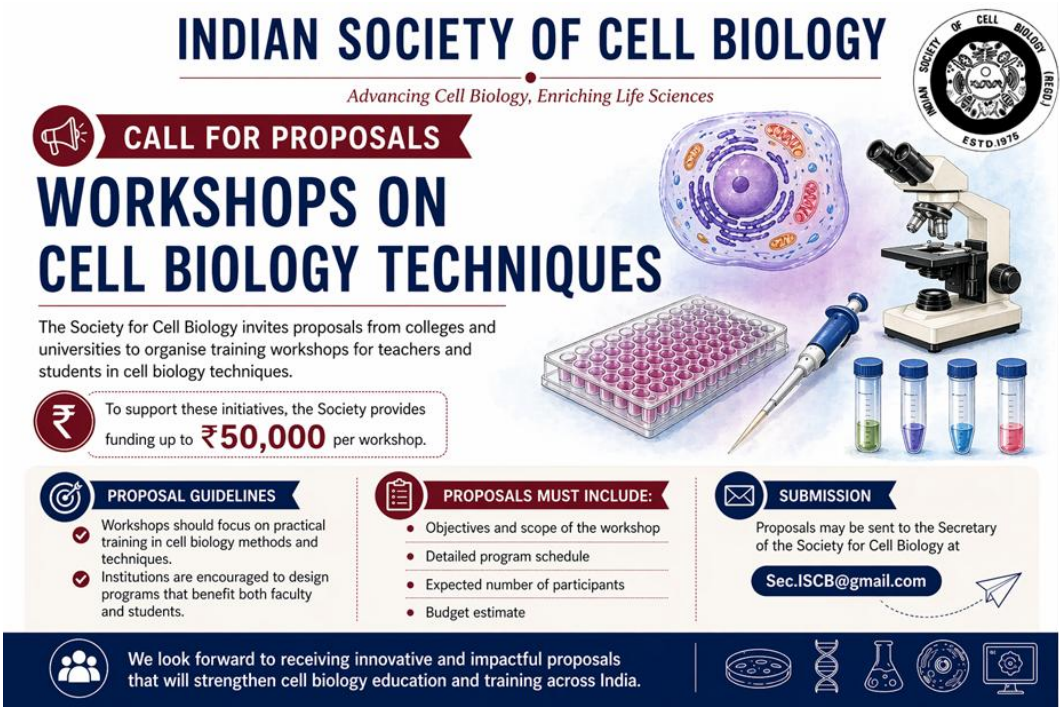
I am especially grateful that they distributed CSF paper fans and were willing to display posters of CSF. India, so it I had assumed I was the only attendee from outside was a real surprise when Dr. Ganesh Pandian Namasivayam from iCeMS (Kyoto University) started speaking to me in fluent Japanese. The warm welcome from the many other participants made this a very fruitful experience. I hope that my visit to this conference will deepen exchanges between ISCB and the JSCB. For your interest, the annual meeting of JSCB will be held in Hokkaido from July 13 to 15, 2026, and in Niigata in 2027. English sessions will be available. We welcome your participation!

CSF website: https://www.jscb.gr.jp/csf/en/

CSF Editorial Team: csf@nacos.com



Call for proposals



Satellite Workshop on Advanced Microscopy: Empowering the Next Generation of Cell Biologists

Venue: Department of Biological Sciences and Bioengineering, Indian Institute of Technology Kanpur
Organizer: Prof. Nitin Mohan
Date: December 10–11, 2025

Following the 48th All India Cell Biology Conference and Symposium (AICBCS-2025) hosted at the Indian Institute of Technology (IIT) Kanpur, a two-day satellite workshop on advanced optical microscopy with hands-on training was successfully conducted from December 10–11, 2025, at the Mehta Family Centre for Engineering in Medicine at IIT Kanpur.

The workshop was designed with a clear goal: to bridge the gap between fundamental biological inquiry and cutting-edge optical imaging technology. The workshop provided an intensive, highly interactive platform for equipping young researchers with the theoretical knowledge and practical skills to leverage advanced microscopy methods in their respective research areas.

Applications were sought from interested students pursuing research from institutions across India, along with registration for the AICBC 2025. All the students who applied for the satellite workshop, a cohort of 24, were invited to attend the workshop. The attendees were divided into five small groups, who took turns observing and gaining hands-on experience with 5 specialised optical microscopes.

Day 1 was filled with an enriching morning session featuring talks from distinguished scientists and industry application experts. The lectures from experts helped the attendees to connect the microscopic events to macroscopic biological phenotypes:

- **Dr Deepak Nair (Professor, IISc Bengaluru)** joined virtually and discussed how super-resolution microscopy methods are used to unravel complex neurobiology in his talk titled, "From Pixels to Polygons: Unveiling Nanoscale Plasticity at Excitatory Synapses."
- **Dr. Gargi Bindal (Scientist, BARC, Mumbai)** explained how she utilized molecular biology and imaging techniques for identifying molecular regulations in micro-organisms, in her work titled, "Live cell imaging reveals reversal of cell division arrest following rac prophage excision in Escherichia Coli."

Fig. 1: Morning lecture session at the satellite workshop: scientists and industry application experts shared insights on how microscopic dynamics influence biological systems.

- **Dr. Sivasurender Chandran (Assistant Professor, IIT Kanpur)** shared his lab's work on non-equilibrium behaviours in micro-organisms revealed by microscopic methods, "Novel Experimental Insights on the Chaotic Behavior of Dense Bacterial Suspensions."

- **Mr. Rishi Kant (ZEISS)** provided comprehensive insights into the instrumentation and image processing of super-resolution and rapid 3D imaging technologies with his talks on "SR Imaging: From Cellular to Organelle Domain" and "Single Snap High-Speed Volume Imaging."

- Experts from **EVIDENT** (including **Dr. Sneha Paul, Dr. Anirban Bose**) thoroughly covered the spectrum of imaging scales, delivering talks on the fundamentals of confocal and super-resolution microscopy, as well as imaging across scales using Widefield, Light-Sheet, and TIRF technologies.

The **second half of day 1 and day 2** were filled with extensive hands-on training sessions. The workshop provided attendees with direct access to five state-of-the-art microscopy systems installed specifically for the event:

- **ZEISS Lattice SIM 5,** with which participants experienced ultra-fast, high-resolution imaging down to 60 nm, utilizing both high-NA oil and water objectives to capture dynamic sub-organelle details.

- **ZEISS Lightfield 4D:** where they learned to capture 3D data in a single snapshot using a 37-microlens array, delivering instant 4D insights.

- **EVIDENT Fluoview FV4000** (Confocal), featuring the breakthrough SilVIR™ detector, this station trained students on achieving high-precision, low-noise biological imaging across the visible and NIR ranges.

- **EVIDENT APX 100** showed participants a benchtop high-end fluorescence microscope that demonstrated how AI-powered, all-in-one systems can streamline the acquisition of publication-quality images.

- **EVIDENT SLIDEVIEW VS200**: showed participants a high-resolution digital slide scanning system where they explored automated whole-slide imaging across multiple modes, including brightfield, fluorescence, and polarization.

To conclude, the Workshop was a resounding success with participants learning to leverage advanced microscopic techniques in their own research and gaining hands - on experience with next-generation imaging technologies. Thanks to the capable Trainers whose invaluable experience from both academia and industry allowed the participants to troubleshoot their specific research bottlenecks in real-time. Overall, the attendees left the workshop with elevated technical confidence, a deeper understanding of optical physics, and fresh perspectives on integrating super-resolution, 4D imaging, and automated microscopy into their ongoing research, from fundamental biology to therapeutic innovation.

Fig. 2: Students getting hands-on experience with advanced microscopes during the hands-on practical sessions with confocal and super-resolution microscopes.

A four-day Seminar cum Hands-on Workshop on "*Recent Cell & Molecular Biology Techniques in Biomedical Research*"

Venue: Molecular & Human Genetics Laboratory, Department of Zoology, University of Lucknow, Lucknow
Organizer: Prof. Monisha Banerjee
Date: February 23-26, 2026

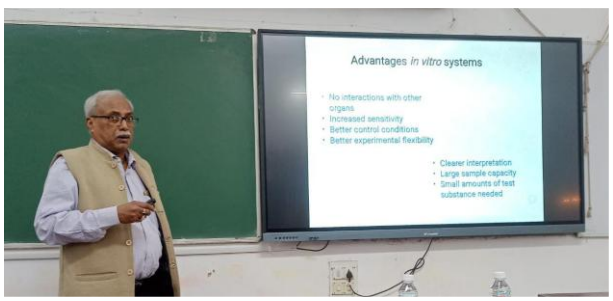
A four-days Seminar cum Hands-on Workshop on Recent Cell & Molecular Biology Techniques in Biomedical Research, sponsored by the Indian Society for Cell Biology, was successfully organized from 23-26 February 2026 by the Molecular and Human Genetics Laboratory, Department of Zoology, University of Lucknow.

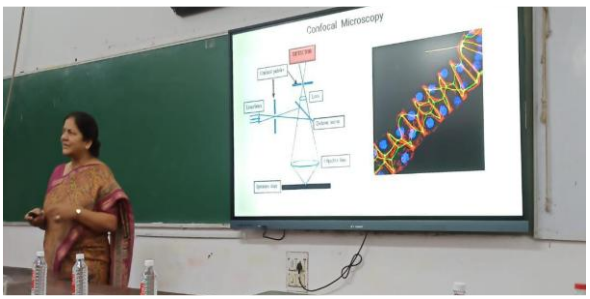
Thirty-seven participants from various universities attended the programme. The workshop featured expert lectures on recent advances in cell and molecular biology. The second, third, and fourth days focused on hands-on training in advanced molecular and cellular techniques, including cell imaging, cell cycle analysis by flow cytometry, molecular approaches for disease diagnostics, and drug discovery.











Workshop @ LU

Fun time!

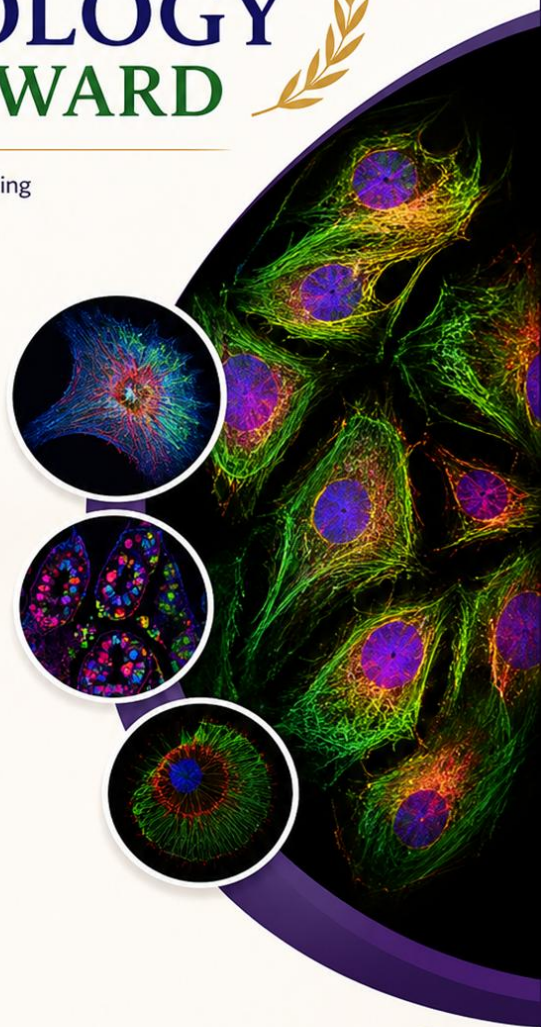
ISCB Awards

ISCB
Indian Society of Cell Biology

The Indian Society of Cell Biology (ISCB) is pleased to announce a new award!

ISCB CELL BIOLOGY IMAGE AWARD

Cell biology is one of the most visually captivating fields of science, producing spectacular images through cutting-edge imaging technologies. To honor and recognize the remarkable work of student members of ISCB, **the Cell Biology Image Award** has been instituted.



ELIGIBILITY

- Student members of ISCB
- Images acquired between Aug 1 (previous year) – July 31 (current year)
- Individual submissions only, certified by the supervisor

SUBMISSION

- Format: 2-page PowerPoint (image + description)
- Deadline: **31 August** each year
- Send to: **Secretary,** ISCB

AWARD

- Three finalists selected annually
- Best image presented at AICBC with a **framed award**
- Certificates for runners-up
- Winning images featured in the **ISCB Newsletter**

Stay tuned for the call!

Celebrate excellence.
Inspire discovery.
Showcase your vision.

Interview with Professor Rajiva Raman: Key Insights

Prof. Rajiva Raman
Cytogenetics Laboratory
Department of Zoology
Banaras Hindu University
Email: *rajiva.raman@gmail.com*

Interviewers: Rashmi Parihar and Deepashree Sheshadri

Early Inspiration in Life Sciences

Deepashree S: You have spent decades exploring genetics and developmental biology. Looking back, what first sparked your curiosity about life sciences and heredity?

Professor Raman: I wasn't a particularly serious student, but when I came to my undergraduate studies, the one subject that immediately caught my attention was genetics. The reason, I believe, was that there was not much to mug up. It was very logical. You couldn't even lose track, and those laws impressed me. I kept wondering how things can follow in such a logical manner when we talk of heredity. That's why the only subject in most of my career that attracted my attention was genetics—because I realized that things can be inherited in a logical and reasonable manner. At that time, genetics was not taught as a separate subject. It was taught only as a part of zoology. The Department of Zoology at BHU was then headed by Professor S. P. Ray Chaudhuri, who did Ph.D with the Nobel Laureate, Prof. H. J. Muller and started animal genetics teaching and research in India. Of course, at that time, we did not know that. To be taught genetics in the manner that it was taught to us—you couldn't have any other liking, at least as far as I was concerned, except genetics.

The other point you asked was about developmental biology. Almost all biologists are always fascinated by how a single cell can grow into a whole organism—development and differentiation. As a young boy, when I was in Class 11–12, we learned that there is an egg and a sperm, they fuse to form a zygote, and from that a whole organism develops. These were the only questions, I should say, that attracted me and made me learn more biology. And that's how it was.

Motivation During Early Career in India

Rashmi Parihar: When you began your career, India's research infrastructure was still evolving. What kept you motivated during those formative years?

Professor Raman: When I did my MSc, you're right—the laboratories were not that well equipped, at least in zoology departments. The Department of Biochemistry and Molecular Biology was not there as a separate subject. But as I said, we were probably the only department in the country doing genetics

experiments—monohybrid crosses, dihybrid crosses, and chromosome preparations at the MSc level. We were not getting good chromosome preparations—that was a different issue—or we were not getting good staining.

But the question that really bothered me at that time came during my MSc special paper—the last lecture—when we learnt about X-chromosome inactivation, the Lyon hypothesis of X-inactivation. This question really fascinated me: how can a whole set of genes—the entire chromosome—get switched off? What makes such a large number of genes switch off all at once? As I went to meet my Head of the Department after my MSc exam, he asked me, *"What are you going to do?"*

. I said, "I'm going to do a PhD with you."

