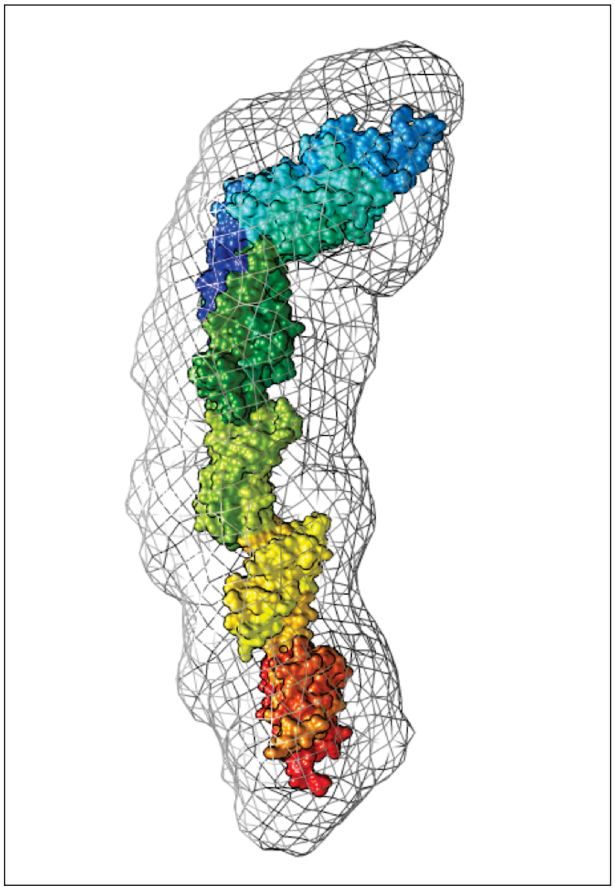
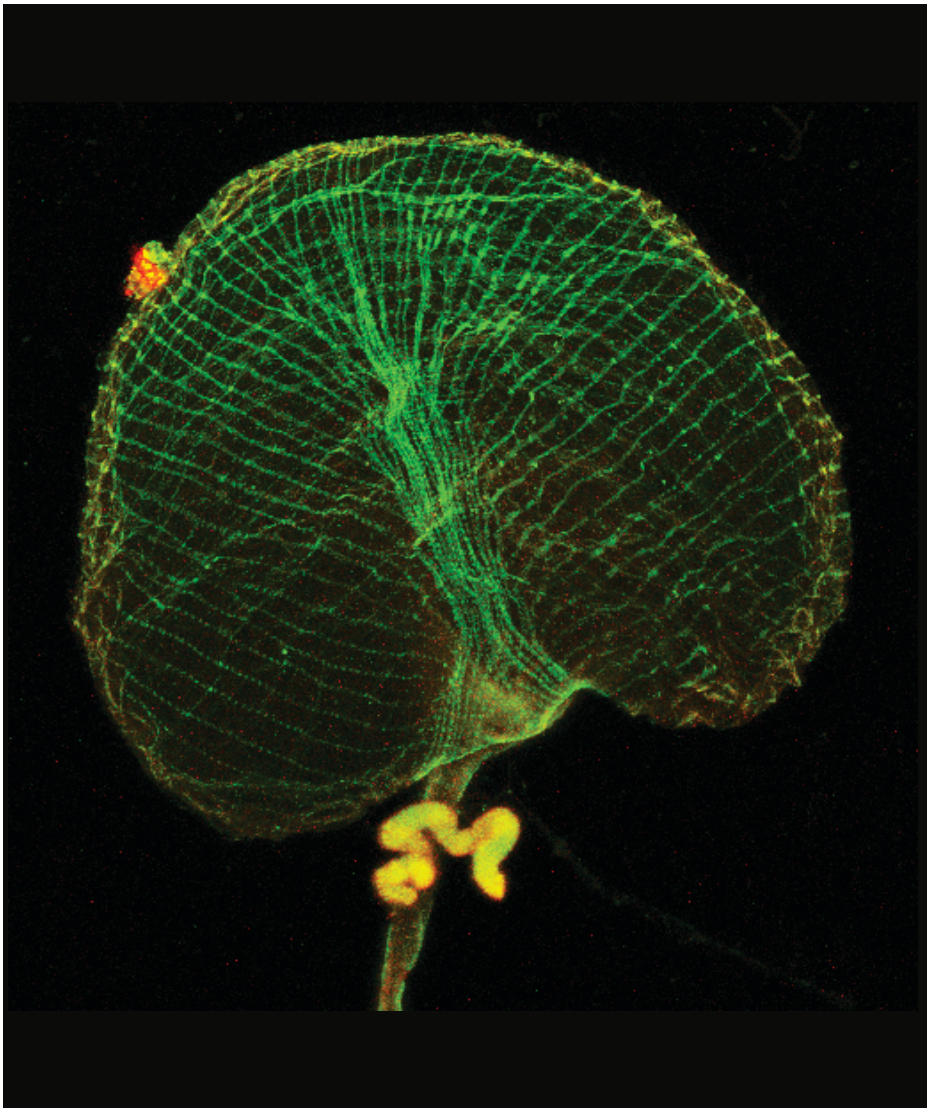
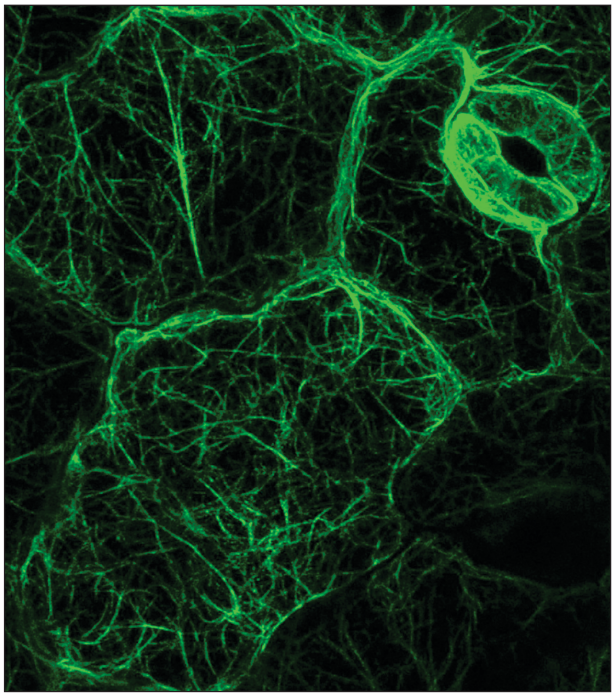
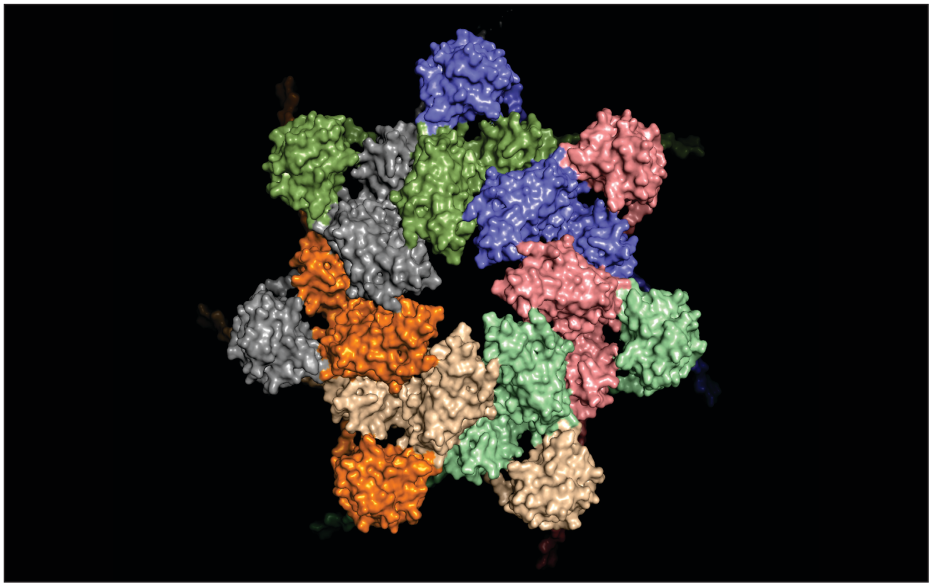
ANNUAL REPORT

2022-2023









United Nations
Educational, Scientific and
Cultural Organization

क्षेत्रीय जैव प्रौद्योगिकी केन्द्र
Regional Centre
for Biotechnology

Courtesy: Anamika Singh

CONTENTS

Mandate of Regional Centre for Biotechnology

The mandate of the Regional Centre for Biotechnology (RCB) is to provide a platform for biotechnology education, training and research at the interface of multiple disciplines. The programmes of the Centre are designed to create opportunities for students to engage in multi-disciplinary research where they learn biotech science while integrating engineering, medicine and natural sciences, to provide solutions for human and animal health, agriculture and environmental technologies.

The vision is to produce human resource tailored to drive innovation in biotechnology, particularly in areas of new opportunities and also to fill talent gaps in deficient areas. The Centre is regarded as a "Category 2 Centre" in terms of the principles and guidelines for the establishment and functioning of UNESCO Institutes and Centres.

The objectives of the Regional Centre are:

a. to disseminate and to advance knowledge by providing instructional and research facilities in such branches of biotechnology and related fields as it may deem fit including technology policy development,

b. to provide capacity-building through education, training, research and development in biotechnology and related academic fields for sustainable development objectives through regional and international cooperation,

c. to facilitate transfer of knowledge and technology relating to biotechnology at the regional level,

d. to create a hub of biotechnology expertise and to address human resource needs in the countries in the region,

e. to promote and strengthen international co-operation to improve the social and economic conditions and welfare of the people,

f. to promote and facilitate a network of satellite centres in the region as well as within India.

The functions of the Regional Centre are:

a. to establish infrastructure and technology platforms which are directly relevant to biotechnology education, training and research,

b. to execute educational and training activities including grant of degrees in education and research in biotechnology and related fields,

c. to produce human resource tailored to drive innovation in biotechnology, particularly in areas of new opportunities and to fill talent gap in deficient areas,

d. to undertake research and development and scientific investigations in collaboration with relevant research centres in the region,

e. to hold scientific symposia and conferences within India or in the region or outside the region and to conduct short-term and long-term training courses and workshops in all areas of biotechnology,

f. to collect universally available information with a view to setting up data banks for bio-information,

g. to collect and disseminate, through networking, the relevant local knowledge in the field of biotechnology, ensuring protection of intellectual property rights of local stakeholder communities,

h. to develop and implement a policy for intellectual property rights which is equitable and just to the stakeholders involved in research in the Regional Centre,

i. to disseminate the outcome of research activities in different countries through the publication of books and articles,

j. to promote collaborative research and development networking programme in specific areas of biotechnology with national, regional and international networks and promote exchange of scientists, at the regional level having regard to issues pertaining to intellectual property rights of collaborating institutions promoting equitable sharing of benefits with collaborating institutions.

From the Executive Director's Desk

Education, training, and research in the broad area of biotech sciences are the key mandates of Regional Centre for Biotechnology (RCB). The Centre has continued its journey towards achieving its mission and making significant progress in these key areas of its mandate. RCB relationship with UNESCO has continued as a category-2 institution; the linkage provides the international reach to our various programs. A detailed account of the various RCB activities is provided in different sections of this annual report.

Research-based learning is the hallmark of the RCB's education and training programs. The RCB academic programs provide an opportunity to the students to work closely with researchers in our laboratories housing the most modern equipment and technologies. RCB offers structured degree programs as well as short-term training programs in highly specialized areas of biotechnology and life science research. The doctoral degree programs are offered in Biotechnology, Bioinformatics, and Biostatistics. More than 100 students work in the RCB laboratories toward their PhD degrees. The integrated MS-PhD program has continued to attract high-quality students from different parts of the country. In the reporting period, 05 students graduated with a Master's degree and 07 students chose to continue with their doctoral research program.

The RCB Act 2016 empowers the Centre to recognize the institutions of higher learning for their various academic programs. This year RCB granted academic recognition to the PhD programs at Institute for Stem Cell Science and Regenerative Medicine (inStem), Bangalore thus bringing the total number of the recognized center to 13. A total of 59 students from these recognized centers were registered for their Master's degree and 431 for the PhD degree with RCB.

This year, RCB organized its first convocation ceremony where degrees were conferred to the students of PhD and Master's programmes by the Chief Guest Dr. V. K. Saraswat, Hon'ble Member, NITI Aayog. A total of 51 students graduated; one PhD in Biotechnology and 50 Master of Science in Biotechnology degrees were awarded to the students.

The COVID-19 pandemic has made it abundantly clear that viruses with RNA genomes can pose a serious public health problem of global scale. The mortality and morbidity due to known RNA viruses are high and the problem is compounded by the appearance of new viruses due to the animal-human conflicts. Several laboratories in different parts of the world are engaged in research to identify critical intervention points in the life cycle of these viruses and exploit this knowledge to develop effective therapeutic and prophylactic strategies. To encourage a productive discussion and to disseminate knowledge about the new advances in this area, RCB organized a focused meeting on the Biochemistry and Molecular Biology of RNA viruses. The meeting was supported by the International Union of Biochemistry and Molecular Biology (IUBMB). The meeting was attended by around 175 young researchers and 30 domain experts from nine countries.

The advancements in technology and instrumentation allow researchers to study the roles of nucleic acids beyond their traditional functions as genetic materials. The biocompatibility and programmability of nucleic acid have allowed their application in DNA nanotechnology to be used in a range of medical and biological applications. Despite all the progress made in this field, there remain open opportunities to explore the development and deployment of innovative applications in this exciting area of science. To discuss these, RCB organized a meeting on 'Functional Nucleic Acids: Recent Landscapes and Therapeutic Applications' under the banner

of the prestigious India-EMBO lecture course. The hybrid mode international meeting saw 25 eminent scientists delivering talks on diverse aspects of nucleic acids. More than 150 research scholars and scientists attended the meeting.

RCB organized the 8th edition of the India International Science Festival (IISF) in Bhopal from January 21-24, 2023 on the theme 'Marching towards Amrit Kaal with Science, Technology and Innovation'. The festival had fifteen programs including the Mega Science and Technology Exhibition showcasing the theme of the festival. IISF is a festival to celebrate the achievements of India's scientific and technological advancements. The festival received a large footfall of several thousand students, innovators, craftsmen, farmers, scientists, and technocrats from different parts of India.

Besides, RCB continues to provide Indian researchers access to the ESRF synchrotron radiation facility. This program has provided tremendous support to Indian structural biologists and has benefited a large number of young research students.

The various scientific programs of RCB can be broadly grouped under the following heads: Structural Biology, Infectious Disease Biology, Molecular Medicine, Cancer and Cell Biology, Agricultural Biotechnology, and Systems and Synthetic Biology. Several advances were made in the various research areas being pursued at the Centre which are discussed in the scientific reports section of the annual report. Our scientists published their research findings in the leading international scientific journals. Their work was supported from various competitive extra-mural grants.

RCB continued to participate in a multi-institutional research program aimed at understanding the biology of preterm birth to identify possible biomarkers to predict birth outcomes. A large cohort of pregnant women has been established by THSTI and the scientists at RCB are conducting a comprehensive study on the proteome of the various tissue samples from these women. The RCB flagship program on antiviral development has also been progressing well. Screening of several small molecule libraries has identified a small number of drug-like molecules showing antiviral activity against the Chikungunya virus in the cell culture and the mouse model. The mechanism of the antiviral activity of these compounds is being studied.

RCB has established a Bio-Incubator on its campus to foster innovation, research, and entrepreneurial activities in biotechnology-related areas. During the reporting period, twenty-six start-up companies were incubating at the Bio-Incubator. Through this mission, we contribute to spurring the economic growth in the region in the biotechnology sector. The Advance Technology Platform Centre (ATC) at RCB provides high-end equipment and technical support to scientists both from industry and academia across the country. The Biosafety Support Unit (BSU) at RCB continues to provide support to the Department of Biotechnology, Govt. of India in its regulatory activities. The Human Resource Development (HRD) Project Management Unit at RCB has been successfully managing the various HRD activities of the Department of Biotechnology (DBT), Govt. of India. Details of these activities are provided in the Research & Innovation Infrastructure section of the report.

On November 4, 2022 Dr. Jitendra Singh, Hon'ble Minister of State (IC), Ministry of Science and Technology, MoS (IC) Earth Science, MoS PMO, Personnel, Public Grievances & pensions, Atomic Energy & Space, Government of India, dedicated the 'Indian Biological Data Center' (IBDC) to the nation. IBDC, established by RCB with support from the Department DBT, is the first national repository for life science data in India. It has a data storage capacity of about 4 petabytes and houses the 'Brahm' High Performance Computing (HPC) facility. The computational infrastructure at IBDC is also made available to researchers interested in performing computational-intensive analysis. IBDC played a pivotal role in supporting the Indian SARS-CoV-2 Genomics Consortium (INSACOG) by curating and analyzing the virus genome data on a real time basis.

INSACOG, established by DBT as an inter-ministerial initiative is being coordinated by RCB. The key objective of INSACOG has been to expand the whole genome sequencing of SARS-CoV-2 across the nation, aiding our understanding of how the virus is spreading and evolving. INSACOG reports on prevailing virus strain/s, and the genetic mutations observed in the virus genome, have helped the government and the public at large develop and follow strategies for COVID management and mitigation.

Finally, I would like to thank my colleagues in the RCB faculty, technical staff, and

administration for their excellent cooperation. I must place on record the continued support of DBT and UNESCO, the members of the RCB Board of Governors, the Programme Advisory Committee, and the various other statutory committees in achieving the various scientific and academic goals of the Centre.

Jai Hind!

Sudhanshu Vrati
Executive Director

EXECUTIVE SUMMARY

Courtesy: Dr. Sudeep Bhar

RCB Mandate

- Human resource development through education and training in the interdisciplinary areas of biotechnology
- To create a hub of biotechnology expertise in the SAARC region, and more generally in the Asian region
- To develop research programs of a global quality through international partnerships

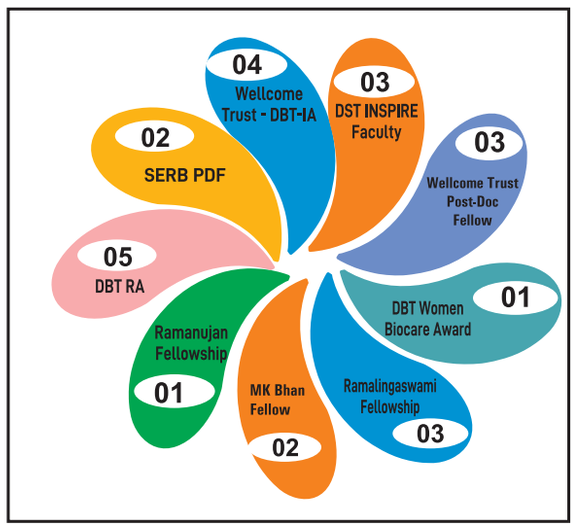
Academic and Training Activities

Post-doctoral Training	Young Investigator Awards	EMR grant Fellows
Doctoral Research Programs	• Biotechnology • Bioinformatics, Biostatistics	
Pre-doctoral Programs	MSc-PhD program	Research Interns

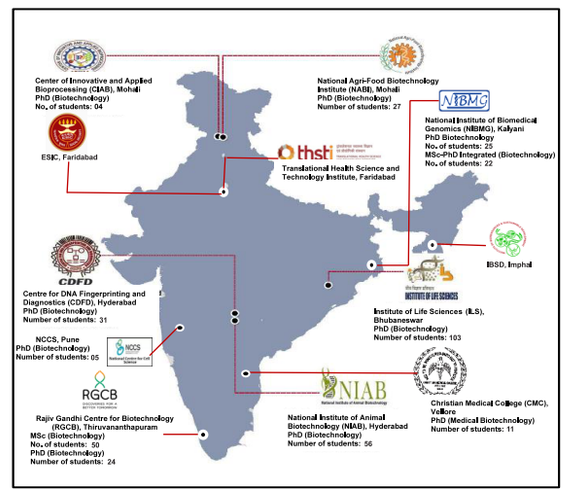
No. of Students studying at RCB

110	PhD (Biotechnology)	MSc-PhD (Biotechnology)	48
07	PhD (Bioinformatics)	PhD (Biostatistics)	04
61	Research Interns	PhD awarded	07

Awards and Fellowships



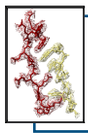
RCB Recognized Centres



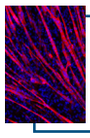
Total number of students registered at RCB: 490

Date	Event Organized
21 June, 2022	International Yoga Day
30 June, 2022	1st Convocation Ceremony 2022
18 July 2022 to 17 August 2022	Summer Research Internship Programme Facilitated By Gujarat State Biotechnology Mission (GSBTM)based
16 - 19 August, 2022	India EMBO 2022
14-27 September, 2022	Hindi Pakhwada 2022
15-18 November, 2022	IUBMB Focused Meeting On Biochemistry & Molecular Biology of RNA viruses
January 21-24, 2023	India International Science Festival (IISF) 2022
28 February, 2023	National Science Day 2023
1 March, 2023	RCB Foundation Day 2023
8 March, 2023	International Women's Day 2023

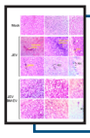
Research Areas



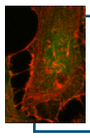
Structural Biology



Molecular Medicine

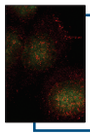


Infectious Disease Biology



Cancer & Cell Biology

Agricultural Biotechnology



Systems & Synthetic Biology

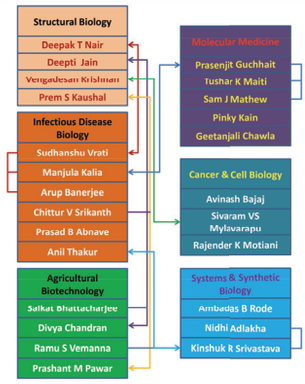
Publications : 89
Patent Filed : 03

Research Highlights

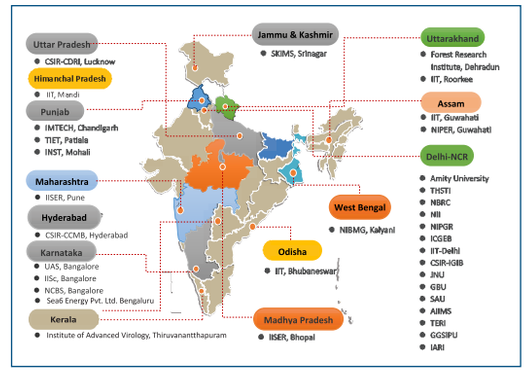
- The crucial role of long non-coding RNA *NEAT1* in mediating antiviral response and mitochondrial dysfunction in dengue infection was highlighted.
- The cryo- EM structure of *Mycobacterium smegmatis* 70S ribosome in complex with RafH protein was resolved at 2.8 Å resolution. Its linker region interacts with the anti-Shine Dalgarno sequence of the 16S rRNA and inhibits the initiation of protein synthesis.
- Elucidated the role of TOR signalling in *Candida auris* that may be responsible for drug-resistance mechanisms and causing pathogenesis.
- Combination of Agrochemicals targeting bZIP23 transcription factors reduces ABA accumulation, enhances the transpiration and yield in plants during mild drought stress.
- A novel ribonucleoprotein (RNP) complexes targeting bacterial type III secretion system developed for crop protection against bacterial diseases in plants.
- *Salmonella* Typhimurium induced gastroenteritis in humans is a significant health problem. It has been shown that Salmonella utilizes a complex mechanism, involving post-translational modification of AP-1 protein to reprogram entire host-signaling to evade host defense.

  The complexity of host-pathogen crosstalk and tunability of immune signaling mechanisms has been highlighted.
- Experimentally demonstrated that targeting genomic RNA conformations in SARS-CoV-2 is a promising antiviral strategy. The developed TPE derivatives can be used as lead molecules for antiviral drug development against SARS-CoV-2 as well as other viruses.
- A high throughput image based screening platform for autophagy modulators was developed. The Spectrum drug library of 2500 compounds was screened, and several novel autophagy inducers and inhibitors were identified.
- The exact mechanism by which fungal strains sense insoluble cellulose is unknown. For this, multi-omics approaches were employed to identify novel cellulase inducers, which boosted the cellulase production in the cellulolytic fungus by 3-fold.
- Crystal structures of pilin subunits (PitA and PitB) that form pili in *Streptococcus oralis*, an early dental plaque colonizer were determined, and new insights into the PI-2 pilus and pili-mediated inter-bacterial interaction were revealed.
- Identified actin dependent-host nuclear movement as a novel susceptibility factor that is crucial for powdery mildew fungal colonization on pea plants.
- A novel physiologically relevant signaling module that transcriptionally increases STIM1 expression has been identified
- Identified the first plasma membrane localized AtGELP7 which can deacetylate xylan polysaccharides upon overexpression in Arabidopsis and improves lignocellulosic biomass digestibility.
- Synthesized and developed novel cholic acid-peptide conjugates as effective antibiotic adjuvants against multidrug resistance gram-negative bacterial infections.
- Developed small molecule-based antimicrobials that can inhibit the development of microbial resistance against vancomycin.
- Engineered lipid-based nanoparticles for oral delivery of siRNA against pro-inflammatory cytokines for mitigating gut inflammation.

Intra-institutional collaborations



National Collaborations



International Collaborations

Infrastructure and Support Services

Advanced Technology Platform Centre

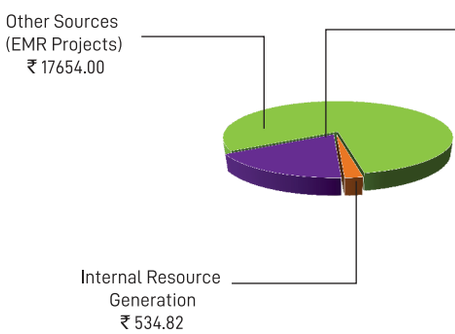
Biosafety Support Unit

BSC BioNEST BioIncubator

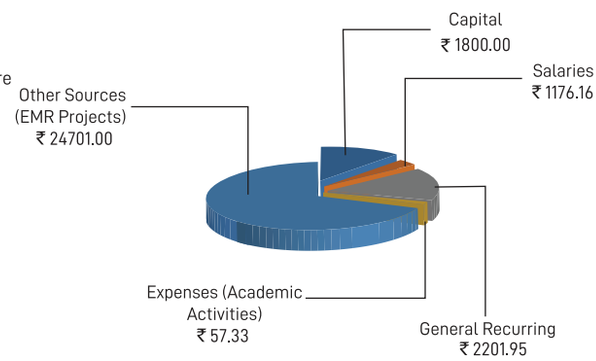
IBDC & DBT HRD-PMU

Financial Figures

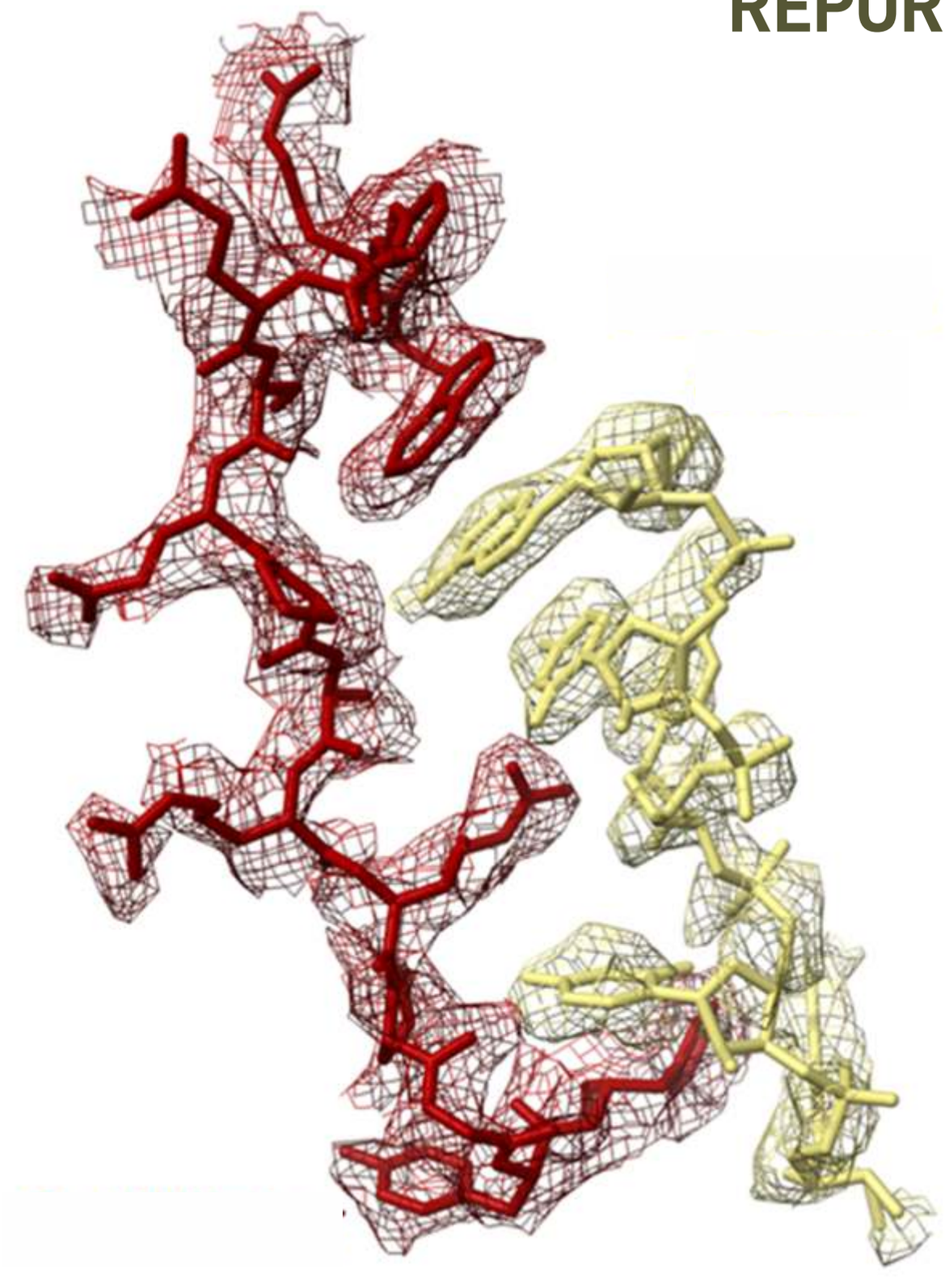
Total Income (Rs. In lakhs) 2022-2023



Total Expenses (Rs. In lakhs) 2022-2023



SCIENTIFIC REPORTS



Structural Biology

Courtesy: Dr. Prem Singh Kaushal

Deepak T Nair
Principal Investigator

Lab Members

Patterson Clement
Dalchand
Thangaraj V
Bhawna Mawri
Ritika
Vaibhav Joshi
Dhiraj Kumar
Minakshi Sharma
Sunil Kumar Yadav
Tuleshwori Sapam
Amit Rathour

Molecular determinants of genomic integrity and plasticity

For all cellular processes to function optimally, the integrity of the genome has to be maintained. Conversely, plasticity in the genome can relieve selection pressures imposed by an adverse environment. These two conflicting requirements have led to the presence of molecules and pathways that either prevent or facilitate changes in the genome. In the case of pathogenic bacteria and viruses, genomic plasticity is implicated in the onset of drug resistance and reduction in vaccine efficacy. We aim to elucidate the structural mechanisms utilized by different molecular determinants of genomic integrity and plasticity to achieve function. Within this broad aim, the biological processes under scrutiny in our laboratory are DNA replication, Stress-Induced Mutagenesis, RNA virus genome replication and Transpostion. The insight gained from our studies will shed light on how organisms evolve and also provide a strong platform for the development of novel therapeutic strategies against pathogenic bacteria and viruses.

