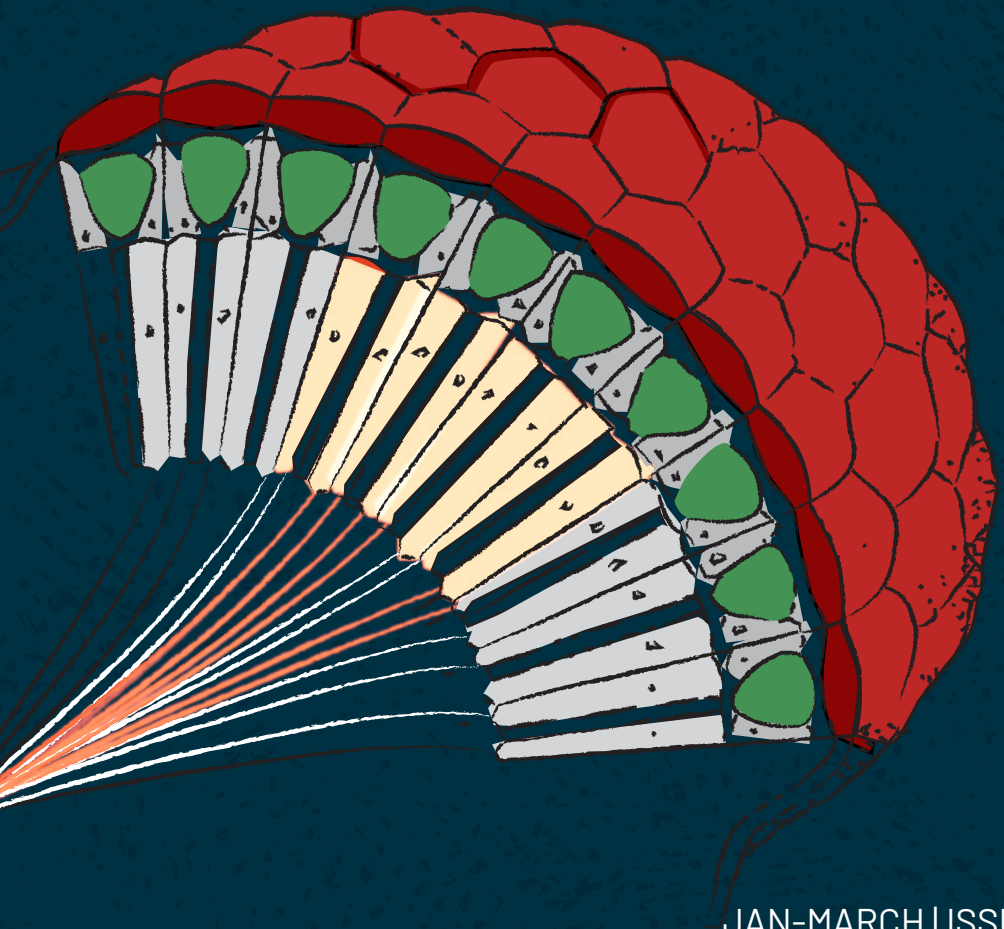
ncbs
National Centre for Biological Sciences
Tata Institute of Fundamental Research

Transcript

Of our research, people, and culture



JAN-MARCH | ISSUE 01

Decoding the Brain:
The Role of AI in Modern Biological Science

Prof. Upinder S. Bhalla

Artificial Intelligence (AI) is transforming modern biology, accelerating research by enabling faster discoveries and improved data analysis. AI techniques such as machine learning (ML), deep learning, and natural language processing (NLP) are helping biologists analyse complex biological systems, model diseases, and develop new treatments. From genomics and cellular processes to neurobiology and ecology, AI has become an indispensable tool in processing vast amounts of data efficiently.

It is already predicting protein structures, mapping neural networks, and analysing cell signalling pathways, aiding breakthroughs in cancer research and beyond. These advancements not only enhance scientific understanding, but also translate into real-world applications in healthcare, agriculture, environmental science, and beyond.

At NCBS, Prof. Upinder S. Bhalla's group uses computer modelling and experiments to understand how the brain maps information across multiple levels—from the molecular to the network level. Their work provides insights into memory, learning, and even the broader question of how intelligence emerges.

AI in Neuroscience: Bridging Biology and Computation

The human brain constructs models of the world to interpret sensory input, predict outcomes, and guide behaviour. For instance, when perceiving a motorcyclist, the brain integrates cues such as speed, direction, and sound to anticipate movement and potential interactions.

"These predictive models are fundamental to navigation and decision-making. Although AI does not yet fully replicate brain function, it provides valuable insights into how such models are formed", says Prof. Bhalla.