He smiled and said, "Oh, with me? And on what problem?"

I said, "I'm going to work on X-inactivation."

He said, "Okay, go back, have your summer vacation, and then come back.

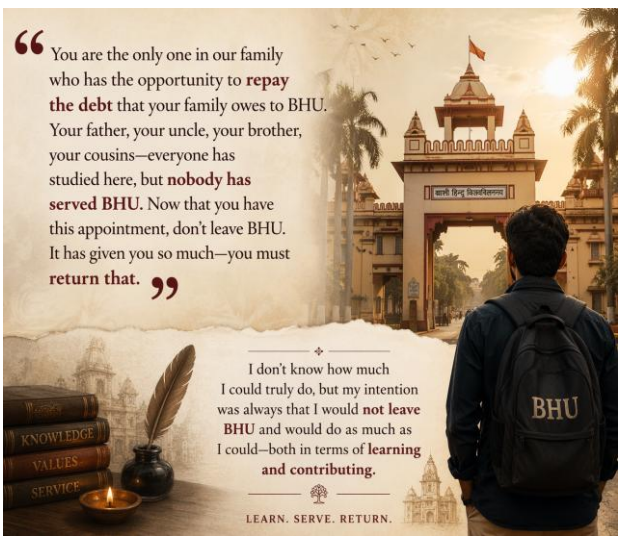
When I returned, he explained that X-inactivation was not feasible to work due to the requirements involved. But he suggested I could work on chromosomes, per se, and later choose any topic once I was ready. Since he was on the verge of retirement he handed me over to Dr Tikaram Sharma, as my Ph.D. supervisor. That's how it started. Our lab was very scientifically engaged—we talked about nothing except science. But it was not boring science; we discussed all kinds of ideas, and nothing else really mattered. I was a cricketer, but I stopped going to the field because the lab took so much of my time. I really enjoyed every moment and kept asking more questions—and that helped me.

Deepashree S: You have been deeply rooted at BHU, an institution with a great scientific tradition. How has the university shaped your philosophy toward research and people?

Professor Raman: BHU is an exceptional university—exceptional in the sense that it was created during British rule with a clear objective: to prepare Indian students—boys and girls—for the future. It was envisioned not only for scientific advancement but also for moral and holistic development. All this was achieved with very little government support—in fact, the government was initially against it. The founder of the university, Madan Mohan Malaviya, travelled across the country to gather donations and build this institution. My father, my uncle, and my maternal uncle—all studied at BHU. So we were imbibed with a strong sense of giving back—of dedicating oneself in order to grow and contribute. That was BHU for all of us. I remember when I became a lecturer and showed my appointment letter to my maternal uncle who was professor in pharmaceutics here. He told me:

"You are the only one in our family who has the opportunity to repay the debt that your family owes to BHU. Your father, your uncle, your brother, your cousins—everyone has studied here, but nobody has served BHU. Now that you have this appointment, don't leave BHU. It has given you so much—you must return that."

I don't know how much I could truly do, but my intention was always that I would not leave BHU and would do as much as I could—both in terms of learning and contributing.



Failures as Turning Points in Scientific Thinking

Rashmi Parihar: Was there a moment in your career when an experiment or hypothesis failed, but later proved to be a turning point in your thinking?

Professor Raman: That's a very interesting question. When I started my PhD, I initially approached Professor Ray Chaudhuri, but since he was retiring, he asked me to join Professor T. Sharma. Professor Sharma was very kind and accepted me. For the first three months, I was working on chromosome preparations, but I wasn't getting good results. So, leave aside hypothesis testing—the method itself was not working. One day, I went to Dr. Sharma and said, "I am your first student, and for three months I have not been able to give you a good chromosome preparation. If you want, I can leave. I don't want you to feel bad that your first student was not good." Dr. Sharma was an exceptional teacher. He laughed and said, "Oh, you're worried about two months? I couldn't do it for six months." He told me**, "Let's try together. If you want to pursue something else, you may—but if you want to stay, remember: failures are part of science. Unless you fail, you won't understand the value of success."**

That stayed with me. Failures are an integral part of success. Unless you fail, you do not truly value success.

Scientific Curiosity and Evolving Research Directions

Deepashree S: Your work spans molecular cytogenetics, chromatin organization, and developmental genetics. What biological question continues to fascinate you the most?

Professor Raman: During my PhD, I worked on chromosomes and on the evolution of rat.

After that, I wanted to explore protein evolution—protein polymorphisms—and see whether I could connect chromosome evolution with protein variation. So I went to Delhi, to the Department of Anthropology, and learned electrophoresis techniques—starch gels, polyacrylamide, cellulose, and so on. When I returned and told Dr. Sharma that I would work on protein polymorphism, he said something that completely changed my thinking: "That problem was given to you by me—that is my problem. Now you must find your own problem." That was a shock. But he explained further: "If you keep working on someone else's problem, you will always remain somebody's student. If you want to become a scientist, you must define your own questions."

At that point, I returned to my original fascination—X-inactivation. I began studying the X chromosome—its function, regulation, and genetics. Over the years, my work has largely focused on sex chromosomes, sex determination, sex chromosome evolution, and related gene functions.

Transition to Molecular Biology and Institutional Change

In 1980, I attended an International Cell Biology Conference in Berlin, with over 3,000 participants. I was shocked that almost everyone was talking in molecular terms—DNA, RNA, Southern blots, Northern blots [PCR was not yet developed]. I returned feeling quite discouraged. I even wrote to my colleague [later we became husband and wife], questioning whether what we were doing was "real science," since we lacked molecular biology infrastructure.

She showed the letter to Professor Sharma. He read it and said, "We should establish a molecular biology lab." It did not happen immediately, but within a few years, we organized a workshop on molecular genetics with Ken Jones. Ed Southern was also invited. When someone questioned why he would come to India for such a workshop, he reportedly said, "I can do molecular biology in my kitchen. This is a scientific lab—I will set it up there."

Although he could not attend eventually, the initiative continued. That is how molecular genetics began at BHU—possibly the first such effort in a zoology department in the country.

Building Human Genetics from Scratch

Later, I felt that unless we moved into human genetics, the field would not progress meaningfully. In 1991, I wrote to the then Vice Chancellor proposing a course in genetics. Surprisingly, he supported the idea. I went to meet him along with Professor Lakhotia, Professor Sharma and Professor Mercy Raman. However, there was strong resistance—even within the zoology department. It took nearly 10 years, and finally in 1999, we were able to start a course in molecular and human genetics. At that time, we had:

- No teachers
- No dedicated funding
- No infrastructure

We used our own research grants, our own lab spaces, and our own teaching time to run the course. When students joined, they asked: "If we study human genetics, where will we do research?" That question compelled us to begin research in human genetics as well. And that is how the journey evolved.

Evolution of Genetics in the Era of Genomics

Rashmi Parihar: Your research connects chromosomal structure, gene expression, and developmental processes. How has the field evolved from when you first began to now, especially with the advent of genomics and high-throughput methods?

Professor Raman: Oh yes—things have changed tremendously. Don't forget, I completed my MSc in 1969. Although DNA as genetic material was established in 1953, but this knowledge reached India quite slowly. Many zoology departments were still not actively engaging with genetics or molecular concepts at that time. We were fortunate to be in a department where teachers like Professor Raychaudhuri and Professor M. S. Kanungo introduced us to genetic material and microbial genetics. But imagine that period, both conceptually and infrastructure-wise, much of biology teaching in India was not ready to embrace what was rapidly becoming an exciting global transformation in science. Our facilities were extremely limited. A centrifuge was considered advanced equipment. Compared to global standards, we had very little. Around the mid-1960s, understanding of chromatin structure improved significantly. It became clear that DNA wraps around histones to form repeating units (nucleosomes). Earlier, there was confusion about whether histones wrapped around DNA or vice versa.

This was a major conceptual shift. Then, in the late 1960s and early 1970s, landmark discoveries began to reshape biology:

- Paul Berg pioneered recombinant DNA technology, for which he was awarded the Nobel Prize in Chemistry (1980).
- Barbara McClintock discovered transposable elements ("jumping genes"), earning the Nobel Prize in Physiology or Medicine (1983).
- Frederick Sanger developed DNA sequencing methods and was awarded the Nobel Prize in Chemistry (1980).

Between roughly 1970 and 1978, biology underwent a dramatic transformation. For the first time, scientists could manipulate DNA itself—something that was unimaginable earlier. Before this, even preparing chromosomes or visualizing cells was considered a major achievement. Our microscopes were limited, and electron microscopes were extremely rare in India—perhaps only a handful existed in the entire country. So studying cellular structures like mitochondria or detailed molecular processes was very difficult. By the time I attended a conference in Germany in 1980, I realized how much the world had moved ahead. Everyone was discussing molecular biology, while we were still largely working at the cytogenetic level. That was a turning point for me. Over the next decade, the pace of change accelerated further. Recombinant DNA technology initially raised biosafety concerns, requiring strict containment facilities. But gradually, these techniques became more accessible. Then came sequencing. Initially, people questioned its utility—what would we gain from sequencing genomes?

Till around 2000, when the Drosophila genome was known, and the human genome was being deciphered, people were still taking it relatively easy. But when the human genome became clear, it brought about a major change.

We began to understand that:

- Large portions of the genome, previously thought to be non-functional, actually have regulatory roles.
- Variations such as SNPs (single-nucleotide polymorphisms) are widespread.
- Not all mutations lead to visible phenotypic changes.
- Complex traits arise from combinations of multiple variants (haplotypes, multifactorial inheritance).

This shifted our understanding from simple Mendelian genetics to highly complex, network-based biology. So, when we talk about monogenic disorders, one may ask whether any disorder is truly monogenic. Possibly not—because even monogenic disorders are influenced by modifier genes and other factors. So actually, what I feel we travelled a very important journey: starting from the dissection of organisms like the fly, the mouse, the squirrel, and the earthworm, and reaching a stage where we can look at DNA, perform sequencing, and ask deeper questions—such as how sex is determined. It has been a fantastic journey. And I am sure that anyone pursuing a career in science will experience how dramatically the world changes as science advances.

I may have spoken at length, but I felt it was important to convey this transition.

Scientific Discovery and the Nature of Inquiry

Deepashree S: In your long academic and research career, if you were to identify one finding that changed your own thinking about biology, what would it be?

Professor Raman: I won't arrogate myself by saying that something I discovered changed my thinking about biology at large. What I experienced were small observations and incremental findings. But the real pleasure was not just in answering questions—it was in how each answer led to new questions. That is the beauty of science: every answer generates further questions. If you remain attentive to those questions, you move forward. If you ignore them, progress slows down. We did some significant chromosome work and identified interesting chromosome mechanisms. One example was a unique sex chromosome system in a tree mouse—X1X2Y/X1X1X2Y—which was quite novel and well-received.

Another important question we addressed was: how does the duration of the S-phase vary?

The DNA content is the same in all cells, yet replication timing differs significantly:

- In early embryonic cells, replication may occur within 7–8 hours.
- In somatic cells, it may take much longer.
- In pre-meiotic cells, it can take days.

So, what governs this variation?

And that was a very fine piece of work we did with one of my colleagues—my PhD student, D D. Dubey—using DNA fiber autoradiography. It was a very painstaking technique. You had to grow cells in 'hot' and 'warm' tritium labeled Thymidine, spread cells on a slide so that the DNA fibers could be visualized. Then, the slide would be exposed to photographic film, and you had to wait for nine to ten months. After that, you would develop the film and finally observe how DNA replicons function. So imagine—after almost ten months, you open the slide, develop it, and only then find out whether your experiment worked. It took almost as long as a gestation period. But what we observed was very interesting. We showed that it is not only the rate of replication or the number of replicons that matters, but that clusters of replicons function together. The number of such clusters is one of the key factors determining the time required for replication. If more clusters are active simultaneously, replication is completed faster. But when clusters are spaced apart or replicate sequentially, the process takes longer.

This was such an interesting observation that when I presented it in the Department of Genetics, one of the very well-known scientists, Lee Hartwell—who later received the Nobel Prize—was not present at the talk. A couple of days later, when I was entering the department, he met me and said, "I'm sorry I could not attend your lecture; my students told me that you have some very interesting findings." He then invited me for lunch, and we had a detailed discussion about the work. He was very excited and said, "We should work together on this." Of course, by the time I had to leave Seattle and return, that collaboration could not materialize. But it remained a very interesting and encouraging moment for me.

Later, I feel very satisfied that I chose to work on a different system. By around 1990, there was growing evidence that the SRY gene on the Y chromosome plays a crucial role in sex determination. Now, we had a common garden lizard in India, which does not possess clearly differentiated sex chromosomes. Reptiles are known to exhibit diverse mechanisms of sex determination—some lack sex chromosomes altogether and instead show environmental influences, such as temperature-dependent sex determination. When genes like *SRY* and *ZFY* were being studied, I thought, why not examine this system? Our initial group of animals showed a clear distinction between males and females, with males showing SRY and ZFY signals, whereas females did not.

At that point, I thought, *"Bingo—we have the answer."*

However, when we increased the number of animals—and this work was being done by Ganesh, your mentor—we found that this was not entirely true. Although most males showed these signals, some females also had them. This indicated that sex determination in this system could not be explained simply by the presence of these molecular markers. Even in the absence of a distinct Y chromosome, these sequences might represent what I would call male-favoured DNA, but they are not strictly male-specific. This raised a more fundamental question: How, then, is sex determined in this organism? So Ganesh explored possible factors such as temperature, hormones, and other influences. However, we found that temperature did not play a decisive role in this case. So the question remained—what determines sex? In fact, I have spent much of my life, and continue even today, trying to answer this question. And the most satisfying part is that it still excites me.

Even this year, I have carried out experiments and generated transcript data, and I am now waiting—very eagerly—for the results. I have sent the samples for analysis, and I am looking forward to understanding what combinations of genes might be involved, and what kind of epigenetic mechanisms could be playing a role. We have examined factors such as yolk, hormones, and other influences, and we are now looking at genome methylation. Because, remember, there is no sex chromosome in this system, and there is no gene that is strictly sex-specific. And yet, sex is clearly determined. So there must be some other mechanism at work. That is what we are trying to understand—and we are enjoying the process.

Nutrition, Genetics, and Population-Specific Effects

The fourth aspect I would like to mention is how nutrition affects gene function.

I focused on a gene called *MTHFR* gene and examined how its SNPs (single nucleotide polymorphisms) influence conditions such as Down syndrome, infertility, and related disorders. What we found was quite interesting. Unlike in many other parts of the world, where this polymorphism is not considered very critical, in India, it appears to have a much more significant impact. Although the frequency of this polymorphism is relatively low, when it does occur, it is often associated with susceptibility to one or more disease conditions. This led us to ask—why does this difference exist? When we submitted our findings for publication, there was initial skepticism.