DNA Replication

DNA-dependent DNA polymerases (dPols) are the primary enzymes responsible for duplication of the genome. We study different dPols from various organisms to understand the chemical mechanisms utilized by these enzymes to achieve their role in replication and evolution.

The DNA polymerase module of the Pfprex enzyme (PfpPol) is responsible for duplication of the circular genome present in the apicoplast organelle of the malaria parasite. The apicoplast genome is particularly vulnerable to the harmful effects of reactive oxygen species due to very high AT content (~87%). We have previously shown that the proofreading activity of PfpPol has the unique ability to remove the oxidized nucleotide from the primer terminus (Sharma *et al*, 2020, Sci. Rep. 10:11157). In addition to the nucleotide pool, ROS can also oxidize nucleotide bases of the genome and give rise to damaged nucleotides such as 8oxodeoxyguanosine (8odG), thymine glycol (Tg) and 2-hydroxydeoxyadenine (2-OHdA). These damaged nucleotides or DNA lesions can be promutagenic or inhibit DNA synthesis. We observe that the PfpPol enzyme has significant ability to accurately bypass the three DNA lesions (Fig. 1) and thus neutralize their adverse effects on genome replication (Sharma et al, 2022, FEBS J. 289:5218). Overall, the proofreading domain and the polymerase domains are able to neutralize the deleterious effects of ROS on the primer and template strands and thus prevent perturbation of the apicoplast genome replication. The proofreading and polymerase activities of the Pfprex enzyme, therefore, represent attractive targets for therapeutic intervention.

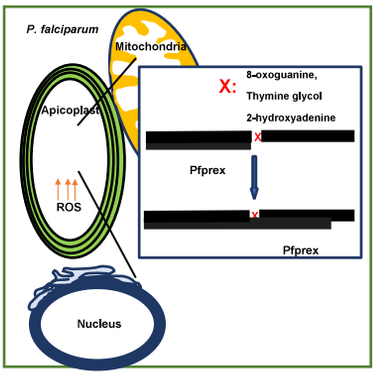


Figure 1: Schematic for the DNA lesion bypass activity of PfpPol.

Strategies to develop improved therapeutic molecules that are resistant to evolution

The presence of molecules and molecular pathways in pathogens responsible for genomic plasticity results in the onset of resistance against therapeutic molecules. As a result, it is imperative to unearth molecules that are resistant to loss of sensitivity due to the appearance of specific mutations in the target protein. We utilize different target proteins,

such as the Spike protein from SARS-CoV-2, to develop strategies to design and test robust therapeutic molecules.

The Spike protein is present on the virus surface and binds to the ACE2 receptor to gain entry into human cells. In collaboration with researchers at the THSTI, NII and AIIMS, we have characterized a monoclonal antibody (mAb) named P4A2 that can neutralize all known Variants of Concern (VoC) of the SARS-CoV-2 in cell culture and animal models. We have determined the structure of the Fab region of P4A2 with the receptor binding domain of the Spike protein (Fig. 2). The structure shows that the P4A2 Fab binds to regions on the Spike-RBD which are important for binding to the ACE2 receptor. The structure of the P4A2 Fab:Spike-RBD complex was used to generate computational models of the P4A2 Fab in complex with Spike-RBD from different VoCs. It was clear that none of the mutations observed in each of the VoCs will adversely impact recognition of Spike-RBD by P4A2 Fab. Due to the overlap between the binding sites of P4A2 and ACE2 on the Spike-RBD, mutations in the Spike-RBD that will lower the binding of P4A2 will also adversely affect the recognition of the ACE2 protein. As a result, the P4A2 mAb may also be effective against future variants of the SARS-CoV-2 virus. Therefore, the humanized form of the murine P4A2 mAb will represent an optimal therapeutic drug to treat COVID19. Our studies with the P4A2 mAb also evince that therapeutic molecules that bind to regions on the target protein that are critical for natural function will be less vulnerable to loss of sensitivity due to mutations in the target protein. Also, the rational structure based protein engineering of P4A2 can be conducted to develop evolved variants that can neutralize newer VoCs of SARS-CoV-2, such as XBB 1.5.

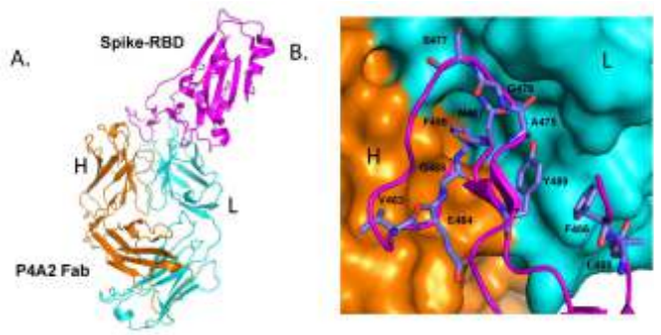


Figure 2: Structure of the P4A2 Fab in complex with Spike-RBD of SARS-CoV-2. *(A) Structure of P4A2 Fab in complex with RBD of Alpha variant. The heavy (H) and light (L) chain of P4A2 Fab are coloured in orange and cyan, respectively and the RBD is coloured magenta.(B) Surface representation of the P4A2 paratope with the RBD epitope is shown.*

We have participated in the characterization of a monoclonal antibody (mAb) named P4A2 that can neutralize all known Variants of Concern (VoC) of the SARS-CoV-2 virus. We have determined the structure of the Fab region of P4A2 with the receptor binding domain (RBD) of the Spike protein. The structural studies and allied computational analysis provide a rationale for the ability of P4A2 to neutralize all known VOCs of SARS-CoV-2. The structural data also provides an opportunity for rational engineering of the P4A2 paratope so that it can bind to Spike-RBD from newer VoCs of SARS-CoV-2. In addition, we have participated in an analysis of humoral immune responses against pathogens that suggests that antibody multispecificity delays the onset of immune evasion by fast mutating pathogens such as SARS-CoV-2.

Vengadesan Krishnan
Principal Investigator

Lab Members

Rajnesh Kumari Yadav
Smita Yadav
Vinay Sharma
Shivangi Tyagi
Sanjoy Das
Lisha
Shivam Kumar Tiwari

Structural biology of host-microbial interactions in health and diseases

Microbial attachment to the host surfaces is the first step in colonization. Subsequent events in the pathogenesis or probiosis depend highly on the initial interaction. Targeting the host-microbial interface is an attractive approach for improving health and combating infections. Since this approach does not directly kill bacteria, it may also serve as an alternative to antibiotics which often results in the development of resistance. However, such an anti-adhesive approach requires detailed knowledge of how microbes attach to the host and how the adhesive strategies differ among microbes. To provide the essential foundations for this approach and understand how microbes adhere to and interact with the host surfaces, we aim to generate structural knowledge by studying key molecules that establish the initial contacts between the host and microbes. We currently focus on hair-like surface organelles (pili) mediating the initial contact with the host surfaces for colonization and biofilm formation.

Our ongoing structural investigation programme covers beneficial and pathogenic strains for insights into tissue tropism and microbial interaction strategies in health and diseases.

Beneficial strains from gut microbiota

The most conventional probiotics are lactic acid bacteria (LAB) from the genera *Lactobacillus*, *Lactococcus*, and *Bifidobacterium*. Pili from LAB play a crucial role in adherence, persistence, and beneficial health effects. We have chosen a few representative LAB strains to understand pilus structures, assembly, and pili-mediated interaction with the host.

Ligilactobacillus (formerly *Lactobacillus*) *rhamnosus* GG (LGG), a well-known probiotic strain for its various health-promoting effects, contains two different sortase-mediated pilus operons (*spaCBA* and *spaFED*). While our previous work revealed new insights about pilus shaft formation and pili-mediated interaction for LGG, we have recently obtained crystal structures of sortases to understand their function. The visualization of LGG pili is in progress.

Ligilactobacillus ruminis (Lru) is a member of the indigenous microbiota present in the gut of humans and animals. Its pilus operon (*lrpCBA*) encodes three pilins (LrpA, LrpB, and LrpC) and one sortase. In contrast to LGG pili, the LrpCBA lacks mucus binding but has an affinity with collagen and fibronectin. Since LrpCBA pilus structure and interaction mechanism differ from LGG pili, it likely represents a third sortase-mediated pilus type in the Ligilactobacillus species. We have produced, crystallized, and obtained structure solutions for Lru pilins.

Lactococcus lactis (Lla) is the best-characterized and most widely used LAB strain in dairy fermentation. The lactococci are used in biotechnological applications such as the delivery of oral vaccines. The Lla pilus operon encodes three pilins (PilA, PilB, and PilC) and a pilus-specific sortase (SrtC). A housekeeping sortase (SrtA) anchors the assembled pilus to the cell wall. We have purified recombinant SrtA and SrtC and characterized them using biochemical, biophysical, and *in silico* techniques. The purified SrtA and SrtC are active against their substrates, as confirmed by FRET-based activity assay and steady-state kinetics. We also included a bifidobacterial strain in the study for structural and functional comparison.

Pathogenic strains from the oral cavity

The oral cavity harbours the second most abundant microbiota after the gut. Certain bacteria (primary colonizers) stick to the surfaces of the oral cavity through their pili and provide attachment sites for other bacteria (secondary colonizers) to develop oral biofilms (plaque). Attachment of primary colonizers (e.g., *Actinomyces oris, Streptococcus oralis*)

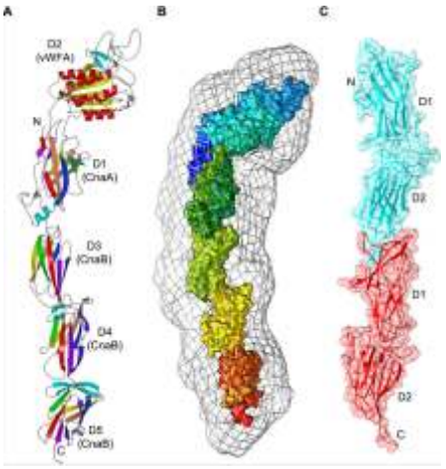


Figure 3: Structural analysis of PitA and PitB. *(A) Crystal structure of mature PitA showing five domains (D2-D1-D3-D4-D5). Core α-helices (red) and β-strands (yellow) of the vWFA domain, core β-strands (rainbow colors from red to violet) of the CnaA and CnaB domains, and additional secondary structural elements (cyan) are indicated. The termini (N and C) are marked. (B) SAXS analysis of PitA. (C) Head-to-tail stacking between PitB (red) – PitB (cyan) units for the PI-2 pilus shaft assembly.*

and their coaggregation promote the growth of plaque, which can lead to many oral diseases (e.g., caries, gingivitis, and periodontitis) and infective endocarditis. In contrast to the typical heterotrimeric sortase-mediated pilus, the PI-2 pilus in *S. oralis* is a heterodimeric structure with only the tip (PitA) and backbone (PitB) pilins. Our recent crystal structural analysis showed four immunoglobulin (Ig)-like domains and a von Willebrand Factor A (vWFA) domain in PitA and two extended Ig-like domains in PitB (Fig. 3). Our SAXS analysis further confirmed the linear arrangement of PitA domains and their orientations. We further revealed the intermolecular interaction, including isopeptide bonds between the pilins in the PI-2 pili by docking and analysis of molecular arrangement in the crystal lattice (Fig. 3). Interestingly, the adhesive vWFA domain containing two unique inserted arms involves in receptor binding through glycans for coaggregation with *A. oris* as shown by bioinformatic analysis, glycan-micro array, coaggregation assay, and yeast two-hybrid screening (Fig. 4). This pili-mediated interbacterial interaction is likely critical for plaque development and serve as a target to control biofilm growth and combat infections.

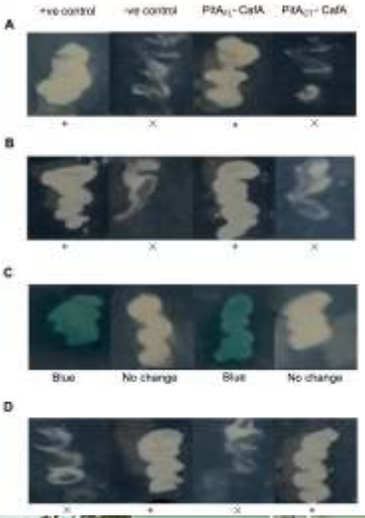


Figure 4: The Y2H screening confirms the direct interaction of S. oralis PitA with A. oris via CafA (coaggregation factor A). *(A) SC-Leu-Trp-His agar plates complemented with 30mm 3AT (3-amino-1,2,4-triazole). (B) SC-Leu-Trp-Ura agar plates. (C) SC-Leu-Trp agar plate complemented with X-gal. (D) SC-Leu-Trp agar plate complemented with 0.5% 5FOA (5-fluorotic acid). PitA$_{FL}$-the full-length PitA; PitA$_{CT}$-the C-terminal PitA consisting of D3, D4, and D5 domains.*

Deepti Jain
Principal Investigator

Lab Members

Vineet Kumar
Pankaj Kumar Sahoo
Shikha Raghav
Sheenu
Moumita Ghosh
Swagatam Maity
Puja Ghosh
Devendra Sharma
Gulshan Maurya
Kaveri Mohela

Transcription Regulation: Structure and Mechanism

Resistance to antibiotics represents an escalating challenge in the treatment of bacterial infections. *Pseudomonas aeruginosa* a gram-negative, opportunistic human pathogen has been listed as the "critical" category pathogen in the DBT-WHO priority list. A significant contribution to the persistence of *P. aeruginosa* is due to its ability to transition from motile to biofilm mode of life. This phenotypic transition is regulated at the level of transcription, which is the pivotal regulatory checkpoint for gene expression in bacteria. We employ an integrated approach, involving structural tools, biophysical techniques, biochemical methods and functional *in vivo* assays to investigate the molecular mechanisms of transcription regulation of flagellar and biofilm genes in *P. aeruginosa*. The mechanistic insights obtained are exploited for the discovery of novel therapeutic agents.

Structural Insights into the regulation of biofilm and flagellar genes by FleR

The two component signalling (TCS) systems couple the environmental or cellular signals to the alteration in the gene expression profile of the bacterium. FleSR is a two-component signal transduction system that regulates flagella and biofilm formation in *Pseudomonas aeruginosa*. Knockout of FleR renders the bacterium non-motile and results in drastic reduction in biofilm formation. FleR is a three-domain protein that harbors receiver or REC domain at the N-terminus, AAA+ ATPase domain at the center and a DNA binding domain (DBD) at the C-terminus. It undergoes phosphorylation at the N-terminus *via* cognate sensor kinase FleS for the assembly of the functionally active form. We have determined the crystal structure of the REC domain and small-angle X-ray scattering structure of the full length phosphorylated and non-phosphorylated form of FleR. The crystal structure of the REC domain displays all the structural features of the active form of the protein. The SAXS structures of full length protein in inactive form and negative stained images of the activated form reveal that FleR, exists predominantly as a dimer in the inactive form and assembles into heptameric discs upon activation (Fig. 5). Further, the REC domain positively modulates the assembly of the functional FleR. Through in vivo experiments we demonstrate that phosphorylated REC domain is required for the transcription activation by FleR. FleR also regulates biofilm formation in *P. aeruginosa.* It activates the genes responsible for synthesis of secondary messenger in the bacterial cells. This serves as a cue for the cells to switch from planktonic to biofilm mode of life. Our lab is currently exploiting this finding for *in silico* screening of database of small molecules that can directly or allosterically inhibit ATP binding to FleR. These molecules will be further examined for their ability to bind and inhibit the ATPase activity of FleR through in vitro assays and eventually for their ability to inhibit biofilm.

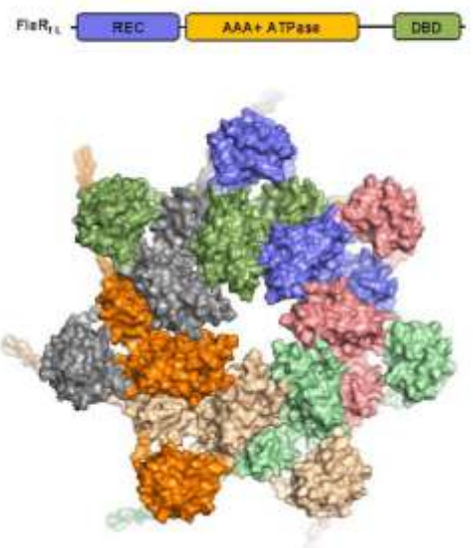


Figure 5: Structure of FleR. *Surface representation of FleR-NTD-Central domain in the phosphorylated active form. The domain organization of full length protein is shown above*

Inhibition and Eradication of Biofilms by *Pseudomonas aeruginosa*

Biofilms are surface attached bacterial colonies that are encapsulated in exopolysaccharide matrix. Bacteria residing within biofilms are tolerant to antibiotics as they are unable to penetrate the matrix. Further, the use and misuse of antibiotics has

resulted in the emergence of resistant bacterial strains. Thus, there is a need to discover and develop new antimicrobials against novel targets to control and manage the bacterial diseases. In collaboration with Prof. Khare at IIT-D we demonstarted biofilm inhibition and eradication by bioactive secondary metabolites produced by rare actinomycetes *Nocardiopsis lucentensis* from halophilic environment. We identified a total of 53 metabolites present in the organic extract pf actinomycetes using gas chromatography-mass spectrometry. Ligands present in the extract were found to target quorum sensing regulators LasR and RhlR *via* molecular docking. Downregulation of quorum sensing genes in the presence of extract of actinomycetes further confirmed LasR and RhlR as the target proteins. Both these regulators belong to LuxR family and contain two domains. The autoinducer binding domain is present at the N-terminus and binding of the ligand regulates the activity of these proteins. We demonstrate that the compounds present in the extract compete for binding of autoinducers. The quorum sensing pathway also regulates the production of virulence factors such as pyocyanin and rhamnolipids. Reduction in pyocyanin and rhamnolipid formation further confirmed that LasR and RhlR pathway was affected in the presence of the metabolites. Docking of the identified secondary metabolites reveals that five of these are capable of binding to both the target proteins, with good energetics. Docking of the representative compounds is depicted in Fig. 6. ADMET (absorption, distribution, metabolism, excretion and toxicity) analysis of the selected metabolites shows that these can be pursued as potential drug candidates. To the best of our knowledge, this is the first-time genus *Nocardiopsis* has been explored to inhibit and eradicate the biofilm of *P. aeruginosa.*

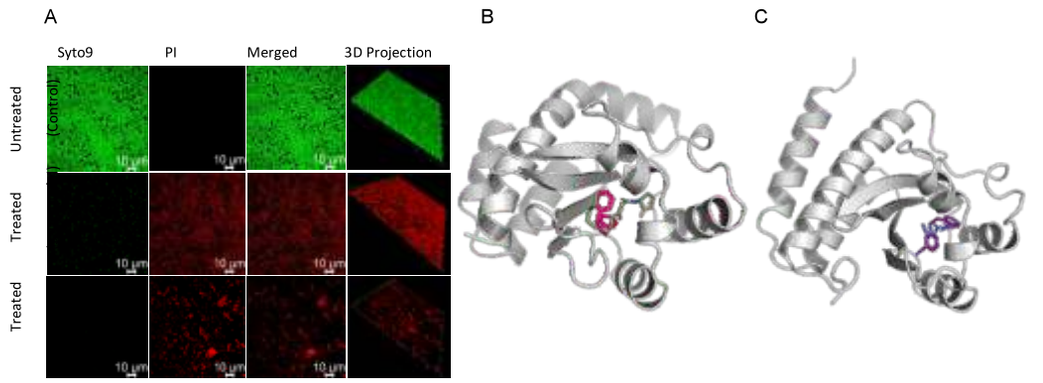


Figure 6: The effect of organic extract of actinomycetes on eradication of 48 hours preformed biofilm of P. aeruginosa: *(A) The CLSM images of untreated biofilm of P. aeruginosa and after treatment for 24 hours at two different concentrations 3.125 µg/µL and 25 µg/µL. Bacterial biomass after eliminating planktonic cells were stained such that live cells were labelled with Syto 9 dye, and dead cells are stained red with propidium iodide (B) Structure of LasR-NTD bound to acylhomoserine lactone (PDB: 2UV0) superimposed with metabolite C30 (C) Alphfold model of RhlR-NTD bound to butylhomoserine lactone superimposed with metabolite C58*

Prem Singh Kaushal
Principal Investigator

Lab Members
Niraj Kumar
Shivani Sharma
Ankita Arora
Shalini Kumari
Soumen Ta
Sreelakshmi R
Tanya Sapra

Structural aspects of translation regulation and ribosome assembly

Our laboratory's research goal is to unravel the structural basis of the functioning of macromolecular complexes involved in translation regulation and ribosome assembly, thereby identifying the potential drug targets. Translation, the protein synthesis, in which genetic information present in mRNA is decoded into a polypeptide, occurs on the ribosome in all cells. Protein synthesis is one of the most energy-consuming cellular processes, consumes nearly 50% of the cell's energy, and the ribosome is a target of nearly 40% of known antibiotics. We focus on understanding the structural aspects of translation regulation in *Mycobacterium tuberculosis* under different stresses and how a mega Dalton protein synthesis machinery, the ribosome, assembles inside the cell. We apply structural biology tool cryo- electron microscopy with molecular biology and biochemistry techniques.

Understanding the mode of mycobacterial ribosome hibernation under hypoxia stress

Ribosome hibernation is a crucial survival strategy bacteria adopt under environmental stress, where a protein, hibernation promotion factor (HPF), transitorily inactivates the ribosome and slows its overall protein synthesis. Hibernation has been well studied in enteric bacteria, where a dual domain, long HPF (HPF^{Long}) induces ribosome dimerization and stabilizes in 100S disome form. However, in mycobacteria, ribosomes are stabilized in 70S monosome form only. We solved a 2.8 Å resolution Cryo-EM structure of *M. smegmatis* 70S ribosome in complex with RafH protein (Fig. 7). The RafH, a dual domain hibernation promotion factor, is essential for survival under hypoxia (low oxygen) stress, which is the major stress encountered by the pathogen (*M. tuberculosis*) in host macrophages. Under stress, the pathogen slows down its cellular processes, including protein synthesis, which causes Latent Tuberculosis Infection (LTBI).

The structural insights reveal that the RafH N- terminus domain is conserved and binds to the similar binding site reported for other HPF. Strikingly, the RafH C- terminus domain is larger and binds to a unique binding site that has not been reported before. Whereas, the linker region connecting these two domains, which till now has been reported as disordered in various reports, makes a remarkable interaction with the anti-Shine Dalgarno sequence of 16S rRNA (Fig. 7). Thus, inhibiting translation initiation by blocking the binding site for the Shine Dalgarno sequence of the mRNA. Further, the *in-vitro* translation assay showed indeed that RafH inhibits protein synthesis in a concentration dependent manner. The modeling study provides a structural interpretation for the incompatibility of the mycobacterial ribosomes to form a 100S like disome architecture.

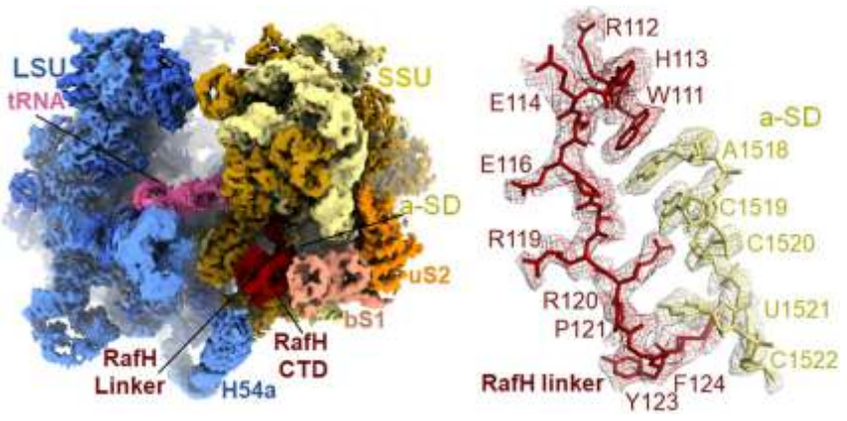


Figure 7. Cryo-EM structure of Mycobacterium smegmatis 70S ribosome RafH complex. *Left panel, the overall architecture of the 70S RafH complex is shown in the mRNA exit site. The SSU 16S rRNA (khaki), SSU r-proteins (dark golden), RafH (maroon), tRNA (pink), the LSU 23S rRNA and 5S rRNA (cornflower blue), LSU r- proteins (royal blue), bS1 (dark salmon) and uS2 (orange) are labeled. The right panel, the cryo- EM density in mesh, and the model in stick representation correspond to the RafH linker region (maroon) and a-SD region of 16S rRNA (khaki), are shown.*

We proposed that RafH has a distinct mode of ribosome hibernation, and it inhibits protein synthesis by blocking the crucial sites for translation initiation on the ribosomal small subunit. RafH binding site also overlaps with the binding of the aminoglycoside class of antibiotics, which hints about its role in antibiotic resistance in LTBI.

Understanding the role of DEAD-box RNA helicases in ribosome assembly

The ribosome is a large assembly of ribosomal RNAs (rRNAs) along with the proteins that decode the message encrypted in the sequence of mRNAs to synthesize proteins. The biogenesis of ribosomes is a complex series of processes, and ribosome particle has to assemble perfectly to perform error-free protein synthesis. In *E. coli*, five DEAD-box RNA helicase proteins (SrmB, DeaD, DbpA, RhlE, and RhlB) are involved in ribosome assembly. Whereas only two DEAD-box proteins (DeaD and RhlE) are present in mycobacteria which share nearly 40% similarity with E. coli DEAD-box proteins.

To gain knowledge about the precise role of DEAD-box RNA helicases in the assembly of ribosomal subunits, especially the 50S subunit, we implemented a CRISPRi technique to prepare Knock-down of RhlE. We co-transformed guide RNA specific to the RhlE in *M. smegmatis* pTetInt-dCas9 cells and selected positive clones. Next, to suppress the RhlE, the Cas9 system was induced by tetracycline (100 ng/ml). Further total RNA was extracted from the cells, cDNA was synthesized, and suppression was confirmed by measuring the expression level of mRNA. We have obtained 70-80% suppression of the protein (Fig. 8a). Furthermore, to understand the essentiality of the gene, an in-vitro growth analysis was performed under the cold condition (16°C) (Fig. 8b). Next, to gain precise insight into the role of the RhlE in assembly, we isolated and purified ribosomes from wild-type (control) and knock-down strains (Fig. 8c). The ribosome fractionation profile clearly shows fewer 50S ribosomal subunits in the knock-down strain as compared to the wild type. Further, the peaks corresponding to the 70S and 50S ribosomes were further analyzed by performing LC-MS/MS mass spectrometry (Fig. 8d-f). We observed the difference in the emPAI values suggesting that the ribosomes isolated from knock-down strain have altered ribosomal protein compositions. We plan further to do cryo- electron microscopy and illustrate the differences in the atomic details.

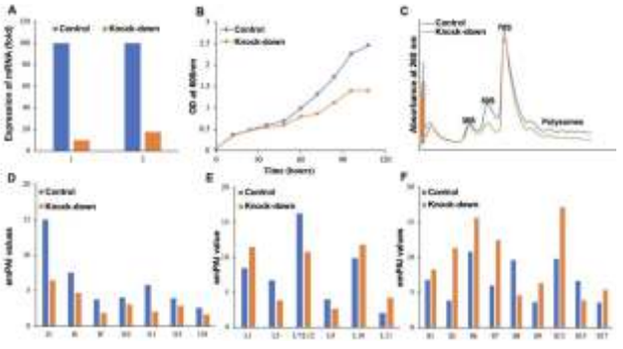
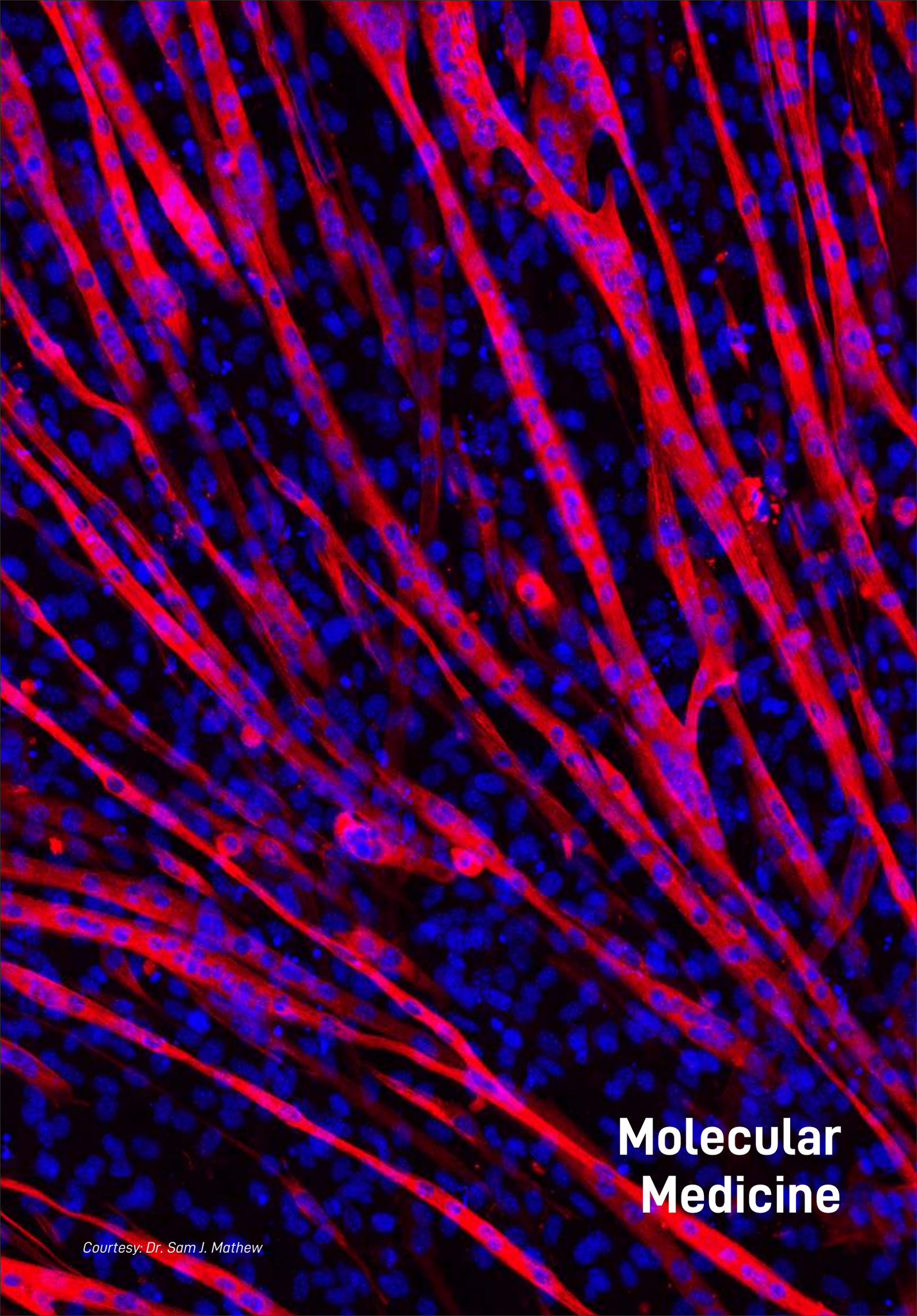


Figure 8: RhlE knockdown characterization. *(a) RhlE silencing using the CRISPRi approach. (b) In-vitro growth analysis of M. smegmatis cells downregulated with RhlE. (c) Ribosome profile. (d-f) Relative abundance of ribosomal proteins in wild-type and knock-down cultures in peaks corresponding to 50S and 70S ribosomal subunits analyzed by mass spectrometry.*



Molecular Medicine

Courtesy: Dr. Sam J. Mathew

Prasenjit Guchhait
Principal Investigator

Lab Members

Sakshi Agarwal
Anamika Singh
Kishan K Gaur
Garima Joshi
Garima Verma
Tejeswara Rao Asuru
Shalu Singh
Simrandeep Kaur
AbhayDeep Pandey
Riya Ghosh
Anushka Das

Thrombosis, Inflammation and Immune Response in Human Diseases

This major research programs focus on studying molecular signaling of thrombosis, inflammation, and innate and adaptive immune responses in human health and diseases, and identifying biomarkers and molecular targets to develop potential therapeutics.