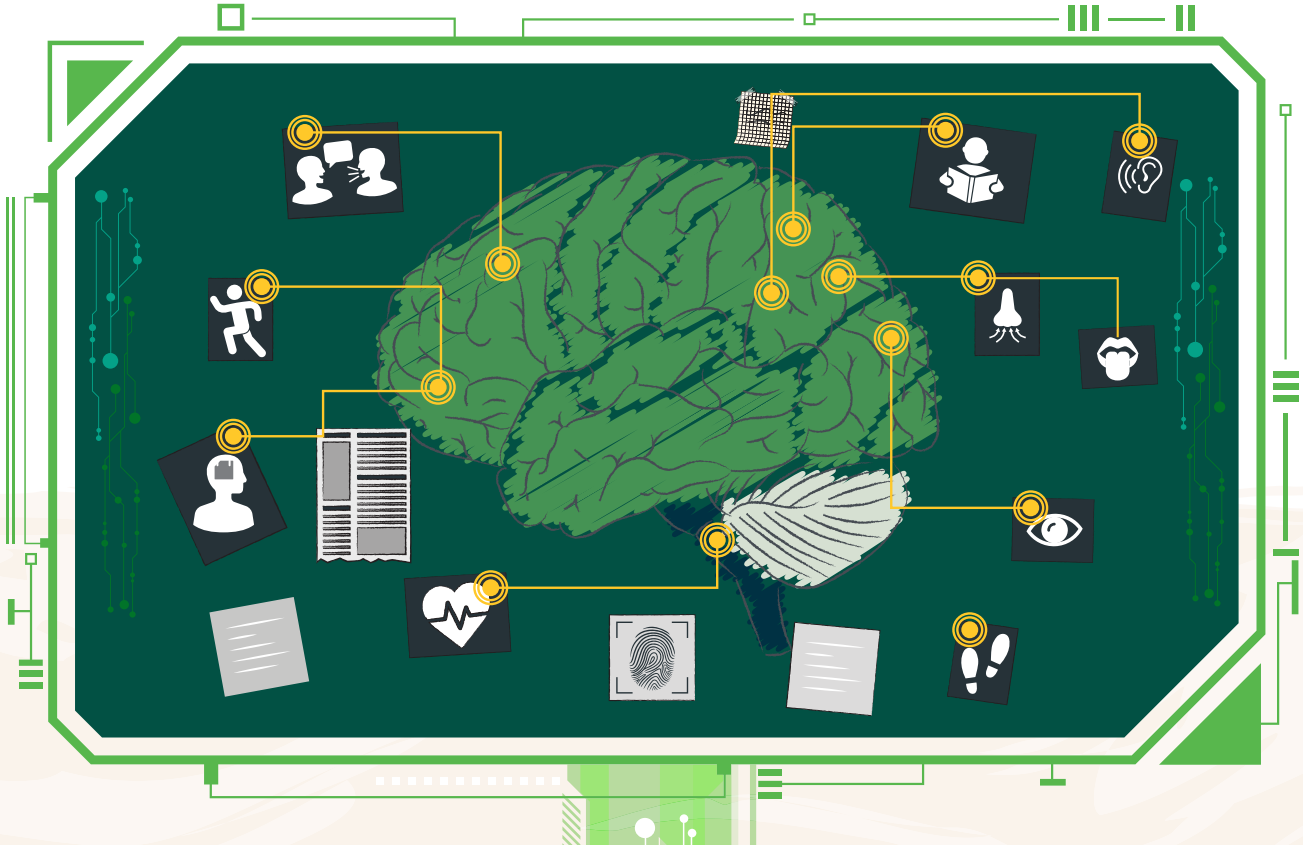
A key focus of Prof. Bhalla's group is understanding the parallels between brain cells and AI units, both of which encode and process information. At the molecular level, signalling pathways extract meaning from timing and context, adjusting synaptic weights—much like how AI fine-tunes its parameters to build representations. The team is investigating how neurons manage these weights to compute, regulate activity, and integrate signals within circuits.

As these processes scale up to larger networks within the human brain, they give rise to sequences and temporal patterns that shape perception and behaviour—ultimately forming an individual's internal model of the world. Time and event relationships underpin cognition and motor functions, allowing the brain to link experiences across different intervals, much like a continuous stream of movie frames. AI, by contrast, lacks an innate sense of time and instead relies on architectures like transformers to impose order on data.

Prof. Bhalla's group also employs AI to analyse neuronal activity patterns, with one key application being real-time brain activity prediction. For example, when monitoring sequences of neural signals, AI helps determine what the brain is doing at a given moment. Researchers can capture snapshots of brain activity and use neural networks to interpret them, predicting the temporal context of specific patterns.

"Conceptually, some of the ideas of AI are very fundamental to how we think about how the brain works," explains Prof. Bhalla. This makes AI both a research tool and a conceptual model for understanding how the brain computes information.