In Europe, for example, nutritional adequacy—particularly with respect to folate and related factors—is relatively common, so the impact of such polymorphisms is less evident. However, in our population, we found widespread deficiencies—particularly in vitamin B12 and folic acid—along with elevated homocysteine levels. This highlighted the strong interaction between genetics and nutrition. Another ongoing part of my work has been to understand how optimal combinations of nutritional factors can be designed to improve health outcomes. Rather than simply recommending "more protein" or "more carbohydrates," the goal is to develop more balanced and context-specific nutritional strategies. That remains my current focus, and I continue to work on it with enthusiasm.

On Scientific Passion and Failure

Science, to me, is deeply exciting. Every day I come to the lab with enthusiasm, waiting for results, asking new questions. Failure should not discourage you. Instead, it should make you ask:

"Where did I go wrong?"

Often, the issue lies in small details—timing, conditions, overlooked variables. There is immense joy in:

- Doing experiments
- Discussing results
- Being challenged—by data or by colleagues

That challenge is what drives science forward.

Advice to Young Researchers: Questions Over Predictions

Rashmi Parihar: What do you think is still missing in our understanding of the genetic basis of development, and where can young researchers contribute?

Professor Raman: Ah, this is a difficult question. I don't think I can answer that, or that anyone can, because the issue is not what is unanswered—many things remain unanswered. The beauty of biology is that systems are extremely diverse. Take sex determination, for example, which is one of the simplest topics I can refer to. On one hand, you have chromosomal systems—XX and XY, or ZW systems. On the other hand, there are organisms that do not have distinct sex chromosomes but instead rely on small DNA elements that are sex-specific. Then there are systems where temperature plays a role. In some cases, genes may override temperature, and in others, temperature may override genetic signals. This diversity is fascinating. The real question is: how do we understand a specific system, and how does that specificity integrate with general biological principles? Specific observations do not contradict general principles—they refine them. The challenge is to understand how a particular feature fits into the broader framework of biology. That is how hypotheses evolve, and that is how science progresses. I would not venture to predict the future of science—none of us can, and perhaps we should not. But each one of you will find something exciting to work on. Whatever excites you—a disease, a biological phenomenon, any question—is worth pursuing.

For example, one may ask why an organism like "*Ascaris*" has such a simple chromosomal system, or why certain genes behave the way they do. These are just random examples. The important thing is to read widely and ensure that the question you are asking has not already been answered. If it has, then you are only repeating the work—though even replication has its value in confirming results. I remember an important lesson from my MSc days. A visiting scientist, Dr. Grüneberg, who was a well-known mouse geneticist, once asked me what I was working on. At that time, I had not yet begun my work, but I said I would work on X-inactivation.

He asked me, "How do you know that the whole X chromosome is inactivated?"

I referred to a recent paper, which suggested that the X chromosome does not incorporate uridine, implying that it is not transcribing.

He then asked, "Have you tested it yourself?"

I said no.

He replied, "And you believe it?"

That was a turning point for me. He told me something I have never forgotten:

"It is not enough to propose a hypothesis—you must prove it also. You don't write a cheques only; you have to cash them also."

So do not accept results blindly. Test them. Validate them. And then build on them. That is how science moves forward.

Mentorship and Qualities of a Good Researcher

Deepashree S: What qualities do you value most in young researchers, whether it's curiosity, perseverance, or creativity?

Professor Raman: All of them—curiosity, perseverance, creativity—but above all: integrity. A very intelligent person without integrity is not desirable in science. The ability to ask questions freely is equally important. You should not hesitate to question—even your teachers. Over the years, I have mentored around 24–25 PhD students. And I can say this with honesty: Every single one of them was better than me in some way. Each student was unique, and each contributed to my learning. If I seem knowledgeable today, it is because of the brilliant students I had the privilege to work with.

Mentorship Moments and Learning from Students

Rashmi Parihar: Looking back, is there a particular student interaction or mentoring moment that has stayed with you?

Professor Raman: Again, it is a difficult question. There are many such moments.

For example, when Chandrashekhar was working with me on DNA methylation, I had assigned him a couple of genes to study. These genes contained introns. However, he came up with a different idea. He said, "Sir, I am looking for a gene that does not have introns. If introns are present and cleavage occurs there, mapping methylation patterns becomes difficult." That was entirely his idea—not mine.

He went on to work on such genes and study developmental methylation patterns. And that approach worked far better than what I had initially suggested. This taught me something important: Sometimes, if students simply follow what you assign, you may not reach the best answer. But when they think independently and challenge the approach, that is when real progress happens.

Building Scientific Communities: Association with ISCB

Deepashree S: You have played leadership roles in academic societies and have been associated with ISCB for a long time. Can you recall your early association with the society?

Professor Raman: Very fondly. You see, it was December 1975. At that time, there was no formal society for cell biology. University of Delhi used to host cell biology conferences, and Professor Seshachar was the Head of the Department—a protozoologist and a cell biologist. In 1975, I attended one such meeting. I had just completed my PhD and presented my work there. It was during that meeting that the idea was proposed that we should have a dedicated society for cell biology—what later became the Indian Society of Cell Biology. There was overwhelming support for this idea. Everyone present felt that such a society was essential—not only for advancing research but also because cell biology was not being taught systematically in Indian universities at that time. Thus, improving the teaching of cell biology became an important motivation behind forming the society. The society was formally established in 1976, and the first meeting was held at BHU and in January 1977, on the 14th, 15th, and 16th. From 1977 to 2026, it has now been nearly 50 years—a remarkable journey.

In the early years, these meetings were largely focused on chromosomes and cytogenetics. Very soon, the field began to expand. Researchers started presenting work on extranuclear systems, nucleocytoplasmic interactions, mitochondrial function, and many other areas. Then, of course, came the onslaught of molecular biology, and the entire scenario changed.

When I attended recent meetings, I found that a large number of presentations were quite advanced, and it took me some time to fully understand what people were doing. The progress has been so rapid that it is not easy to keep pace with everything. But I can say this with confidence—every piece of work I have done in my career has been presented at the Indian Society of Cell Biology meetings. Many of my students also received awards for their poster and oral presentations there. But that is not the main point. The real value of such meetings lies in the fact that you meet people who understand your work, question you, and contribute to the growth of your knowledge. Any scientific meeting is worthwhile only if it helps you grow intellectually. And I truly feel that I have grown through these interactions. In many ways, the Cell Biology Society has been one of the biggest catalysts in my scientific journey and I have always felt very satisfied about that.

Science Beyond the Lab: Music and Balance

Rashmi Parihar: We've seen your musical side as well. How does music fit into your life as a scientist, does it help you think differently or find balance?

Professor Raman: (Laughs) I have a habit of humming. I keep humming all the time—whether I am working or **not**. But I hum so badly that I prefer nobody notices it! That said, it plays an important role. It keeps me balanced. For example, when you are doing microscopy for long hours, there are moments when you feel dull or drowsy. If you hum while working, it keeps you alert and engaged. It also gives you a sense of companionship—you are not alone. When I am writing or working quietly, humming helps me stay focused. It is also a kind of stress buster. I would encourage everyone to develop some hobby like this—something that helps you stay balanced during challenging times.

What Continues to Inspire a Life in Science

Deepashree S: After so many years in academia, what continues to inspire you— is it students, discovery, or simple curiosity?

Professor Raman: Simple curiosity—most important. And being questioned.

If a student walks into my room—someone I don't even know—and asks me a question, I feel very privileged. That student believes I may be able to help, and that gives me a sense of value. Every day I come to the lab, I feel fulfilled. In fact, on days when I cannot come, I feel something is missing as if I have skipped a meal. Except when I am out of station, or on Sundays, I come to the lab regularly—whatever the circumstances. These days, even if I am not doing major research, I try to write articles for students—on topics like dosage compensation or sex determination. If even a few students benefit, I feel my purpose is served.

Influence of Family and Values from India's Freedom Movement

Rashmi Parihar: We have heard that your family was somehow connected to India's freedom movement. How did those values influence your journey?

Professor Raman: I was born in 1948, just after independence. Both sides of my family—my maternal and paternal families—were influenced by the freedom movement. I would put it this way: my mother, throughout her life, never wore anything but Khadi. In 1942, during the Quit India Movement, my father's house was searched by the police for possessing what was considered "incriminating literature." At that time, such material could include books like the autobiographies of Jawaharlal Nehru or Mahatma Gandhi. Fortunately, they were not arrested. Similarly, during the Salt Satyagraha, my maternal uncle, as a young boy, participated in symbolic acts of protest—such as attempting to extract salt from river water. For such acts, they were detained and taken away, though later released.

I would not say that my family members were active freedom fighters, but the spirit of freedom—especially through non-violence—was deeply ingrained. For me, even today, Mahatma Gandhi represents one of the greatest human beings humanity has known.

If you look at the world today, one often feels the need for values embodied by leaders like Gandhi. If the problems of the world are to be solved, you need people like Mahatma Gandhi, Martin Luther King Jr., Jawaharlal Nehru, and John F. Kennedy—or leaders of that kind. At times, one feels that the world today lacks such values. We are living in a difficult phase, and I often wonder whether this is the kind of world that we envisioned. The idea of using non-violence as a force—even in the face of the most powerful adversaries—and still succeeding, was a remarkable achievement. As individuals, we may not truly become Gandhians or Nehruvians—that is very difficult. But even to be inspired by them, and to believe that such a way of life is possible, is itself a privilege. Studying at Banaras Hindu University, founded by Mahamana Madan Mohan Malaviya, reinforced these values. He was a visionary and a freedom fighter who believed that independence was not just about removing British rule, but also about building the nation simultaneously. BHU was an embodiment of that vision—it aimed to prepare young minds for the future, so that when the country became free, it would be ready to stand alongside developed nations. And I believe we have not done very badly.

Advice to Young Scientists

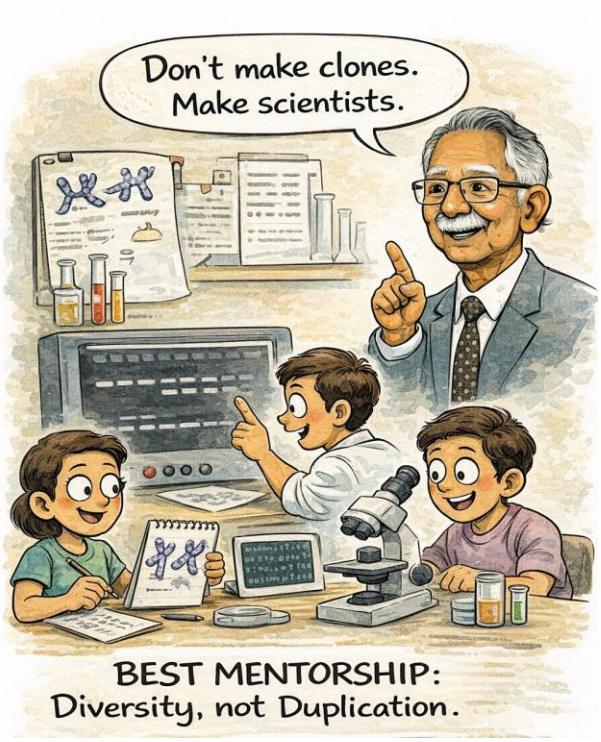
Deepashree S: What advice would you give to young scientists who want to combine scientific excellence with creativity and personal growth?

Professor Raman: My advice is nothing; I am not very good at giving advice. But if I must say something: Have a question—and pursue it with complete integrity. Do not be afraid of failure. Accept it, and ask yourself: where did I go wrong? As Isaac Newton said, sit before your results like a child. Be curious, be open, and listen to what the data is telling you. Science is not about doing big things. It is about consistently doing small things with honesty and curiosity. Even today, I come to the lab expecting that something new might emerge. Perhaps I will finally answer a question I have been asking for 30–40 years. That process itself is fulfilling. If you are in science, the field itself will guide you. It will teach you more than any advice can.

A Lesson on Mentorship

There is one important lesson I would like to share.

When I took my first PhD student, I went with him to my mentor, Dr. T Sharma. After speaking to the student, he turned to me and said: **“Congratulations on becoming a mentor. But remember one thing—you are not here to create your clones. Do not try to see yourself in your students. You are here to help create independent scientists. Shape them, but do not chisel them**.” I have tried to follow that throughout my career.




Rashmi Parihar and Deepashree Sheshadri serve as Research Establishment Officers at IIT Kanpur.

Snapshots!

Professor Rajiva Raman is a distinguished Indian geneticist and Professor Emeritus at Banaras Hindu University (BHU). Specialising in human molecular genetics and cytogenetics, his pioneering research has advanced understanding of sex determination in vertebrates, chromatin organisation, and genetic disorders. A Fellow of all three national science academies, Professor Raman has also made notable contributions to the Indian Society of Cell Biology (ISCB). He served as the Society's Secretary (1997–1999), as the Vice-President (2001-2003) and later as President (2005–2007), playing a pivotal role in strengthening cell biology research in India and in organising national symposia that fostered collaboration and innovation in the field. The image shows the felicitation of Prof. Raman, followed by a group photograph with his colleagues and former students, taken during the Annual Conference of the Society at IIT Kanpur in December 2025.

Professor Sandhya Srikant Visweswariah is a distinguished cell biologist, currently serving as an Honorary Professor in the Department of Developmental Biology and Genetics at the Indian Institute of Science, Bangalore. An accomplished scientist, she has made pioneering contributions to cyclic nucleotide signalling, elucidating cAMP pathways in mycobacteria and cGMP signalling in the human gut. In recognition of her significant contributions to cell biology and cell signalling, the Indian Society of Cell Biology (ISCB) has conferred upon her the 13th Professor Jyotirmoy Das Memorial Lecture Award. In the accompanying article, Prof. Visweswariah walks us through her work.

Gut reactions and gut instincts: regulation of intestinal homeostasis by receptor guanylyl cyclase C (GC-C)

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The important role that the gut plays in directing and modulating the well-being of the entire organism cannot be underestimated. We are beginning to dissect molecular players that are intrinsic to the functioning of the epithelial cells of the gut, which, in turn, control the responses of various tissues. Here, I provide an overview of our research activities over the past 2 decades related the role of a receptor guanylyl cyclase, GC-C, in regulating fluid-ion homeostasis, cell proliferation, and the microbiome in the gut.

The intestinal epithelium is constantly exposed to the environment and performs diverse functions. It is also one of the most rapidly proliferating tissues in mammals, undergoing regeneration every 5-7 days. A single layer of epithelial cells separates the intestinal lumen from the lamina propria and is responsible for the digestion and absorption of nutrients, regulating fluid-ion balance, and acting as the first line of defence against external agents. In the small intestine, the epithelial layer forms finger-like projections called villi, which extend into the lumen to increase the absorptive surface area, with deep invaginations between the villi. The large intestine lacks the villi, and the epithelial layer covers only the crypt-like invaginations. The immense regenerative potential of the intestinal epithelium arises from 4-6 stem cells at the crypt bottom, which undergo repeated rounds of division to give rise to specialised epithelial cell types along the crypt-villus axis. The stem cells undergo asymmetric division to form a daughter stem cell and a progenitor cell or transit-amplifying (TA) cell. Terminally differentiated cell types migrate upward along the villus axis and, upon reaching the villus tip, shed into the intestinal lumen by anoikis.