COVID-19: We investigated the mechanism of SARS-CoV-2 induced inflammation, clot formation and apoptotic cell death in the lungs resulting into hypoxemia in infected-animals. We have shown that dietary supplementation of a common metabolite, namely α-Ketoglutarate (αKG) rescued the above effects (Shrimali *et al,* 2021, Agarwal *et al,* 2022). Further, we describe the mechanistic insights in the severity of lung inflammation in SARS-CoV-2 infected mice with diabetic background (both type 1 and type 2 diabetes). The dietary supplementation of αKG along with metformin found to potent therapeutics against SARS-CoV-2 in T1D/T2D in animals (Figure-9, unpublished).

Dengue and JEV: Recently we reported that platelet factor 4 (PF4) is pro-viral for both Japanese Encephalitis virus (JEV) and dengue virus (DENV). PF4 inhibits interferon (IFN)α and promotes viral replication (Ojha *et al*, 2019). Further, we describe that PF4-/- mice are less susceptible to both JEV and DENV infection showing better survival. In mechanism we described that PF4 is a potent inhibitor of autophagy and PF4-/- monocytes displayed better autophagic flux in degrading virus containing vesicles, and also promoting type 1 interferon (IFNα/β) synthesis (unpublished). Furthermore, we developed a small-molecule antagonist to CXCR3 (receptor of PF4) and described that compound 7D is a potent inhibitor to the DENV2 infection in mice and improved both IFN and IgG responses (unpublished).

Diabetes: The db/db mice with a chronic T2D phenotype or patients with T2D with recurrent cardiovascular disease (CVD) symptoms displayed an elevated systemic inflammation and increased pro-thrombotic phenotype. The T2D mice displayed chronic lung inflammation, which was further rescued by dietary treatment of αKG. The αKG inhibited the phosphorylation of both Akt and P65 and decreased activation of T2D platelets in leukocytes from patients, suggesting a potential therapeutic role of αKG against thromboinflammation and CVD in T2D (unpublished).

AMS and HAPE: Recently, we have shown that the Tibetan specific mutations in prolyl hydroxylase-2 (PHD2, gene *EGLN1*), known as $PHD2^{D4E/C127S}$ protects these highlanders form hypoxia-triggered inflammatory response and related symptoms like AMS and HAPE (Bhattacharya S *et al*, 2021). Further, our data described a significant protection of $PHD2^{D4E/C127S}$ monocytes from viruses like DENV and JEV under hypoxic microenvironment, other hand, these mutant monocytes are susceptible to these infections under normoxic environment. The wild type showed the opposite trend of the mutant. We described that HIF1α signaling regulated the above (unpublished).

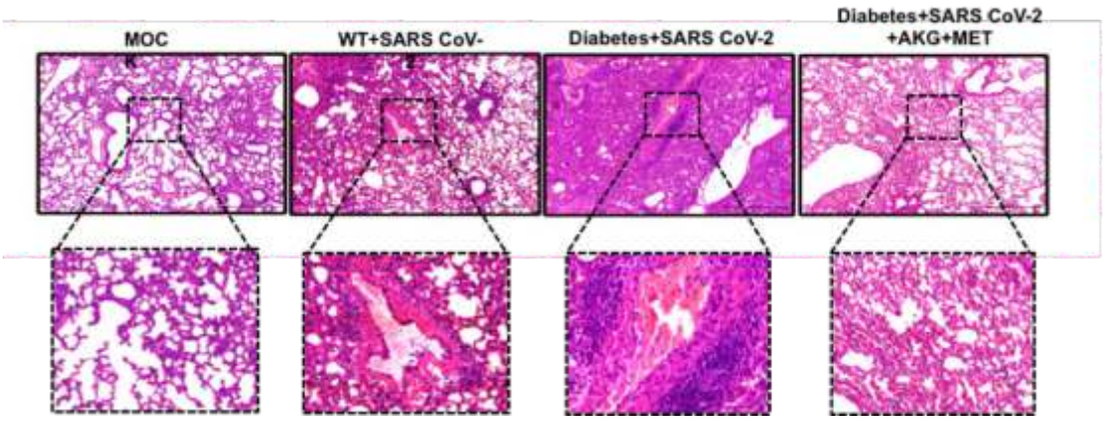


Figure 9: *H&E images of the lung section from SARS-CoV-2 infected mice showed elevated accumulation of inflammatory cells and microthrombus. The diabetic mice with SARS-CoV-2 infection showed further elevation in the above symptoms. The dietary supplementation of αKG along with metformin significantly rescued these (unpublished).*

Based on the research findings, the following are proposed to be carried out:

1. Investigating the therapeutic potential of dietary αKG against ARDS and pulmonary fibrosis in Covid-19 infection in mice. Finally, proposing a clinical trial of αKG in COVID-19 treatment.
2. Investigating the severity of dengue infection in heterotypic DENV infection in diabetes.
3. Proposing clinical trial of 7D against dengue treatment.
4. Investigating novel clinical, molecular genetics and anthropological insights Lethal Aortopathy syndrome associated with novel FBLN4^{D203A} Mutation among Mappila Children of Malabar, Kerala.
5. Assessing the role of OxLDL mediated CD36 signaling in the development of thrombo-inflammatory complications in T2D patients.
6. Investigating the role of PHD2$^{D4E/C127S}$ in infection among Tibetans.

Tushar Kanti Maiti
Principal Investigator

Lab Members

Nitu Singh
Archana Prasad
Shakuntala Bai
Arundhati Tiwari
Sandhini Saha
Sushanta Majumder
Krishna Singh Bisht
Naman
Swati Agarwal
Ankit Biswas
Chandrayee Dey
Nitin Kumar

Understanding the protein homeostasis mechanism in human diseases

Protein metabolism is essential for normal cellular functions and it involves synthesis, folding, transport and degradation of proteins in a cell on a constant basis. Chaperones post-translationally promote the transformation of nascent proteins into their correctly folded functional forms. Protein translocation machinery, proteasome and autophagy-related processes are the critical events for protein subcellular localization and degradation. Stress and aging confront chaperone functions as well as protein clearance networks leading to protein misfolding, overload and cellular dysfunction. Protein misfolding, aggregation and impaired protein clearance mechanism are the features of many neurodegenerative diseases, cancer and metabolic diseases in humans. The aim of our research is to delineate the underlying mechanisms of protein misfolding, aggregation and quality control systems in cancer, neurodegenerative diseases and metabolic disorders.

Dysregulated protein homeostatic network in hepatic lipotoxicity

The free acid accumulation in liver due to nutrient surplus promotes hepatosteatosis. Free fatty acids cause cellular stress, organelle adaptation, and ultimately cell death in cultured hepatocyte and hepatocellular cancer cell lines. Despite extensive investigation, the exact process causing lipotoxicity and the mechanism of cell death are still unknown. Using hepatocellular carcinoma cells as a model, we applied proteomics technique to circumvent the mechanism of lipotoxicity. The quantitative proteomics studies with hepatocellular carcinoma cells exposed to palmitic acid (PA) show an alteration of biological processes including apoptosis signaling, post-transcriptional regulation of gene, mRNA splicing, nuclear-cytoplasmic transportation, cytoskeleton organization, negative regulation of proteolysis, negative regulation of hydrolase activity and negative regulation of mitotic cell cycle phase transition. Protein-protein interaction network analysis shows very strong connectivity with the regulated proteins of cell cycle-cell death and ubiquitin dependent catabolic process. Biochemical analysis also strongly confirms dysregulation of ubiquitin proteasomal system upon PA exposure to HepG2 cells. Activity based chemical profiling of deubiquitinating enzymes and their quantification by targeted mass spectrometry showed a global reduction of majority of deubiquitinases indicating a severe compromise in protein quality control process. In a landscape of deregulated deubiquitinases, we efficiently explored the mechanism of palmitic acid-induced negative regulation of USP7 in hepatocytes. The expression of the deubiquitinating enzymes USP7 was partially decreased by palmitic acid. Reduction of USP7 destabilizes p53 and encourages cells to reside more time in mitosis. Global phosphoproteomics analysis also provides a strong evidence of an altered cell cycle checkpoint proteins' expression that abrogates early G2/M checkpoints recovery with damaged DNA and induce mitotic catastrophe leading to hepatocyte death. We have discovered that palmitic acid favours AIF-mediated cell death via depolarizing mitochondria and translocating AIF from mitochondria to nucleus. In conclusion, the current work shows that palmitic acid causes hepatocellular mortality via deubiquitinase USP7 downregulation and subsequent mitotic catastrophe (Fig. 10).

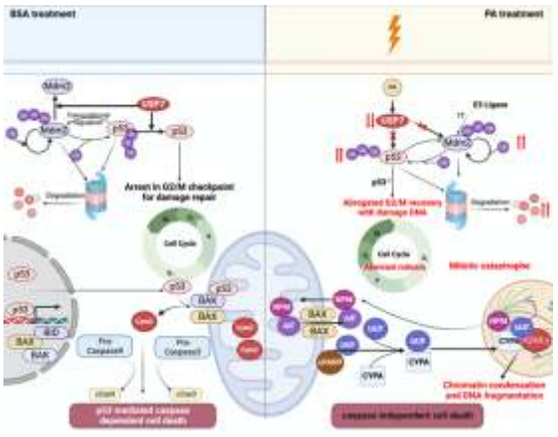


Figure 10: *USP7-p53-Mdm2 axis facilitates AIF-mediated caspase-independent mitotic catastrophe in PA-treated HepG2 cells. The partial reduction of UPS7 by PA causes the destabilisation of p53 and Mdm2. The USP7-p53-Mdm2 axis enhances caspase-independent death over caspase-dependent death by activating AIFM1 cleavage and translocating cleaved AIF into the nucleus. The phosphoproteome and AIFM1 interactome analyses reveal Nucleophosmin1 (NPM1) as a significant component that affects mitochondrial membrane potential and promotes AIF-mediated cell death. The recovery of disrupted G2/M checkpoints with damaged DNA triggers mitotic catastrophe as a novel pathway for hepato-lipotoxicity and consequent hepatocyte death during PA treatment.*

Understanding the protein quality mechanism in Parkinson's disease

Parkinson's disease (PD) is the second most common neurodegenerative disorder, which is characterized by the death of dopaminergic neurons in the midbrain. Lewy body (LB) formation is the hallmark of PD pathology. PD is accompanied by shaking, rigidity, slowness of movement, difficulty with walking and ultimately death. Genetic factors, ageing and excessive exposure to environmental toxins contribute to the etiology of PD. Recent studies have shown that more than 500 proteins are present in the LB and many of them are co-enriched with α-synuclein. These proteins belong to the family of kinases, deubiquitinases, ubiquitin ligases, chaperones and oxidative stress regulators. The functional role of a few proteins has been studied. Recently, we have demonstrated that OTUB1, a deubiquitinating enzyme of OUT family, sequesters in Lewy body due to its amyloidogenic nature. We have identified two hotspot sites in OTUB1 that contribute structural instability and these mutants follow completely different folding intermediates in invitro condition.

Development of prenyltransferase-based labeling technology for imaging applications

Selective labeling of proteins in cells is a key for investigating cellular processes and alterations associated with different diseases. Although fluorescent protein tags are commonly used for visualisation of protein-of-interest (POI), their large size, weak fluorescence, and rapid photobleaching limit the usefulness. Chemical fluorophores, on the contrary, are smaller, brighter, and more photostable. However, site-specific labeling is challenging in complex cellular milieu. This paradigm motivates us to develop specific and enhanced labeling-system that can be used for site-specific labelling of proteins/peptides for varied applications. Considering the numerous advantages of the enzyme-based reactions, we aim to develop a method for site-specific conjugation of fluorophore to protein/peptide using prenyltransferases. In this effort, we present a novel enzyme-based protein/peptide labelling using PagF, a prenyltransferase from *Planktothrix agardhii* that recognises short-peptide motif and conjugates it with isoprenoid moiety (Fig. 11). We demonstrate that PagF can selectively conjugate fluorogenic isoprenoid molecule to the proteins tagged with minimal motif 'PYLYGGGGSGG' or 'YPYDVPDYA'. Our data provides a *proof-of-concept* for the applicability of a bacterial prenyltransferase as a biotechnological tool for labelling of proteins or peptides.

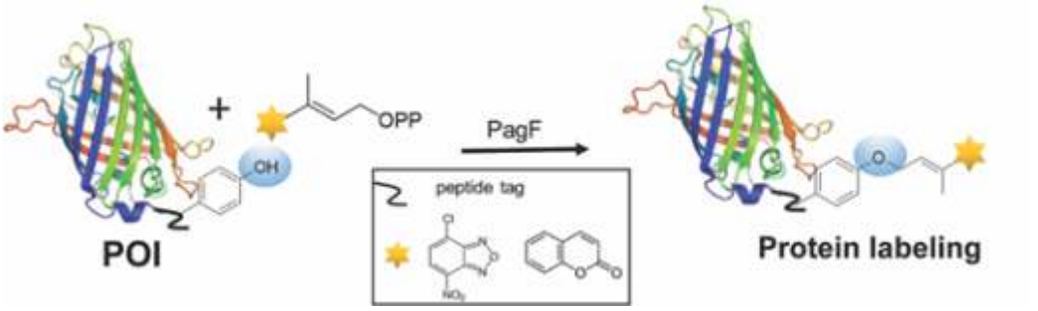


Figure 11: *Scheme for in vitro prenylation of protein of interest (POI) using fluorogenic prenyl donor in presence of PagF. The peptide tag consists of residues "YPYDVPDYA' and the fluorophores are nitrobenzofurazan or coumarin derivatives.*

Sam J Mathew
Principal Investigator

Lab Members

Masum Saini
Lakshmikanthan P
Preedia Babu
Pankaj Kumar
Akashi Sharma
Shreyasi Das
Anushree Bharadwaj
Subhashni Sahu
Aatifa Zehra
Jaydeep Sharma
Mahima Kumari
Somnath Mondal
Saumya Kathuria
Arvind Sahu
Jagriti Singh
Aparna Rai
Jyoti Kamlakar Jadhav

Signals that regulate skeletal muscle structure and function

The skeletal muscle is the largest tissue in our body, essential for vital functions such as locomotion, support, posture maintenance, and regulation of whole-body metabolism. We are investigating the mechanisms that regulate skeletal muscle formation and controls its function. Skeletal muscle damage or injury occurs in accidents, during physical activity such as sports, or due to congenital diseases such as muscular dystrophy. Muscle stem cells also known as satellite cells, present in the skeletal muscle, help in its repair and regeneration. We are studying how skeletal muscle repair and regeneration occurs, identifying and characterizing genes involved in this process. We are also studying a cancer type called rhabdomyosarcoma, where the tumor cells exhibit properties of muscle cells, to identify signaling pathways that can be targeted for therapies to treat such tumors.

Myh3 expression is regulated by a 4.2 kb genomic region

The skeletal muscle is made up of different cell types, among which myofibers are long, multinucleate, contractile cells which arise by a process of fusion and differentiation of myogenic progenitors during development. The myofibers contain sarcomeres, which are functional contractile units, composed of thin and thick filaments. Myosins are the primary contractile proteins that constitute the thick filaments, composed of different subunits, of which Myosin heavy chains (MyHCs) are the major subunit. Several MyHC isoforms exist, among which one, MyHC-embryonic encoded by the *Myh*3 gene, is expressed exclusively during muscle development. MyHC-embryonic is normally not expressed in adult muscle fibers, except during muscle injury or disease and associated regeneration. Mutations in *MYH3* lead to human congenital musculoskeletal disorders such as Freeman-Sheldon and Spondylocarpotarsal Synostosis Syndromes. It is therefore vital to understand the functions of MyHC-embryonic and decipher its regulation, which will help develop strategies to treat such muscle disorders and promote muscle regeneration.

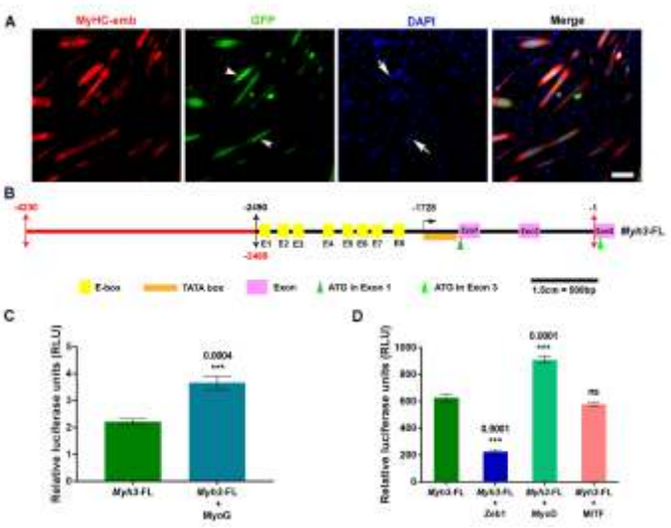


Figure 12: *A 4.2 kb genomic region regulates Myh3 expression. (A) C2C12 mouse myogenic cells labeled for MyHC-embryonic (red), GFP (green) and DAPI (blue), at day 5 of differentiation, with arrowheads marking differentiated myofibers (scale bar 10µm). (B) Schematic showing the 4.2 kb Myh3 full length (Myh3-FL) construct with the promoter and upstream enhancer elements. (C-D) Graphs showing the effects of MyoG (C), Zeb1, MyoD and Mitf (F) on Myh3-FL promoter activity in C2C12 cells.*

We identified a 4.2 kb genomic region upstream of the mouse *Myh3* coding sequence, which regulates MyHC-embryonic expression. This 4.2 kb *Myh3* promoter-enhancer was cloned upstream of a GFP reporter, transfected into C2C12 myoblasts and allowed to differentiate, where GFP recapitulated the expression of MyHC-embryonic detected by a monoclonal antibody (Fig. 12A). Thus, the 4.2 kb genomic sequence upstream of the MyHC-embryonic ATG start site (termed *Myh3-FL*) contains all the necessary *cis*-regulatory elements necessary for *Myh3* expression (Fig. 12B). We performed a candidate-based approach to identify *trans*-factors that bind to the *Myh3* promoter-enhancer to regulate its expression. We found that the basic helix-loop helix (bHLH) transcription factor MyoG, known to promote muscle differentiation, elevates *Myh3-FL* expression (Fig. 12C). We tested another candidate, the Zinc finger E-box binding homeobox 1 protein (Zeb1), reported to function as a repressor. Co-transfection of Zeb1 led to reduced *Myh3-FL* expression, indicating that Zeb1 represses *Myh3* promoter activity (Fig. 12D).

To decipher the specific role of Zeb1 in myogenic differentiation, we performed siRNA-mediated knockdown of *Zeb1* during C2C12 cell myogenic differentiation (Fig. 13). At day 5 of differentiation, *Zeb1* knockdown resulted in an increased number of myofibers (Fig. 13A). Upon quantification of the fusion and differentiation indices, which measure the number of nuclei per myofiber as a fraction of the total number of nuclei, an approximately three-fold increase was observed upon *Zeb1* knockdown (Fig. 13B-C).

These results indicate that *Myh3* expression is controlled by *cis*-elements located 4.2 kb upstream of the *Myh3* promoter, where *trans*-elements bind. We identify Zeb1 as a novel repressor in skeletal muscle differentiation and regeneration, which could be of importance in developing therapies to treat muscle injury and diseases.

Research undertaken by India Alliance Early Career Fellow Dr. Masum Saini

Modulation of MET signaling and its role in myogenesis

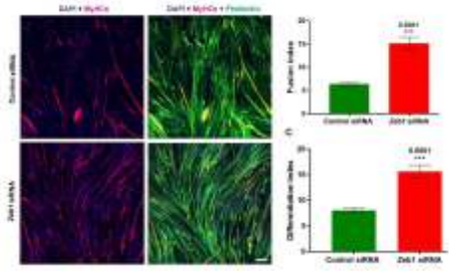


Figure 13: Zeb1 is required for proper muscle differentiation. *(A) Immunofluorescence images of C2C12 cells treated with control (upper panel) or Zeb1 siRNA (lower panel), labelled for MyHCs (red), phalloidin (green), and DAPI (blue) at day 5 of differentiation (scale bar 100μm). (B-C) Graphs showing fusion index (B) and differentiation index (C) in control and Zeb1 siRNA treated cells at day 5 of differentiation.*

Masum Saini

Receptor tyrosine kinases (RTKs) are cell surface receptors that respond to specific stimuli by transducing signals through downstream effectors, and thus generate cellular outcomes. RTK mediated signaling cascades regulate developmental and homeostatic physiological processes, whereas dysregulated RTK signaling underlies numerous human diseases including cancer. The proto-oncogene MET is one such RTK important for normal development, particularly crucial to the migration of muscle precursors during skeletal muscle formation (myogenesis). Postnatally, MET signaling is reactivated in the muscle stem cells during post-injury muscle regeneration. MET is also known to show aberrant expression in Rhabdomyosarcoma, a pediatric soft-tissue cancer characterized by maintenance of an undifferentiated myogenic state. Thus, MET signaling is a common thread between muscle development, regeneration and disease. To determine its role and regulation in myogenesis I am using genetically engineered mice to delete MET specifically in the muscle progenitor cells. Notably, in the absence of Met, animals survive the developmental stages but the loss proves fatal after birth. I am trying to identify the cause(s) of postnatal mortality and characterize possible defects in skeletal muscle formation in the Met knockout animals. This work will provide insights into context-dependent roles of Met signaling in developmental and regenerative myogenesis.

Pinky Kain Sharma
Principal Investigator

Lab members

Saptorshi Bandopadhyay
Navya Chauhan
Kajal Kamboj
Vikas Kumar
Santanu

Understanding Taste and its Modulation using *Drosophila Melanogaster*

In humans, abnormal nutrient consumption and alterations in taste sensitivities is a major cause of obesity and various metabolic issues. Despite this burden on society, role of neural circuits that regulate appetite and influence feeding behaviors are not fully understood. To understand the neural basis of taste preferences, we are using genetic model system *Drosophila melanogaster* that can sense the same taste stimuli as mammals (sweet, sour, water, salt, umami and bitter). We are interested in understanding how the taste information is wired in the brain that gets modulated by physiological state, intrinsic and extrinsic factors. Understanding how taste preferences reshape taste curves to promote overconsumption of food in flies leading to overeating and metabolic issues can help in understand underlying mechanisms that drive changes in the neural activity. Answering these questions may open up avenues to reduce diet-related diseases and other neurological disorders.

Identification of novel feeding circuits in *Drosophila* brain

Insects localize food source by distant chemoreception like smell during flight and land close to the source of the smell. Their search for the food on the ground depends on contact chemoreception like taste. *Drosophila* and other insects have taste receptors and hairs in their front legs that allows them to taste the food as they walk and sit on it. After finding a suitable source of food, they stop, extend their proboscis, and feed. If the food source or patch is not enough to satiate them, they get engage in "local search" for more food.

In all animals including *Drosophila* local food searching behavior is an adaptive foraging approach. Disease-carrying and crop- destroying insects also use their senses of taste and smell to find hosts and food and probably the same foraging strategies. Searching behavior has been studied in other insects like honeybee and ant using a behavioral approach, but due to poor availability of tools and genetics, the neural circuits and molecular mechanisms involved are not completely understood and have never been explored. This behavior is dependent on the hunger state, genetic background and distribution of food items in the environment. In order to understand where the foraging and feeding information is integrated in the fly brain, my group has identified novel satiation state-dependent central taste circuit (Fig. 14) that help flies in both foraging and feeding. The newly identified neurons use short Neuro Peptide F (sNPF) and Dopamine signaling to mediate these behaviors. Targeting neuronal pathways for food elicited foraging behavior may lead to novel tools for safe and affordable strategies for insect control that cause loss to the agricultural industry every year.

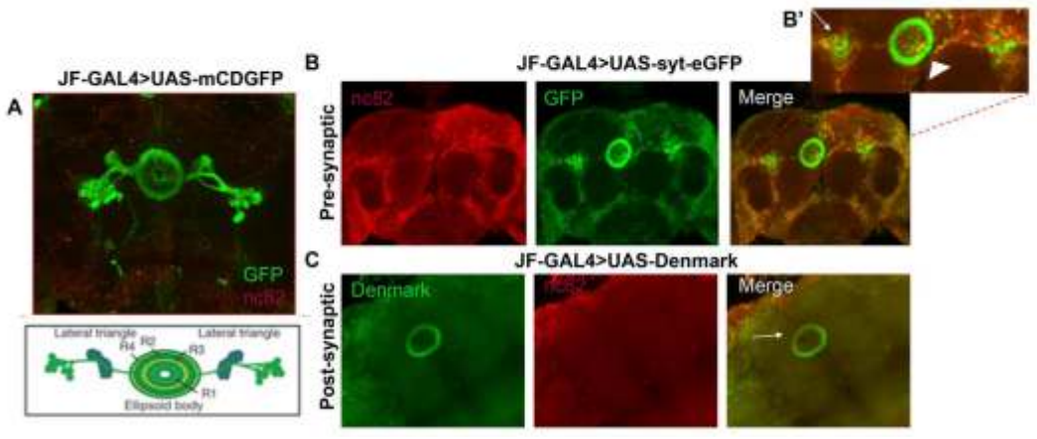


Figure 14: *Newly identified Foraging-feeding circuit in adult fly brain. A. JF-GAL4 (JF-GAL4>UAS-mCD8GFP) line marking ring neurons of Drosophila central complex (visualized with anti-GFP- green). Structure of ring circuit shown below. For all brain images, neuropil is stained with anti-nc82 (red). B. Pre-synaptic terminals marked with genetic construct JF-GAL4>syt-eGFP (B' is a zoomed image of GFP expressing region). C. Post synaptic areas marked with genetic construct JF-GAL4>UAS-Denmark (m-cherry).*

Understanding post-ingestive gut brain circuitry using *Drosophila melanogaster*

In animals including *Drosophila*, sweet compounds are detected by specific taste receptor cells at the periphery. Activation of sweet taste receptor cells send hardwired signals to the brain to elicit recognition of sweet-tasting compounds. Surprisingly, even in the absence of a functional sweet-taste pathway, animals can still acquire a preference for sugar. Overconsumption of sugar is an important contributor to increase in obesity rates.

Flies have a simple and similar to humans- gut system (Fig. 15) divided as foregut, midgut and hindgut. To elaborate on the prime function of intestine in neural and dietary connectivity by comprehending the role of nutrition intake and usage, we started looking at the role of novel gustatory receptors (GRs) in the fly gut to dissect the neural basis for sweet taste preference. In a gut specific screen, we identified potential GRs that are present in the gut and play a key role in modulating sweet taste behaviour. We are now looking at the mechanism by which these taste circuits talk to the brain through neuropeptides that give rise to final behavioural output.

The post-ingestive sensing system in the gut assures that signaling only occurs after nutrients reach their desired target for effective absorption and metabolic consumption. The association between the activation of this gut-to-brain circuit paired with the recognition of compounds like sugar by the taste system combines nutrition with the basic sense of taste and afford animals the fundamental capacity to identify, develop and reinforce a strong and durable preference for sugar-rich food sources. Our study will lay the foundation for the molecular and genetic analysis of internal responses that occur upon the sensing of nutrients or harmful substances in the fly intestine. Understanding what goes on in that workspace may give clinicians new levers to pull in treating diseases ranging from diabetes to obesity to irritable bowel disease.