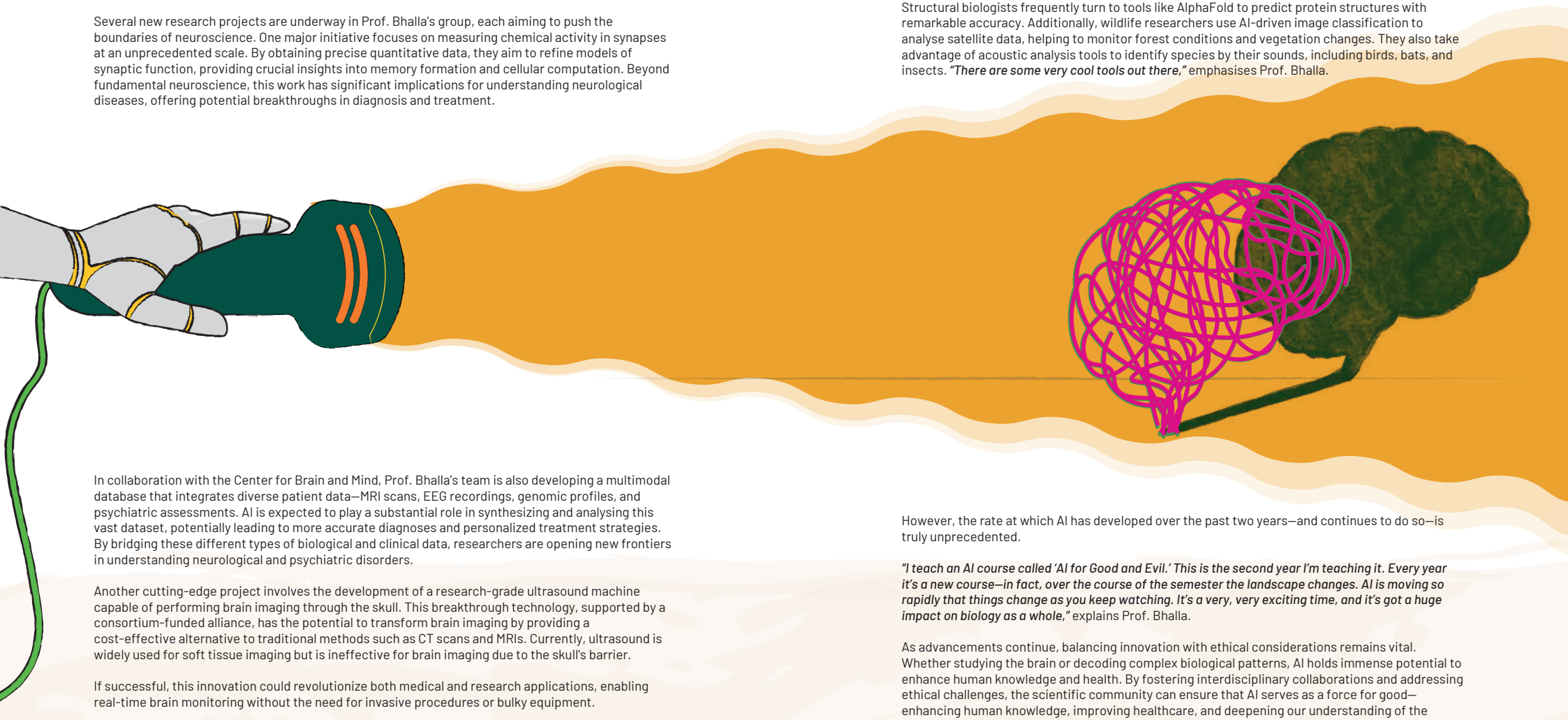
Prof. Bhalla's team has also developed pioneering tools to support their work. MOOSE, a multi-scale simulator, models brain activity at various levels using fundamental equations governing chemical processes, electrical activity, and neuronal excitability. FINDSIM manages experimental data for accurate simulations, while SANKET serves as a centralised portal for accessing datasets. These tools are crucial for synthesizing data and building comprehensive frameworks for understanding neural dynamics.



Transforming the Neuroscience Research Landscape: Current Projects and Future Directions

AI is providing remarkable insights into higher-level brain functions, offering clues that were previously inaccessible. A particularly intriguing shift is AI's impact on the philosophy of mind—long- standing debates about cognition and consciousness are now being tested with empirical data. What was once confined to theoretical discussions can now be examined through AI models, challenging traditional perspectives on the nature of intelligence and what makes the brain unique.

Several new research projects are underway in Prof. Bhalla's group, each aiming to push the boundaries of neuroscience. One major initiative focuses on measuring chemical activity in synapses at an unprecedented scale. By obtaining precise quantitative data, they aim to refine models of synaptic function, providing crucial insights into memory formation and cellular computation. Beyond fundamental neuroscience, this work has significant implications for understanding neurological diseases, offering potential breakthroughs in diagnosis and treatment.



In collaboration with the Center for Brain and Mind, Prof. Bhalla's team is also developing a multimodal database that integrates diverse patient data—MRI scans, EEG recordings, genomic profiles, and psychiatric assessments. AI is expected to play a substantial role in synthesizing and analysing this vast dataset, potentially leading to more accurate diagnoses and personalized treatment strategies. By bridging these different types of biological and clinical data, researchers are opening new frontiers in understanding neurological and psychiatric disorders.

Another cutting-edge project involves the development of a research-grade ultrasound machine capable of performing brain imaging through the skull. This breakthrough technology, supported by a consortium-funded alliance, has the potential to transform brain imaging by providing a cost-effective alternative to traditional methods such as CT scans and MRIs. Currently, ultrasound is widely used for soft tissue imaging but is ineffective for brain imaging due to the skull's barrier.

If successful, this innovation could revolutionize both medical and research applications, enabling real-time brain monitoring without the need for invasive procedures or bulky equipment.

These advancements illustrate how AI is rapidly reshaping neuroscience, offering new ways to study brain function, diagnose diseases, and improve treatment outcomes.

AI at NCBS: Expanding the Frontiers of Biological Research

At NCBS, it isn't just Prof. Bhalla's team,researchers across various departments are seamlessly integrating AI into daily research workflows, enhancing efficiency and enabling discoveries across multiple disciplines. AI is being leveraged for tasks such as text analysis, data processing, and coding, making it an indispensable tool in modern biology.

For example, Dr. Shruti Viswanath utilizes AI directly to model how proteins come together, while Dr. Shaon Chakrabarti focuses on developing models to understand cellular mechanisms. Structural biologists frequently turn to tools like AlphaFold to predict protein structures with remarkable accuracy. Additionally, wildlife researchers use AI-driven image classification to analyse satellite data, helping to monitor forest conditions and vegetation changes. They also take advantage of acoustic analysis tools to identify species by their sounds, including birds, bats, and insects. ***"There are some very cool tools out there,"*** emphasises Prof. Bhalla.

However, the rate at which AI has developed over the past two years—and continues to do so—is truly unprecedented.

"I teach an AI course called 'AI for Good and Evil.' This is the second year I'm teaching it. Every year it's a new course—in fact, over the course of the semester the landscape changes. AI is moving so rapidly that things change as you keep watching. It's a very, very exciting time, and it's got a huge impact on biology as a whole," explains Prof. Bhalla.