We have been studying the role of a key signalling axis, mediated by receptor guanylyl cyclase C (GC-C) and cyclic GMP (cGMP), in regulating overall intestinal homeostasis. The GUCY2C gene, containing 27 exons, is located on chromosome 12 in humans and chromosome 6 in mice. Guanylyl cyclase C is the receptor for heat-stable enterotoxins (ST) produced by enterotoxigenic E. coli (ETEC), the causative agent of traveller's diarrhoea. Endogenous ligands of GC-C in mammals, the gastrointestinal peptide hormones guanylin and uroguanylin, were purified from rat intestinal mucosa and urine. Upon ligand stimulation, GC-C catalyses the conversion of guanosine-5'-triphosphate (GTP) to cyclic guanosine 3',5'-monophosphate (cGMP). GC-C is expressed in the epithelia of murine small intestine and colon and single-cell transcriptomic analysis in murine ileum and human colon showed that GC-C transcripts exist in all intestinal epithelial cell types, including the Lgr5+ crypt base columnar stem cell. The primary sequence of GC-C discloses a

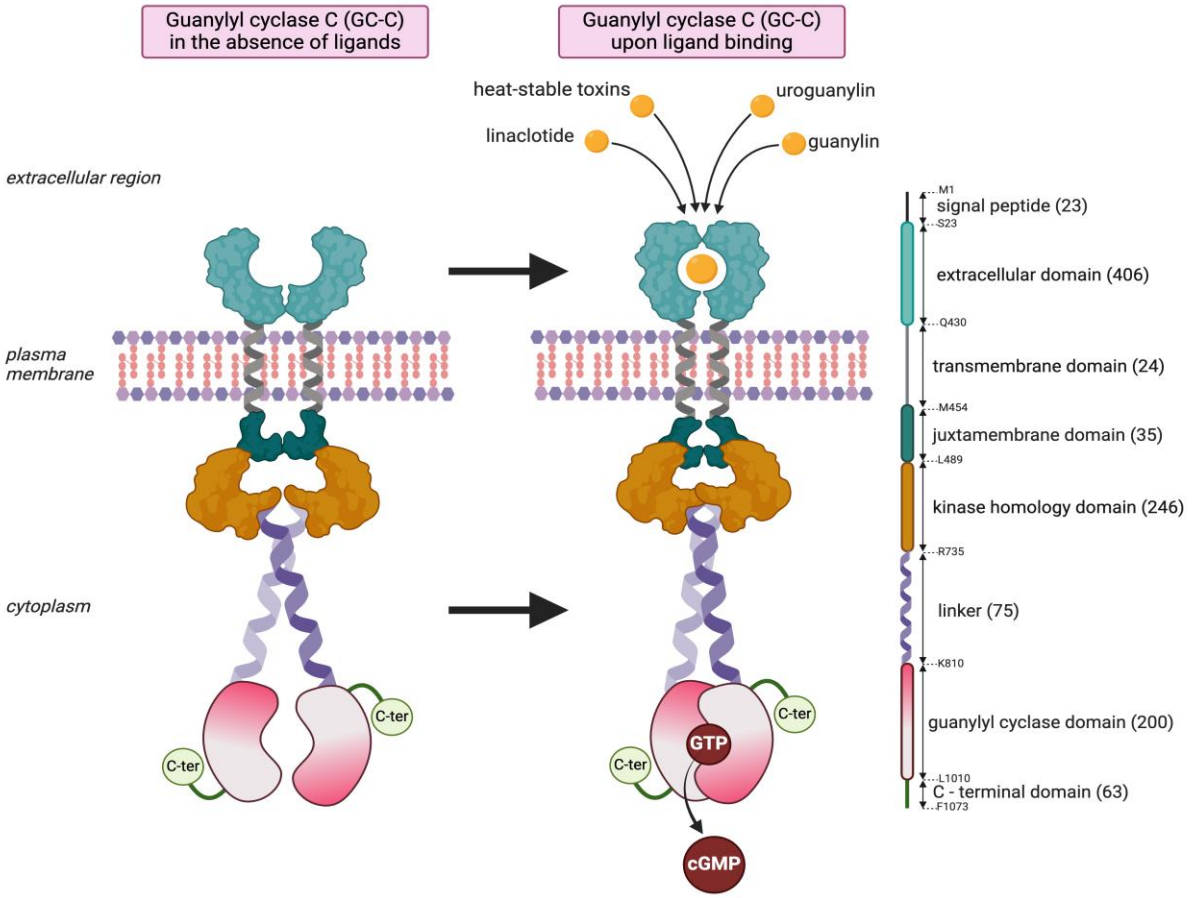

Figure 1. Schematic representation of the overall domain organization in receptor guanylyl cyclase C (GC-C). GC-C is a multi-domain, homodimer transmembrane receptor with seven conserved functional domains: ligand-binding extracellular domain (ECD), single membrane-spanning transmembrane domain, intracellular juxtamembrane domain, regulatory kinase-homology domain (KHD) which binds ATP, a coiled-coil linker region, catalytic guanylyl cyclase domain, and a C-terminal domain which anchors the receptor to the cytoskeleton. The ECD binds to endogenous guanylin and uroguanylin, the exogenous heat-stable enterotoxin (ST) produced by enterotoxigenic E. coli (ETEC), and the Food and Drug Administration (FDA)-approved ST analogue, linaclotide. Based on recent structural observations in receptor guanylyl cyclase A (GC-A), we speculate that upon ligand binding in the ECD of GC-C, conformational changes ensue across the length of the receptor, whereby, the coiled-coil linker region facilitates the optimal head-to-tail dimerization of the GCD to enable the catalytic conversion of guanosine 5'-triphosphate (GTP) to cyclic guanosine 3',5'-monophosphate (cGMP). The linear representation of the domain organization indicates the domain boundaries with the single-letter amino acid code and the length of each domain within brackets. The figure has been created with Biorender.

multi-domain architecture (Figure 1). The stretch of 1-23 amino acid residues represents a putative signal peptide that directs the receptor to localise to the cell surface. Residues 24-430 comprise the extracellular domain (ECD), and this is followed by a single membrane-spanning transmembrane domain (residues 431-454). The intracellular region begins with a short juxtamembrane domain (residues 455-489) and a regulatory kinase-homology domain (KHD) encompasses residues 490-735. The KHD is followed by a linker region (residues 736-810), connecting the KHD to the catalytic guanylyl cyclase domain (GCD) (residues 811-1010). A C-terminal domain is present, spanning residues 1011-1073. Ligand binding to the ECD of GC-C results in conformational changes along the length of the receptor that relay the signal to the

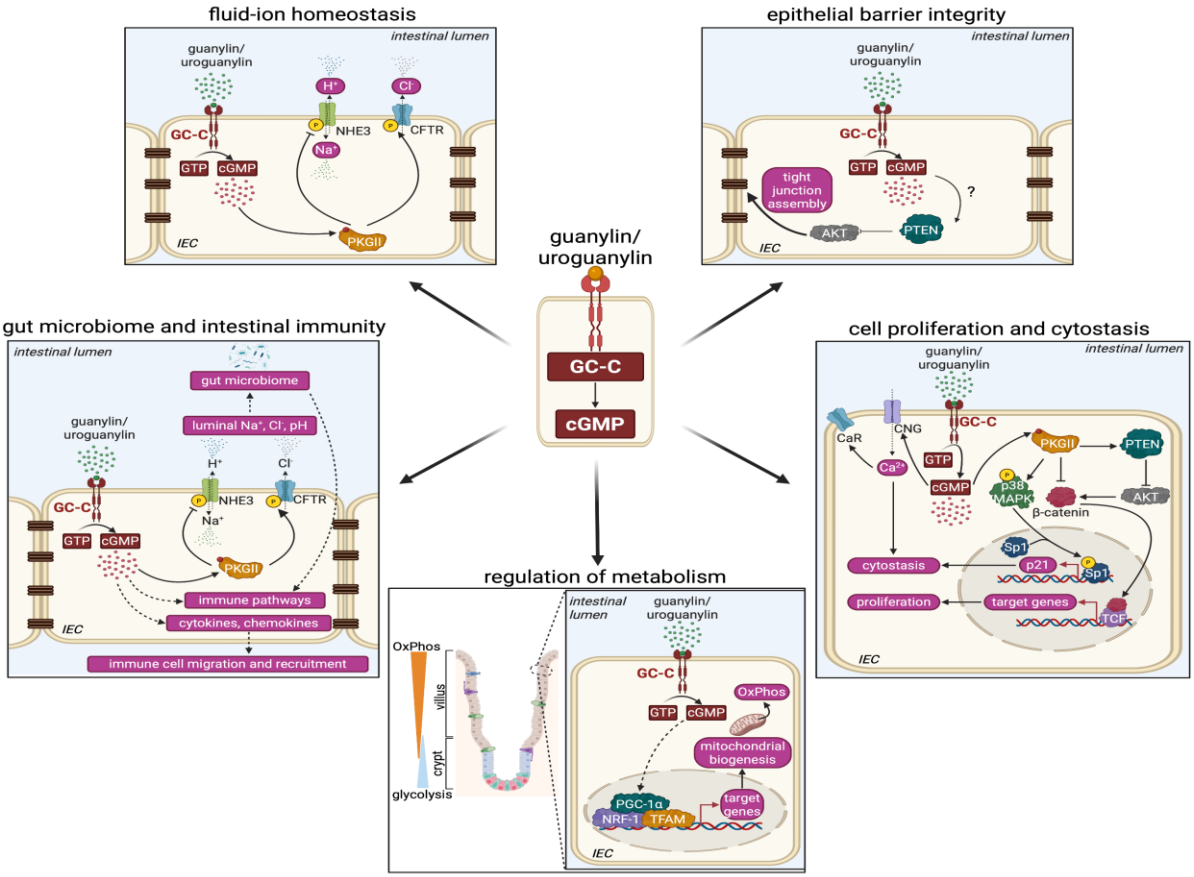

Figure 2. Schematic overview of GC-C/cGMP signalling within the intestinal epithelium. Binding of guanylin and uroguanylin to GC-C induces the catalytic conversion of guanosine 5'-triphosphate (GTP) to cyclic guanosine 3',5'-monophosphate (cGMP) in intestinal epithelial cells (IECs). Cyclic GMP, through epithelial cell-intrinsic and extrinsic pathways, elicits diverse outputs. Cyclic GMP binds to and activates cGMP-dependent protein kinase II (PKGII), which regulates fluid-ion homeostasis by phosphorylating sodium hydrogen exchanger 3 (NHE3) and cystic fibrosis transmembrane conductance regulator (CFTR). PKGII suppresses AKT activation via Phosphatase and tensin homolog (PTEN), which can lead to greater expression of tight junction proteins, thereby enhancing epithelial barrier integrity. The GC-C/cGMP/PKGII signalling axis also regulates cell proliferation and cytostasis. PKGII can suppress □-catenin directly or via PTEN, thereby inhibiting cell proliferation. PKGII-mediated phosphorylation of p38 mitogen-activated protein kinase (MAPK) results in Sp1 phosphorylation, leading to an upregulation of p21 and cytostasis. Cyclic GMP can directly regulate calcium influx via cyclic nucleotide-gated ion channels (CNG), which further induces cytostasis. The increased calcium influx can lead to greater calcium receptor (CaR) accumulation on the cell surface. Cyclic GMP can regulate the metabolism within IECs by upregulating genes that induce mitochondrial biogenesis and oxidative phosphorylation (OxPhos), such as peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1□), nuclear respiratory factor 1 (NRF-1), and mitochondrial transcription factor A (TFAM). Cyclic GMP can indirectly regulate gut microbial composition and intestinal immunity by affecting the luminal microenvironment or directly influencing immune-associated pathways within the IECs. The figure has been created with Biorender.

GCD through the KHD and linker region, thereby inducing the catalytic conversion of GTP to cGMP [1] (Fig. 2). Guanylin and uroguanylin regulate fluid-ion homeostasis by cGMP-mediated activation of cGMP-dependent protein kinase II (PKGII) (Fig. 2).

PKGII phosphorylates and activates cystic fibrosis transmembrane conductance regulator (CFTR) located on the apical surface of intestinal epithelial cells. CFTR secretes chloride and bicarbonate ions from the epithelial cells to the intestinal lumen. PKGII phosphorylates and inhibits NHE3, which absorbs sodium ions from the intestinal lumen into the epithelial cells and simultaneously releases hydrogen ions from the epithelial cells into the intestinal lumen. The increased activity of CFTR and inhibition of NHE3 induced by cGMP/PKGII lead to increased chloride and sodium levels in the intestinal lumen, which creates an osmotic pressure and causes secretion of water from the epithelial cells into the intestinal lumen [2]. Guanylin and uroguanylin regulate this fluid-ion secretion to ensure the passage of luminal contents along the intestine. However, stimulation of GC-C by its super-agonist ST leads to elevated levels of cGMP, which results in increased fluid-ion secretion into the intestinal lumen due to greater activation of CFTR and inhibition of NHE3, leading to diarrhoea.

The gastrointestinal tract is home to a diverse range of microbes, including bacteria, archaea, fungi, and viruses, that account for almost 1014 microorganisms, ~10 times greater than the total number of cells present in the human body. Since GC-C regulates fluid-ion homeostasis in the gut, the GC-C/cGMP signalling axis would affect the luminal microenvironment and, in turn, impact the gut microbial composition. Indeed, the Gucy2cS839I/S839I mouse model with a hyperactivating mutation in GC-C showed gross microbial dysbiosis [3]. The effects of GC-C/cGMP signalling on regulating gut microbiota could have implications in diseases caused by aberrant GC-C activity. In line with this, most of the genera found to be enriched in Gucy2cS839I/S839I mice are also enriched in IBD patients, and include members of the genus Paraprevotella.

Human diseases associated with GC-C/cGMP signalling in the intestine

Familial GUCY2C diarrhoea syndrome (FGDS) was identified in 2012 in a Norwegian family of 32 members as the first human disease to be associated with mutations in GUCY2C [4]. Affected individuals showed diarrhoea characterised by loose, watery stools with meteorism and occasional abdominal pain. A whole-genome single nucleotide polymorphism (SNP)-based linkage analysis followed by exome sequencing of these patients revealed that they harboured a point mutation in GUCY2C (c.2519G>T in exon 22), which resulted in a missense mutation of Ser840 in the guanylyl cyclase domain of GC-C to Ile (p.S840I). All 32 members were found to be heterozygous for the mutation, which showed autosomal dominance and full penetrance. Biochemical characterisation of the mutant receptor using HEK293T cells exhibited higher cGMP production on ligand addition.