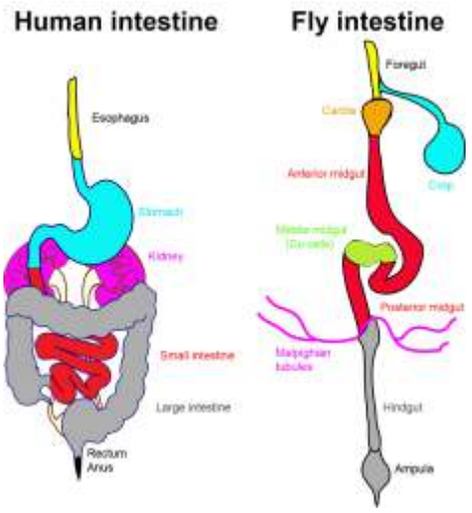
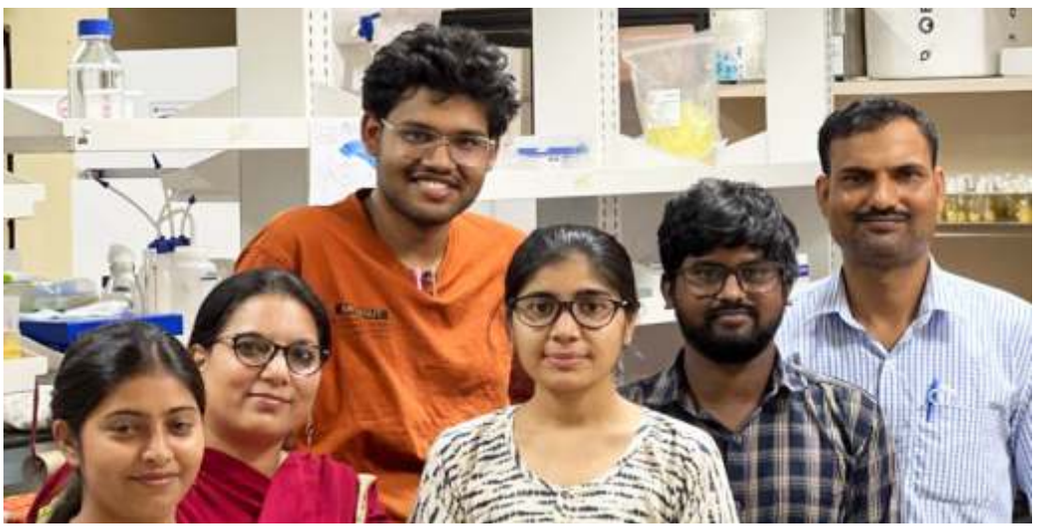


Figure 15: *Comparison between human and Drosophila gut. Organs with similar functions are coded with same colors. Drosophila contains many tissues/organs that functionally resemble to most essential human gastrointestinal system: Esophagus (foregut), midgut (small intestine) and large intestine (hindgut), stomach (crop), kidneys (Malpighian tubules).*



Geetanjali Chawla
Principal Investigator

Lab Members
Manish Pandey

MicroRNA biology

MicroRNAs (miRNAs) are a class of small non-coding RNAs that regulate gene expression by directing effector complexes to target mRNAs. These regulatory RNAs play critical roles in several biological processes, including aging, development, differentiation, and cell fate determination. The precise spatiotemporal control of miRNA levels is largely determined by the mechanisms that regulate biogenesis. Many of the miRNA loci reside in clusters that are transcribed as capped and polyadenylated primary transcripts. These clustered miRNAs are predominantly co-expressed and regulate functionally related target mRNAs. Since, these clusters are transcribed as a single primary transcript, fine-tuning of the downstream effector pathways is achieved by post-transcriptional regulatory mechanisms that determine the processing efficiency. The cis-acting sequence and structural features of the primary miRNA that interact with the processing machinery are critical determinants of the processing efficiency of the primary and precursor miRNAs. One major goal of our laboratory is to characterize molecular mechanisms underlying differential processing of miRNAs.

Molecular dissection of a conserved cluster of microRNAs

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. In our recently published study, we have dissected the role of cis sequences in the expression of a

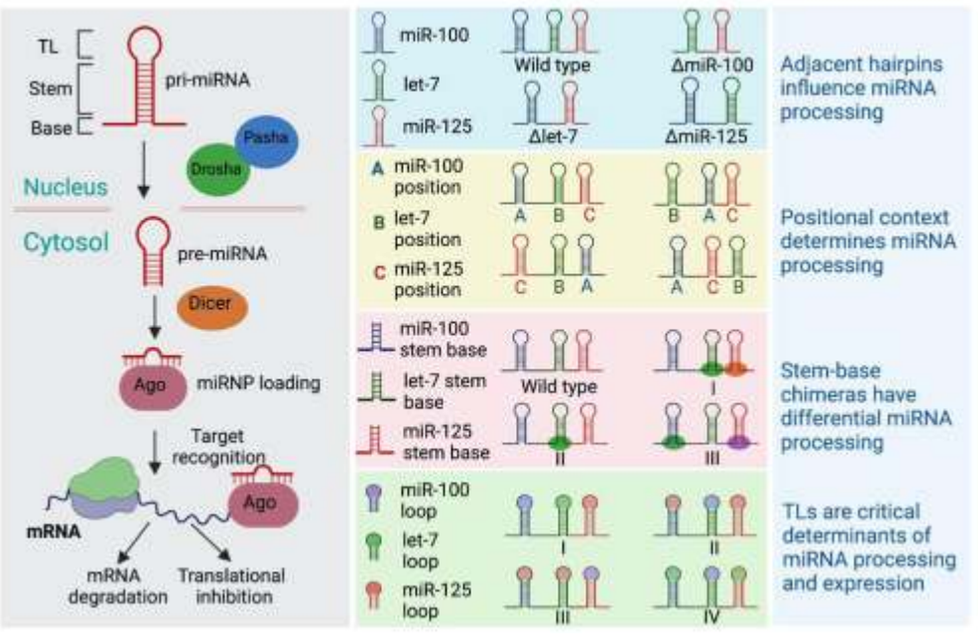


Figure 16. Molecular dissection of a conserved cluster of miRNAs identifies critical structural determinants that mediate differential processing. *Differential processing of let-7-Complex miRNAs (miR-100, let-7 and miR-125) is determined by the position, order, presence of adjacent miRNAs, stem base and terminal loops of the primary hairpins.*

conserved cluster of miRNAs encoded by the *Drosophila melanogaster let-7-Complex* (*let-7-C*). We constructed a series of chimeric variants of *let-7-Complex* that encodes three evolutionary conserved and differentially expressed miRNAs (*miR-100*, *let-7* and *miR-125*) by swapping the position, stem-base and terminal loops of the primary miR-100 (pri-miR-100), primary let-7 (pri-let-7) and primary miR-125 (pri-miR-125) transcripts. The expression of the three processed miRNAs was examined in transgenic flies and a *Drosophila melanogaster* cell line. The kinetic effects of Drosha and Dicer processing on the chimeric precursors were examined by *in vitro* processing assays. Furthermore, the functional activity of the chimeric constructs was assessed by miRNA sensor assays. Our results highlight the importance of

stem-base and terminal loop sequences in the 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 (*Pandey et al., 2022*) (Fig. 16). This study provides specific guidelines for achieving differential expression of a particular miRNA in a cluster by structurally induced changes in primary miRNA (pri-miRNA) sequences.

Purification and characterization of nutrient-dependent exosomal proteins

Exosomes are a class of extracellular vesicles that play a role in intercellular signaling under diverse contexts. These vesicles are secreted by almost all kinds of cells under different contexts and serve as carriers of nucleic acids (DNA, RNA, microRNAs and long noncoding RNAs), proteins, lipids, metabolites, and other bioactive substances. The tissue and cell type signature of exosomes and their availability in bodily fluids such as saliva, urine, and blood plasma have led to a significant interest in exploiting these extracellular vesicles as a potential source of disease biomarkers, and this interest has led to a plethora of studies that have employed high-throughput technologies including lipidomics, transcriptomics, and proteomics. However, low yield, purity, and heterogeneity are some issues that need to be tackled before exosomal technologies can be introduced into clinical practice. In our recent publication, we have described a protocol that has been optimized for the isolation and characterization of exosomes from a *Drosophila melanogaster* cell line using size exclusion chromatography (SEC) (*Pandey and Chawla, Front. Cell and Dev. Biol., 2022*). The specific focus of this protocol was to examine the starvation-induced exosome loading of a Flag-tagged protein, and its application has been described in our previously published study that examined the role of miR-125 in dietary restriction-mediated enhancement of lifespan. To summarize, we have optimized a protocol for the isolation and validation of exosomes from a *Drosophila* cell line that is subjected to starvation or nutrient deprivation and to characterize proteins that are selectively enriched onto exosomes under these conditions.

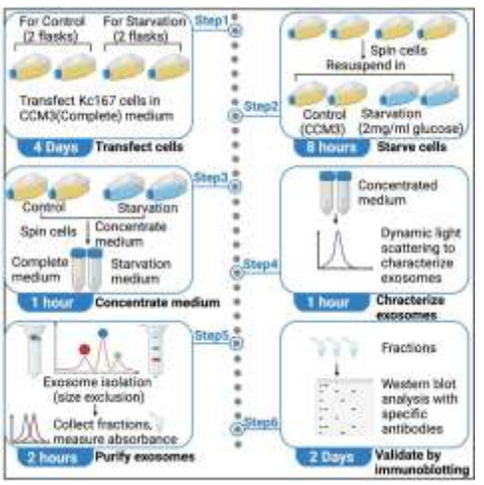
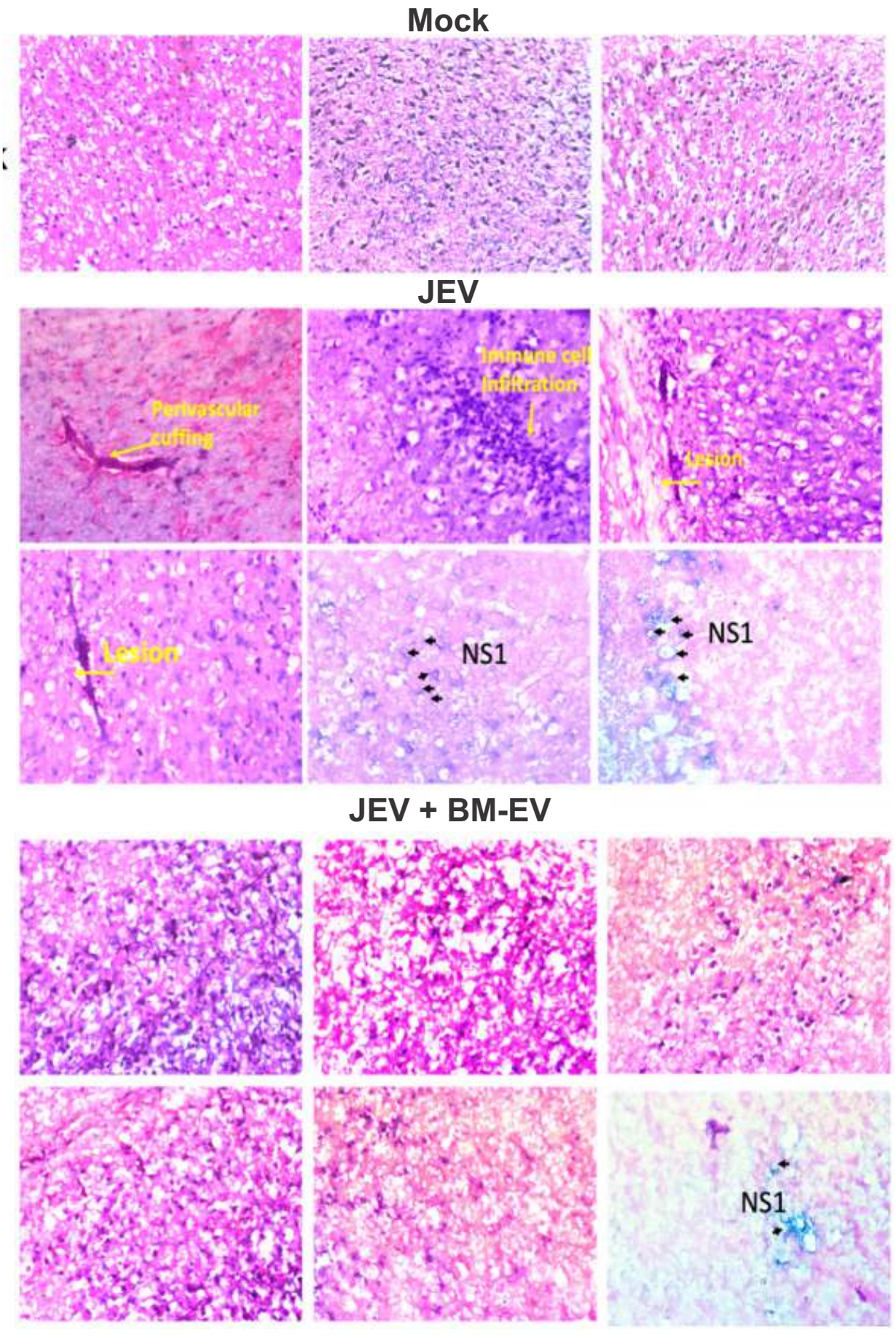


Figure 17. Purification of exosome-enriched proteins produced in a Drosophila cell line by size exclusion chromatography. *Graphical representation of the optimized protocol for the isolation and characterization of exosomes from a Drosophila melanogaster cell line.*



Infectious Disease Biology

Courtesy: Dr. Arup Banerjee

Sudhanshu Vrati
Principal Investigator

Co-Principal Investigators
Manjula Kalia
Arup Banerjee
Kanchan Bhardwaj
Deepak T Nair
Deepti Jain

PhD Scholars
Arundhati Deb
Brohmomoy Basu
Shivani Balyan
Harsh Thakur

Project Fellows (RA/ SRF/ JRF/ PA)
Shweta Duggal
Kiran Bala Sharma
Anshula Sharma
Khashpatika Ganesh
Ghanshyam Sharma
Archana Rout

Collaborators
Dr. Sweety Samal (THSTI)
Dr. Renu Wadhwa (AIST, Japan)
Dr. Anirban Basu (NBRC, Manesar)
Dr. Gulam Seyed (ILS, Bhabaneshwar)

Biology of Medically Important Viruses

Viruses pose an ever-increasing threat to the well-being of the human population at large and this scenario is particularly ominous in the Indian context where epidemics of various viral infections are reported at regular intervals. Understanding the biology of virus infection, replication, and pathogenesis will help in designing novel antivirals for effective therapeutic and prophylactic interventions. We are studying the biology of CHIK, DEN and JE viruses to understand their replication and pathogenesis with a view to design novel antiviral strategies.

Several projects relating to the goals of the research program are being pursued. Provided below is a summary of some of the key projects under the program.

Identification of novel antivirals: To deal with the ever-increasing incidence of CHIK, JE, and DEN viruses, efficacious and affordable antivirals are highly desirable. High throughput assays for testing the antiviral activity of small molecules have been developed in the lab and these are used to screen the medicinal plant extracts and chemical compound libraries. From a library of ~30000 compounds that includes small druggable molecules, we have identified lead compounds that show inhibition of CHIK virus infection in 3 different cell types at micromolar concentration. A mouse model of CHIK virus infection in mice has been established where some these compounds show antiviral activity. Attempts are underway to understand the mechanism of antiviral action of these compounds. Bigger chemical libraries with a variety of scaffolds are now being screened for antiviral activity.

Cellular imaging based-high content screening of natural compounds against CHIK virus identified Withaferin A (WFA), a steroidal lactone isolated from the plant Withania somnifera, also known as Ashwagandha, as a potent antiviral agent. Additionally, WFA significantly reduced the morbidity caused by CHIKV virus in the C57/BL6 mouse model, demonstrating the potential of WFA as an antiviral.

The cell culture experiments indicated that WFA restricted CHIK virus infection at the early translation/replication stage, post-entry. The drug showed IC50 in the range of ~0.5 μM and SI index of ~20 in embryonal rhabdomyosarcoma cells. Testing of WFA against JE virus and DEN type-2 showed no viral inhibition and established its specificity against CHIK virus infection. WFA treatment was seen to alter various cellular pathways such as Unfolded protein response (UPR), autophagy, and elevated intracellular calcium levels, collectively which might be responsible for the generation of the antiviral cellular state. These are being investigated further.

Nucleolin has a proviral role during the Japanese encephalitis virus replication

Japanese Encephalitis Virus (JEV) is an arthropod-borne, plus-sense ssRNA virus, and is the most common cause of viral encephalitis in humans with a case fatality rate of ~25%. The largest and the most conserved protein of JEV is the non-structural protein 5 (NS5). It performs two important functions – viral RNA replication, and 5' capping of viral genomic RNA. Due to the central role played by the protein in the viral life cycle, NS5 is considered a promising target to control virus replication. In this direction, identifying the host protein interactors of NS5 would be helpful. We have identified Nucleolin as one of the several NS5-interacting host proteins using multiple approaches. Interaction of JEV NS5 with Nucleolin in virus-infected cells was demonstrated by colocalization of the proteins by confocal microscopy, co-immunoprecipitation, and proximity ligation assay. Nucleolin has a proviral role during the JEV replication cycle in cultured cells as its siRNA-based silencing significantly decreased the virus titers. On the other hand, JEV grew to higher titers in cells over-expressing Nucleolin. Further, in-silico studies predicted NS5 interaction with the RRM4, RRM3 and RGG domain of Nucleolin. This was validated in the cell culture by transfecting the truncated forms of Nucleolin. We also found that overexpressing nucleolin rescued JEV replication from the antiviral effect of the Nucleolin binding aptamer AS1411 as well G-quadruplex ligand BRACO-19. These data indicate that Nucleolin is a part of the virus replication complex and it might bind to the G-quadruplex structure present in JEV 3' non-coding RNA, thus helping in virus replication.

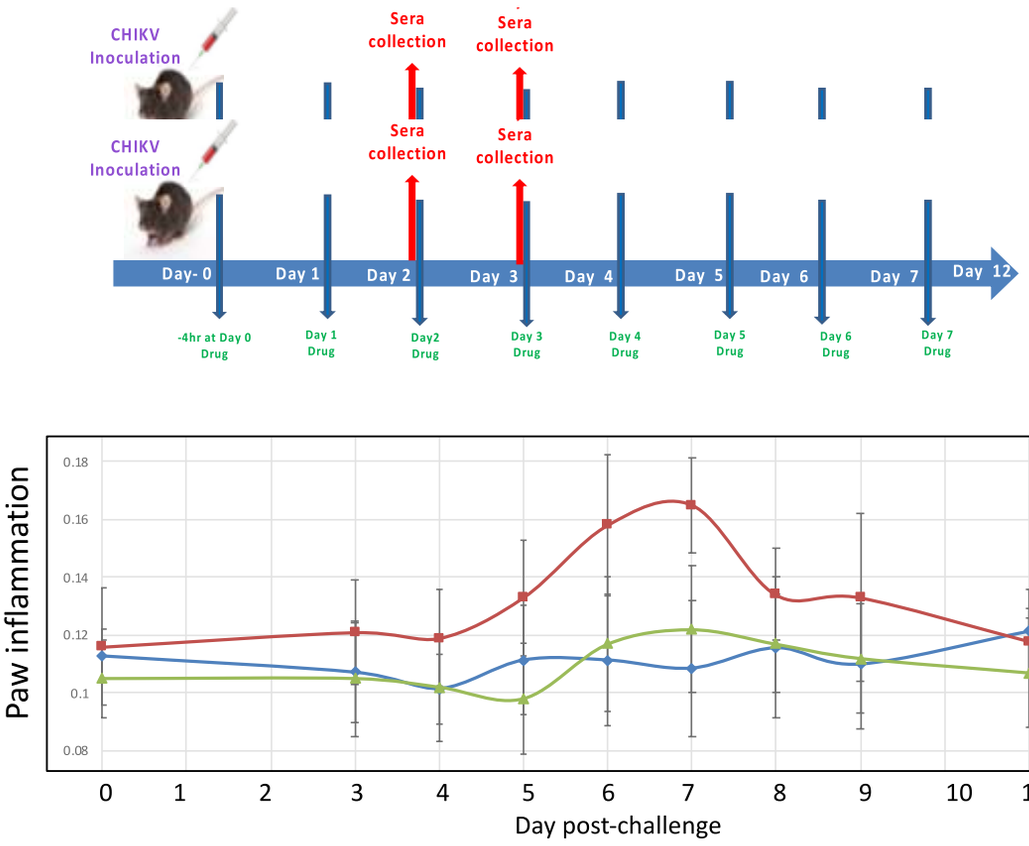


Figure 18. *Antiviral activity of Withaferin A in the mouse model of CHIK virus infection. C57/BL6 mice (10-12 weeks old) were injected with 10e4 PFU of CHIK virus sub-cutaneous in each of the hind limbs. Withaferin A was dissolved in PBS+0.5% CMC+26% ethanol and delivered intra-peritoneal at a dose of 5 mg/Kg twice daily. Paw inflammation was measured using a plethysmometer. The blue line represents the paw inflammation in control uninfected mice, red line represents virus-infected mice, while green line represents virus-infected mice treated with Withaferin A.*

Chittur V Srikanth
Principal Investigator

Lab members

Pharvendra Kumar
Hridya Chandrasekhar
Preksha Gaur
Sonalika Maurya
Rohan
Rajiv Babar
Yesheswini Rajendran
Ezhuthachan Vishnu
Ashok Kumar
S. Nandha Kumar
Kirti Kajal
Vishal Madanlal Angnani
Bhagyashree Srivastava
Anmol Jain

Molecular biology of infectious and idiopathic inflammation of the gut

Several gut illnesses, including those arising from infections caused by *Salmonella* Typhimurium (*STm*), are accompanied with uncontrolled inflammation. This research programme is focused on understanding the molecular mechanisms that govern infection, inflammation and autoimmune disorders of the gut. The key interest of is to identify critical molecular pathways that regulate inflammation during *STm* infections and those that arise during Inflammatory bowel disease (IBD). In the current report, we describe our recent efforts to understand how the SUMOylaton, a post-translational modification (PTM) pathway, and host cell signalling are modulated by *STm* during infection.

Identification of AP-1 as a regulator of SUMOylation pathway genes, UBC9 and PIAS1

The Gram-negative pathogen *Salmonella enterica* serovar Typhimurium (*STm*) is a causative agent of foodborne illness gastroenteritis. The disease occurs due to a localized intestinal infection, which triggers acute diarrhoea, accompanied by abdominal cramps and/or fever. With a few exceptions, gastroenteritis is self-limiting yet result in several hospitalizations across the globe. *S*uccessful infection is caused by a battery of virulence-associated effector proteins of *STm* which are directly secreted by the pathogen into host cytoplasm in an extremely controlled manner. These effectors bestow several pathogenicity related functions including host entry, invasion, replication and evasion of host defence. We earlier published that *STm* modulates host SUMOylation pathway, a post-translational modification (PTM) mechanism, through the action of its effector proteins. Downregulation of SUMOylation mechanism was necessary for a successful infection. A prerequisite for SUMOylation alteration during infection was seen to be the downregulation of two enzyme of SUMOylation pathway, i.e. Ubc9, an E2-SUMO-conjugase and PIAS1, E3 SUMO-ligase. However, the regulation of SUMO-gene downregulation remained unknown.

To address these unanswered questions, we carried out an *in-silico* analysis of promoter region of SUMO pathway genes in an attempt to find conserved motifs that may represent binding regions of transcription factors. Using Gene Bank Database around -10.6 Kb promoter region was analyzed. Several potential regulatory motifs, including that of NF-kB, PPARγ, c-Fos, c-Jun, NFAT and CREB, could be identified in these genomic regions of SUMO-genes (Fig. 19). Notably, multiple Activator Protein 1 (AP-1) binding motifs ('5-TGAG/CTCA-3') were significantly overrepresented as discerned by in silico tools.

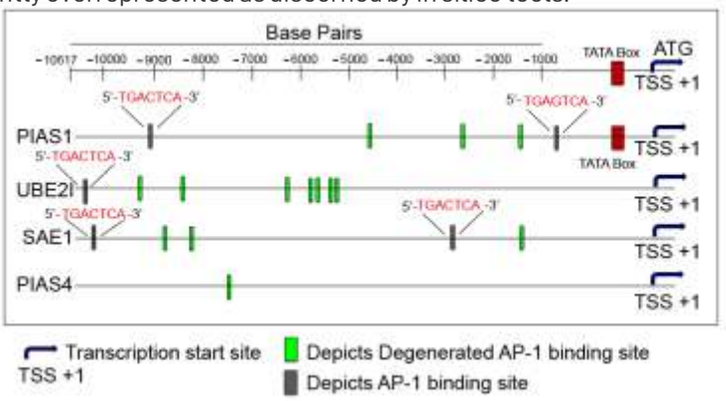


Figure 19: Identification of potential regulatory proteins binding motifs in SUMO pathway genes. *Graphical representation of the identified transcription factor binding motifs of various regulatory proteins in the promoters of SUMO pathway genes (UBC9, PIAS, SAE2, PIAS2) using various computational tools. Consensus sequence and degeneracy of regulatory motifs (indicated as gray and green boxes, respectively).*

AP-1 works as a heterodimer involving different combinations of c-Fos, c-Jun, ATF and JDP family proteins. They are known to regulate gene expression programs in response to a variety of stimuli including infections. Considering the importance of AP-1 in inflammation induced by *STm,* we investigated its role in regulation of Ubc9 and PIAS1.

Initially, a direct binding of AP-1 to the identified motif was confirmed using Electrophoretic

Mobility Shift Assay (EMSA) and Chromatin immunoprecipitation (ChIP) based assays. Furthermore, in line with this finding, experimental knock-down of c-Fos resulted in decreased expression of Ubc9 and PIAS1, on the other hand its upregulation led to an increased expression of these SUMO-genes. Interestingly, the effect of perturbation of c-Fos was not same for other AP-1 target genes, such as CCL-2 and CCL-19, thereby suggesting existence of a differential regulation program. The basis of differential gene regulation was investigated using a range of c-Fos mutants by imaging and biochemical experiments. Together these experiments pointed towards involvement of PTM modifications (such as SUMOylation) in modulation of c-Fos function.

AP-1 SUMOylation governs host inflammatory signalling and Salmonella burden

Possible consequences of differential regulation of target genes displayed by AP-1 was investigated in the context of PTMs duing infection. Murine embryonic fibroblast cells engineered to express either wild-type c-FOs (c-FOS-KO$^{WT\text{-}FOS}$) or a SUMOylation deficient c-FOS (c-FOS-KO$^{SUMO\text{-}def\text{-}FOS}$) were subjected to *STm* infection followed by 3'mRNA sequencing. Multiple pairwise comparisons, between these cells and their mock infected counterparts, were done to identify a total of 2416 differentially regulated genes (FDR < 0.05). The differentially expressed genes were further represented as a Venn diagram to understand the unique genes in each case. Biological process analysis of various groups further led to the identification of affected genes representing pathways related to Immune system, defence response, cytokine (Fig. 20).

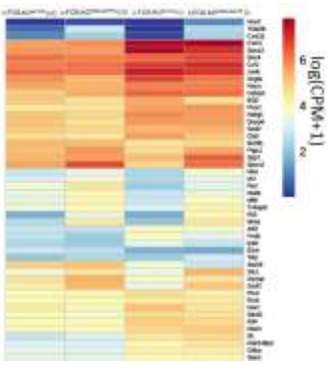


Figure 20: c-Fos PTM-mediated modulation of immune response in MEFs upon STm infection. *Heat map representing the normalized expression counts of a key subset of genes under each cell type expressing the indicated form of c-Fos. UI: uninfected, I: infected with STm for 4 hrs, Counts per million, CPM.*

Thus the analysis reveal a PTM dependent control of immune gene regulation by c-Fos. Subsequently importance of AP-1 and its PTMs on *STm* pathogenicity was investigated. Healthy and *STm* infected cells overexpressing c-FOS$^{WILD\text{-}TYPE}$ or different PTM varients of c-FOS (i.e. c-FOS$^{PHOS\text{-}DEF}$, phosphor-mimetic c-FOST232D, c-FOS$^{PHOS\text{-}MIMIC}$ or c-FOS$^{SUMO\text{-}DEF}$) were tested. A significant variation of *STm* colony forming units (CFU) was observed in cells expressing different PTM variants of c-Fos . The CFU was lowest in case of c-FOS$^{WILD\text{-}TYPE}$, while the effect was lesser in case c-FOS$^{PHOS\text{-}DEF}$ and c-FOS$^{PHOS\text{-}MIMIC}$. Together these data reveal a PTM of c-FOS dependent mechanism of modulation of immune pathway genes. Thus, these mechanisms have a direct bearing on survivability of intracellular pathogens. We are now investigating the consequences of c-Fos PTMs in various host defence mechanisms and persistent infections of *STm*. Separately, we are also investigating the cellular and molecular mechanisms related to PTMs in other gastrointestinal diseases.

Manjula Kalia
Principal Investigator

Lab Members

Eira Chaudhary
Riya Sarkar
Surendra Kumar Prajapat
Puja Sharma
Simran Chhabra
Sakshi Khera
Laxmi Mishra
Ananya De
Sahil Kumar
Mukesh Tanwar

Host-Pathogen Interactions of Flaviviruses

Japanese Encephalitis Virus (JEV), a mosquito-borne flavivirus, is the leading global cause of viral encephalitis, which results in 68,000 cases with 13,600–20,400 deaths each year. The virus is endemic mainly in East and South-East Asian countries. In India, epidemics occur every year where many children succumb to the disease. The virus infection leads to acute brain fever (encephalitis). Though vaccines are available, no drugs or therapeutics against JEV have been developed. Treatment for the disease is only supportive and hence there is an urgent need for the development of antiviral treatment. During virus infection, a constant battle between the host and virus decides the course of the disease. This ranges between two extremes- complete recoveries to death. We are trying to understand how the virus invades the different cells of the human body including the brain and how it exploits the cellular machinery to grow and spread. We are actively engaged in testing FDA-approved drugs for any antiviral potential using the animal model of JEV. We also study how the infected host mounts an immune response and what parameters are essential for inhibiting infection. This gives us clues to design and/or test drugs that can block the infection and/or enhance immunity. We aspire towards identification and development of anti-viral strategies and drugs.

Role of human Guanylate-binding protein 1 in virus replication

A detailed understanding of the host-virus interaction is critical for the development of effective antivirals. RNA virus infection triggers interferon (IFN) receptor signaling, leading to the activation of hundreds of interferon-stimulated genes (ISGs). Guanylate-binding proteins (GBPs) belong to one such IFN inducible subfamily of guanosine triphosphatases (GTPases) that have been reported to exert broad anti-microbial activity and regulate host defenses against several intracellular pathogens. There are 7 GBPs in human that are involved in various cellular functions such as inhibition of cell spreading and proliferation, activation of inflammosome and antimicrobial activities against viruses, bacteria and protozoans. Mechanistically GBPs and their associated family members have been shown to target and lyse the pathogen-containing vacuole membranes and destroy the residential habitat of vacuolar protozoan and bacterial pathogens. Several reports have suggested that IFN priming and induction of GBPs is crucial for caspase-4 (murine caspase-11) dependent pyroptosis and destruction of the bacterial replication niche

Here, we investigated the role of human GBP1 (hGBP1) in Japanese encephalitis virus (JEV) infection of HeLa cells in both an IFNγ unprimed and primed environment. We observed enhanced expression of GBP1 both at transcript and protein levels upon JEV infection, and GBP1 association with the virus replication membranes. We speculated that GBP1 recruitment to the virus replication complex could be an antiviral host defense mechanism similar to what has been described for bacterial pathogens. Depletion of hGBP1 through siRNA had no effect on JEV replication or virus induced cell death in the IFNγ unprimed environment. IFNγ stimulation provided robust protection against JEV infection. Knockdown of GBP1 in the primed environment upregulated expression and phosphorylation of signal transducer and activator of transcription 1 (STAT1) and significantly reduced JEV replication and titres. Our data suggests that in the presence of IFNγ, GBP1 displays a proviral role by inhibiting innate immune responses to JEV infection.