As advancements continue, balancing innovation with ethical considerations remains vital. Whether studying the brain or decoding complex biological patterns, AI holds immense potential to enhance human knowledge and health. By fostering interdisciplinary collaborations and addressing ethical challenges, the scientific community can ensure that AI serves as a force for good—enhancing human knowledge, improving healthcare, and deepening our understanding of the natural world. The future of AI in biology is vast and promising, and its potential is only beginning to unfold.

Research Stories

Dendritic Computations and Neural Network Functionality

Prof. Upinder Bhalla's group developed computational models demonstrating that neurons can discriminate complex neural activity patterns through dendritic computations, even in randomly connected networks. They found that synaptic inputs from co-active or sequential neural ensembles can cluster on dendrites, enhancing neuronal activation and computational power. This suggests that dendritic processing contributes significantly to neural network functions.

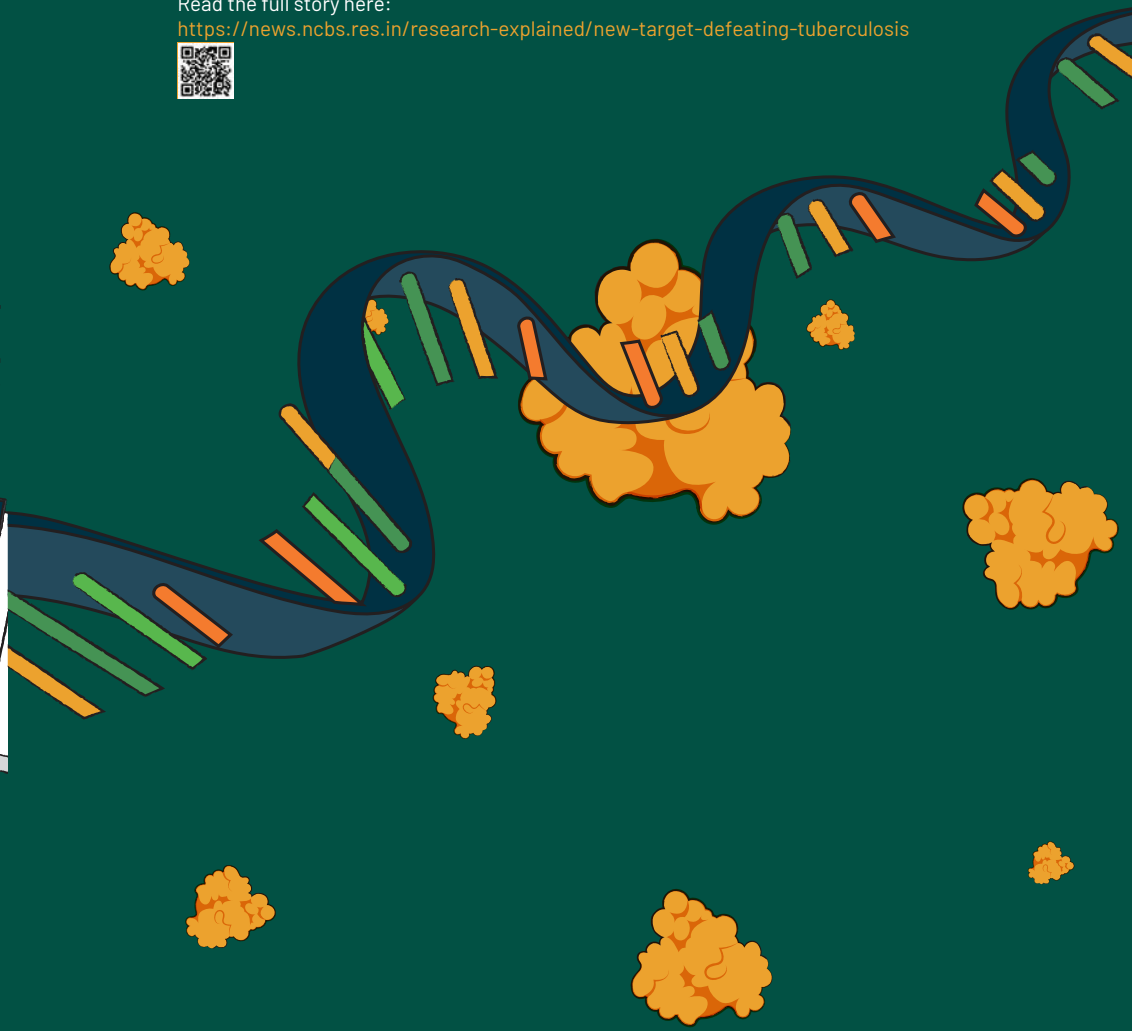
Read the article here:
https://news.ncbs.res.in/research-explained/inside-brain-dendrites-help-identify-patterns

Investigating the Role of RbpA in Mycobacterium tuberculosis

Prof R Sowdhamini's group used computational techniques to investigate the role of RNA polymerase-binding protein A (RbpA) in Mycobacterium tuberculosis. They observed significant structural rearrangements in RNA polymerase upon RbpA interaction and identified crucial amino acids involved in transcriptional regulation.

These findings enhance our understanding of RbpA's function and can inform the development of targeted therapeutics against tuberculosis.