Four de novo hyperactivating mutations were found in GUCY2C patients suffering from congenital sodium diarrhoea [5]. A transition of A>G at position 1519 was found in a female French/Algerian child, substituting Lys507 with Glu. The child exhibited a large abdomen owing to intestinal dilation after delivery. She required parenteral nutrition for up to 2 years and experienced frequent diarrheal incidents. The mutant receptor produced higher levels of cGMP both in the absence and in the presence of ligand stimulation, greater activation of CFTR, and enhanced inhibition of NHE3, which was reflected in the elevated faecal sodium levels of the patient (110 mmol/L compared to 25-50 mmol/L in healthy individuals) [5].

Two dominant mutations were found in the linker region. A G>C transversion at position 2376 results in a conversion of Arg792 to Ser, while in the second instance, a T>C transition at position 2324 results in Leu775 being replaced by Pro [5]. Both mutant receptors produced higher levels of cGMP even in the absence of ligands. Interestingly, while the mutant receptor with R792S produced ~100-fold higher cGMP in the absence of ligands, stimulation by ligands generated even higher levels of cGMP. The fact that this receptor was unresponsive to ligands indicates that the disease phenotypes observed

are due to constitutively higher levels of cGMP in the enterocytes, irrespective of the concentration of guanylin or uroguanylin in the gut.

A fourth mutation was found in the guanylyl cyclase domain (transition of A>G at the 2548 position), substituting Asn850 with Asp [5]. The patient exhibited higher levels of sodium in the ileum and faeces and required parenteral nutrition in the first 2 years of her life. This mutant receptor produced marginally high levels of cGMP in the absence of ligands and was hyperactivated upon ligand stimulation, leading to the disease phenotypes observed [5].

Due to congealed meconium, meconium ileus (MI) is an obstruction in the neonatal bowel, particularly in the terminal ileum and caecum. The first genetic aetiology for non-CF-associated MI was discovered in an Israeli Bedouin family where four siblings were affected with MI, but none of them had CF. A detailed study involving sequence analysis and comparison across affected and unaffected patients revealed a mutation in GUCY2C, where a transition of A>G at the 1160 position created a mutant receptor harbouring Glu instead of Asp387 [6]. The mutant receptor showed lower catalytic activity and cGMP production, which might lead to reduced activation of CFTR and inhibition of NHE3, rendering the patients with the mutation prone to develop MI [6].

Recently, Crowley et al. conducted a retrospective study with 1005 paediatric IBD patients in The Hospital for Sick Children, Toronto, to identify the prevalence of monogenic causes amongst very early onset IBD (VEOIBD). They found 17 patients with monogenic CD and 14 with monogenic UC, identifying mutations in 21 genes. Among these VEOIBD patients with monogenic IBD, two showed autosomal dominant mutations in GUCY2C (GC-C) (p.G549S, p.F525L) [7].

GC-C signalling inhibits cell cycle progression, reduces cell migration, maintains genomic integrity, and regulates epithelial barrier integrity. Indeed, guanylin and uroguanylin are the most frequently lost gene products during transformation in intestinal tumours [8-10]. GC-C expression is seen in several primary tumours of the gastrointestinal tract, including oesophageal (59%), stomach (68%), colorectal (98%), and pancreatic cancers (64%). GC-C has, therefore, been proposed as a marker for metastatic colorectal cancer.

Since GC-C signalling is implicated in several human diseases, targeting GC-C with agonists or antagonists might be a therapeutic approach. GC-C agonists have been developed to treat patients with idiopathic constipation or IBS-C. Two FDA-approved agonists of GC-C, linaclotide and plecanatide, are effective in IBS-C. Linaclotide and plecanatide are analogues of ST and uroguanylin, respectively. Both agonists can be consumed orally, and they are not absorbed systemically.

Conclusion and future perspectives

The GC-C/cGMP signalling axis is widely considered one of the most important mediators of fluid-ion homeostasis in the intestine. However, our recent studies using animal models have highlighted the role of this signalling pathway in regulating other aspects of intestinal homeostasis, such as gut microbiota, epithelial barrier integrity, intestinal immunity, and epithelial proliferation and differentiation. The broad influence of this signalling axis on maintaining intestinal homeostasis is also evident from the disease phenotypes observed in patients with loss or gain-of-function mutations in GUCY2C.

Although FDA-approved agonists of GC-C are available, pharmacological antagonists of GC-C are not described due to the lack of structural information on the receptor. Given the broad impact of GC-C on intestinal homeostasis, further studies are required to elucidate the mechanistic details. This can be achieved by using pre-clinical mouse models lacking GC-C or harbouring gain-of-function mutations in GC-C.

A systematic approach using these mouse models is needed to understand the consequences of altered activity of the GC-C/cGMP signalling on intestinal homeostasis, epithelial-immune-microbiota crosstalk, and epithelial proliferation and differentiation during infection and regeneration. However, we have recently shown that mouse and human GC-C differ markedly in their biochemical properties, which include a lower affinity for ligands seen in mouse GC-C and, importantly, a much-reduced activity of the GCD [11]. These changes, therefore, should be borne in mind while utilising mice as preclinical models for the development of therapeutics directed towards the GC-C/cGMP signalling axis.

Our current research activities relate to the identifying mutations associated with paediatric IBD in the Indian population through whole exome sequencing, and also studying the role of GC-C in affecting a secondary infection with a gut-associated pathogen. We hope these studies are of clinical relevance and also provide an avenue for alleviating the debilitating outcomes of repeated diarrhoeal disease in children in Sub-Saharan and South Asian countries.

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ISCB @ APOCB 2026!

The Indian Society of Cell Biology (ISCB) is a member organization of the Asian-Pacific Organization for Cell Biology (APOCB). In partnership with its member organizations, APOCB convenes the APOCB Congress once every four years. This year, the meeting was held in Hefei, China, where the office bearers of ISCB were invited to deliver talks and participate in the APOCB Executive Committee meeting. Prof. Thelma (President), Prof. Ganesh (Secretary), Prof. Nitin Mohan (Treasurer), and the ISCB representative to APOCB, Dr. V. Radha, participated in the meeting. Several students from India also participated and presented their work, highlighting the vibrant contributions of young researchers. Dr. Radha will be succeeded by Prof. Nitin Mohan as the ISCB representative to APOCB for a period of two years, beginning September 2026. The Hefei meeting underscored the importance of the APOCB umbrella structure, which plays a vital role in promoting cell biology research and fostering collaboration across the Asia-Pacific region.

RNA and Dietary Interventions in Geroscience: Advancing Lifespan and Healthspan

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Ageing is the most significant risk factor for several chronic diseases, including Type 2 Diabetes mellitus, most cancers, neurodegeneration, and cardiovascular diseases. Increasing evidence has implicated dietary restriction (DR), i.e., reduced nutrient intake without malnutrition, as a simple means of enhancing healthspan and counteracting age-related disease. This nutritional intervention increases lifespan in diverse species, indicating that the molecular mechanisms underlying DR are evolutionarily conserved [1]. Studies in several model organisms have shown that dietary/caloric restriction prolongs lifespan predominantly through protein-coding mRNAs. Since non-coding RNAs account for more than 70% of the human genome, our research has focused on identifying and evaluating components of non-coding RNA networks that can be targeted for therapeutic development. A class of non-coding RNAs known as microRNAs (miRNAs) has been recently recognized as key players in aging and late-onset diseases. Despite growing evidence that miRNAs are altered during aging, there is little evidence on dietary restriction-dependent positive effects on miRNAs and their targets or the pathophysiological consequences of these alterations. We are employing genetic, molecular, metabolomic, and proteomic strategies to test whether RNA-mediated mechanisms operating downstream of DR can promote healthy lifespan and ameliorate symptoms associated with late-onset diseases

Post-transcriptional regulators of lifespan and healthspan

Our laboratory uses the short-lived and genetically amenable Drosophila melanogaster to study how microRNA networks modulate aging and dietary restriction (Fig 1) [2]. Age- and nutrient-related changes in microRNA (miRNA) abundance and their biogenesis factors have been linked to organismal longevity [1, 3-5]. Our small RNA-seq analysis of RNA extracted from wild type flies that were fed an ad libitum (AL) and dietary-restricted (DR) diet identified miR-100, let-7, and miR-125, encoded by the let-7-Complex locus, as upregulated by dietary restriction. These three highly conserved and co-transcribed miRNAs are encoded by the let-7-Complex locus [6]. Furthermore, loss-of-function mutations in let-7 and miR-125 dampen DR-dependent lifespan extension.

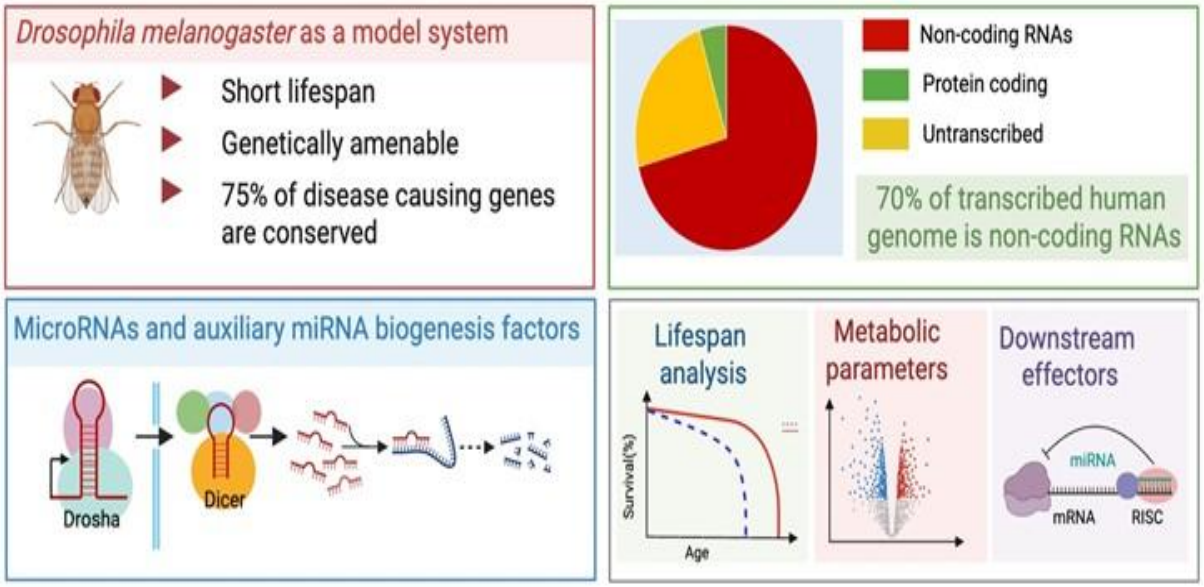

Figure 1. *Drosophila melanogaster* as a model system to study RNA biology of aging (This schematic was created with Biorender).

The DR phenotype associated with loss of miR-125 results from derepression of its target, Chronologically Inappropriate Morphogenesis (chinmo). Functional characterization of miR-125 demonstrated its role in neurons, while its target, chinmo, acts in both neurons and fat tissue to modulate fat metabolism and longevity. Proteomic analysis revealed that Chinmo exerts its DR effects by regulating the expression of FATP, CG2017, CG9577, CG17554, CG5009, CG8778, CG9527 and FASN1[2]. Our analysis has also uncovered a previously unknown mechanism of nutrient-dependent post-translational control of Chinmo that may be linked to a novel nutrient-dependent non-nuclear role for this protein. Consistent with the miR-125 loss-of-function DR phenotype, increasing the dosage of human miR-125 in the fat body increased longevity. Taken together, we have identified a conserved miRNA that mediates the effects of DR by promoting tissue-to-tissue communication, demonstrating its potential as an RNA-based therapeutic that can mimic DR's beneficial effects. Some of the miRNAs that we are currently examining have been implicated in circadian rhythm and sleep. Increasing evidence suggests that sleep disturbances increase the risk of age-related chronic diseases. We hope that our functional analysis of DR-modulated miRNAs that play significant roles in fat metabolism and circadian rhythm will translate into therapeutic approaches to improve health.

Differential processing is a hallmark of clustered microRNAs (miRNAs), and the role of position and order of miRNAs in a cluster, together with the contribution of stem-base and terminal loops, has not been explored extensively within the context of a polycistronic transcript. To elucidate the structural attributes of a polycistronic transcript that contribute towards the differences in efficiencies of processing of the co-transcribed miRNAs, we constructed a series of chimeric variants of Drosophila let-7-Complex and examined the expression and biological activity of the encoded miRNAs (miR-100, let-7, and miR-125). The kinetic effects of Drosha- and Dicer-mediated processing on the chimeric precursors were examined using in vitro processing assays. Our results highlight the importance of stem-base and terminal loop sequences in differential expression of polycistronic miRNAs and provide evidence that

processing of a particular miRNA in a polycistronic transcript is, in part, determined by the kinetics of processing of adjacent miRNAs in the same cluster[7]. We are currently characterizing the role of auxiliary RNA-binding proteins that may be responsible for the differential processing of let-7-complex miRNAs.

Evaluation of natural dietary interventions in promoting health

Enhancement of nutrient quality and bioavailability through biofortification of food crops has been employed by developing countries to increase the availability of essential nutrients and other health-promoting compounds, such as anthocyanins. Given the mechanistic conservation of antioxidative mechanisms and oxidative stress, Drosophila has been extensively utilized to evaluate antioxidants in vivo. In one our studies, we utilized Drosophila to test the effectiveness of biofortified wheat varieties in slowing down the ageing process. These anthocyanin-rich blue wheat (BLW), purple wheat (PW), and black wheat (BW) breeding lines with good yield potential were developed by crossbreeding and characterized for anthocyanin type and content by scientists in the National Agricultural Biotechnology Institute (NABI), Mohali. The BW lines had the highest anthocyanin content (185 ± 17.3mg/kg), followed by BLW (113.3 ± 3.8 mg/kg), PW (40.7 ± 0.5mg/kg), and amber/white (WW) (2.2 ± 0.1mg/kg)[8].