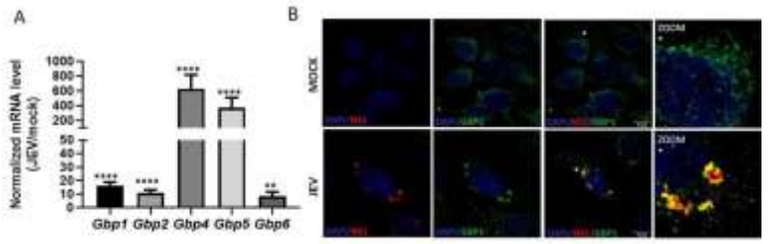


Figure 21: GBP1 localises to virus replication complex. *(A) HeLa cells were mock/JEV infected (1 MOI) for 24 h, and mRNA levels of Gbps were quantified by qRT-PCR. Graph shows the relative expression level of gene transcripts in mock/JEV infected samples. (B) Mock/JEV-infected (3MOI) HeLa cells were fixed at 24 hpi and immunostained for GBP1 and JEV NS1. Images were acquired on a confocal microscope using a ×60 objective. Scale bar 10μm.*

Development of a high-throughput image based platform for measuring autophagy flux

Autophagy is a conserved intracellular degradation pathway that is essential for maintaining cellular homeostasis. Recent studies have shown that pharmacological modulation of autophagy holds tremendous therapeutic potential for disease conditions such as neurodegeneration and cancer. Given its critical role in several disease conditions, recent studies are focussed on identifying drugs/small molecules with autophagy modulating capacity for potential clinical applications. The measurement of autophagy is done by monitoring the lipidated levels of microtubule-associated protein light chain 3 (LC3) protein that specifically incorporates into autophagosomes. Other techniques involve direct visualization of autophagosomes through fluorescence or electron microscopy. The degradative capacity of the pathway or autophagy flux is analysed by using specific inhibitors of autophagosome-lysosome fusion either through western blotting for LC3-II levels or by using ratiometric fluorescence based assays. Here, we describe the development and characterisation of a quantitative image-based high content screening platform for autophagy flux measurements using the human melanoma A375 cell line that stably expresses the GFP-LC3-RFP probe. The GFP-LC3 is incorporated into autophagosomes, while RFP serves an internal control. The GFP/RFP fluorescence intensity ratio gives an accurate indication of autophagy induction (low ratio) vs blockage of autophagy flux (high ratio), and was validated with the autophagy inducer Torin1 and inhibitor Bafilomycin A_1. This assay was used to screen the Spectrum collection library comprising of 2560 compounds, to identify autophagy modulators. In addition to known autophagy effectors, several novel autophagy inducers and inhibitors were identified in our study. Further three FDA approved drugs that are widely used in skin-care products: Avobenzone, Guaiazulene and Tioxolone, were validated as potent autophagy inducers that function in an mTOR independent manner.

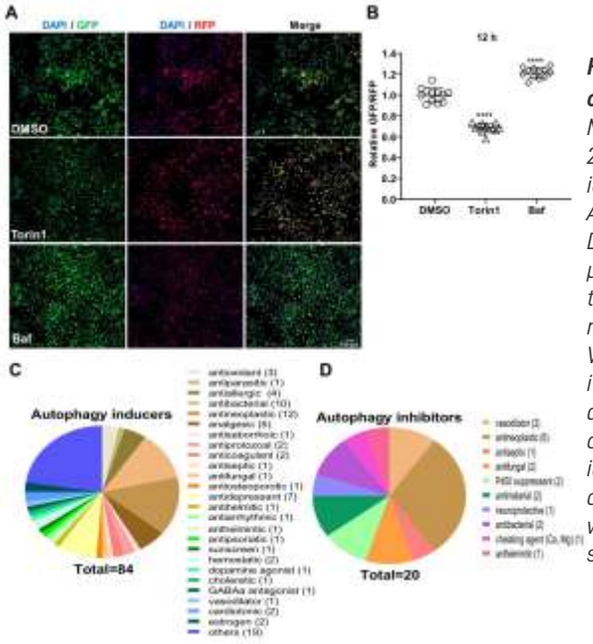


Figure 22: High throughput imaging screen of Microsource spectrum library. *(A) The Microsource spectrum library consisting of 2560 drugs were screened for the identification of autophagy flux modulators. A375 (GFP-LC3-RFP) cells were treated with DMSO/ Torin1 (100 nM)/ Baf (20 nM)/ drugs (10 μM) for 12 h in biological duplicates or triplicates. (B) GFP/RFP ratios were measured and normalized to DMSO control. Values show relative GFP/RFP ratios from 3 independent experiments. (C-D) Venn diagram showing the categorical classification of different molecules identified as autophagy inducers (ratio <0.8) or inhibitors (ratio >1.2). One-way ANOVA was used to determine statistical significance, **** P < 0.0001*

Arup Banerjee
Principal Investigator

Lab members

Surender Rawat
Jaya Saini
Sharda Kumari
Rohit Soni
Sakshi Nimesh
Prasanjit Jena
Shweta Duggal
Shubham Kumar
Naina Soni
Kusuma B

Understanding Pathobiology of Flaviviruses Prevalent in India

The outcome of viral infection is primarily driven by the immune cells interacting with the viruses and eliciting either protective or detrimental immune responses. Dengue and Japanese Encephalitis virus (JEV) infection cause notable morbidity and mortality and are recognized as important pathogens in India. However, it is not clear what molecular triggers cause severity. The immunopathogenic mechanisms that drive disease progression are ill-understood. Virus infection modulates the microenvironment leading to phenotypic and functional changes in the immune cells, thus altering disease outcomes. However, there is a lack of in-depth knowledge of the phenotypic heterogeneity of immune cells that arise due to viral infection. How virus-induced phenotypic changes are related to cell-fate decisions in the immune response and imparting adverse disease outcomes is unclear. Phenotypic heterogeneity may arise due to direct virus-cell interaction. Or it could be a contact-independent process where virus-infected cells secrete bioactive molecules by releasing extracellular vesicles. Transfer of those vesicles to the recipient cells may affect phenotype and functions. Thus, we have undertaken multiple projects to decipher the mechanisms of immune modulation at the cellular and molecular levels. Our work encompasses studying the impact of viral infection on various immune cell phenotypes and functions.

Understanding the impact of dengue virus infection on neutrophil phenotypes and functions

Neutrophils are the most abundant, phenotypically heterogeneous, and exert both detrimental and protective roles during anti-viral response. Uncontrolled neutrophil activation and subsequent modulation in effector functions can contribute significantly to cytokine storms and direct or indirect host tissue damage. Dengue virus (DV) has been reported to activate neutrophils. However, there is a lack of in-depth knowledge of the phenotypic heterogeneity and modulated effector functions of neutrophils during DV infection. In our study, we investigated the interaction of DV with neutrophils and studied its effector functions. We noticed that DV induces phenotypic modulation of neutrophils by down-regulating CD62L expression (Fig. 23). We observed that DV has a profound effect on neutrophil survival and cytokine expression, which is dependent on intracellular signaling involving PI3K and NF-κB activation. Furthermore, the DV-stimulated neutrophil secretome was found to have significant paracrine effects on both naïve neutrophils and platelets. The secretome of DV-treated neutrophils contained TNF-α, blocking TNF-α with neutralizing antibody accelerated neutrophil apoptosis, confirming TNF-α promoted survival effect on naïve neutrophils. Thus, our findings support the hypothesis that the neutrophil–DV interaction modulates the phenotype of neutrophils to enhance a pro-inflammatory microenvironment.

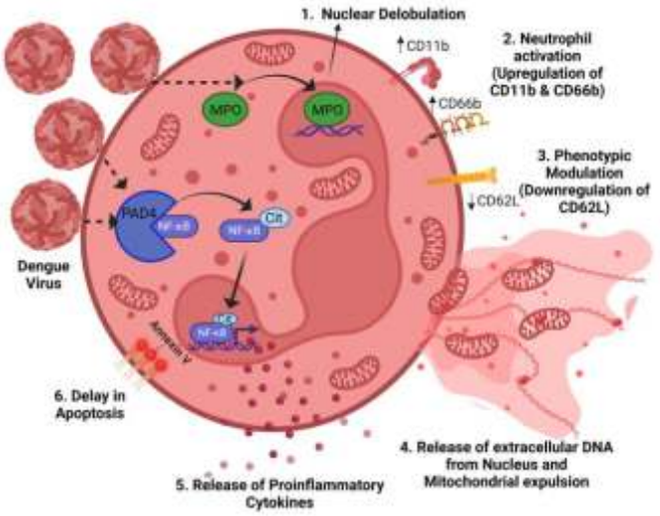


Figure 23: Multifaceted effect of Dengue virus (DV) on neutrophil biology.

Impact of dengue virus on neutrophil biogenesis

We also studied the effect of DV infection on neutrophil biogenesis in the bone marrow. Using an *ex vivo* expansion of mice progenitor cell model, we demonstrated that the presence of DV alone or with GM-CSF or G-CSF in culture conditions accelerates the differentiation of mice progenitor cells towards $CD11b^{+}Ly6C^{+}Ly6G^{+}$ granulocyte population. We further observed an expansion of $CD11b^{+}Ly6C^{int}Ly6G^{low}$ myeloid cells in the bone marrow of DV-infected mice, suggesting that DV infection modulates bone marrow myeloid cell proliferation and differentiation (Fig. 24). We also observed an increased number of monocytes and neutrophils in circulation. We further studied the importance of Myeloperoxidase (MPO), a vital granular enzyme, in DV-induced neutrophil differentiation. When we treated the bone marrow progenitors cells with ABAH, an MPO inhibitor, DV-induced proliferation, and differentiation were significantly affected and ROS production was halted significantly. Our study thus provides evidence that DV can accelerate the differentiation of bone marrow progenitor cells into neutrophils through MPO.

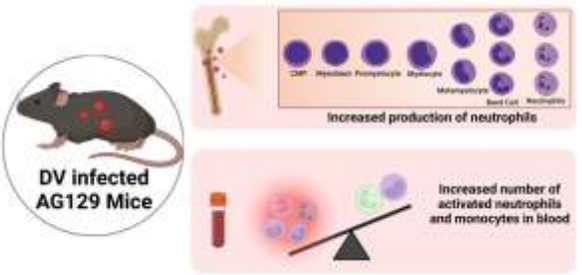


Figure 24: Schematic diagram representing the effect of dengue virus (DV) infection in the bone marrow and blood of AG129 mice.

Characterization of circulating extracellular vesicles and their immunopathogenic role in dengue virus infection

Extracellular vesicles are small membrane structures (size range up to 30 – 200 nm) that are produced by most cells and can be detected in several body fluids. EVs can affect recipient cells either by delivering the cargo into the recipient cells or can interact with receptors present on the surface and triggering intracellular signaling. However, there is less clarity on how EVs influence proliferation activation and functions of immune cells during dengue virus (DV) infection. Considering the versatile roles of circulating EVs, we hypothesize that circulating EVs in dengue patients can interact with the immune cells and shape the immune response that eventually contributes to disease progression. We have included plasma from healthy donors (HD), dengue-negative other febrile illness (OFI), and mild and severe dengue (DV) patients. In our ongoing research work, we have shown that severe dengue infection is associated with an increased release of platelet-derived extracellular vesicles in plasma compared to MILD_DV-EVs, HD-EVs, and OFI-EVs. We also noticed that the surface proteins of EVs are crucial for mediating signals to T cells. The EVs isolated from severe dengue patients' plasma carried an increased level of Programmed death-ligand 1 (PDL-1) which suppressed T cell proliferation. When we blocked the PD-L1 with an antibody, we observed that severe DV-EVs-induced immunosuppressive activity was partially reduced. Overall, our study highlights the immunosuppressive property of DV-EVs which might contribute to immune pathogenesis by shaping the adaptive immune response. Further study is in progress to understand the effect of EVs on endothelial barrier dysfunction.

Investigating Adult Stem Cells Dynamics in the Infection Scenario

Prasad Abnave
Principal Investigator

Lab members

Sahil Kumar
Shivam Kumar Tiwari
Riddhi Bhardwaj
Biplab Ghosh
Kishan Khandelwal
Puja Bharti
Shruthi Sunil

Adult stem cells (ASCs) with self-renewal and differentiation abilities, play a crucial role in maintaining tissue health by repairing damaged tissue during homeostasis, injury or disease. However, severe bacterial, viral or fungal infections can severely hinder tissue regeneration, as recent research has shown that ASCs' function and behavior are negatively impacted by these infectious agents. As a result, the inability to maintain healthy tissue often leads to fatal diseases. Therefore, our research aims to investigate the molecular mechanisms in ASCs that are affected during bacterial infections. We seek to understand how pathogens affect ASCs' behavior and determine the outcome of regeneration. Ultimately, the knowledge gained from this study would enable us to enhance ASCs' ability to tolerate infections, which would have significant biomedical implications.

Infection and regeneration

Many organs and tissues within our bodies, such as the liver, lung, skin, and bone, have the ability to regenerate and contain stem or progenitor cells. However, during certain infections, these cells often fail to efficiently repair the tissue. Recent studies suggest that mammalian stem cells may become exhausted and differentiate completely in circumstances where rapid proliferation or differentiation is needed to replace severely infected tissue. This leads to the question of why stem cells frequently fail to regenerate tissue effectively during severe infections. Our research program aims to answer this question by investigating how bacterial pathogens impact the dynamics of stem cells, including their proliferation, differentiation, and survival, potentially altering the regeneration capacity of infected tissue. Pathogens may have multifaceted effects on stem cells, resulting in diverse outcomes that affect one or more of their functions. To study this complex interaction, we require an in vivo system that enables monitoring of stem cell dynamics in their natural microenvironment. We are using planarian flatworms as a model system for these investigations. Planarian *Schmidtea mediterranea* is renowned for its remarkable regeneration ability, possessing a pool of pluripotent adult stem cells that enable it to regenerate an entire body from a small tissue fragment. Various lineage-committed stem cells and their progeny can be conveniently studied in vivo in planarians. The genetic machinery essential for stemness in mammalian stem cells is conserved considerably within planarian stem cells. Furthermore, planarian stem cells can be readily isolated by flow cytometry in large quantities for next-generation sequencing applications, such as RNA-Seq and ChIP-Seq. Consequently, the planarian has emerged as a convenient model system for studying adult stem cell dynamics in vivo.

Exploring the interaction between Planarians and Bacteria

Currently, there is limited knowledge on the interaction between planarians and bacteria, leaving much room for exploration. To gain a better understanding of how planarians recognize and respond to bacterial pathogens, we are investigating fundamental questions such as the effects of bacterial infection on planarian regeneration and how planarians recognize bacteria. Although several potential pattern recognition receptors (PRRs) have been identified in planarians, their role in bacterial recognition and immune response remains unclear. Therefore, we are focusing on one well-conserved PRR, the Peptidoglycan Recognition Proteins (PGRPs), to decipher its role.

Our homology search using known vertebrate and invertebrate PGRP sequences identified seven PGRP domain-containing transcripts in *Schmidtea mediterranea*. We designated the smaller ones (~20 kDa) as PGRP-S1 to -S3 and the larger ones (~90 kDa) as PGRP-L1 to -L4 based on their size. The phylogenetic tree showed their similarity with different vertebrate and invertebrate PGRPs. For example, PGRP-S1, S2, and S3 are the closest orthologs of mammalian PGRP2. We performed a multiple sequence alignment of PGRP domains from humans, mice, drosophila, and planarians, and found that the amino acid residues essential

for amidase catalytic activity were conserved in all three small PGRPs in planarians. This suggests that these small secreted PGRPs may have amidase catalytic activity and could function as effector PGRPs (Fig. 25). The residues required for substrate binding and Zn binding were mostly conserved in all planarian PGRPs (Fig. 25).

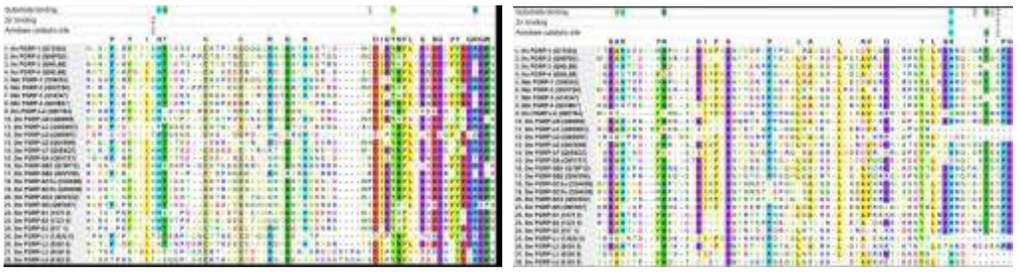


Figure 25: Multiple sequence alignment of 28 different PGRPs from four different organisms. *Amino acid residues with >60% conservation are highlighted. Amino acid residues present at the substrate binding site, zinc binding site and amidase catalytic site are mentioned on the top.*

To determine the expression patterns of PGRPs in whole animals and specific cell types, we used fluorescence in situ hybridization on intact planarians. We found that all seven PGRPs had distinct expression patterns and were expressed in a variety of tissues such as the intestine, epidermis, secretory cells, parenchymal cells, and stem cells (Fig. 26).

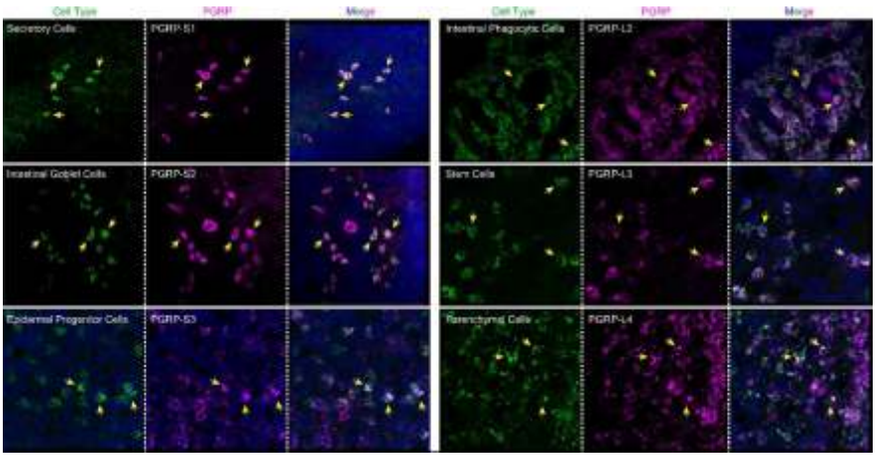


Figure 26: Fluorescence in situ hybridization images showing the expression of PGRPs in various planarian cell types. *Green- specific cell type marker, magenta- PGRP, and blue- nuclei.*

In order to understand how PGRPs contribute to planarian regeneration, we examined their expression patterns throughout the regeneration process. Our analysis, conducted using RT-qPCR, revealed that a number of PGRPs exhibited rapid over-expression in response to injury, indicating that these proteins may play a role in safeguarding the injured tissue from potential bacterial infections.

Anil Thakur
Principal Investigator

Lab members

Aishwarya Rana
Nidhi Gupta
Shumaiza Asif
Biswambhar Biswas
Sandeep Hans
Ajeet Kumar
Rashmi Yadav

Translational control of gene expression in yeast and fungal pathogens

Our research group studies translational control of eukaryotic gene expression. Translational control plays an essential role in the regulation of gene expression and it is important in defining the proteome, maintaining homeostasis, growth, and development. Translation is executed by ribosomes with the assistance of translation factors and ribosomal proteins. Recognition of the start codon in the mRNA is one of the initial events in translation and it determines the reading frame to be decoded. However, little is known about the translatome employed by human fungal pathogens during infection. Transcriptional profiling of fungal cells exposed to phagocytes have indicated major influences on ribosome biogenesis and protein synthesis. However, the translational regulation that fine-tunes the translation of subgroups of mRNA for host adaptation needs to be thoroughly investigated. Our quest is to probe the translation process of yeast and pathogenic fungi to identify novel therapeutic targets to treat fungal diseases in humans.

Regulation of protein synthesis in response to oxidative stress and nutrient starvation in the fungal pathogen Candida glabrata

Candida species are opportunistic fungal pathogens of humans, and *Candida glabrata* is the second most common cause of infection. *C. glabrata* infections are difficult to treat and this fungus has intrinsic resistance to antifungal drugs. The mechanisms of pathogenicity of *C. glabrata* are not yet fully understood. *C. glabrata* can survive in macrophages and even replicate within a phagosome although it is deficient for nutrients and trace elements. However, *C. glabrata* is highly resistant to oxidative killing compared to *Candida albicans* and *Saccharomyces cerevisiae*. Whole-genome expression and transcription profiling studies have confirmed that the host infection altered the expression profiles and other stress-protective molecules of pathogens following exposure to macrophages and neutrophils. This is achieved by implementing complex regulatory mechanisms including a global inhibition of protein translation. We found this translation inhibition mainly depends on the kinase Gcn2 which phosphorylates the alpha subunit of eIF2, which binds with initiator methionyl-tRNA (Met-tRNA$_i$), in a ternary complex (TC) during scanning of the start codon for translation initiation. Phosphorylation of eIF2α reduces global protein synthesis and induces expression of stress-responsive genes and assists the mRNA decay pathway in degrading accumulated mRNAs.

One of the stress-responsive factor is Gcn4 a master transcriptional regulator, studied for its roles during starvation and stress. During amino acid starvation and oxidative stress, the translation of Gcn4 mRNA increases, through the activation of the Gcn2 kinase. The Gcn4 function as a transcriptional activator to induce transcripts involved in amino acid biosynthesis. This allows cells to restore amino acid levels and survive in starvation and under oxidative stress. We found that the *gcn4* mutant is defective in the utilization of proline as a nitrogen source (Fig 27A). In eukaryotes, Cytoplasmic proline is transported into the mitochondria where it is converted back to P5C by proline oxidase (*PUT1*). The mitochondrial P5C is converted to glutamate by the *PUT2* which is then converted to α-

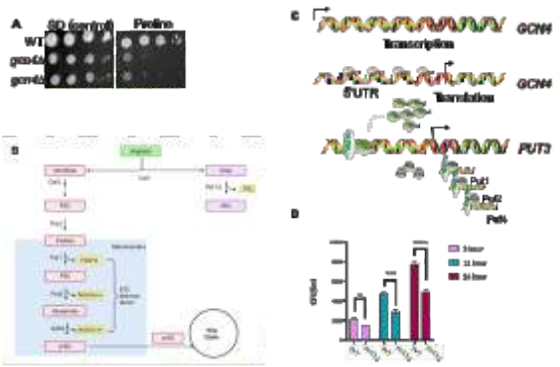


Figure 27: Effect of C. glabrata Gcn4 and Put3 on proline catabolic pathway: *A) Ten-fold serial dilution of WT, gcn4Δ strain of C. glabrata were spotted on SD, Proline. B) Scheme of proline catabolic pathway. C)The proposed mechanism of regulation of PUT3 transcription factor and in turn proline catabolism for utilization of proline as a nitrogen source. D) Differentiated THP1 macrophages were infected by WT and put3Δ in MOI of 1:15 for two hours and the plating was done at specific time points.*

ketoglutarate *via* Gdh2 to enter in the citric acid cycle (Fig 27B). In our study, we found that Gcn4 regulates the Put3 transcription factor for the expression of both *PUT1* and *PUT2* genes which allows the pathogen to degrade proline to use it as a nitrogen source (Fig 27C). The *put3Δ* strain is defective in survival in the host cells (Fig 27D). We concluded *PUT3* is the main proline pathway regulator important for *C. glabrata* to survive in the host. It suggests the ability of *C. glabrata* to freely obtain proline from the host system as a nitrogen source that may help it thrive as a commensal and opportunistic pathogen.

Ribosomal protein Rps14 control the accuracy of start codon selection by translation pre-initiation complex

In eukaryotes, translation initiation generally occurs via a scanning mechanism, wherein the small (40S) subunit of the ribosome recruits methionyl initiator tRNA (Met-tRNA$_i$) in a ternary complex (TC) with GTP-bound eukaryotic initiation factor 2 (eIF2), this reaction is stimulated by initiation factors eIF1, eIF1A, and eIF3. The resulting 43S preinitiation complex (PIC) attaches to the 5' end of mRNA and scans the 5'UTR for an AUG start codon. In scanning PIC, eIF1 and eIF1A promote an open, scanning-conducive conformation of the 40S subunit with TC bound in an unstable open conformation "P_{OUT}", which facilitates the inspection of successive triplets in the peptidyl (P) decoding site for complementarity with the anticodon of Met-tRNA$_i$. The GTP bound to eIF2 can be hydrolyzed, but eIF1 blocks release of inorganic phosphate (P_i) at non-AUG codons. Start codon recognition triggers dissociation of eIF1 from the 40S subunit, enabling both P_i release from eIF2-GDP·P_i and more stable TC binding to the PIC, with Met-tRNA$_i$ fully accommodated in the closed state "P_{IN}" (Fig. 28A).

Recent Cryo-EM structures have revealed interactions between RPS14 with the backbone of mRNA, including the -3 nucleotide of the "Kozak" context enhancing AUG selection. We found that substitutions at interacting residues of RPS14- L137R with mRNA increased recognition of a UUG start codon at *HIS4* reporter and L137R reduced dissociation of the eIF2·GTP·Met-tRNA$_i$ ternary complex (TC) with a UUG start codon *in vitro,* indicating destabilization of the open complex. L137R substitution also increased usage of poor-context AUGs in *SUI1* mRNAs *in vivo*. In contrast, RPS14-R135 interacts with the rRNA backbone only in the closed complex, and the R135E substitution reduced initiation at UUG codon and poor-context AUGs, while increasing TC dissociation at UUG codons *in vitro*, indicating destabilization of the closed complex. Thus, distinct interactions of RPS14 with mRNA or rRNA stabilize first the open and then closed conformation of the PIC to influence the accuracy of initiation (Fig. 28B). Currently, we are also identifying the roles of additional ribosomal proteins of small 40S subunit to determine the high-fidelity selection of AUG initiation codons.

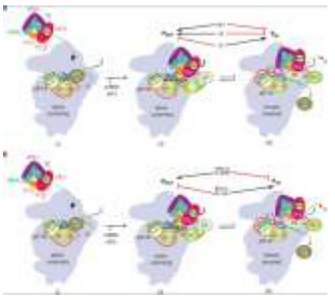
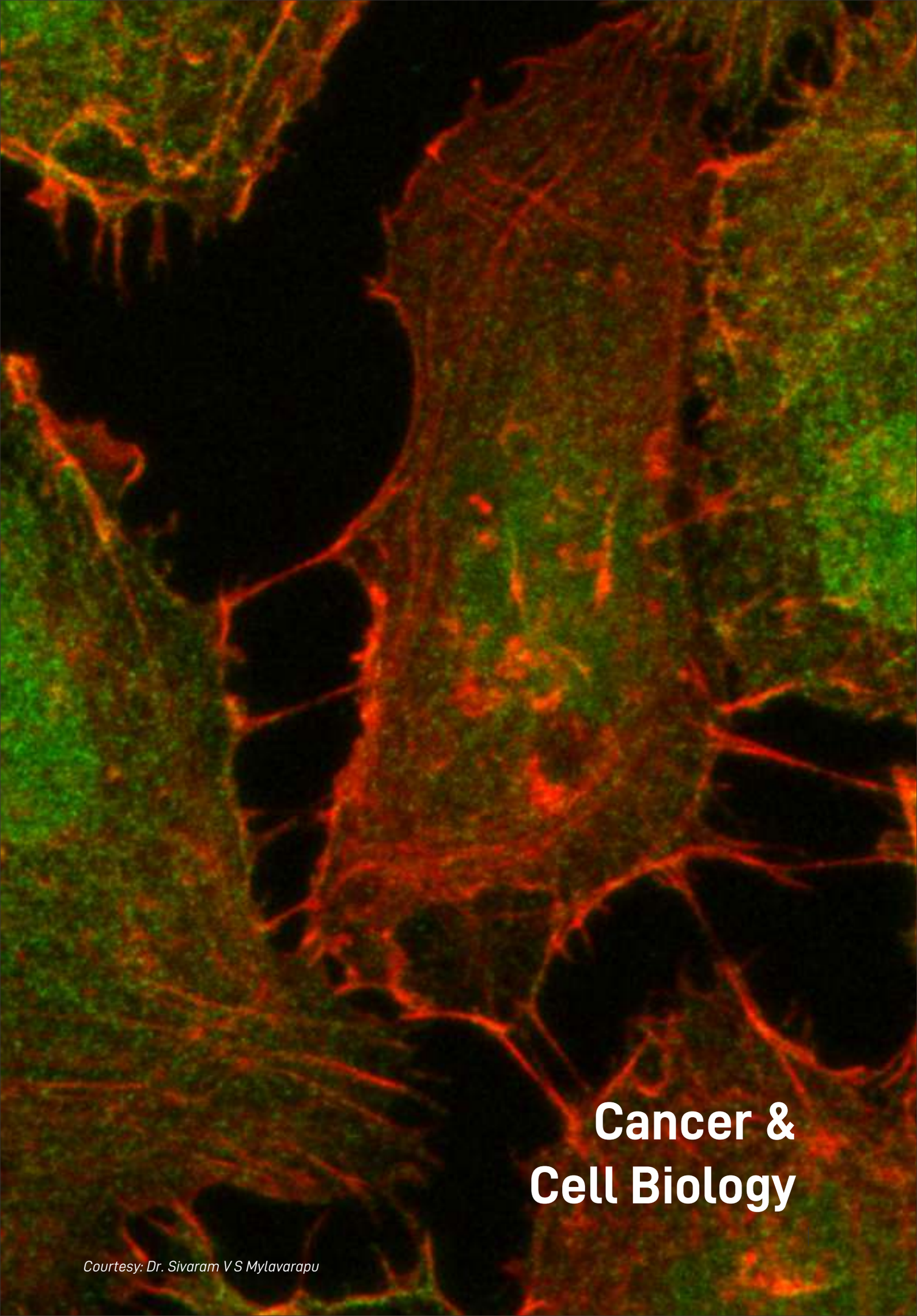


Figure 28: Model describing conformational rearrangements of the PIC and roles of RPS14 residues in start codon recognition *(A) Assembly of the PIC and start codon selection in WT cells. (i) eIF1 and eIF1A elements stabilize an open conformation. (ii) Scans mRNA. (iii) On AUG recognition, the Met-tRNA$_i$ moves from the P_{OUT} to P_{IN} state. (B) Interaction of RPS14-L137 with mRNA enhances scanning (ii). Interactions of RPS14-E135 with rRNA stabilize the closed conformation (iii).*



Cancer & Cell Biology

Courtesy: Dr. Sivaram V S Mylavarapu

Avinash Bajaj
Principal Investigator

Lab Members

Dr. Ruchira Chakraborty
Poonam Yadav
Kajal Rana
Dolly Jain
Varsha Saini
Somesh K Jha
Nishant Pandey
Bharti Agarwal
Shalu
Devashish Mehta

Engineering of Nanomaterials for Biomedical Applications

We are using interdisciplinary approaches like synthetic chemistry, cell biology, microbiology, cancer biology, nanotechnology, lipidomics, genomics and bioinformatics to address challenges in the area of cancer biology and infectious diseases and to develop nanomaterials for effective therapeutics.