Read the full story here:
https://news.ncbs.res.in/research-explained/new-target-defeating-tuberculosis

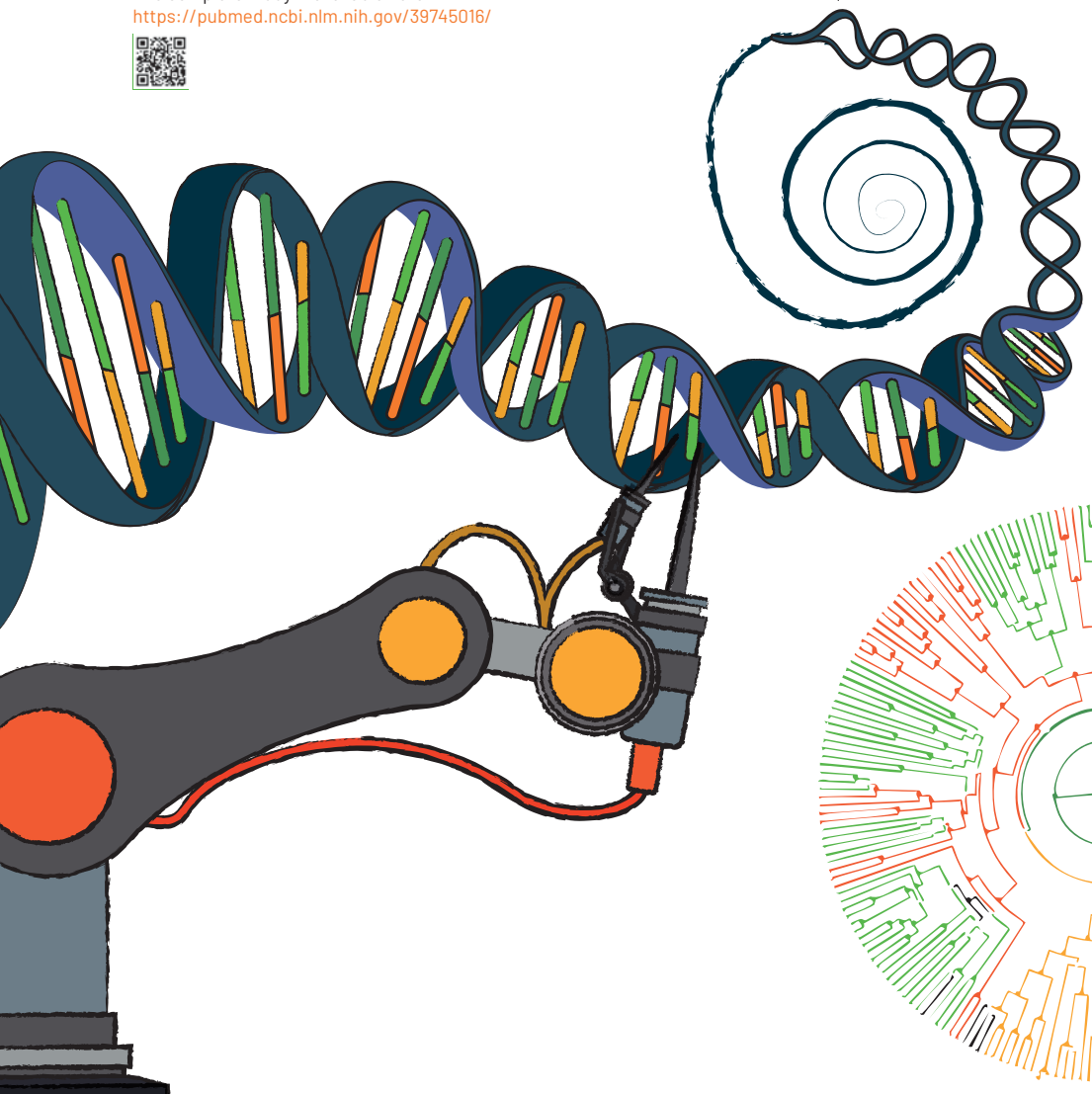


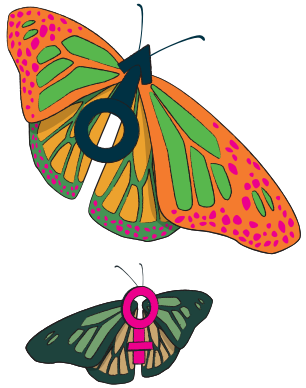
Publication Highlights

Structural Insights into PALB2: Role in DNA Repair and Cancer Suppression

Dr. Ranabir Das' group elucidated the structure of the PALB2 protein. By analysing specific genetic mutations within the coiled-coil domain, they found a strong correlation between structural disruptions and reduced DNA repair efficiency. These insights enhance the understanding of PALB2's role in cancer suppression and could improve genetic counseling.

The complete study is available here:
https://pubmed.ncbi.nlm.nih.gov/39745016/





What Butterfly Wing Coloration Reveals About Natural and Sexual Selection

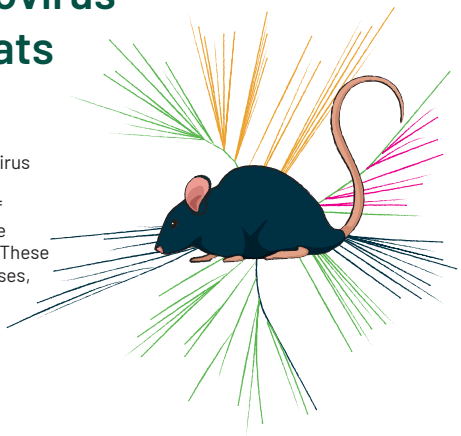
Dr. Krushnamegh Kunte's group studied butterfly wing color patterns across 20 species to explore natural and sexual selection effects. Males showed brighter, more saturated colors than females, with vivid dorsal surfaces. They found that while selection pressures shape color characteristics, they do not necessarily affect the extent of variation in these patterns.