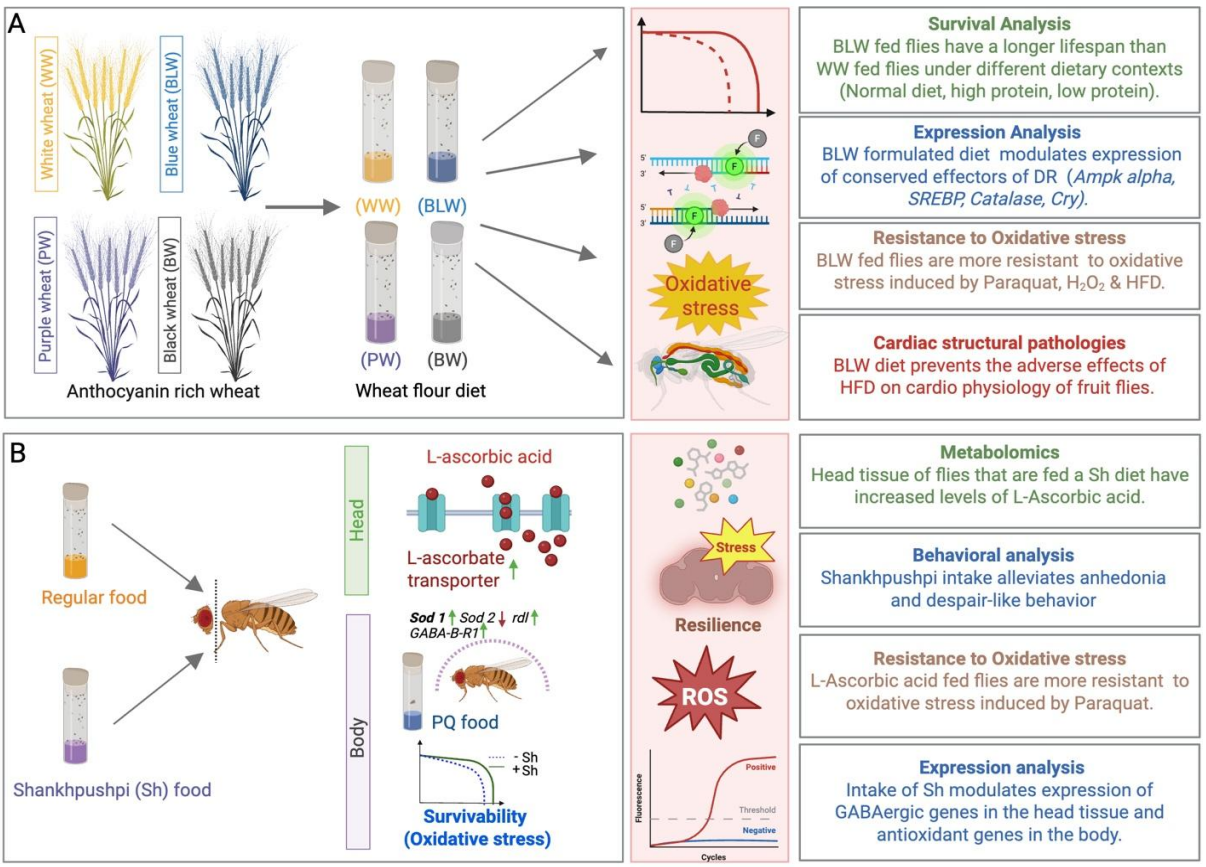

Figure 2. Natural dietary interventions in healthy aging. (A) Biofortified anthocyanin-rich wheat prolongs lifespan under ad libitum and dietary restriction, promotes expression of conserved effectors of dietary restriction, enhances resistance to oxidative stress and prevents structural defects in the adult heart under a high-fat diet. (B) *Convolvulus pluricaulis* mediates its pharmacological effects via sod1, rdl, glut1, GABA-B-R1 and CG6293 orthologs in *Drosophila melanogaster* (This schematic was created with Biorender).

We examined the long-term impact of these native-colored wheat varieties on Drosophila lifespan. We found that anthocyanin-rich blue wheat (BLW) prolongs lifespan under ad libitum (AL) conditions. Gene expression analysis of RNA extracted from AL and DR-fed whole flies indicates that BLW diet exerts its effects by modulating the expression of genes involved in DR-dependent lifespan extension (AMPK alpha, SREBP, and Catalase), suggesting that blue wheat-mediated antioxidant and DR mechanisms operate to extend lifespan in *Drosophila*. The BLW diet also enhanced the survivability of fruit flies upon exposure to paraquat or high-fat diet-induced oxidative stress and delayed the degeneration of myofibrils in flies that were fed a high-fat diet. Together, these data indicate that biofortified wheat-formulated diets enhanced healthspan and prevented cardiovascular age-related pathologies [9].

In a more recent study, we used metabolomic and molecular approaches to identify metabolic and molecular pathways modulated by the consumption of *Convolvulus pluricaulis* (Shankpushpi) [10]. Shankhpushpi has been traditionally used to manage disorders of the nervous system, including depression and anxiety. Metabolomic profiling of flies fed Shankhpushpi identified significant increases in L-Ascorbic acid, glucose, and adenosine monophosphate levels in head tissue. Consistent with the metabolomics data we observed significant modulation of Glut1 (glucose transporter 1), CG6293 (L-Ascorbate transporter), rdl (resistant to dieldrin), GABA-B-R1 (GABA-B receptor 1), and Sod1 (superoxide dismutase 1) upon intake of Shankhpushpi. We established a short variable stress-induced depression model of *Drosophila* to examine the antidepressant effects of Shankhpushpi. Intake of a Shankpushpi-supplemented diet led to a significant reduction in anhedonia and despair-like behavior of stressed flies. Furthermore, knockdown of CG6293 eliminated the antidepressant effects, and knockdown of CG6293, Sod1, Glut 1, or GABA-B-R1 reduced the antioxidant effects of Shankhpushpi. Lastly, supplementation of L-Ascorbic acid mimicked the behavioral and oxidative resilience conferred by Shankhpushpi. Together, these findings reveled conserved mechanisms underlying the pharmacological effects of Shankhpushpi.

In the future, we would like to expand this research program to investigate noncoding RNAs and their modifications in preclinical models of prevalent age-related diseases in preclinical models and human patients[11, 12]. We would also like to continue using the genetically tractable Drosophila model to uncover the molecular mechanisms underlying the beneficial effects of diet in promoting health during aging.

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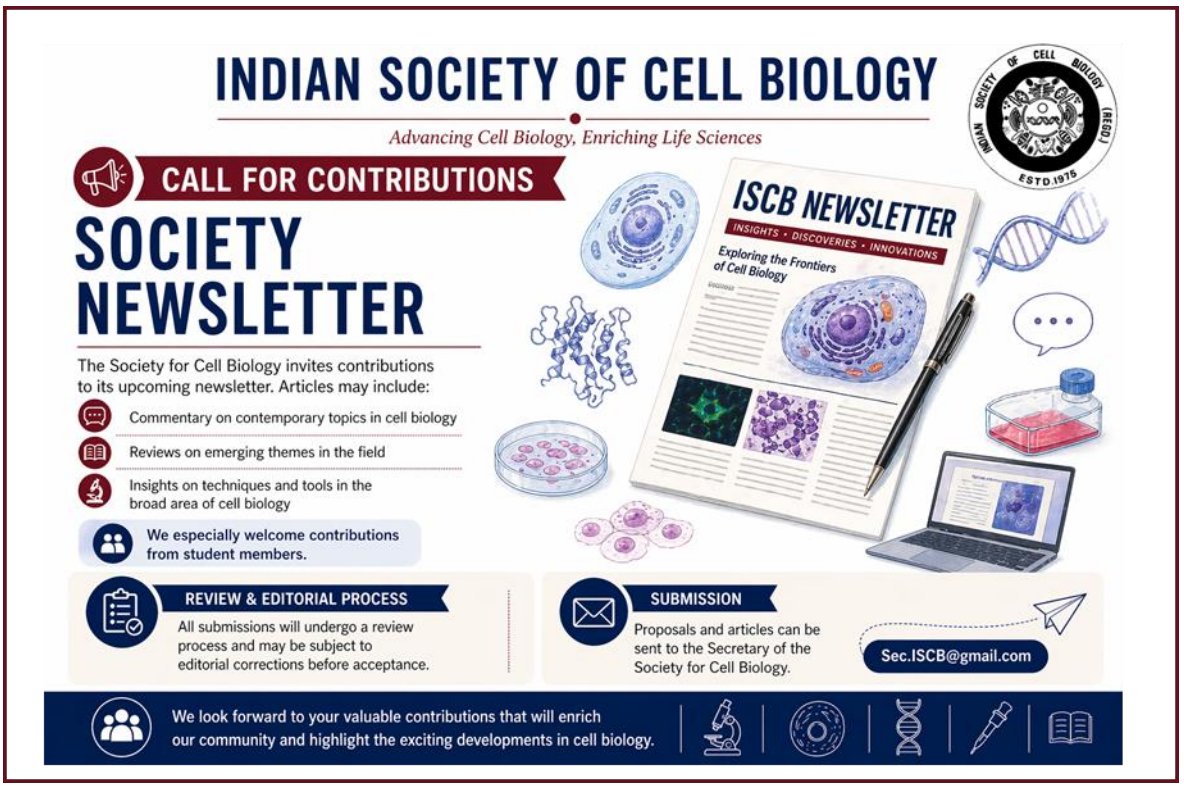
Call for Contributions



Lysosomal ion channels as therapeutic target against neurodegenerative disorders

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Abstract

Lysosomes, once regarded as simple degradative organelles for cellular waste disposal, are increasingly being recognized as dynamic metabolic and signaling hubs essential for neuronal health. Key lysosomal ion channels and transporters regulate pH, membrane potential, calcium homeostasis, autophagy, trafficking, and exocytosis. The dysfunction of lysosomal channels such as ATP13A2, TRPML1, TMEM175, TPC1/2, and chloride transporters disrupts proteostasis and promotes toxic protein accumulation in neurodegenerative disorders, including Parkinson's, Alzheimer's, Amyotrophic Lateral Sclerosis, and Huntington's disease. This review highlights the role of lysosomal ion channels in neuronal homeostasis and evaluates their therapeutic potential as targets in neurodegeneration.

Introduction

The most common forms of neurodegenerative disorders, Alzheimer's disease (AD), Amyotrophic Lateral Sclerosis (ALS), and Parkinson's disease (PD), are associated with the accumulation of misfolded/mutated proteins (1). Alzheimer's is associated with the accumulation of amyloid plaques or the deposition of microtubule-associated protein tau (2). Protein aggregates form inclusion bodies in ALS. Similarly, Parkinson's is characterised by the accumulation of Lewy bodies containing α-synuclein (α-syn) aggregates. At present, as these neuropathies have no cure, patients have to survive with drugs that delay disease progression (3). However, with growing age, these misfolded/mutated proteins accumulate, increasing the severity of the disease.

Majority of the misfolded/mutated proteins are degraded through the proteasome or endo-lysosomal autophagy, which constitute the protein quality control mechanisms (4). However, several proteins involved in neurodegeneration rapidly oligomerize into aggregates thus making them nearly resistant to the proteolytic pathways (4). These aggregates can cause cytotoxicity and neuronal cell death, unless the compartments they are localized in, the lysosomes, undergo exocytosis to expel out their toxic contents (5). Impaired lysosomal exocytosis exacerbates the pathology by causing more lysosomal dysfunction, loading, and enlargement (5).

Brain autopsy of patients with AD and PD show abnormal lysosomal phenotypes similar to those with lysosomal storage disorders (6–12). It is increasingly evident that the primary causative mechanism in several neurodegenerative disorders like AD and PD may not be accumulation of misfolded/mutated proteins, but rather the presence of dysfunctional lysosomes (13–17). Several clinical trials involving drugs to prevent accumulation of these proteins have failed (18,19), thus calling for new approaches and drugs to expel aggregated proteins from the neurons. Lysosomes have emerged as promising therapeutic targets for neurogenerative diseases (Figure 1) (20). The major challenge has been to identify the lysosomal components and appropriate modulatory drugs that can restore the function of the dysfunctional lysosomes and promote lysosomal exocytosis.

Studies have demonstrated that impaired lysosomal exocytosis in patients with mutations in the PD associated lysosomal protein ATP13A2/PARK9 leads to accumulation of α-synuclein inside fibroblasts and fibroblast derived dopaminergic neurons. Wild type α-synuclein that exists in soluble or filamentous form can be readily degraded by the proteasomal or endolysosomal machinery. The mutations in ATP13A2/PARK9 lead to lysosomal dysfunction leading to decreased exosomal secretion, impaired lysosomal proteolysis, reduced lysosomal exocytosis, and decreased secretion of α-synuclein, without appreciable intracellular α-synuclein accumulation at early time points. Notably, with prolonged culture, α-synuclein accumulated to toxic levels in neurons due to defective secretion and impaired lysosomal degradation (21–25). Lysosomes are major intracellular Ca^{2+} stores of cells (26). Using cytosolic and lysosome-targeted Ca^{2+} sensors, it was demonstrated that ATP13A2/PARK9 deficiency leads to higher basal cytosolic Ca^{2+} and decreased lysosomal Ca^{2+} release. Even stimulation with lysosomal Ca^{2+} release inducers failed to trigger detectable Ca^{2+} release from mutant cells, whereas overexpression of ATP13A2/PARK9 restored optimal lysosomal Ca^{2+} release (21,27–30).

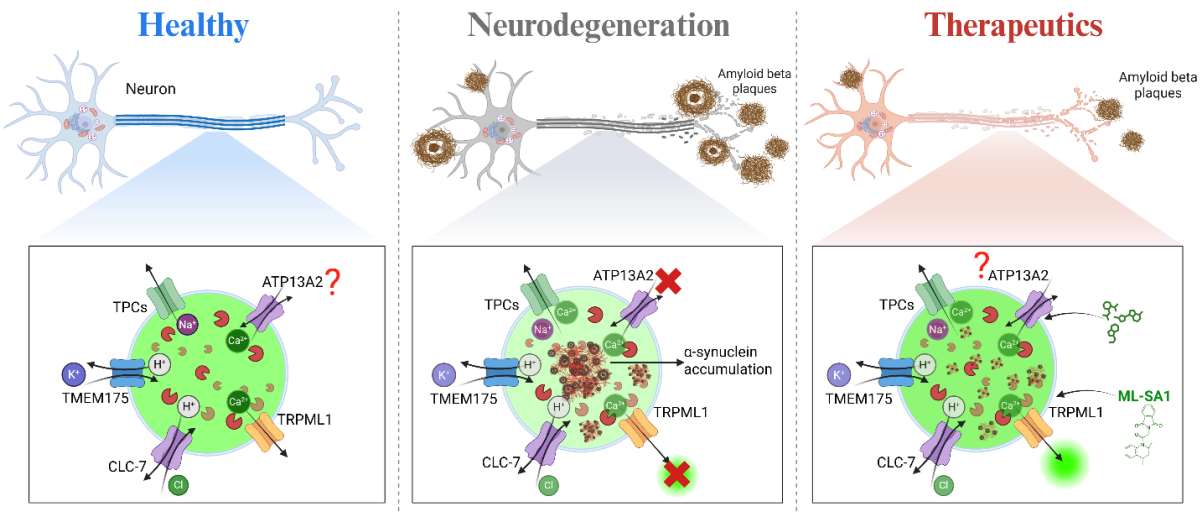

Figure 1. Model depicting lysosomal ion channels activity at basal level in healthy neurons (left), their dysfunction in neurons leading to neurodegeneration (center) and boosting their activity as a therapeutic approach to restore neuronal function (right)

Further investigations assessed whether reduced lysosomal Ca^{2+} sequestration underlies impaired Ca^{2+} release. It was shown that defective lysosomal Ca^{2+} release was due to pathologically low luminal Ca^{2+} levels in ATP13A2/PARK9 mutant cells. Stimulation failed to increase extracellular lysosomal enzyme activity or cell-surface lysosomal membrane protein expression in mutant/deficient cells, confirming that ATP13A2/PARK9 regulates lysosomal exocytosis through control of lysosomal Ca^{2+} levels. Chelation of cytosolic Ca^{2+} prevented lysosomal exocytosis, whereas blocking Ca^{2+} release from the endoplasmic reticulum had no significant effect, further confirming that release of Ca^{2+} stored within lysosomes is indispensable for lysosomal exocytosis (21,25,31,32).