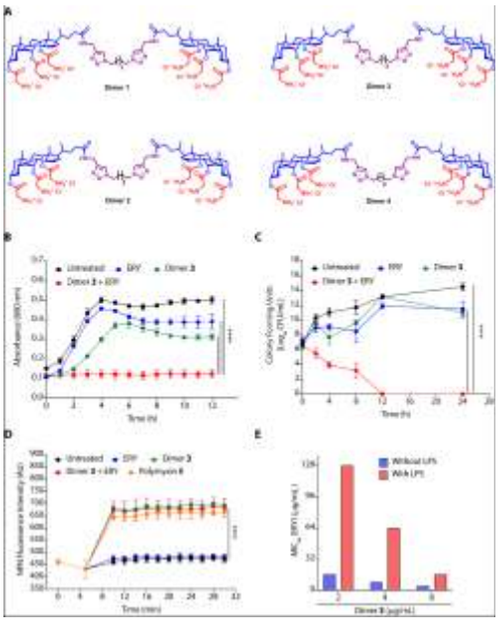
We investigated the antimicrobial activities of four dimers against three different Gram-negative bacterial strains *Escherichia coli* (MTCC443), *Pseudomonas aeruginosa,* (MTCC1688), *and Klebsiella pneumonia* (MTCC3384) (Fig. 29A). We found that most of the dimers are active against Gram-negative bacteria with MIC_{99} of 32-64 g/mL. We selected dimer 2 and 3 as these dimers are least toxic, and possess no effective antimicrobial activity themselves. To find the potential adjuvant activity of dimer 2 and 3, we examined the activity of these dimers in combination with erythromycin (ERY) against *E. coli* and *P/ aeruginosa* using chequerboard assay. MIC_{99} of ERY against *E. coli* gets reduced from 128 to 1 µg/mL in presence of 32 µg/mL of dimer 2, and there was a 32-fold reduction in MIC_{99} of ERY against *P. aeruginosa* in presence of 4 µg/mL of dimer 2. Fractional Inhibitory Concentration (FIC) values calculated for this combination against the three strains range from 0.039-0.13, thereby confirming the synergism between dimer 2 and ERY. Similarly, we observed a significant decrease in MIC_{99} of ERY on using dimer 3 against *E. coli* as we observed MIC_{99} of 2.0 µg/mL for ERY in presence of 2 µg/mL of dimer 3 with an FIC of 0.039. Dimer 3 also enhanced the activity of ERY against *P. aeruginosa* where MIC_{99} of ERY was found to be 0.5 µg/mL when used in combination with 2 µg/mL of dimer 3 with FIC of 0.066.

Growth kinetic studies showed that combination of dimer 3 and ERY did not allow *P. aeruginosa* and *E. coli* to grow (Fig. 29B), whereas there was negligible effect on growth kinetics on treatment with dimer 3 or ERY alone. Similarly, combination of dimer 3 and ERY was able to kill *P. aeruginosa* within 12h of treatment (Fig. 29C). NPN-stained *P. aeruginosa* displayed high fluorescence on treatment with dimer 3 displaying outer membrane permeabilizing property of dimer 3 (Fig. 29D). Similarly, combination of dimer 3 and ERY also caused outer membrane permeabilization in Gram-negative bacteria. Dimer 3 also caused inner membrane permeabilization in *P. aeruginosa*. Flow cytometry analysis showed that dimer 3 and combination of dimer 3 and ERY causes significant increase in number of PI-positive cells. Dimer 3 at 8 g/mL caused ~50% PI positive cells whereas combination of dimer 3 and ERY induces >70% PI-positive *P. aeruginosa* cells. Combination of dimer 3 and ERY showed a synergistic effect against *P. aeruginosa* at a combination ratio of 8 and 4 g/mL, 4 and 8 g/mL, and 2 and 16 g/mL respectively**.** In contrast, LPS made the ERY ineffective as MIC_{99} of ERY increased to 128 g/mL in presence of 2 g/mL of dimer 3 (Fig. 29E). Flow cytometry analysis witnessed that LPS induced a 6-7-fold decrease in PI-positive *P. aeruginosa* and *E. coli* cells on treatment with combination of dimer 3 and ERY, thereby confirming the LPS-mediated effect of dimer 3 on bacterial cell death. Upon testing the combination of dimer 3 and ERY in presence of salts, we observed that in presence of 0.25 mg/mL of $MgCl_2$, dimer 3 could not restore the activity of ERY.

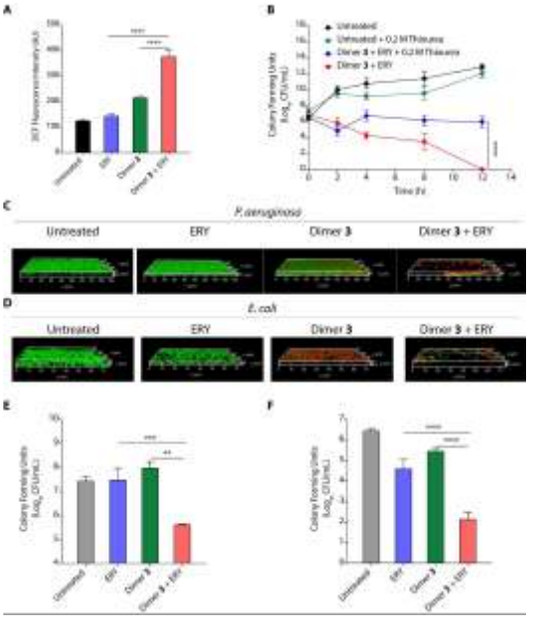
We observed that ERY alone treatment did not display any effect on protein synthesis, whereas there is >10-fold decrease in protein synthesis on treatment of *P. aeruginosa* and *E. coli* cells with combination of dimer 3 and ERY. Combination of dimer 3 and ERY caused many fold increase in ROS over untreated, only dimer 3, and only ERY treated *P. aeruginosa* bacterial cells (Fig. 30A). Presence of thiourea, a quencher for intracellular ROS, inhibited the bactericidal effect of combination of dimer 3 and ERY *P. aeruginosa* bacterial cells. (Fig. 30B). Quantification of bacterial load in biofilms showed that combination of dimer 3 and ERY induced a 5-6 log decrease in CFUs of *P. aeruginosa* and *E. coli* biofilms, and there was minimal decrease in CFUs on treatment of dimer 3 or ERY alone. Confocal fluorescence imaging clearly demonstrated that combination of dimer 3 and ERY can degrade *P. aeruginosa* and *E. coli* biofilms (Fig. 30C, 2D). Quantification of CFUs showed that treatment

of dimer 3 or ERY alone did not cause any change in bacterial load in *P. aeruginosa* and *E. coli* infected mice, whereas combination of dimer 3 and ERY induced a 2-log decrease in bacterial load (Fig. 30E, 30F). Antimicrobial studies witnessed that combination of dimer **3** and ERY is highly effective against all the clinical strains of *E. coli* and *P. aeruginosa*).

In summary, our study showed discovery of a unique combination of cholic-acid derived dimeric amphiphiles and ERY for Gram-negative bacterial infections that can be further tuned for clinical applications.



fp= 29- ,½ इस अध्ययन में कोलिक एसिड–व्युत्पन्न डिमर्स की आणविक संरचनाओं की जांच की गई। बी) डिमर 3, ERY और डिमर 3 तथा ERY के संयोजन की उपस्थिति में P-एरुगिनोसा के विकास का गतिज अध्ययन। सी) P-एरुगिनोसा पर विभिन्न उपचारों के प्रभाव को दर्शाने वाला कोशिका की मृत्यु का गतिज अध्ययन। डी) विभिन्न उपचारों पर NPN–उपभेदी P-एरुगिनोसा की प्रतिदीप्ति तीव्रता में परिवर्तन। ई) LPS की अनुपस्थिति और उपस्थिति में डिमर 3 की विभिन्न सांद्रता का उपयोग करने पर P-एरुगिनोसा में ERY के MIC_{99} में परिवर्तन।



fp= 30 ,½ P.एरुगिनोसा के विभिन्न उपचारों पर ROS की मात्रा निर्धारित करते हुए DCF की प्रतिदीप्ति तीव्रता में परिवर्तन। बी) थायोयूरिया की अनुपस्थिति और उपस्थिति में विभिन्न उपचारों पर P.एरुगिनोसा की कॉलोनी बनाने वाली इकाइयों में परिवर्तन। (सी, डी) विभिन्न उपचारों पर SYTO9/PI युक्त P.एरुगिनोसा (सी) और E. coli (डी) बायोफिल्म के प्रतिदीप्ति माइक्रोग्राफ। CIPF सिप्रोफ्लोक्सासिन होता है। (ई, एफ) विभिन्न उपचारों से चूहों के घावों में P.एरुगिनोसा (ई) और E. coli (एफ) के सीएफयू में परिवर्तन।

Sivaram V S Mylavarapu
Principal Investigator

Lab Members

Chandan Kumar
Diksha Pathak
Neeraj Wasnik
Mahendra Singh
Mahima Singhal
Harsh Oza
Manya Batra
Anushka Das
Sukirti Khantwal

Molecular mechanisms of cell division, intercellular communication and cellular dynamics

We study the molecular regulation of cell division and intercellular communication, two vital and dynamic cellular processes essential for cell survival and organism development. These processes are subverted in both infectious and non-infectious diseases, underscoring the relevance for future therapeutic exploitation. Under this broad objective, we aim to elucidate the mechanisms of formation of novel modes of cell-cell communication, currently focusing on enigmatic structures called tunneling nanotubes, and aim to understand the host cell biology of pathogenic microorganisms. We also wish to understand the regulation of cell division by the intracellular motor dynein and the mechanisms of cytokinesis, the final step of cell division. The broad objective is to obtain a holistic understanding of the molecular mechanisms that govern these processes through multi-disciplinary approaches. Knowledge gained from these studies could be exploited towards strategies for the amelioration of disease conditions.

Nucleolin is required for multiple centrosome-associated functions in early vertebrate mitosis Nucleolin is required to maintain prophase centrosome attachment to the nuclear envelope

In order to examine whether nucleolin is required for centrosome attachment to the nuclear envelope (NE), we depleted nucleolin from HeLa cells stably expressing end-binding protein 1 (EB1) tagged to GFP (EB1-GFP) to visualize centrosomes and histone 2B-mCherry (H2B-mCherry, to visualize chromosomes) using treatment with sequence-specific siRNAs. Live cell, time-lapse fluorescence confocal imaging of G2/prophase synchronized cells revealed the position of the centrosomes to be closely attached to the G2 NE in control cells, while treatment with nucleolin siRNA led to a marked dissociation of the centrosome(s) from the NE (Fig. 31A-D). We quantified the fraction of cells showing centrosomes detached from the nuclear envelope and observed an increase in this population by approximately 3-fold compared to control cells (Fig. 31E). Closer analysis revealed that a significant proportion of mitotic cells showed a large centrosome displacement (> 2 µm) from the NE, a distance limit that was rarely breached in control cells (Fig. 31F). Overall, these results confirmed a novel function for nucleolin in maintaining the attachment of G2 centrosomes to the NE in mammalian cells.

The two duplicated centrosomes normally stay together until just prior to NEB, when they disengage and separate from each other along the nuclear envelope, enabling the eventual formation of a bipolar spindle to facilitate chromosome segregation. Upon nucleolin siRNA treatment, we observed through time lapse fluorescence confocal imaging that the two G2/prophase centrosomes untethered from each other normally, but failed to separate completely from each other (Fig. 32A). Quantitative analysis of our live cell confocal imaging

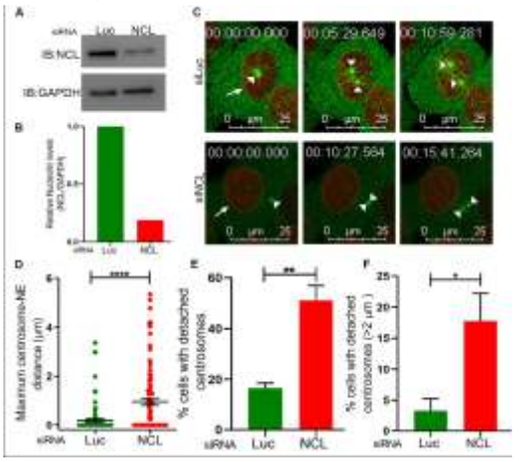


Figure 31: Nucleolin depletion leads to centrosome-NE attachment defects. *A) Western blot showing nucleolin (NCL) depletion from HeLa cells stably expressing H2B-mCherry (red, chromatin in C) and EB1-GFP (green, microtubule plus ends in C), upon treatment with the indicated siRNAs (top). Luc = luciferase (negative control siRNA). IB = immunoblot. GAPDH = loading control. B) Densitometric quantification of A. C) Representative stills from time-lapse videos of the cells treated in A and B. Arrowheads = centrosomes, arrows = NE. D) Maximum centrosome-NE distance measurements. 90 G2 cells counted over three independent experiments per condition. E, F) Quantification of the fraction (%) of G2 cells showing at least one centrosome detached from the NE (E), or detached and separated from the NE for at least 2 µm (F), from the movies depicted in C. Error bars = mean +/- SEM. *P<0.05, **P<0.01, ****P<0.0001. (D: Mann Whitney test; E, F: unpaired t-test).*
Nucleolin is required for inter-centrosome separation at G2

data revealed that the average inter-centrosome distance at G2/prophase reduced significantly upon nucleolin siRNA treatment (Fig. 32B), suggesting that nucleolin is required to ensure the proper separation of G2/prophase centrosomes along the NE. Our observations suggest that in addition to maintaining a bipolar spindle in metaphase as earlier reported, nucleolin may also facilitate the formation of a proper mitotic spindle by ensuring the optimal separation of the duplicated G2/prophase centrosomes.

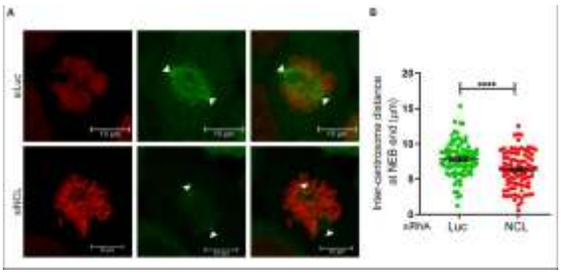


Figure 32: Nucleolin depletion leads to reduced inter-centrosome separation following NEB. *A) Representative stills from time-lapse videos of HeLa cells stably expressing H2B-mCherry (red, chromatin) and EB1-GFP (green, microtubule plus ends) upon treatment with the indicated siRNAs. Arrowheads = centrosomes. B) Inter-centrosome linear distance measured from analysis of the live cell movies. 90 G2 cells counted over three independent experiments per condition. Error bars = mean +/- SEM. ****P<0.0001. (B: unpaired t-test). Nucleolin is required for ensuring timely nuclear envelope breakdown*

Inter-centrosome separation at prophase to position the two centrosomes at opposite sides of the nucleus is closely followed by the onset of NEB, so as to enable the formation of a bipolar mitotic spindle. We analyzed the live cell movies of HeLa cells stably expressing EB1-GFP::H2B-mCherry to examine whether nucleolin is required for the timely onset and completion of NEB following separation. Treatment with nucleolin siRNA led to a modest but consistent delay in the time taken from initial centrosome-centrosome disengagement to the dissolution of the nuclear envelope, and also to a delay in the time taken to complete NEB, characterized by the disappearance of any remnants of a sharp boundary demarcating the chromatin from the cytoplasm. To examine whether nucleolin is required for the progression of NEB itself once initiated, we analyzed the duration between NEB onset and NEB end in luciferase and nucleolin depleted cells. We observed no significant changes in NEB duration in nucleolin depleted cells as compared to luciferase control. These observations suggested that nucleolin plays a role in ensuring the timely onset of nuclear envelope disintegration at the beginning of mitosis, but not in its progression once initiated.

Nucleolin is required for maintaining spindle length in metaphase

Bipolar spindle formation and mitotic spindle integrity are critical for proper chromosome segregation. Nucleolin is required for proper chromosome congression and maintenance of spindle pole integrity in mitosis. In order to understand whether nucleolin has a role in regulating spindle length during mitosis, we depleted nucleolin in U2OS cells using sequence-specific siRNAs and confirmed efficient knockdown by immunoblotting. We performed immunofluorescence analysis of the cells, imaged them by confocal microscopy and measured the interpolar distance from 3D reconstructions. Nucleolin depletion led to a significant increase in the average mitotic spindle length, as depicted by the representative linescans of the inter-centrosomal spindle axes. The fluorescence intensity profile of gamma-tubulin (centrosomes) clearly peaked at the centrosomal area, but was significantly reduced along the spindle axis. The average distance between the two gamma tubulin peaks was greater upon nucleolin siRNA treatment by about 12% as compared to control treatment. These observations confirmed that nucleolin has essential roles in maintaining optimal metaphase spindle length during mammalian cell division.

Rajender K Motiani
Principal Investigator

Lab Members

Akshay Sharma
Jyoti Tanwar
Nutan Sharma
Samriddhi Arora
Suman Sourav
Kriti Ahuja
Sharon Raju

Understanding molecular mechanisms regulating calcium signaling and their role in human pathophysiology

Ca^{2+} signaling regulates plethora of cellular functions and thereby plays a critical role in maintaining tissue homeostasis and health. Perturbation in Ca^{2+} dynamics causes impairment of cellular physiology eventually leading to diseases. The focus of our group is to understand the role of Ca^{2+} signaling in Skin pigmentation, Tumorigenesis and Cancer metastasis. We are aiming to: 1) Delineate the role of organellar Ca^{2+} dynamics in these pathophysiological conditions; 2) Elucidate detailed molecular mechanisms connecting dysregulated Ca^{2+} signaling to Cancers and Pigmentary disorders; 3) Eventually, we aim to utilize this knowledge for devising strategies for better management and treatment of these pathophysiological conditions.

Calciomics of skin pigmentation

Skin pigmentation plays a vital role in protection against UV induced cancers. Perturbations in pigmentation pathways result in pigmentary disorders like solar lentigo, melasma, and vitiligo. These disorders are considered as social stigma; impart long-term psychological trauma and are huge economic burden. The current therapeutic regimes are not efficient in alleviating pigmentation defects. Therefore, it is critical to identify the novel molecular players regulating pigmentation and devise strategies for targeting them. For identifying novel regulators of pigmentation, we performed microarrays on hyperpigmented and hypopigmented human melanocytes. Interestingly, we observed significant deviations in the Ca^{2+} homeostasis in these cells. Although role of plasma membrane Ca^{2+} handling proteins is reported in pigmentation, the significance of organellar Ca^{2+} signaling and functional relevance of intracellular Ca^{2+} handling proteins remains unappreciated. Therefore, this program is focused on understanding the role of inter-organellar crosstalk, via Ca^{2+} dynamics, especially ER-Mitochondrial and Mitochondrial-Melanosome communication in regulating pigmentation.

We had earlier identified ER Ca^{2+} sensor, STIM1 as a novel regulator of pigmentation. STIM1 expression is enhanced with increase in pigmentation. This year, we report that Microphthalmia-associated transcription factor (MITF) is a critical regulator of STIM1 expression. We show that physiological melanogenic stimuli α-Melanocyte Stimulating Hormone (αMSH) increases STIM1 mRNA and protein levels. Further, αMSH stimulates STIM1 promoter-driven luciferase activity, thereby suggesting transcriptional upregulation of STIM1. We report that downstream of αMSH, MITF drives STIM1 expression. By performing knockdown and overexpression studies, we corroborated that MITF regulates STIM1 expression and activity. Next, we conducted extensive bioinformatics analysis and identified MITF binding sites on STIM1 promoter. We validated significance of the MITF binding sites in controlling STIM1 expression by performing ChIP and luciferase assays with truncated STIM1 promoters. Moreover, we confirmed MITF's role in regulating STIM1 expression in primary human melanocytes. Finally, analysis of publicly available datasets substantiates a positive

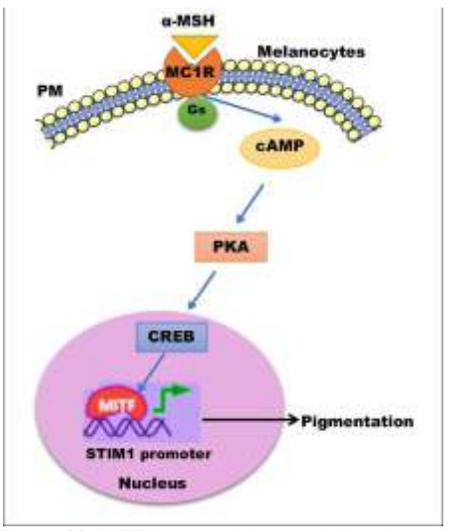


Figure 33. MITF is a novel transcriptional regulator of STIM1 during melanogenesis. *Downstream of αMSH stimuli, MITF-M regulates STIM1 expression by enhancing transcription of STIM1. We show that MITF-M binds on the STIM1 promoter and thereby drives STIM1 promoter activity and its expression. Figure adopted from our recent publication Tanwar et al., Journal of Biological Chemistry Dec. 2022.*

correlation between STIM1 and MITF expression in sun-exposed tanned human skin, thereby highlighting physiological relevance of this regulation. Taken together, we have identified a novel physiologically relevant molecular pathway that transcriptionally enhances STIM1 expression (Fig. 33).

Targeting calcium signaling for curtailing tumor growth and metastasis

Pancreatic Cancer (PC) is one of the deadliest cancers that accounts for lakhs of deaths annually and has mean survival time of less than 5 years. Most of the PC deaths are associated with late diagnosis, secondary metastasis and chemoresistance. For developing effective treatment strategies, it is necessary to understand the molecular mechanisms that drive PC metastasis and chemoresistance. Ca^{2+} signaling plays a critical role in tumorigenesis by regulating the hallmarks of cancer progression such as cellular proliferation, invasion and metastasis. Cancer progression is often associated with altered cellular Ca^{2+} levels and dysregulated functioning of Ca^{2+} channels. In non-excitable cells including pancreatic cells, Store Operated Ca^{2+} Entry (SOCE) mediated by Orai channels is the most important Ca^{2+} influx pathway that regulates cellular physiology. Mammals consist of three distinct Orai proteins (Orai1, 2 and 3). Orai1 is ubiquitously expressed and contributes towards "classical" SOCE in most of the non-excitable cell types. Interestingly, recent findings implicate that instead of Orai1, Orai3 is the major contributor of SOCE in estrogen receptor-expressing (ER+) breast cancer cells and in non-small cell lung cancer (NSCLC).

We recently reported that Orai3 forms a functional SOCE channel in PC cells and regulates PC metastasis *in vivo*. Further, we reported that Orai3 is overexpressed in PC tissue samples and higher Orai3 levels are associated with poor prognosis. However, the molecular mechanisms working downstream of Orai3 for poor survival remain completely unappreciated. Chemo-resistance is one of the key factors that contribute to poor prognosis in PC. Gemcitabine either alone or in combination with other drugs is frequently used as a first line therapy in PC management. Gemcitabine resistance (GemR) is associated with poor clinical outcomes in PC patients. However, the signaling cascades that drive GemR and connect GemR to poor prognosis remain poorly understood. Based on literature survey, unbiased analysis of GemR transcriptomics data and our pilot studies (**Fig. 34**), we hypothesize that Orai3 contributes to GemR and associated poor clinical outcomes. Therefore, we are currently elucidating the role of Orai3 in PC GemR.

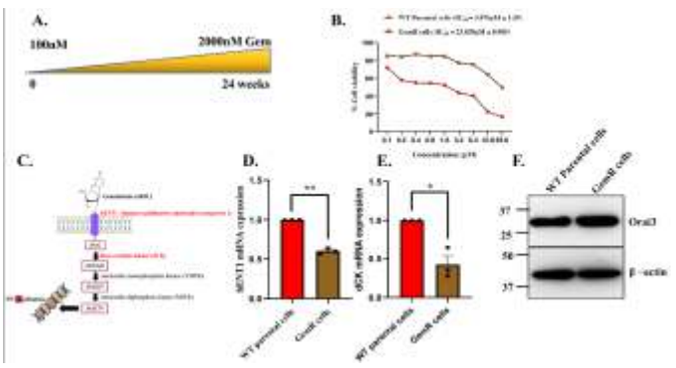


Figure 34. Orai3 is upregulated in GemR PC cells. *We have generated and characterized GemR PC cells (A to E). F. We observed that Orai3 levels are significantly higher in GemR PC cells in comparison to WT Parental cells.*

Karthigeyan Dhanasekaran
Principal Investigator

Lab Members

Himanshi
Tulasiram Mora
Zidhan Subair
Neha Sharma
Aparna Upadrasta
Shankar S

Understanding the structure and function of centriole based organelles

Centrosomes are microtubule-based membrane less organelle. These subcellular structures are being studied for more than a century but their significance has been limited to cell division and the associated pathogenesis in aneuploidy and cancer until the recent developments witnessed in the field of cell biology. Today we understand the biogenesis of centrosome and cilia to a large extent and yet fail to connect all possible events from nucleation to faithful segregation. This is partly due to the deficiency of tools and partly due to the dearth of a more focused research involving physiological context based centrosome biology. Our lab is majorly focused towards the centrosome and ciliary functional aspects regulating the physiological and pathological events revolving around these centriole based structures. We are motivated to study the structural composition as well as the regulatory aspects controlling the genesis and maintenance of Centriolar structures especially while facing challenges like DNA damage and viral infection. Beyond this our group is also actively involved in understanding the centrosome signalling component which operates actively in response to such pathological cues.

Impact of flaviviral proteins on centrosomes.

The centrosome is a multifunctional organelle that consists of a pair of centrioles embedded in the pericentriolar matrix (PCM). They are involved in many cellular processes and defects caused by changes in centrosomal structure or number have been associated with human diseases ranging from congenital defects to cancer. Recent reports have suggested the hijacking of centrosomes by several retroviruses during their pathogenesis in host cells. Yet the underlying mechanisms are not completely deciphered at this juncture. Based on our literary survey we could appreciate the fact that different viruses have varying levels of centriolar involvement across a wide variety of hosts. Further, the outcome of these phenotypes depends a lot based on the nature of tissue and the overall impact on the infected organs prime function.

Flaviviruses including Zika Virus, Dengue Virus, Hepatitis C virus, West Nile Virus, Yellow Fever Virus, etc. are vector borne and highly pathogenic single stranded RNA viruses which are reported to cause severe illness in humans. Among the flaviviral members, Zika viral helicase and replicase and Dengue viral replicase are known to localize on centrosomes. These viruses are also known to induce centrosome abnormalities, thereby regulating cell division, differentiation and death. Centrosomal amplification is a very dominant phenotype post viral infection in few of the instances documented till date. While we are now able to appreciate the strong connection of viruses with centrosomes still we do not know the extent of their involvement in regulating viral propagation or altering the host homeostasis needs to be probed in depth during the future course of our study.

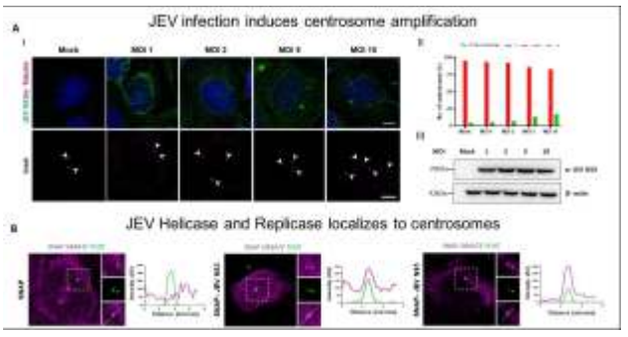


Figure 35. JEV infection involves host cell centrosome *(A) Confocal micrographs representing centrosome amplification 24 hpi in HeLa cell. (I) Three-color overlay of JEV (green), γ- tubulin (magenta) and nucleus (blue) are shown. Scale bar, 10 μm. Inset scale bar, 5 μm. (II) Quantification of percent cells with indicated number of centrosome in panel (I). (III) Western blot showing the expression of JEV NS3 and β- actin (loading control). (B) Confocal micrographs of SNAP alone or fused with JEV ns3 and ns5 (magenta) associating with centrosomes marked by PCNT (green). Scale bar, 5.5μm. Arrowheads in magnified inset points centrosomes. Line graph besides each panel represents the intensity profile of PCNT and SNAP tag.*

So far we have identified that JEV is capable of inducing centrosome amplification (Fig 35A) for the first time and also we have discovered the centrosome localization of both JEV helicase (ns3) and replicase (ns5) using the viral free screening system (Fig 35B). Currently we are trying to understand the mechanistic details of this localization and subsequently its functional impact over the host centrosomes. These

insights would be important milestones in the identification of novel targets to intervene JEV infection in future.

CHIKV infected host cell biology

Chikungunya virus (CHIKV) is a mosquito-transmitted alphavirus responsible for epidemic outbreaks in the recent past with no available vaccine or an effective antiviral till date. CHIKV causes debilitating musculoskeletal disorders in humans. Understanding the molecular interactions between the virus and host cell is necessary in identifying more promising viral and / or host directed therapeutic targets.

Up till now the effect of CHIKV infection on the centrosomes have not been previously characterized. Understanding the fact that no centriolar phenotypes are reported till date we started exploring their involvement at the subcellular level upon infection. For the first time ever, we observed that infection of human cell lines with CHIKV could lead to centrosome amplification which needs careful evaluation under all possible physiological state of the host cell (Fig 36A). Also we have documented the centrosomal association of CHIKV helicase, nsp2 (Fig 36B). Very recently we have discovered a pool of CHIKV Capsid protein to be incorporated into the nuclear membrane (Fig 36C) and this is expected to have some new roles beyond what is known. Our work provides new insights that would allow us to look at these subcellular structures like centrosome, cilia and nuclear envelope as a target for Chikungunya viral pathogenesis intervention.