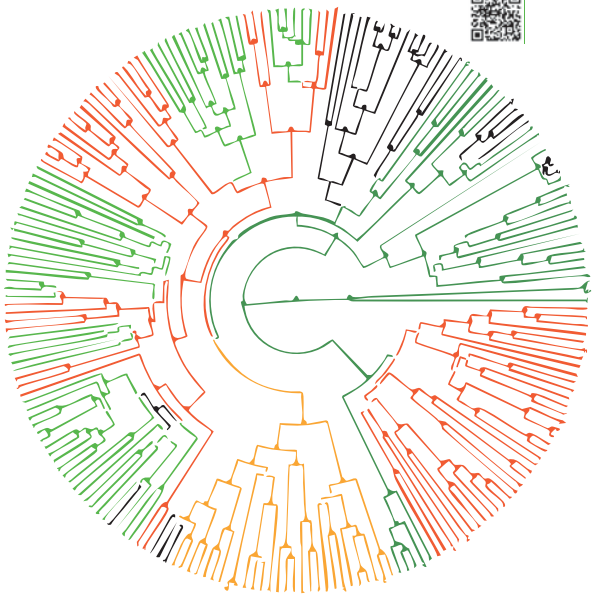
You can read the full article here:
https://bmcecolevol.biomedcentral.com/articles/10.1186/s12862-024-02346-8

Uncovering Novel Adenovirus Diversity in Western Ghats Rodents

Prof. Uma Ramakrishanan and group investigated adenovirus diversity in small mammals within the Western Ghats, a biodiversity hotspot. They discovered a high prevalence of adenoviruses, identifying five distinct lineages with unique mutations in the endemic rodent species, Rattus satarae. These lineages differ significantly from known murine adenoviruses, suggesting novel adenovirus diversity in this region.

You can read more here:
https://pubmed.ncbi.nlm.nih.gov/39903359/





Evolution of Transcription Factor Superfamilies and Organismal Complexity

The evolution of transcription factor (TF) superfamilies across eukaryotes was examined by **Dr. Aswin Sai Narain Seshasayee's** group. They found that the diversity of TFs is linked to organismal complexity, with more complex organisms possessing a greater variety of TFs. This expansion likely facilitated the development of intricate gene regulatory networks essential for complex life forms.

The full study is available here:
https://www.sciencedirect.com/science/article/abs/pii/S0022283625000257?via%3Dihub

Extended Synaptotagmin: A Key Calcium Sensor in Brain Health

A latest study from National Centre for Biological Sciences (NCBS-TIFR) has proposed that a key protein found in the brain can act as a natural smart sensor hinting at impending neurodegeneration in cells. The study was conducted by **Professor Raghu Padinjat's** group and published in the *Journal of Cell Biology*.

Cells in the brain need to communicate and stay updated about the developments and all ongoing activities within its neighbourhood in order to support the brain and bodily functions. But how is it accomplished? The exterior region of a cell constitutes the plasma membrane (PM) and endoplasmic reticulum (ER). The region where their ER-PM boundaries meet are known as the Membrane Contact Sites (MCS). These sites facilitate intra-cellular signalling, transport of essentials like lipids and calcium between organelles and are vital for cell health. Whereas, PM is responsible mainly for maintaining two-way communication of the cell and filtering material into the cell.

Recent research has identified around 20 proteins at MCS, but their specific roles in maintaining cell health remain an active area of study.

Padinjat's lab at NCBS had, previously, shown how the presence of Retinal Degeneration B (RDGB) – an essential protein sitting at the MCS. Back then, researchers had concluded that the absence of RDGB blinded the flies. In other words, the MCS density depended on the incoming light intensity.

Aimed at advancing the scope of understanding the importance of MCS and the role of calcium in their new study, researchers tracked how some of these proteins found near MCS regulated cell functioning at this site. With the help of the Drosophila fly model, researchers observed the changes in the photoreceptors (light sensitive neurons in the fly's retina) when they were subjected to visible light during the experiment. The calcium present at MCS monitors the incoming light and signals the cells to undertake lipid transfers.

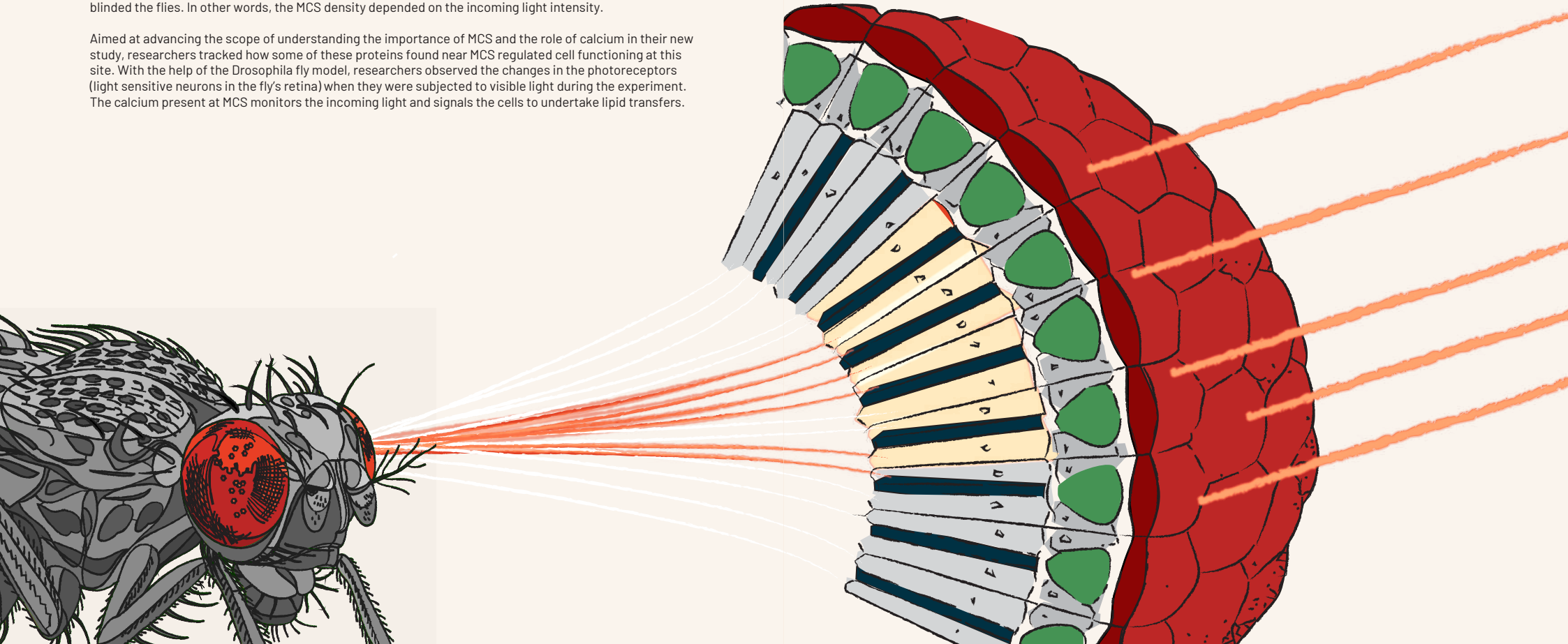
In the process, the team identified a new protein named Extended synaptotagmin (Esyt) at MCS which is the first to sense the variation in the calcium levels and instantly signal the same to the cells. It possesses a C2 domain that has the ability to bind and detect calcium.