Lysosomal ion channels TRPML1-3 (33,34) sense lysosomal pH and mediate Ca2+ release from lysosomes, which forms an essential step in lysosomal exocytosis (35). TRPML channels have also been shown to regulate endo-lysosomal trafficking and function, promote expulsion of bacteria from epithelial cells and release of granzyme-B from NK cells (36–38). Activation of TRPML1 has been shown to clear deposition of amyloid β-peptides (Aβ) in neurons by promoting lysosomal calcium efflux, luminal acidification, and lysosomal exocytosis (39). TRPML1 regulates lysosomal remodeling along with lysosomal trafficking (40) and mutations in TRPML1 have been implicated in severe endolysosomal damage (41). TRML1 deficiency has been shown to impact mitochondrial structure and function (42).

TRPML1 activation has been shown to increase α-synuclein expulsion by restoring lysosomal exocytosis by ensuring release of luminal Ca2+ from lysosomes into cytosol. ATP13A2/PARK9 silencing abolished TRPML1 activator induced lysosomal exocytosis, indicating that cooperativity exists between the two lysosomal proteins ATP13A2/PARK9 and TRPML1. The above observation also raised the question whether TRPML1 overactivation is the cause of pathologically low levels of luminal Ca2+ in lysosomes. This possibility was discarded from their observation that silencing TRPML1 doesn't affect impaired release of luminal Ca2+ levels in lysosomes in ATP13A2/PARK9 mutant fibroblasts. ATP13A2/PARK9 sequesters while TRPML1 releases lysosomal Ca2+, and are partially responsible for the critically low Ca2+ levels in lysosomes that prevents lysosomal exocytosis (21,25,28,43).

iPSC-derived human cortical neurons expressing APOE ε4, which resemble late-onset AD, have impaired TRPML1-induced endolysosomal Ca2+ release, and subsequently disorganized endosomal-autophagic-lysosomal system (44). Blocking TRPML1 function by depleting its endogenous agonist PI(3,5)P2, in primary cortical neurons recreated multiple features of endosomal-autophagic-lysosomal neuropathology evident in late-onset AD. Notably, TRPML1 reactivation using its synthetic agonist ML-SA1 rescued these AD-like neuronal defects, further implicating TRPML1 activators as therapeutic agents against neurogenerative diseases (44). Several start-ups have come up with novel TRPML1 agonists. In May 2026, Lysoway Therapeutics is initiating first-in-human Phase 1 clinical trial of LW-1017, a potent and highly brain penetrant TRPML1 agonist in Australia. In 2026, Casma Therapeutics is initiating clinical trials to test its TRPML1 agonist CSM-101, which has shown pre-clinical efficacy in reversing pathological phenotype of GBA-associated Parkinson's disease and idiopathic Parkinson's disease, lowered toxic alpha-synuclein levels and preserved dopaminergic neurons. Caraway Therapeutics, a company focused on developing lysosomal ion channel-based drugs to treat genetically defined neurodegenerative and rare diseases, was acquired by Merck for $610 million in 2023, highlighting the interest of big-pharma companies in this line of therapy.

TRPML channels are emerging as an alternative approach to rescue the impaired lysosomal exocytosis, an essential mechanism that prevents accumulation of pathogenic protein aggregates to toxic levels. High lysosomal Ca2+ levels are essential for lysosomal trafficking and exocytosis as well as for optimal TRPML functioning (5). However, the mechanism that inactivates TRPML1 in aggregate laden lysosomes and lysosomal calcium importing channels remains to be elucidated (21,45–48).

Another important lysosomal ion regulator is TMEM175. It differs from classical potassium channels in its structure and primarily functions in lysosomes. It helps keep the membrane potential and pH stable, and supports the ability to break things down. Genome-wide association and functional studies have associated TMEM175 with the risk of Parkinson's disease. Reduced TMEM175 activity reduces lysosomal proteolysis and causes α-synuclein accumulation, both of which are strongly linked to the vulnerability of dopaminergic neurons. Consequently, TMEM175 is becoming increasingly popular as a potential target for PD treatment (49–53).

The lysosomal membrane contains Two-Pore Channels (TPC1 and TPC2) as well as complex chloride transport systems, which contribute to its functional diversity. TPCs are critical for mediating sodium and calcium flux, regulating vesicle trafficking, endosome maturation, and the formation of contact sites between the lysosome, mitochondria, and endoplasmic reticulum (54). Although the gating mechanisms of TPCs are still being studied, these channels are recognised as key components in intracellular signalling pathways that influence autophagy and neuronal responses to proteotoxic stress. Disruption of TPC-mediated ion homeostasis is increasingly associated with synaptic failure and cellular collapse in neurodegenerative diseases (55–59).

In addition to cation flux, lysosomal function depends on maintaining anionic balance, which is primarily regulated by CLC-7 and other chloride transport proteins. These systems create an electrical shunt that balances the positive charge generated by proton (H+) pumping by the V-ATPase. This makes sure that the lumen is properly acidified (60–62). Insufficient chloride conductance prevents the lysosome from achieving the pH required for optimal enzymatic degradation, leading to metabolic accumulation. The significance of this balance is demonstrated by the neurological abnormalities observed in inherited chloride transport disorders, underscoring that precise anionic regulation is as essential as proton regulation for sustained brain health (63–65).

Approaches directed at increasing luminal levels of lysosomal Ca2+ and their optimal release could prove to be more beneficial in ensuring normal rates of lysosomal exocytosis and be novel therapeutic intervention in treating neurodegenerative diseases (Figure 1). It includes identification such lysosomal Ca2+ importers and development of specific drugs targeting them. In the absence of such drugs, pharmacological drugs targeting TRPML are likely to prove beneficial and safe for multiple neurodegenerative diseases, as TRPML channels are almost exclusively localized in the lysosomes. Several TRPML activators are in preclinical trials for neurodegenerative diseases (66) and offer a ray of hope for the patients and their families. Alternative approaches, such as activating TFEB or increasing lysosomal biogenesis, could help when channels do not function fully. New techniques in electrophysiology, cryo-electron microscopy, fluorescence imaging, and drug screening are speeding up the progress of drug discovery. Proteins in lysosomes that were once hard to study are now possible targets for therapy.

In conclusion, lysosomal ion channels have become key players in maintaining neuronal stability, rather than being merely unknown organellar proteins. They determine whether neurons can withstand cellular stress by regulating acidification, calcium release, membrane potential, trafficking, autophagy, and exocytosis. Targeting lysosomal ion homeostasis signifies a promising avenue for developing disease-modifying therapies for currently incurable neurogenerative disorders.

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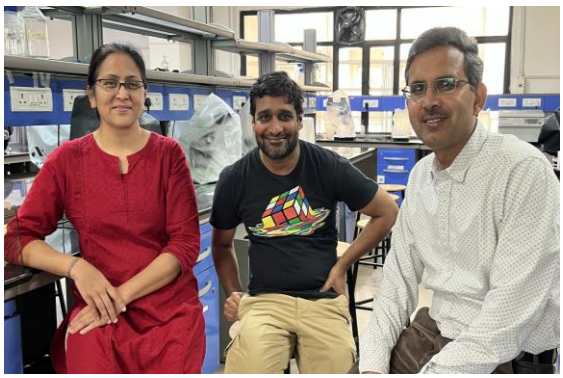
Hands-on Training to Students of Large Undergraduate Classes Based on Real-life Cell Biology Questions



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With access to rapidly evolving technologies, routine training practices/methods can draw limited attention among the students. Adopting new approaches, including hands-on training, is a complex task, especially in laboratory courses with large numbers of students. Teachers face time constraints with uncertainty in Biology experiments, while institutions face financial constraints in providing expensive facilities. Therefore, innovative approaches are needed to give ample hands-on training in large classes and to excite students' curiosity. Towards these goals, we adopted certain pedagogy approaches in an introductory course for a large undergraduate biology class. After training in basic laboratory skills, we encouraged students to ask real-life questions about microorganisms in fermented milk products/foods using readily available equipment and resources. We recently published these practices in the Journal of Microbiology and Biology Education (Das et al., 2025). We are also introducing these approaches to the educators/teachers from different organizations in India through an in-house teacher-training program. Insight of J. Gowrishankar on this pedagogy approach is included as concluding remarks.

The transition from schools towards higher education is a critical phase in academia, when students should identify their true potential and have the opportunity to explore it. Early hands-on training for students is an essential component to develop the ability to solve problems, not only those given by their teachers but also those they encounter. In the process, students acquire the skills to identify and test new ideas and develop keen interests in a specific subject.

Higher educational institutes are expected to educate students in sufficient depth. Since students may have received limited practical training earlier at their schools, teachers need to start from the fundamentals. Often, class sizes can be substantially large in many institutions (~300 students are enrolled in a common undergraduate program at our institute). Courses requiring rigorous hands-on training often demand student-centric approaches. Conducting such courses for large classes become challenging for educators, as the tasks include conducting diverse exercises, giving students enough opportunity for exploration, and careful evaluation of their performances.

The complex and time-consuming nature of certain exercises, along with the added uncertainty and variability of tests involving living organisms, make hands-on training in Biology even more challenging. Often, educators are also constrained by limited facilities/ equipment available at their disposal. Therefore, students are allowed to perform only a limited number of exercises following well-established protocols. They get minimal opportunities for exploration.

However, answering queries through experiments enhances learning outcomes from the course. It not only improves students' analytic capabilities, but also enhances their problem-solving skills and enables them to identify novel and interesting questions. Therefore, students should have the opportunity to explore, as new and unexpected outcomes essential to education arise from investigations based on observation and curiosity. In the process, students gain a sense of achievement from their learning, while teachers get a sense of accomplishment from their innovative methods.

We have been training large undergraduate classes in a basic biology laboratory course for the last 4 years by making simple modifications to the assigned exercises. The large majority of students had received limited experimental training in their schools. This introductory course, which typically runs for ten weeks, with one weekly three-hour session, is designed to train students in basic laboratory practices, including principle and handling of micropipetting, weighing balances, autoclaves, and centrifugation; preparation of solutions, buffers and media; working under aseptic condition (laminar hood); principle and usage of microscopes for visualising cells and Gram staining for distinguishing different classes of microorganisms, etc.

To ensure that each student got opportunities to perform the exercises independently, the large classes were divided into three sessions. Students in a session were further distributed into sections, sub-sections, and smaller teams (Table 1). An optimal number of course instructors, tutors, teaching assistants (TAs), and laboratory staff (collectively referred to as educators) were critical for the training. Course instructors were teachers/faculty who managed the classes with assistance from TAs and staff. TAs were researchers working on Master or PhD theses, and post-doctoral projects. The educators arranged resources for the exercise, ensured that students followed safety protocols, introduced the basic concepts and methodology, and guided students in troubleshooting difficulties. Printed protocols were distributed at the start of the lab. This practice saved time by avoiding long introductions in the limited three hours available for each session. Importantly, the educators remained available for interactions throughout the sessions. The educators also discussed real-life applications of the exercises with the students and assessed their performance through written records and personal interactions. Students completed their lab journals within the session and submitted the records at the end for evaluation.

Table 1: Organization of large classes.

Student numbers	240-300
Distributed in lab sessions	3
Students trained in a lab session	80-100
Teachers in a session	4
Teaching Assistants (TAs) in a session	8-10
Segregated lab space for a session	2
Students within a lab space	40-50
Students assigned to a TA	10
Students on a workbench	5
Lab duration	3 hours
Number of labs	10

After training in the tasks mentioned above, students were advised to utilize their skills to measure the sizes of different prokaryotic and eukaryotic cells using basic light microscopes and to compare their results with values reported in the literature.

Figure 1. Illustration showing imaging approach using basic microscope and smartphone camera (created by B. Mohapatra using Google Gemini).

They took pictures of their slides with smartphone cameras after adjusting the gadget on the microscope's eyepiece (Fig 1).

Cell dimensions were back-calculated after accounting for the total magnifications of the microscopes (eyepiece and objectives) and the smartphone camera. Alternatively, cell sizes could be estimated from magnified images relative to the microscope's field of view (FOV). FOVs, if not already marked on the eyepiece and objectives, was calculated by imaging a graph/ruled paper. The exercise resembled imaging cells with high-end microscopes equipped with a pre-installed camera (which would be difficult to arrange in large numbers).

Gram staining was proposed for Gram-negative *Escherichia coli* because it was readily available in the laboratory. However, we wanted to demonstrate Gram-positive *Lactobacilli*, but it was difficult to culture under aerobic conditions. We wondered about natural sources of Gram-positive microorganisms and advised students to explore microorganisms present in fermented milk products: homemade curd (dahi), commercial curds, and probiotics. Interestingly, students readily detected Gram-positive *Lactobacilli, Streptococci*, and yeast in homemade curd. On the other hand, commercial curd appeared to have a homogeneous population of Gram-positive *Streptococci* (suggesting the possibility that Lactobacilli may not have been used to prepare those commercial curds). Surprisingly, probiotics, which were expected to contain a dense population of Gram-positive Lactobacilli, showed highly variable counts for reasons unknown. Homemade curd proved to be the best source of *Lactobacilli* (Fig 2).

Students realised health benefits of homemade food and traditional knowledge associated with their preparation. The fermentation of milk into curd (dahi) dates back to the dietary practices in ancient India (see [1], and references therein). Unsurprisingly, Lactobacilli are used as probiotics for treating various colon ailments.

In the modified course, students learned basic laboratory skills, microscopy principles, acquired imaging skills and measured the size of microorganisms with the help of basic microscopes. They observed that prokaryotic cells are not always smaller than eukaryotic cells, and further explored the microbial content in fermented milk products (see [2] for further details).

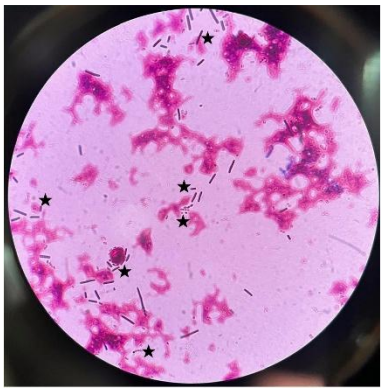

Figure 2. Gram-staining of homemade curd. The picture of a Gram-stained slide of homemade curd (dahi) mounted under microscope with 100x objective was taken by a student using smartphone camera. Gram-positive Lactobacilli are seen as purple-colour rods (marked with stars). Lightly stained (Gram-negative) cocci and large clumps of milk casein can also be seen.