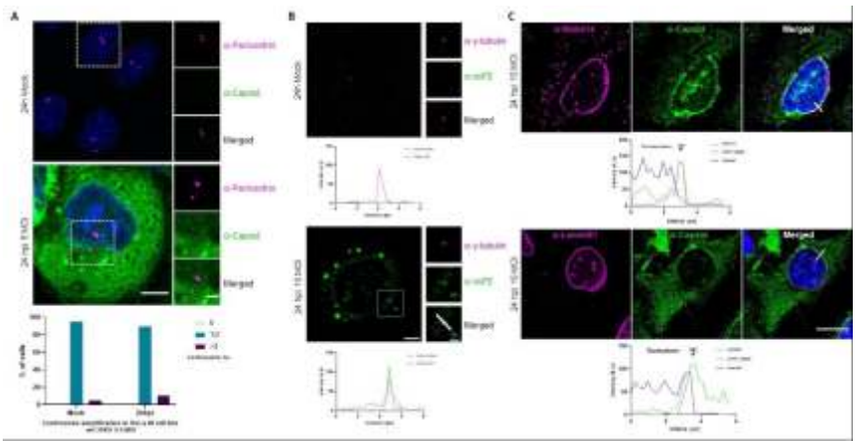


Figure 36. Phenotypes observed following CHIKV infection. *(A) CHIKV infection induces centrosome amplification in HeLa-M cell line 24 hpi. The number of centrosomes (pericentrin in magenta) were quantified and the graph was plotted below. Scale bar-20 µm, Inset Scale bar-5 µm. (B) CHIKV nsP2 localizes at the centrosome in HuH-7 cell line. Line profiles of fluorescence intensity at the centrosome is given below for γ-tubulin (magenta) and nsp2 (green). Scale bar-10 µm, Inset Scale bar-2 µm. (C) CHIKV Capsid protein localizes at the nuclear envelope in RPE-1 cells. Line profiles indicating capsid protein accumulation at the nuclear envelope with the indicated markers. Scale bar-10 µm.*

Put together we are interested in identifying the common host centrosome related phenotypes associated across RNA viruses if it exists. Further we are trying to understand the mechanism used by viruses to subvert these sub cellular structures to their own benefit ultimately. Likewise, the same is true to find out if this organelle is contributing towards host cell immunity against these mosquito borne viruses involved in our current research.

Agricultural Biotechnology

Courtesy: Sahil Kumar

Saikat Bhattacharjee
Principal Investigator

Lab Members

Shraddha Dahale
Krishnendu Goswami
Medha Noopor
Sandeep Kumar
Pinky Yadav
Komal Gupta
Ishana Bhattacharya
Ashruti Chitra
Gargi Ghosh
Priya Yadav
Priya Chaudhary
Pawan

Molecular mechanisms of signal transduction in innate immune responses of plants

Phytopathogenic effectors constantly manipulate plant responses that hinder pathogen colonization in the host. Evolution of an effector virulence activity also incorporates genetic changes that simultaneously attempt to evade effector-triggered immunity (ETI), elicited by the cognate resistance protein, in resistant plants. Using a class of rapidly evolving effectors from *Pseudomonas syringae* (*Ps*) pathovars that are differentially sensed across different plant systems, we are identifying their virulence activity, and the mode of immune activation when sensed in resistant plants. Immune sentinels deployed at strategic cellular locations couple to downstream signaling and defense-associated gene-expression networks. The molecular mechanistic of these signal transduction processes remains largely unknown. With versatile activities as signaling messengers, we are exploring the roles of selective inositol phosphates (InsPs) in the transduction of immunity. Lastly, as a part of an ongoing national biotechnological effort, we are characterizing anti-viral defense-promoting functions of natural, bio-safe and commercialized seaweed extracts (SWEs) on plants.

HopA1effectors do not directly bind mRNA-cap but interfere with the activity of eIF4E1

Ps encoded HopA1 effectors determine host-range and pathogenicity. In *A. thaliana*, *RESISTANT TO PSEUDOMONAS SYRINGAE6* (*RPS6*) gene confers ETI against $HopA1_{pss}$ derived from *Ps* pv. *syringae* strain 61 but not to $HopA1_{pst}$ from the tomato pathovar. These responsive differences between the two HopA1s represent a unique system to study pathogen adaptation skills and host-jumps. We recently reported that the expression of several *A. thaliana* resistance genes which under steady-state are regulated by alternative splicing (AS) and nonsense-mediated decay (NMD) pathway, are induced by $HopA1_{pss}$. The effector suppressed the polysome association of the defense transcripts and exhibited strong translational inhibition in *in vitro* reporter-expression assays. Moreover, $HopA1_{pss}$ interactome includes several *A. thaliana* proteins with functional implication in post-transcriptional regulation of transcripts. Taken together, these results implied that HopA1 attempts to suppress post-transcriptional events associated with PTI. A weak structural similarity of HopA1s ($HopA1_{pss}$ and $HopA1_{pst}$) to the eukaryotic translation initiation factor 4E1 (eIF4E) predicted previously, is not further explored. As a part of a multiprotein eIF4F aids the formation of translation initiation complex, and interacts with 5'-m^7G(5')ppp(5') (hereafter referred to as cap) of mRNAs to promote the assembly with ribosome subunits. To determine whether the two HopA1s harbour mRNA cap-binding efficacies, we first tested this activity using recombinant effectors and eIF4E1 as the positive control. Equimolar amounts of His-$HopA1_{pss}$, His-$HopA1_{pst}$, or His-eIF4E1 incubated with m^7-GTP-agarose enriched only His-eIF4E1 (Fig. 37A). When expressed transiently via Agrobacterium in *Nicotiana benthamiana* leaves, again Myc-eIF4E1, but not Myc-$HopA1_{pss}$ or Myc-$HopA1_{pss}$, was enriched with the m^7-GTP-agarose beads (Fig. 37B). Thus, HopA1s do not directly bind mRNA cap, and may affect other processes associated with this eIF4E1 role. To evaluate whether HopA1s instead interfere with eIF4E1 mRNA cap-binding propensity, we co-expressed Myc-$HopA1_{pss}$, or Myc-$HopA1_{pst}$ with HA-eIF4E1 and performed the cap-binding assay on plant

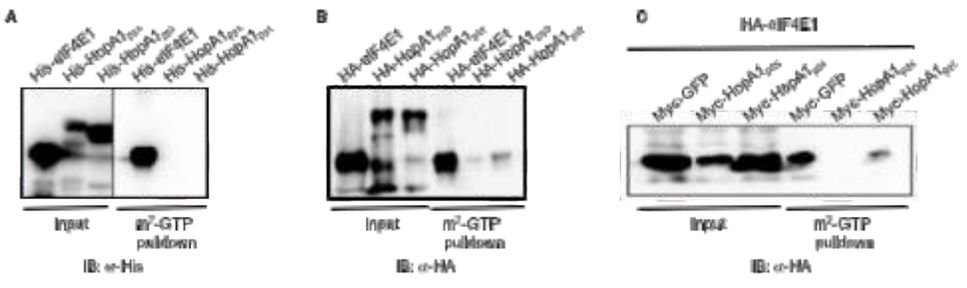


Figure 37: HopA1s do not bind mRNA M^7-GTP cap, but interfere with the cap-binding activity of eIF4E1. *(A) Enrichment of M^7-GTP cap-binding proteins from E. coli cells expressing His-eIF4E1, His-$HopA1_{pss}$, or His-$HopA1_{pst}$. (B) Enrichment of M^7-GTP cap-binding proteins from N. benthamiana leaves transiently expressing HA-eIF4E1, HA-$HopA1_{pss}$, or HA-$HopA1_{pst}$. (C) Enrichment of HA-eIF4E1 using m^7-GTP beads from N. benthamiana leaves co-expressing Myc-GFP, Myc-$HopA1_{pss}$, or Myc-$HopA1_{pst}$. The eluates were probed with the indicated antibodies.*

extracts, as earlier. Remarkably, both HopA1s, but not the Myc-GFP control, reduced the binding efficiency of HA-eIF4E1 to m^7-GTP-agarose beads (Fig. 1C). Considering that HopA1 co-enriched proteins are populated with known eIF4E1-interactors, these findings implied that HopA1 effectors interfere with eIF4E1 functions indirectly. Suppression of polysome loading of defense-associated transcripts in the presence of HopA1 is thus a likely consequence of this interference.

eIF4E1 genetically functions as a negative immune regulator and intercepts $HopA1_{pss}$

A modest reduction in total HA-eIF4E1 accumulation was noted when co-expressed with $HopA1_{pss}$ but not with $HopA1_{pst}$(Fig. 37C). Co-expression of AvrRps4, an unrelated but avirulent effector, did not change endogenous eIF4E1 levels (Fig. 38A). These results implied that plant surveillance specifically senses $HopA1_{pss}$-mediated perturbation on eIF4E1 functions and elicits immunity, whereas $HopA1_{pst}$ likely has evolved to evade or suppress these consequences. These additionally indicate that eIF4E1 may hence function as a negative immune regulator. To test this hypothesis, *eIF4E1* mutant (named as *cum1-1*) were evaluated for their defensive efficacies. Homozygous *cum1-1* plants displayed delayed bolting compared to Col-0 (Fig. 38B). Pathogen accumulation of virulent *Ps* pathovar tomato strain DC3000 (*PstDC3000*) was significantly lower in *cum1-1*, supporting eIF4E1 role as a negative immune regulator (Fig. 38C). In the complemented lines expressing CaMV 35S promoter-driven HA-epitope-tagged eIF4E1 cDNA (*HA-eIF4E1/cum1-1*), delayed bolting observed for the parent *cum1-1* was abolished, implying functional complementation by the expressed transgene (Fig. 38B). To test whether increased expression of positive defense modulators enhanced defenses in *cum1-1*, basal levels of several defense-associated proteins were evaluated via immunoblots. Interestingly, accumulation of PATHOGENESIS-RELATED 1 and 2 (PR1/PR2), and the resistance protein SUPPRESSOR of NPR1-CONSTITUTIVE 1 (SNC1) were higher in *cum1-1* than Col-0 (Fig. 38D). The complemented *HA-eIF4E1/cum1-1* lines displayed Col-0-comparable levels of the above tested immune-related proteins. Taken together, our investigations suggested that eIF4E1 suppresses defense, and when perturbed by activities of effectors such as $HopA1_{pss}$, leads to elicitation of ETI in resistant plants. Consolidated, our investigations have identified promising node of HopA1 virulence in post-transcriptional regulation of defense-associated transcripts, and have revealed a novel mode of immune surveillance that intercepts effector-mediated manipulation of plant processes.

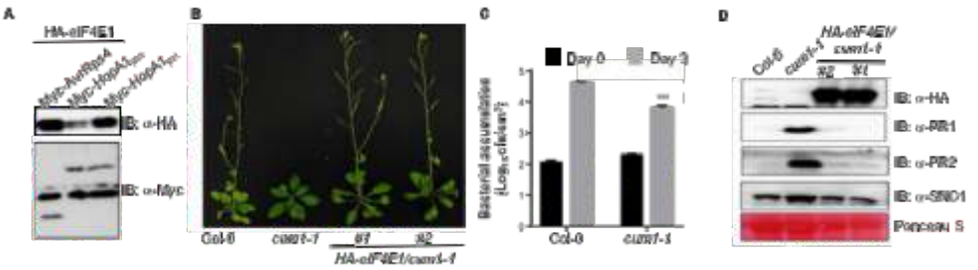


Figure 38: Expression of $HopA1_{pss}$, but not $HopA1_{pst}$, destabilize eIF4E1 to elicit ETI. *(A) Accumulation of HA-eIF4E1 in N. benthamiana leaves co-expressing Myc-AvrRps4, Myc-$HopA1_{pss}$, or Myc-$HopA1_{pst}$. (B) Plant phenotypes of wild-type (Col-0), eIF4E1 mutant (cum1-1), and complemented lines (HA-eIF4E1/cum1-1). (C) PstDC3000 accumulation in Col-0 versus cum1-1 plants. Statistical analysis is according to Student's t-test (*** p<0.0001). (D) Basal levels of defense-associated proteins PR1, PR2, and SNC1 in Col-0, cum1-1, and complemented lines. Immunoblots were performed with the indicated antibodies.*

Divya Chandran
Principal Investigator

Lab Members

Naini Burman
Babitha K C
Ankita Alexander
Kesiraju Karthik
Chetan Chauhan
Arunima Gupta
Akriti Sharma
Debashish Sahu
Poonam Ray
Abhilash K V
Gulshan Thakur
Rabishankar Ohja
Ankita Verma
Meghna Dhar

Investigations into the molecular mechanisms underlying legume-powdery mildew interactions

Powdery mildews (PM) are biotrophic fungal pathogens that cause substantial yield losses in grain and forage legumes, such as pea, lentil, and Medicago. Our research program aims to identify molecular targets for PM disease management in legume crops. Specifically, we study the molecular interplay between the pea PM pathogen *Erysiphe pisi* and two legume hosts, *Medicago truncatula* and *Pisum sativum* (pea), to identify host resistance/susceptibility factors and pathogen virulence determinants that significantly impact disease development.

Changes in host nuclear and actin dynamics precede fungal ingress during compatible pea powdery mildew interactions

Proper nuclear positioning in plant cells, a process regulated by the cytoskeleton, is crucial for developmental processes and response to (a)biotic stimuli. Notably, cytoskeletal rearrangements, which are one of the earliest cellular responses to pathogen invasion, impact pathogen penetration efficiency. Yet, the connection between host nuclear movement and fungal ingress is still elusive, particularly in legumes.

Our investigations on host nuclear dynamics during compatible pea-PM interactions show that the host nucleus moves towards the initial site of PM penetration and associates with the newly developed primary haustorium, the key fungal structure that enables host colonization. However, the nucleus migrates away from the primary infection site as the infection progresses toward colony expansion and sporulation. Treatment of pea leaves with an actin polymerization inhibitor abolished host nuclear movement towards the fungal penetration site and restricted PM growth. In contrast, treatment with a microtubule-polymerization inhibitor had no effect. In addition to nuclear movement, host actin filaments strongly polarized towards the site of initial fungal contact at early infection stages. Collectively, our results suggest that actin polarization mediates host nuclear movement to the fungal penetration site and facilitates successful colonization during compatible pea-PM interactions [Fig. 39; *Sharma & Chandran Planta 2022*].

Inner nuclear envelope SUN protein regulates nuclear morphology, pathogen-induced nuclear movement, and PM resistance in pea

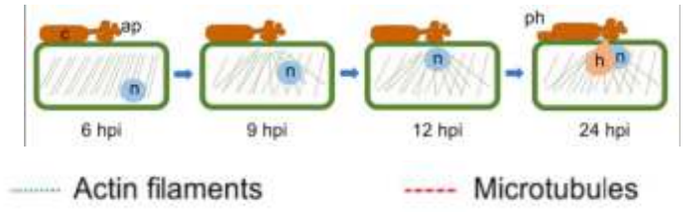


Figure 39: Proposed model showing actin-dependent migration of the pea nucleus towards the site of PM penetration and its close association with the primary haustorium during early infection stages. *ap, appressorium; c, conidium; h, haustorium; hpi, hours post-inoculation; ph, primary hypha*

The nuclear-envelope bridging LINC (Linkers of Nucleoskeleton and Cytoskeleton) complexes, composed of inner and outer nuclear membrane proteins, regulate nuclear movement in plants during developmental events and symbiotic interactions. The C-terminal type inner nuclear membrane SUN proteins form an integral component of LINC complexes and are broadly conserved in opisthokont and plants. Therefore, we investigated whether the C-terminal SUN proteins play a role in PM-induced host nuclear movement.

Pea has a single C-terminal SUN nuclear envelope protein (Fig. 40). *PsSUN* is weakly induced during the early stages of PM infection with transcript levels increasing ~1.5 to 2-fold at 24 hpi and returning to basal levels by 72 hpi. Transient knockdown (KD) of *PsSUN* produces nuclei with increased circularity and sphericity, an established phenotype of plants with low SUN levels. *PsSUN* KD also impairs host nuclear movement towards the site of fungal penetration, resulting in fewer conidia with a primary haustorium at 24 hpi. However, colony formation at 72 hpi is not significantly impacted, indicating that primary haustorium formation is delayed but not abolished on *PsSUN* KD. Further, the expression of key defense genes is not perturbed on *PsSUN* KD, indicating that the PM resistance phenotype is not a consequence of enhanced host immunity.

For additional functional insights into PsSUN, we generated *PsSUN* overexpressing (OE) transgenics in Arabidopsis. *PsSUN*-OE lines display altered nuclear morphology with reduced nuclear sphericity and deformed nuclear envelope. Basal levels of several defense-related genes, particularly those involved in salicylic acid signaling, are significantly higher in the *PsSUN*-OE lines compared to empty vector control plants. Additionally, *PsSUN*-OE lines exhibit elevated salicylic acid levels and enhanced bacterial resistance compared to control plants.

Taken together, our results suggest that PsSUN may promote fungal colonization during the early stages of legume-PM interactions by regulating host nuclear movement, and consequently, primary haustorium development. However, SUN expression appears to be tightly regulated during plant-PM interactions as high levels of the SUN protein lead to a hyperactive immune response. Whether the specific transcriptional changes induced by SUN dysregulation are a consequence of altered chromatin organization is a question we are currently investigating.

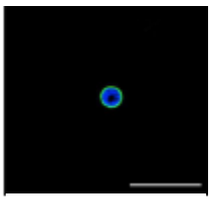


Figure 40: *PsSUN is a nuclear membrane protein. PsSUN-GFP fusion protein (green) localizes to the nuclear membrane when transiently expressed in Nicotiana benthamiana leaves. The nucleus (blue) is stained with DAPI. Scale bar, 20 µm*

Functional characterization of HY5 homolog in rice

Light is an important environmental signal which is perceived by plants to adapt to ambient conditions. Photoreceptors perceive the light signal and pass it on to master regulators, which in turn, bring about changes in downstream components, leading to changes in gene expression. One of these master transcriptional regulators is HY5 and three HY5 orthologs were identified in rice based on the presence of COP1-binding and bZIP domains. One ortholog, OsbZIP48, is known to form heterodimers with other bZIPs, transcription factors involved in a wide variety of plant growth and development pathways. *In silico* analysis identified ~18 bZIPs transcription factors and their interaction with OsbZIP48 was checked using BiFC. The promoters of selected bZIPs were scanned for HY5 binding sites and surprisingly almost all were found to harbor light regulatory elements. The majority of the selected bZIPs interact with OsbZIP48 and OsbZIP48 also binds to their promoters indicating that OsbZIP48 regulates these transcription factors via protein-protein interaction and transcriptional control.

Dr. Naini Burman
DST Inspire Faculty

Modulation of stomatal aperture regulating genes to improve carbon gain and crop yield

Plants adapt to drought by synthesizing the ABA hormone, which not only limits water loss through stomatal regulation but also induces the synthesis of osmoprotectants and ROS scavengers. The dehydration control by stomatal regulation usually limits the uptake of CO_2, and thus, growth and productivity. We aim to minimize ABA-induced stomatal closure without affecting ABA-regulated cellular tolerance mechanisms to improve carbon gain under moderate stress conditions by targeting genes encoding anion channels ALMT12 (Aluminium-activated malate transporter) and SLAC1 (Slow anion channel-associated 1) using CRISPR-Cas9 approach and chemical genomics in rice. Genome-edited plants in rice targeting ALMT12 and SLAC1 were developed and small molecule inhibitors for these genes were identified by protein docking studies. Cowpea, green gram, wheat, and rice treated with small molecules showed robust plant growth, larger stomatal openings, higher photosynthesis, and improved yield. Arabidopsis guard cell transcriptomics identified two E3 ligases with a role in stomatal regulation.

Dr. Babitha K.C.
DBT Women BioCARe Awardee

Ramu S Vemanna
Principal Investigator

Lab Members

Akashata Dawane
Garima Pal
Shobhna Yadav
Libin Thomas
Kishan Gurjar
Shankar Mavinamar

Functional genomics and crop improvement for stress adaptation

Plants are exposed to multiple stresses in field conditions, such as drought and bacterial infection by *Xanthomonas oryzae* pv. *oryzae (Xoo)*, that affect productivity. To maintain cellular homeostasis and disease resistance, the negative regulators of plant growth and defence need to be modulated to realize the potential yields of plants during stress. Our emphasis is on developing stress-mitigating strategies to protect plants from biotic and abiotic stresses. We aim to identify small molecules targeting plant stress-responsive genes, especially negative regulators, and characterize their functional relevance to improve plant health and sustain nutritional quality and yield.

Small molecules to improve plant processes under drought condition

Drought induces the accumulation of Abscisic acid (ABA), reactive oxygen species (ROS), reactive carbonyl compounds (RCC), etc., which affects plant metabolic reactions. Under drought, maintaining plant-water relations is very important to sustain metabolic activities and productivity. Several transcription factors have been identified to play important role in drought stress as positive and negative regulators of many target genes. The negative regulators have emerged as candidate target genes for gene editing or by inhibiting their role using small chemical compounds. We have identified DREB2A and bZIP23 from rice seedlings exposed to oxidative stress. The structure-assisted drug designing approach is used to design small molecules targeting these proteins. The 3D protein structures of OsDREB2A and OsbZIP23 were predicted and using the DNA binding domain of the transcription factors virtual screening was performed in the Schrodinger tool with the ZINC chemical library. The molecules Pronetalol (binding to OsDREB2A), serotonin and indolyl-ethyl amine (IEA) (binding with OsbZIP23) were identified and custom synthesized. To test the efficacy of the small molecules, a robust oxidative stress-mediated screening platform was developed. Rice seedlings exposed to methyl viologen (MV) induced oxidative stress treated with pronetalol, showed susceptible phenotype (Fig. 41A-D). Pronetalol inhibited the DREB2A transcription factor activity and suppressed the expression of its target genes *LEA7* and *HSF-A3* (Fig. 41E). The results demonstrate that small molecules could effectively inhibit the transcription factor activity.

We targeted OsbZIP23 which regulates the ABA biosynthesis and signaling genes and improves drought tolerance, however, it reduces seed germination and productivity. The small molecules serotonin and IEA inhibit OsbZIP23 transcription factor activity (Fig. 41F-H) and enhanced seed germination in rice, wheat and soybean. The inhibition of OsbZIP23 by these small molecules reduced the expression of *NCED4* involved in ABA biosynthesis and *PP2C49* involved in signaling. The exogenous application of small molecules to rice leaves showed enhanced water loss indicating reduced ABA levels (Fig. 41I). The drought-exposed rice plants sprayed with serotonin or IEA molecules showed increased stomatal conductance and photosynthesis which resulted in higher spikelet fertility and yield under mild drought conditions (Fig. 41J-L). Our results demonstrate that serotonin and IEA small molecules have the

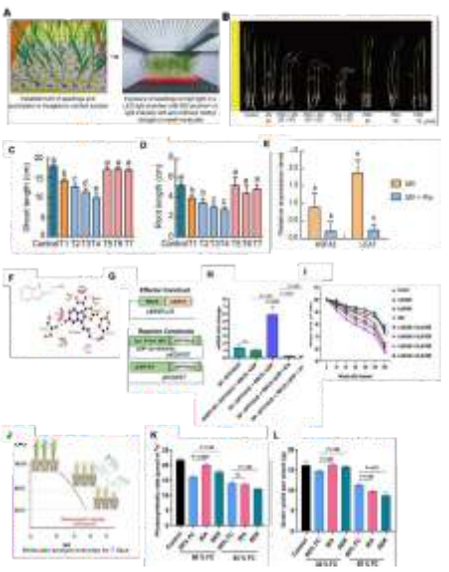


Figure 41: Responses of rice seedlings treated with small molecules. *(A) Seedlings exposed to high light (B) Seedling growth at different concentrations of pronetalol (C-D) Shoot and root growth (E) Expression of DREB2A target genes (F) bZIP23 protein and small molecule structures (G) Effector and reporter constructs (H) Relative expression of GFP/GUS gene (I) Water loss from rice leaves sprayed with molecules (J) Drought stress at flowering stage (K) Photosynthesis rate (L) grain yield*

potential to improve yields under mild drought stress conditions.

Double-stranded RNAs (dsRNAs) to target plant genes regulating growth and disease resistance traits

To maintain cellular homeostasis and disease resistance, the negative regulators of plant growth and defence need to be modulated to realize the potential yields of plants during stress. Conventionally, the susceptible genes were downregulated by virus-induced gene silencing (VIGS), or RNA interference (RNAi) technology, however, it involves technical expertise and regulatory issues concerning transgenes that hinders their use in agricultural application. We have targeted plant endogenous genes using foliar application and root uptake of dsRNA to modulate the plant processes. In plant cells, dsRNAs are processed in the nucleus as siRNAs, subsequently along with argonaute protein and RISC, the target genes are silenced. The major limitation is the highly unstable nature of dsRNAs. Therefore, we have used cationic nano polymers which help in maintaining dsRNA stability for efficient delivery into the plant cells. The results suggest that dsRNAs could be encapsulated by polymer and the complexes are stable at high temperature, and different pH up to several days (Fig. 42A). The systemic movement and root uptake were detected through labelled polymer. Polymer does not show any toxicity on rice seedlings as germination rate, shoot and root length were similar to control seedlings. Naked dsRNA and dsRNA-polymer complex could effectively downregulate *GFP* transgene in Arabidopsis plants, however, dsRNA-polymer showed prolonged effect in silencing the gene (Fig. 42B). The *Flowering Locus T (FT)* and *Phytochrome Interacting Factor* 4 (*PIF4*) in Arabidopsis were silenced using dsRNA to delay the flowering and plants showed more biomass (Fig. 42C-F). Rice plants in which root uptake of dsRNA was tested by targeting the *Phytoene desaturase* (*PDS*) gene showed photobleaching or yellowing of leaves and stunted growth (Fig. 42G). The effect of dsRNA was tested on rice disease susceptible genes *SDIR1 (Salt and Drought-induced ring box 1)* and *SWEET14 (Sugar Will Eventually be Exported Transporter)* through foliar application (Fig. 42H-K). The dsRNAs could effectively downregulate the genes and improve resistance against bacterial leaf blight (BLB) causing *Xanthomonas oryzae pv. oryzae (Xoo).*

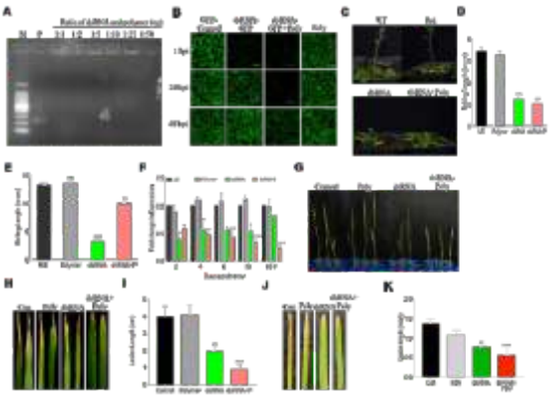


Figure 42: Delivery of dsRNA to target plant genes. *(A) Complex of dsRNA:TAC6 Polymer on agarose gel (B) Confocal images showing GFP in dsRNA-treated plants. (C) FT gene targeted by dsRNA (D) Bolting length (E) PIF4 targeted plants showing bolting length (F) Expression of PIF4 in dsRNA treated plants (G) Dwarf and albino phenotype of PDS targeted rice seedlings (H) BLB symptoms on TN1 rice leaves targeting SDIR1 (I) Lesion length (J) BLB symptoms on SWEET14 targeted plants (K) Lesion length*

Prashant Mohan Pawar
Principal Investigator

Lab Members

Lavi Rastogi
Deepika
Manju Singh
Rajan Kumar Sah
Bhagwat Dewangan
Arunima Gupta
Apurva Gangal
Navdeep Kaur
Rahul Kumar
Shouvik Das

Understanding the role of GELP family in polysaccharide acetylation

Our research group focuses on understanding the molecular mechanism of plant cell wall biosynthesis and exploring novel ways of altering its wall structure for effective conversion to value-added products. One of the critical factors which play a vital role in wall assembly and disintegration is acetyl groups, substituted on polysaccharide backbone or side chain. Finetuning the level of polysaccharide acetylation increases the digestibility potential of hydrolytic enzymes and fermentation of plant lignocellulosic biomass. Our group is interested in identifying plant and microbial polysaccharide esterases and exploiting them to redesign cell walls for different bioenergy applications.

Characterization of GELP family in plants

Glucuronoacetylated xylan (GAcX) is one of the most abundant polysaccharides present on the earth. GAcX backbone consists of β (1,4) linked xylose residue and is substituted with glucuronic acid and acetyl groups. These groups allow limited hydrolysis of xylan to xylan degrading enzymes. Moreover, xylan itself or through these groups interact with cellulose and lignin, which are the main components of the cell wall. Disrupting the xylan acetylation also destabilises the xylan and wall component's interaction. Therefore, understanding xylan acetylation is necessary to understand the complexity of plant cell walls. Xylan is acetylated in the Golgi membrane and transported to the apoplastic space via vesicles. The acetylation level is regulated in both Golgi and cell walls, and esterase plays a vital role in determining its level. In this study, we are exploring the role of the GDSL esterase/lipase (GELP) family in maintaining polysaccharide acetylation.

In plants, GDSL esterases/lipases represent a large gene family encoding more than 100 members in Rice and *Arabidopsis thaliana*. Plant GDSL esterases/lipases contain five conserved domains and four amino acid residues in their catalytic region that are involved in catalysis. Because of these four conserved amino acids i.e., S, G, N, H, GDSL esterases/lipases or GELP, are also called SGNH lipases. Some gene members of this family are widely expressed in different developmental stages of plant growth, and others are expressed in specific tissues or developmental stages. So far, very few gene members of this family have been fully characterized in plants; therefore, there is still much to investigate regarding the plant GELP family having either lipase or esterase function. They play crucial roles in plants' biochemical and physiological processes, such as in plant growth and development, lipid metabolism, and biotic and abiotic stresses. Based on bioinformatics analysis, we have identified 12 GDSL genes, which are further categorized into four groups (Groups 1-4) based on sequence similarity (Fig. 43).