"Esyt's strategic presence at the contact site allows it to first decode the calcium binding to the C2 domain. Loss of this ability makes the cell incapable of adjusting its functioning to the varying light intensities," said Raghu Padinjat, professor and senior author of the study.

Healthy and adequate number of MCS are essential for cell functioning. It is the calcium which signals to the cells if there is a need for creating more MCS, thereby ensuring continuous lipid transfer into the cell, said Vaisaly Nath, lead author of the study.

Researchers said that Esyt could be used as a smart sensor that can point to the onset of neurodegeneration in cells. "Esyt monitors incoming light and accordingly signals the cells in the fly's eyes to adapt its working machinery. A failure in this signalling could result in the onset of loss of cell structure, commonly referred to, with respect to the brain, as neurodegeneration. And in case of the Drosophila fly, it suffered retinal degeneration," said Padinjat.

You can read the full article here:
https://rupress.org/jcb/article/224/5/e202407190/277301/Ca2-binding-to-E



Narrowing the Access Gap in Science Education

How Outreach is Critical to Shaping Scientific Interest in Marginalised Communities

The Outreach Team

Access to higher education can be a transformative experience, not just for individual students, but for entire families. For first-generation learners and students from marginalised communities, research institutions can seem like daunting spaces; the barriers to their access go beyond merely financial constraints. Often, there are additional challenges with navigating the collegiate experience, evaluating career and research opportunities, and manoeuvring networking and communication. Outreach programs are an essential component of demystifying the college experience, welcoming first-generation students, and maximising the benefit they receive from their programmes.

With scientific disciplines, there is often an added layer of inaccessibility because of its exclusive, jargon-heavy language, the limited importance of science communication, the complex, every-growing corpus of scientific work. First-generation learners may additionally lack the means for extra-curricular tuition and mentorship—one of the most common ways through which Indian students learn how academia and research work. First-generation students are also more likely to come from schools with underfunded laboratories, further limiting their early exposure to science.

The need to address these inequities was the driving force behind the founding of NCBS' Science Education and Outreach Initiative. The programme aims to narrow the gap between people who traditionally have access to spaces like NCBS—such as students from urban communities or those whose parents are likely to be educated—and those who do not—such as students from Tier-II and Tier-III cities and first-generation learners. We spoke to Dr. Krithi Nandimath, Program Manager at the Science Education and Outreach Office, about the mission behind the initiative, as well as its current programs.

Modulating the reputation of science: Improving access on every front

Science in general has a reputation for being 'tough'. Students, especially first-generation students, may consider NCBS to be an intimidating place due to its research history. The mission of the Science Education and Outreach Office is to not only make NCBS more accessible, but to make science more accessible as well. Beyond that, the Office also aims to introduce students to the breadth of career opportunities in science and underscore that there is no longer a dichotomy between research and industry.

Dr. Nandimath, who was at IISc for several years before joining NCBS, says, ***"I enjoyed a career in research because I loved being in the lab and running experiments. But at the same time, I didn't want to become a principal investigator (PI). I wanted to do something with education and outreach. It was at this inflection point in my career that I met Prof Raj Ladher from NCBS. We quickly realised we had a mutual desire to improve science education and outreach. I joined NCBS last year, and after applying for some grants etc., the Science Education and Outreach Office was established earlier this year."***

The Science Education and Outreach Office now has a team of four individuals who work on different verticals, including teacher training, digital content, and network building. A majority of the work at the Office boils down to creative thinking and brainstorming on the best ways to design and execute the many programmes they are working on.

In January of this year, the Office successfully collaborated with the NGO, JKScientists, to conduct a two-month winter internship programme for undergraduate and postgraduate students from the Jammu and Kashmir region. During these two months, the participating students attended labs, lectures, and networking sessions. Another similar internship programme is due to be held in May, in collaboration with Project EduAccess. The programme will host a pan-India cohort of first-generation learners, students from marginalised backgrounds, and students who have experienced setbacks that have limited their opportunities for education. This internship programme will focus on research and skill-building in equal parts, so that students additionally learn the basics of writing a statement of purpose (SOP), strategies for science communication, and how to handle technical interviews.