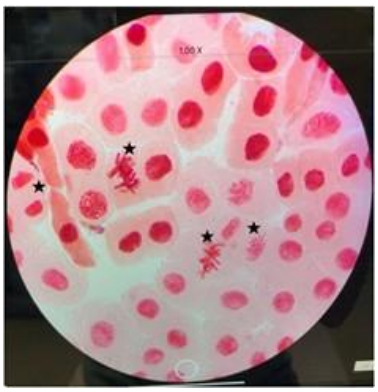

Figure 3. Mitotic cells in onion root tip. The picture of dividing cells in onion root tip observed under a microscope with 40x objective was taken by a student using a smartphone camera. Aceto-Orcein/Acetocarmine was used for staining mitotic nuclei. Distinct stages of mitosis are shown by stars.

These exercises can be extended to visualise cells in samples of different origins and to study cellular processes such as growth and division. Students visualised single-celled eukaryotic organisms, the budding yeast Saccharomyces cerevisiae and fission yeast *Schizosaccharomyces pombe*, and measured their sizes following the methods described earlier. They could observe and image different stages of mitosis in root tips of onion bulbs (Fig 3).

In our experience, hands-on training for large practical classes can be managed effectively and efficiently, even with limited resources and time, if planned and executed properly, and supported by the right manpower. Through simple modifications in existing exercises, we could also introduce real-life examples to students. Such introductory training can be expanded with more advanced molecular and genomic techniques in higher classes. The approaches can be readily adopted in diverse educational setups without increasing their financial burden.

We have been introducing these practices to teachers and instructors of undergraduate students from other organizations. We conducted an in-house teacher training program for college teachers during the 2025 summer. Teachers were selected through an open competition based on their application and expression of interest. Priorities were given to teachers from government educational organisations with limited resources and training facilities for their students. The next training program is scheduled for 2026 summer.

J. Gowrishankar (formerly at IISER Mohali and now at the University of Hyderabad) shared his views on our pedagogy approach: “This is indeed an excellent initiative, encompassing both imaginative ideas from the faculty and hands on experiments by a large cohort of students. I am happy that it uses the bacteriology of curd, which I personally believe is India's health gift to mankind – we Indians are likely the ones that consume it (and buttermilk in its various avatars) the most amongst all the people in the world.

Another point, that is elegantly exploited in your paper, is that so much of the yoghurt and buttermilk consumption in India even today is of the product made at home for consumption by the family and not for sale – and it is not pasteurized (which would, of course, kill the bacteria and render the experiments unsuccessful). This tradition is unlikely to be prevalent in any other large community around the world. These experiments also remind me of the hugely successful efforts of Prof Graham Hatfull at the University of Pittsburgh to engage high school and undergraduate college students in exciting research through the isolation and characterization of mycobacteriophages from diverse soil samples [3]."

Disclaimer: The use of smartphones was permitted only for learning. Students who did not own a device could borrow from their teammates. Representative pictures taken by MS25 students are shown in Fig 2 and 3.

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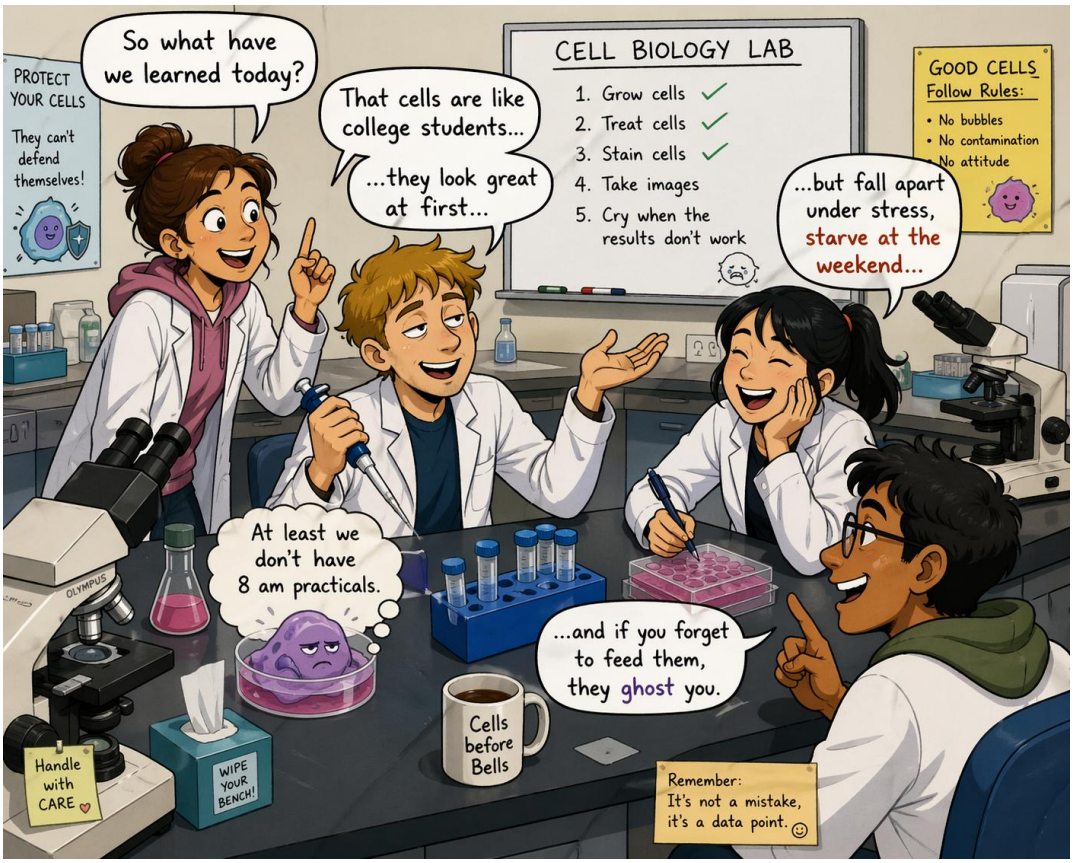
Fun time!



ISCB Outreach

ISCB–CACTUS JOINT WEBINAR SERIES (2025–2026)

CACTUS Communications

Advancing Cell Biology Research & Communication

MODERATOR
Prof. Debdeep Dutta
IIT Kanpur

SPEAKERS
- Prof. S. C. Lakhotia (BHU, Varanasi)
- Prof. Jyotsna Dhawan (CCMB, Hyderabad)
- Dr. Indranil Banerjee (IISER, Mohali)
- Dr. Rashna Bhandari (CDFD, Hyderabad)
- Dr. Sunaina Singh (Editage)

OVERVIEW

- **ISCB**, in partnership with Cactus Communications, organized a national webinar series (2025–2026).
- **Objective:** Integrate rigorous research with effective communication.
- **Audience:** Faculties, students, and researchers across India.
- **Format:** Expert talks, live Q&A, active participation, and meaningful dialogue.
- **Focus:** Advances in cell biology, scientific communication, and career advancement.

WEBINAR SESSIONS AT A GLANCE

1 Drivers of Research: Compulsion, Fashion and Passion
Prof. S. C. Lakhotia (BHU, Varanasi)
Inaugural Lecture 13 Oct 2025
181 Registrants
40% Students
30% Researchers
20% Faculty
Informative & Impactful

2 Quiescent muscle cells are active communicators
Prof. Jyotsna Dhawan (CCMB, Hyderabad)
15 Nov 2025
290 Registrants
42% Students
18% Researchers
16% Faculty
Strong scientific content & clear presentation

3 Navigating the early career maze (Panel Discussion)
- Dr. Indranil Banerjee (IISER, Mohali)
- Dr. Rashna Bhandari (CDFD, Hyderabad)

21 Jan 2026
143 Registrants
39% Students
33% Researchers
14% Faculty
Highly positive feedback

4 Visualizing Science: Enhancing Research Communication Through Visuals
Dr. Sunaina Singh (Editage)
18 Feb 2026
132 Registrants
23% Students
17% Researchers
29% Faculty
Widely praised for practical value & engaging format

IMPACT & OUTCOMES

- All participants received session recordings and certificates.
- Strong engagement across career stages and institutions.
- Enhanced awareness of research philosophy, career options, and research communication.
- Bridged the gap between bench science and research communication.
- Contributed to capacity building and strengthened professional networks within the Indian cell biology community.

WHAT'S NEXT?

Building on the success of the 2025–2026 series, expanding the initiative to include hands-on workshops in:

Manuscript Writing | Grant Development | Editing | Peer Review

Continued collaboration willl be essential for advancing the quality and impact of scientific research in India.

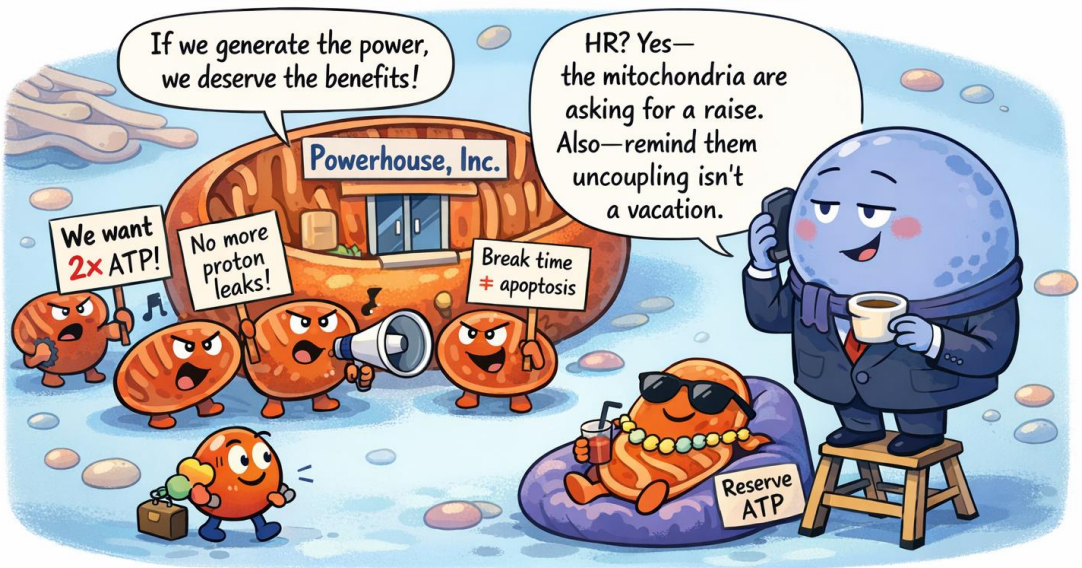
We acknowledge the technical support from **Cactus Communications** for making this webinar series possible.

Report by Debdeep Dutta

Fun time!

Golgi: The Ultimate Stylist

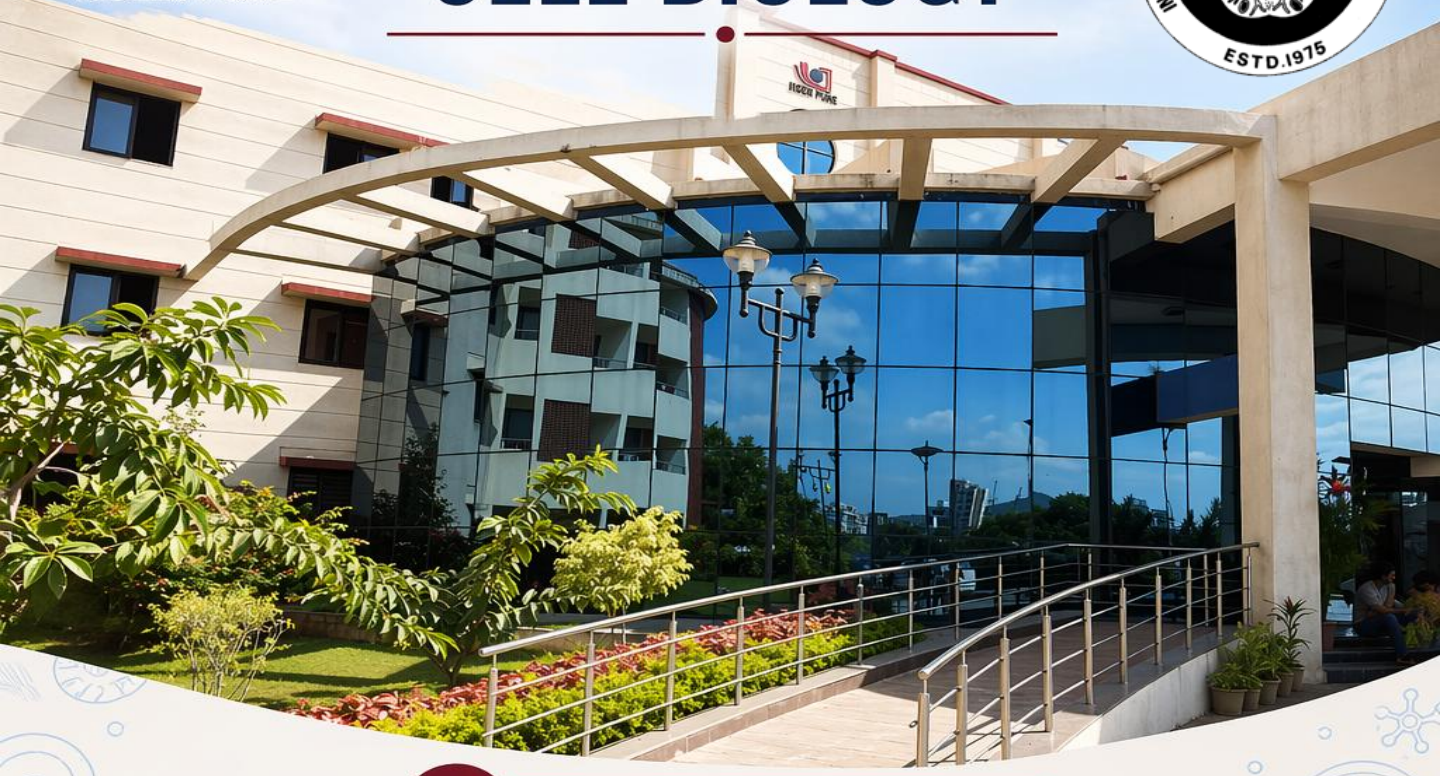
Mitochondrial Union



Collective bargaining — cellular edition.

IISER PUNE

INDIAN SOCIETY OF CELL BIOLOGY



ANNOUNCEMENT

49th ALL INDIA CELL BIOLOGY CONFERENCE AND SYMPOSIUM

DECEMBER 10–12, 2026 | **IISER PUNE**

We are delighted to announce that the 48th All India Cell Biology Conference and Symposium will be hosted at IISER Pune from **December 10–12, 2026.**

Further details will be shared with members soon. Please stay tuned for the call for abstracts and applications for awards.

We look forward to welcoming you to IISER Pune this December for an engaging and inspiring scientific gathering!

Science. Collaboration. Inspiration. | **SEE YOU AT IISER PUNE!**