"Research as a career choice needs to be accessible to more people," says Dr. Nandimath. ***"If someone chooses not to be in academia, then they should be making that choice after exploring research instead of making the choice out of a lack of knowledge. At the same time, the aim is not to get everyone into a PhD. It's about overall development. The skills you learn as a scientist, such as critical thinking, can be applied outside academia as well."***

Catching them young: Inculcating scientific interest from a young age

Beyond internship programmes for first-generation learners, the team also puts considerable effort into its outreach programmes for younger students. In November of last year, the Office hosted an event for 7–8 year old students from The Earth School in Bengaluru. Keeping in mind the scientific syllabus of that age group, the office designed activities that exposed the students to the scientific method, without overwhelming them with overly complex concepts. Some of the techniques employed by the Office include card games, flashcards, board games, role-playing games, scientific demos, and hands-on experiments—each activity tailored based on the expected scientific understanding of the participating students. Another memorable school visit was conducted in January, where middle school students from marginalised backgrounds at Gubbachi Learning Center, Bengaluru, were exposed to experiments in entomology and microscopy.

Rounding out NCBS' own students: How outreach in reverse serves as capacity building

NCBS's Communications Office conducted school visits even before the Science Education and Outreach Office was established. But managing these visits alongside other activities was challenging with fewer people, making it harder to design experiences tailored to visitors. Now, with a dedicated communications team at the Science Education and Outreach Office, the workload is distributed among a larger number of people, giving everyone involved the bandwidth to customize visits based on visitors' needs. Additionally, resource persons now spend less time on these activities, as the team ensures that all the backend work is handled efficiently.

"The resources we call upon for our programmes are usually our own graduate or post-doctoral students who have shown an interest in education and outreach. However, their primary focus remains their research. With a dedicated team managing logistics, they no longer have to divert their attention from their work," explains Dr. Nandimath. *"Ultimately, we also want to build capacity for our own students as well. We want them to become well-rounded scientists who think about society at large; participating in these kinds of outreach events is a great way to make that happen."*

In the next few years, the office hopes to establish a network of interns from internship programmes who can support each other in their scientific journey. We also hope to maintain sustained connections with our interns and support them as best we can in their careers and scientific journeys. The team further hopes to release toolkits for science teachers by the end of the year, with a focus on how to conduct practical work even with a low budget.

Measuring the impact of this kind of work is nearly impossible at present. Its effects will only make themselves clear in the long term. For now, the team is satisfied when they are able to reach people and make it clear to them that science is accessible to everyone.

Dr. Nandimath sums it up succinctly, *"If we can make students think that science is wonderful—give them not just a bulleted list of isolated facts but instead give them the biology, history, and current developments in the field in one place—then that is impact enough. The hope is to have NCBS known not only for its high-quality research but also for providing opportunities to students from communities that do not usually have access to a place like NCBS. The hope is that they go back to their communities and amplify the learning. We see this as a long-term vision of having a sustainable transformation where it is most needed."*

Meet Our Recent Awardees

Hindustan Unilever Fellowship for Women in STEM

"Receiving the HUL Award is an incredible encouragement for women in STEM, supporting our journey toward higher academic positions. This fellowship not only provides crucial research funding, enabling me to present my work at international conferences but also offers mentorship opportunities to gain insights into both academic and industrial research landscapes. My research focuses on identifying biomarkers to predict cancer patients' response to immunotherapy, which can help optimize treatment strategies and improve accessibility to advanced therapies. I am grateful to NCBS for fostering such opportunities on campus; creating an environment where young researchers can thrive."

Disha Kshirsagar
Research Fellow
Sabarinathan Radhakrishnan Lab

"Through the HUL Women in Stem Fellowship, I aim to study how tree seeds cope with desiccation stress along the Western Ghats Mountain range. This research could provide a peek into how global warming might impact rainforest tree communities. It's been an enriching few months travelling across the Western Ghats to conduct this research, and I am very thankful for the funding and support from HUL for making this possible."

Aparna Krishnan
Research Fellow
Mahesh Sankaran Lab

Marie Skłodowska-Curie Actions Postdoctoral Fellowship

"The MSCA postdoctoral fellowship means a lot to me as it will allow me to work with brilliant scientists at the University of Cambridge, expose me to the state of the art research in my field of interest, and provide the necessary thrust to boost my career as an independent scientist.

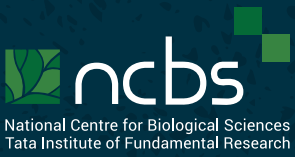
I think the most important thing that helped me in getting the award is the research proposal that we came up with as it leverages the cutting edge tools of genomics to understand intricate concepts of evolutionary biology. Of course, having the appropriate research experience and preparing a good application also mattered a lot."

Vinay Sagar
Former Ph.D. Scholar, Uma Ramakrishnan Lab
(Current Post Doctoral Fellow, University of Kansas)

David H. Smith Conservation Research Fellowship

"The David H. Smith Conservation Research Fellowship (Smith Fellowship) means a lot to me, as it is one of the most prestigious and competitive fellowships in the field of conservation science.
Being the first fellow from India makes this award even more special, but also a responsibility.
The best part of the Smith Fellowship is becoming part of a community of incredible conservation scientists.
I believe the exposure I gained during my PhD played a key role in helping me secure this opportunity.
During my fellowship, I will be working on the conservation genomics and connectivity of North American River Otters, using cutting-edge genomic and epigenetic tools at Purdue University."

Abhinav Tyagi
Post Doctoral Fellow
Uma Ramakrishnan Lab



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