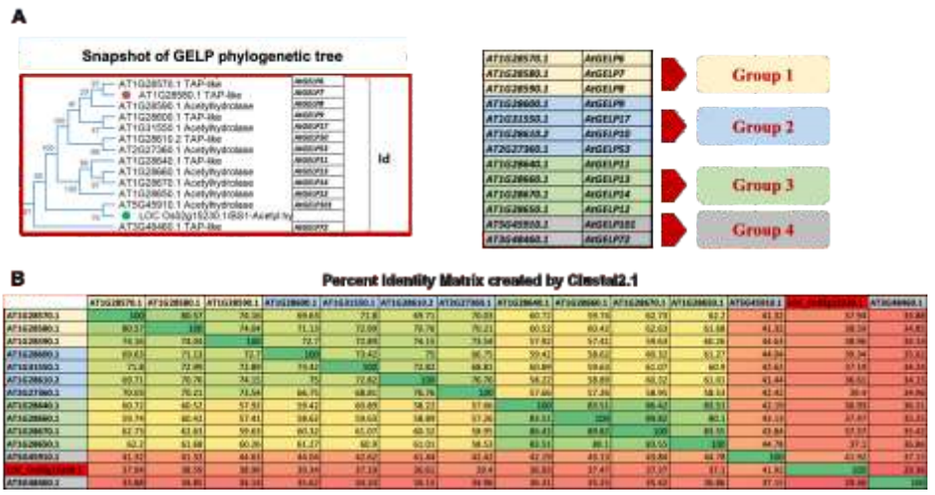


Figure 43: Bioinformatics analysis GDSL lipase/esterase or GELP family *(A) Snapshot of phylogenetic tree showing GELP family clade Id generated by MEGA5 with 1000 bootstrap and divided them into groups based phylogenetic tree (B) Identity matrix generated for clade Id (13 genes) of GELP family as compared to rice Os02g15230/BS1 by clustalw method.*

To further understand the role of these 12 GDSLs, we generated transgenic Arabidopsis lines expressing MYB46 transcription factor which regulates gene expression of cell wall biosynthetic genes. All five independent MYB46 lines showed more expression than wild type plants. Overexpression - 2 (OE) was a highly expressed line among all with five-fold expression, followed by OE-3 and OE-5 with approximately three-fold expression. All MYB46 OE lines look like wild type plants. We found that PAL2 expression was elevated in OE-2 and OE-5 lines, which was correlating with previous findings (Data not shown). We tested the expression of selected genes from clade Id and Ic. We did not see any change in *At2G27360 (AtGELP53), At1G28670 (AtGELP14), At1G28570 (AtGELP6), At5G45910 (AtGELP10)*, and *At1G09390 (AtGELP2*). But we found that *At1G28580* or *AtGELP7* expression was increased by 55-fold in both MYB46 OE lines (Fig. 2). This suggests that AtGELP7 is likely to function in cell wall biosynthesis. To further validate this, we generated independent transgenic lines overexpressing *At*GELP7. We found these lines showed an elevated level of acetyl xylan esterase expression in stem tissue. Therefore, we tested polysaccharide acetylation in the stem and it was decreased by 14% in all transgenic lines as compared to wild type. Fourier transform Infrared spectroscopy (FTIR) analysis further confirmed that acetyl to xylan linkages were reduced in transgenic lines confirming that *At*GELP7 is a polysaccharide esterase (Fig. 44).

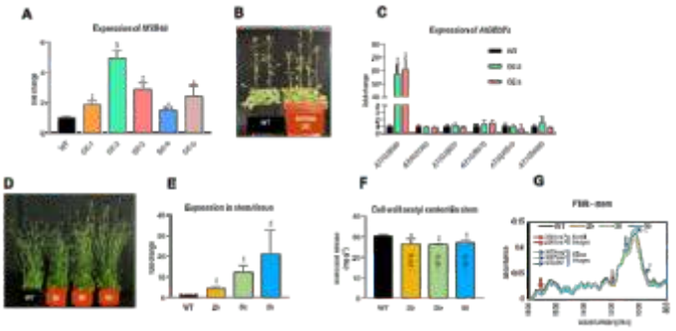
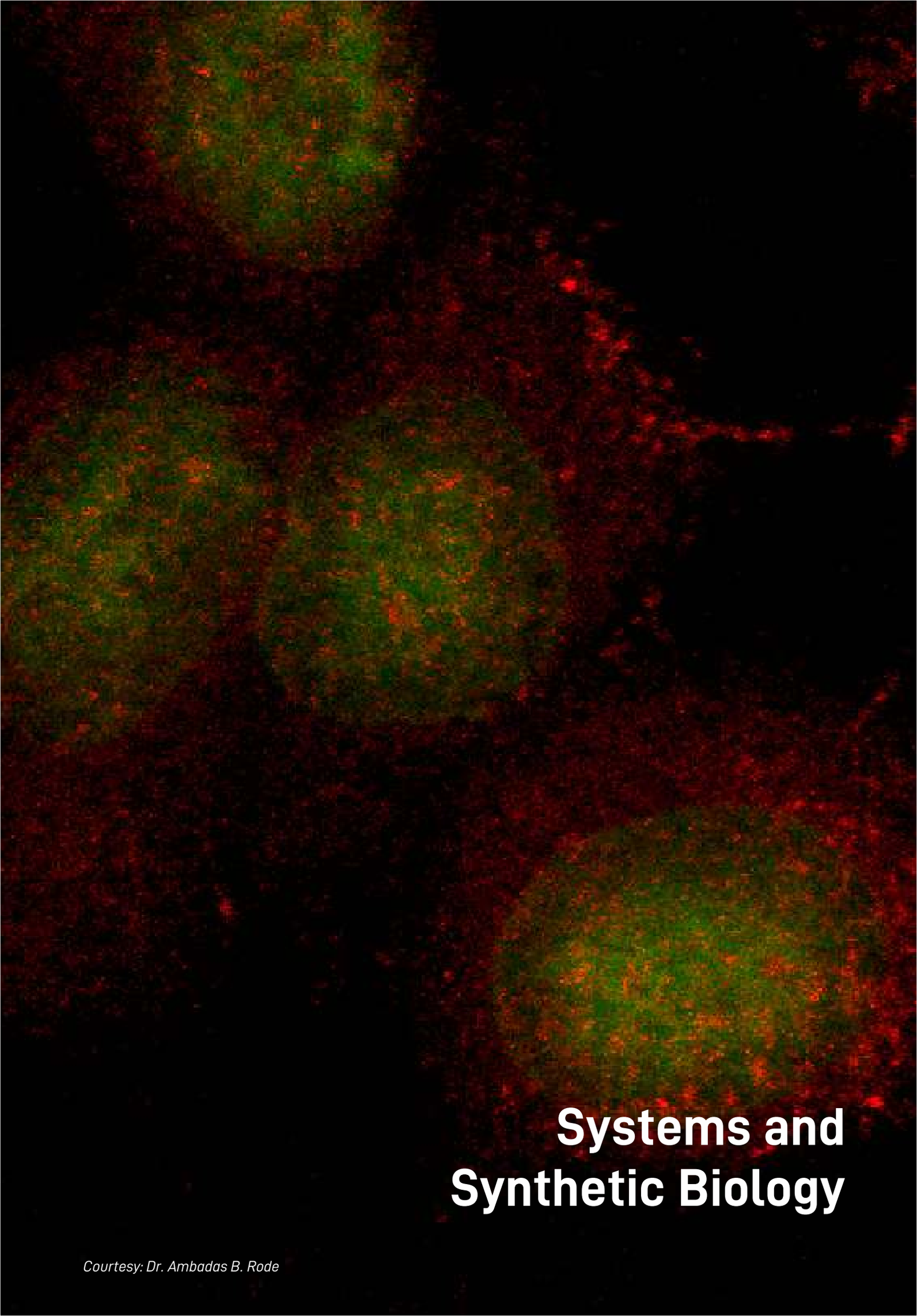


Figure 44: Characterization of MYB46 and AtGELP7 lines. *(A) Expression of MYB46 in overexpressing (OE) transgenic lines (B) Representative picture of WT and MYB46 (C) Expression of GELPs MYB46 OE lines (D) Picture of WT and transgenic lines expressing AtGELP7 (E) Expression of GELP7 gene in stem tissue (F) Acetyl content (G) FT-IR spectra represents acetyl and xylose linkages in the cell wall. Data represents mean ± SE, n = 3-4 biological replicates, Student's t-test at **p ≤ 0.05, *p ≤ 0.1.*

An integrated molecular genomic approach to unveil genomic and epigenetic complexity of adaptive traits, like flowering time, seed size and plant cell wall trait in mungbean

Mungbean (*Vigna radiata* (L.) R. Wilczek) is a warm-season legume (2n=2x=22) native to India and Central Asia. The adaptive traits like flowering time, seed size and plant cell wall composition vary with changing climates and follow a quantitative inheritance pattern. Our aim is to decipher complex genetic inheritance patterns of these traits. Therefore, we performed a genome-wide association study (GWAS) in a 144 mungbean association panel which led to identifying candidate genes regulating seed size by controlling amyloplast division and starch synthesis. Moreover, the diversity of plant cell wall composition has been analysed by FTIR and chemical methods in the mungbean association panel. GWAS resulted in the identification of cell wall-associated genes and we are currently doing functional characterization of these mungbean genes.



Systems and Synthetic Biology

Courtesy: Dr. Ambadas B. Rode

Rajendra P Roy
Principal Investigator

Lab Member

Sumit Murmu
K Shampathkumar

Peptide Ligation and Protein Semisynthesis

We are interested in developing chemoenzymatic strategies for protein semi-synthesis to generate synergy in protein engineering with a view to facilitate protein labeling and bioconjugation for addressing questions in mechanistic biology and biotechnology. In recent years, the transpeptidase sortase of *Staphylococcus aureus* (SrtA) has been found extremely useful in this endeavor. However, new sortases (natural or engineered) with disparate/ orthogonal substrate specificity are needed to expand the sortase toolkit.

Sortase enzymes present in the Gram-positive bacteria link the surface proteins containing LPXTG type of sequence to the pentaglycine branch of the peptidoglycan leading to covalent anchoring of proteins to the cell wall. SrtA-catalyzed ligation of the recombinant or synthetic LPXTG polypeptide to an aminoglycine derivatized moiety occurs efficiently *in vitro* and has inspired numerous applications.

Engineering specific chemical marks in histones

The installation and erasure of epigenetic marks on chromatin serves as a fascinating regulatory mechanism for chromatin associated processes. Biochemical interrogation of histone PTMs is a formidable challenge owing to the lack of defined modified histones. Therefore, well-defined engineered histones carrying specific marks are necessary for probing the individual and cooperative contribution of modifications to the overall epigenetic regulatory mechanism.

The acetyl mark on specific Lys residues of histones are installed by the action of histone acetyl transferases (HATs) are erased by histone deacetylases (HDACs). There are 18 human HDACs (including Sirtuins). The site-specificity of HDACs for histones is largely unknown. In previous years, we assembled two well-defined semisynthetic acetylated histones with a view to delineate the specific eraser(s) of acetyl mark at Lys-5 in H2B and Lys-4 in H3. Toward this, acetyl modification at the designated site (H2BK5Ac and H3K4Ac), were assembled by a peptide ligation reaction catalyzed by the transpeptidase sortase. The site-specific deacetylation of histones was ascertained with lysates prepared from individual HDACs overexpressed in HEK 293 cells and purified recombinant HDACs, both in isolation as well as in assembled nucleosomes nested with modified histones.

The in vitro deacetylation assays revealed HDAC1 as the prime eraser of H2BK5Ac. In order to establish the selectivity of HDAC1 in the cellular context, HEK293 cells were treated with siRNAs targeting HDAC1 specifically. As a control similar treatment was performed using siRNAs targeting GFP and then probed the corresponding cell lysate for the knockdown status of HDAC1 as well as the H2BK5 acetylation levels upon siRNA treatment. In parallel H3K56Ac mark, which is a known target of HDAC1, was also compared across these samples as a positive control. The acetylation signal was found to be significantly increased for both H2BK5Ac and H3K56Ac marks in the sample that was treatead with si-HDAC1 compared to control while the HDAC1 immunoblot analysis revealed nearly 80% knockdown in the treated lysate compared to control. In a similar way, HEK293 cells were treated with either pyroxamide or tichostatin which is a pan-class I and II HDAC inhibitor, and their acetylation status was compared with respect to the DMSO treated control. Here again H2BK5Ac levels were found to be enhanced in both the treated lanes. The same was also tested on a previously reported histone target of HDAC1 namely, H3K56Ac. The acetylation signal was markedly enhanced in both the treated lanes compared to DMSO control while the total HDAC1 levels remained unaltered across all treatments. Together, the catalytic inhibition was sufficient to confirm the specificity of HDAC1 towards H2BK5Ac in the cellular context. Thus, these observations unambiguously establish HDAC1 as a *bona fide* eraser of H2BK5 acetyl mark. The delineation of HDAC specificity for H3K4Ac is in progress.

Probing the altered specificity of a new class E sortase

The study of enigmatic substrate recognition propensity of the Class E sortase from *Thermobifida fusca* namely, TfSrtE, remained the continued focus of our work. As reported earlier, the 64-residues N-terminal truncated catalytic domain, referred to as Δ64TfSrtE, preferred LAXTG pentapeptide substrates as against the canonical LPXTG substrates. This substrate discrimination by Δ64TfSrtE was found to be dictated by a critical Tyr residue (Tyr222) present in the vicinity of the catalytic cleft. Interestingly, Tyr222 mutants displayed disparate substrate preference and catalytic behaviour. Attempts to crystallize Δ64TfSrtE was not successful. However, a further truncated version namely, Δ90TfSrtE yielded diffraction quality crystal.

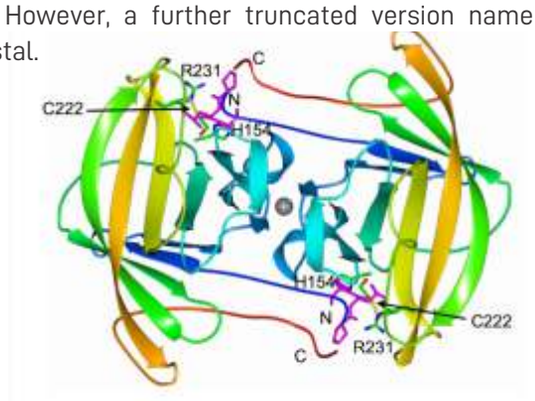


Figure 49. Structural features of SrtE from Thermobifida fusca (TfuSrtE). *Ribbon diagram of the two TfSrtEΔ_{N90} molecules in asymmetric unit in blend through colour (N-terminal in blue and C-terminal in red). A metal ion at the centre of two molecules (in the sphere) and conserved Arg-Cys-His triad (in sticks) are shown. The PLP peptide is shown in violet.*

The crystal structure of Δ90TfSrtE comprises of two protomers in the asymmetric unit, and each of these displays a conserved sortase β-barrel fold. Interestingly, N-and C-termini are in close proximity and point toward the active site cleft of adjacent molecules in the asymmetric unit (Fig. 49). The two molecules in the asymmetric unit are also stabilized by a metal ion. The conserved catalytic triad (His, Cys, and Arg) residues are seen at the top of the β-barrel as observed in the sortase family of enzymes. Curiously, the active site in each protomer is occupied by a tripeptide sequence (Pro92-Leu93-Pro94) coming from the N-terminal region from the other molecule. In the tripeptide, residue Pro92 points away from the active site while Leu93 and Pro94 point towards the active site. The PLP tripeptide is stabilized by numerous hydrophobic contacts: Side chains of Leu93 and Pro94 form contacts with several hydrophobic residues. Interestingly, the active site arginine residue (Arg231) holds the carbonyl oxygen from Pro92 and Leu93 of PLP tripeptide which likely mimics a portion of the LPXTG sorting motif. The presence of the PLP peptide, although fortuitous, may serve as a fount for the analyses of sortase-substrate interactions in TfSrtE. Accordingly, Pro94 has been mutated to Ala to observe a LAXTG mimic (PLA akin to PLP) bound to the active site of Δ90TfSrtE. Contemporaneous with this, double mutants of Y128F/A, P94A have also been created. The crystal structure of wild type Δ90TfSrtE together with the above

Ambadas B Rode
Principal Investigator

Lab Members
Payal Gupta
Rushikesh M. Khadake
Krushna Shinde
Divya Ojha
Shounak Panja
Manisha Devi

Molecular Engineering of Functional Nucleic Acids for Biomedical and Biotechnological Applications

Our research focuses on harnessing the nucleic acids structure-mediated gene regulation in humans and bacteria for biomedical applications. The propensity of nucleic acids to control cellular processes not only relies on their base-pair identities but also on the inherent ability to form tertiary structures such as triplexes, G-quadruplexes and riboswitches, etc. These structures are diverse and are involved in a remarkably broad spectrum of biological processes, from gene expression to genome maintenance. Thus, these structures gained attention as therapeutic targets. Besides this, the modular nature of nucleic acid structures makes it a promising synthetic biology tool. We are developing synthetic riboswitches for conditional and spatiotemporal gene regulation for diverse applications. We also aim to design and synthesize novel synthetic molecules to target Hairpin-G-quadruplex (Hp-GQ) conformational equilibria for anticancer therapy.

Rational reengineering of riboswitches for precise control of gene expression and its applications

Synthetic riboswitches have emerged as a promising synthetic biology tool for their applications in biotechnology, medicine and environmental protection. Riboswitches have several interesting features that inspired researchers to develop synthetic riboswitches based on the functional mechanism of natural riboswitches. Synthetic riboswitches have the potential to reprogram bacteria and human cellular functions for therapeutic and synthetic biology applications. Like their natural counterparts, the synthetic riboswitches are triggered in response to a specific inducer molecule. The key feature of synthetic riboswitch-based gene regulation systems is that they are conditional, thus useful for diverse biomedical applications. The aptamer domain that recognizes the specific ligand is indispensable for the function of both natural as well as synthetic riboswitches.

Despite the promise, one of the biggest hurdles while using these synthetic riboswitches for *in vivo* applications is the unsuitability of the existing aptamer domains and their regulatory ligands. Majorly RNA aptamers have been selected *in vitro* using an iterative process called systematic evolution of ligands by exponential enrichment (SELEX). Although the SELEX method generates aptamer domains with high binding affinity for the chosen ligand, these aptamers have some limitations to use in constructing synthetic riboswitches. To date, several aptamers have been selected by SELEX, however due to limitation only three aptamers i.e., theophylline, neomycin and tetracycline aptamers are mostly used for *in vitro* applications but these are also found unsuitable for *in vivo* applications due to its toxicity and

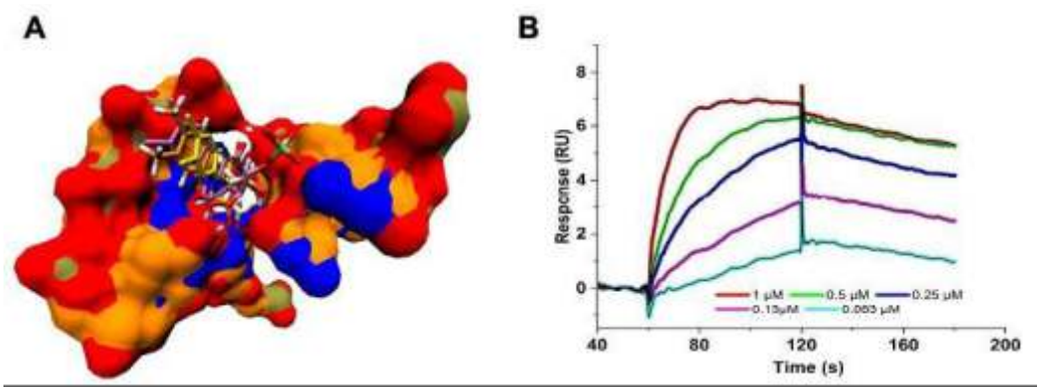


Figure 45: *(A) Docking pose showing binding of synthetic ligands with reengineered riboswitch aptamer domain (B) Representative SPR sensorgram illustrating riboswitch aptamer-ligand binding in a concentration-dependent manner as shown in Red (1 μM), Green (0.5 μM), Blue (0.25 μM), Magenta (0.13 μM), Cyan (0.063 μM) color*

poor cell permeability.

An alternative approach, which has been little explored to date, would be to reengineer existing natural riboswitches. A major problem in using natural riboswitches without reengineering is that the ligands for natural riboswitches are typically metabolites ordinarily present at varying levels in the cell, which severely limits their applicability as generic small-molecule responsive expression systems. To overcome these limitations, in this project, we aim to develop new orthogonal riboswitches through further genetic manipulation and by developing new and more effective synthetic ligands which will allow more precise and dynamic control of gene expression. We used a structure-based molecule design strategy to design novel molecules that can bind to selected riboswitches similar to their cognate ligands. Based on the computational docking results, we have selected the compounds with good docking scores (Fig. 45A) for chemical synthesis. We have synthesized a series of synthetic analogs, purified and then characterized them by using Nuclear Magnetic Resonar

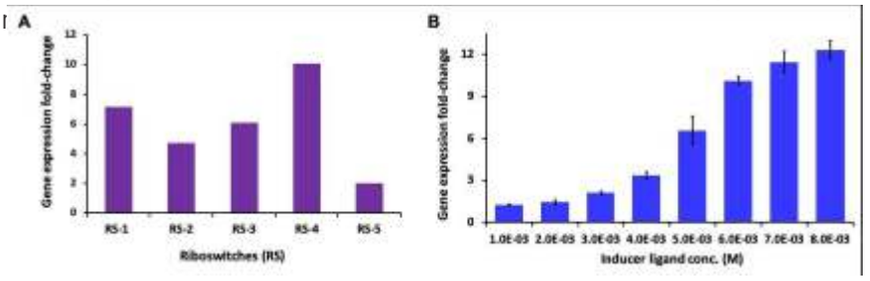


Figure 46: *(A) Functional screening of representative reengineered riboswitches in E. coli (B) The effect of inducer ligand concentration on riboswitch-mediated induction in GFP expression in E. coli.*

Next, we use biophysical techniques such as surface plasmon resonance (SPR) to investigate the riboswitch aptamer-ligand interaction and affinity (Fig. 1B) as well as reporter gene assays (Fig. 46) to investigate the functions of reengineered riboswitches. We have constructed novel synthetic riboswitches by developing more effective aptamer ligands that allowed more precise and dynamic control of gene expression. To validate the function of the riboswitches, the green fluorescent protein (GFP) gene was expressed under the control of constructed riboswitches in *E. coli*. Activation ratios in the range of 2 to 10-fold were observed in most reengineered switches (Fig 46A), with lower background expression in the absence of ligands. The riboswitch-mediated induction in GFP expression was ligand concentration-dependent (Fig 46B). Next, we have used developed riboswitches for balanced gene expression in multienzyme pathways which are crucial for engineering metabolic pathways to improve the yield of biosynthesis of product. We observed a significant increase in biosynthetic product yield in the presence of inducers that we have developed

Nidhi Adlakha
Principal Investigator

Lab Members
Sudipt Kumar Dalei
Shriya Singh
Shivam Aggarwal
Kunal Meena
Siddhi Pavale
Murlidhar Madhukar

Synthetic biology to understand and improve the production of value-added products

Our research focuses on the development of biocatalysts for industrial and biomedical applications using systems and synthetic biology approaches. The lab aims at optimizing the existing microbial cell factories and improving the cost economics of enzymes or bioproducts synthesis. Another goal of our group is to understand the underlying mechanism that biocatalysts employ, with the aim to augment the yield and productivity of value-added products from engineered microbes. Our initial efforts will be directed at the following projects.

Stoichiometric balance ratio of cellobiose and gentiobiose induces cellulase production in *Talaromyces cellulolyticus*

The major goal of our research is to develop superior biocatalysts for pharma, chemical, food, flavors, and agro-based industries. We intend to build a technology that is greener and reduces cost, with improved sustainability. For agro-based industries, the lab aims at the development of superior enzymes for cellulose degradation. Over ninety percent of cellulose-disintegrating enzymes are known to be induced by the polysaccharide substrate, yet the precise molecular mechanism behind the perception of insoluble cellulose by fungi and the secretion of enzymes is still unclear. Recent research indicates the role of soluble saccharides generated during initial polysaccharide degradation. The soluble inducer molecules are believed to enter the fungal cell and mediate cellulase production. Till date, a few saccharides have been screened for their role in induction, however rational scrutiny of early metabolome for deciphering natural cellulase inducer is still missing.

The current research aims at understanding the induction mechanism and rationally engineering filamentous fungi for improved enzyme production. The knowledge of induction mechanisms and inducers will provide a new perspective on the production of microbial cellulases. The objectives of the current study are:

Scrutiny of early metabolites and its role in cellulase induction

Talaromyces cellulolyticus transcribes a baseline level of CAZymes on the outer surface of the spores. Additionally, the membrane protein extract indicated the presence of endoglucanase and glucosidase-type activity, which may act on polysaccharides and produce inducer molecules. Therefore, we planned a series of experiments to identify the inducers for our model strain, *Talaromyces* sp. First, we incubated the resting spores ($1X10^9$ spores/ml) with 1% avicel and the early metabolites generated by the action of spore surface enzymes were recovered in the supernatant by centrifugation. The reaction was performed at 50°C (optimum temperature for cellulase activity) for 72h. The spore only, avicel only, and spore incubated with starch reactions were used as negative control (Fig. 47A).

The direct effect of the recovered metabolite mixture was tested through a supplement experiment. Analysis of the contribution of transglycosylation product mixtures to cellulase induction revealed a 57% increase in total cellulase as compared to the controls (Fig. 47B). In concordance, it also led to significant upregulation in the transcript levels of core cellulase enzymes, i.e., cellobiohydrolase I (*cbh1*), cellobiohydrolase II (*cbh2*), beta glucosidase-1 (*bgl1*) and endoglucanase 1 (*egl1*) (Fig. 47C). Overall, the trans-glycosylated products generated by the action of spore surface enzymes on avicel facilitate secretion of cellulolytic enzymes by the filamentous fungi. We furthered our study to scrutinize the saccharides present in the mixture using GC-MS. Expectedly, GC-MS results showed that the soluble sugars were the primary differential metabolites between avicel-treated and control samples (Fig. 47D).

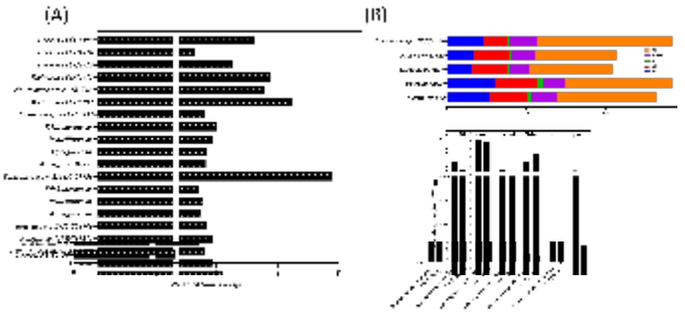


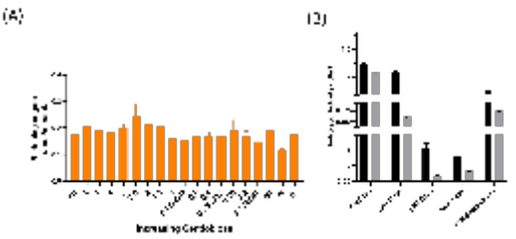
Figure 47: Inducer generation upon co-incubation of spores and avicel *(A) A schematic representation of experimental setup for production of potential inducer metabolite cocktail. (B) The transglycosylated metabolites, produced by co-incubation of 1% avicel with 1x10^7 spores, were supplemented to liquid culture for evaluating their role as potential inducers. Post 48h, the culture supernatant was analysed for its effect on cellulolytic activity. (C) Effect of inducers on the expression of key cellulolytic genes was performed. (D) GC-MS predicted saccharides obtained by the action of spore surface enzyme on cellulose-based polysaccharide.*

Submerged cultivation to evaluate effect of optimized inducer

To evaluate the effect of the optimized inducer on the biomass hydrolyzing capability of the strain, we compared the efficiency of the crude enzyme prepared using a stochiometric balanced inducer ratio with that of uninduced crude enzyme. For this, the Talaromyces inoculum was raised for 36h in PDB and used for inoculating the complex media containing 12.5mM cellobiose and 5mM gentiobiose, and no inducer was used as a negative control. As expected from our previous results, the activity of crude enzyme preparation in the presence of inducer outperformed that of the negative control (Fig. 48A). Precisely, it was perceived that there was a 175% increase in the cellulase production in the presence of inducer in terms of FPU.

According to Klein-Marcuschamer et al., (2011), the saccharification of complex biomass with the following conditions: 20% solids loading; 20 mg (0.5 FPU/mg) enzyme cocktail per gram of polysaccharide led to the development of an effective technoeconomic model for inexpensive biofuel production. We performed saccharification studies on pre-treated wheat straw at 0.5FPU/g and compared it with a commercial enzyme cocktail (cTec3). It was observed that crude enzyme preparation from our study hydrolyzed 65-76% of the total sugars from pre-treated wheat straw, whereas only 55-68% hydrolysis was observed with commercial cellulase preparation after a 12h reaction (Fig. 48B).

Figure 48: Submerged cultivation to evaluate effect of optimized inducer on cellulase production. *(A) The inducers were supplemented to complex culture medium. The supernatant was harvested after 6 days and different cellulolytic activity was estimated. (B) Comparison of Ctec3 and induced secretome from Talaromyces in terms of % saccharification.*



SARS-CoV-2 related Research and Development

Prof. Prasenjit Guchhait

1. Mechanism of inflammation and thrombosis in the lung leading to hypoxemia in SARS-CoV-2 infected animals and patients (Kaur *et al*, 2022, Agarwal *et al*, 2022).
2. Investigation on the mechanism of ARDS and Pulmonary Fibrosis in SARS-CoV-2 infected animals.
3. Investigation on the mechanism of severity of SARS-CoV-2 pathogenesis in animals and patients with diabetes.

PUBLICATIONS & PATENTS

Courtesy: Ritika

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Book Chapter(s)

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Patent Application(s)

1. Guchhait Prasenjit, Eswaran S V (June' 2019) Water Soluble Fullerene C60 Adducts for Nano-Medicine & Materials Science; Application/ Registration Number 201811020894. From the Regional Centre for Biotechnology, Faridabad, India.

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3. Adlakha N, Meena K (2022). Method for the production of phenylalanine free diet through the reuse of phenylalanine ammonia lyase. Indian Patent Application No. 202211016821 (Complete application).

ACADEMIC & TRAINING ACTIVITIES

Academic Programmes

1. PhD Programme in Biotechnology

RCB offers doctoral programme in Biotechnology to students holding a post-graduate degree (or an equivalent) in any field of science, medicine or technology and interested in pursuing research at the interface of multiple disciplines in the areas related (but not limited) to structural biology, molecular medicine, infectious disease biology, agricultural biotechnology, systems and synthetic biology, cancer & cell biology.

Currently, 110 students are working at RCB for the PhD degree in Biotechnology. During the period of this report, 07 students were awarded PhD degree.

2. PhD Programmes in Biostatistics & Bioinformatics

RCB offers an interdisciplinary doctoral programme in Biostatistics and Bioinformatics supported through a collaboration with the global pharmaceutical giant, GlaxoSmithKline Pharmaceuticals India Private Ltd. (GSK). These programmes are subject to RCB statutes, ordinances and regulations.

In addition to RCB faculty members, a virtual adjunct faculty pool created from partner institutions (IIT Delhi, NII New Delhi, ICGEB New Delhi, NIBMG Kalyani) act as mentors for the students admitted to these programme. Students receive a consolidated fellowship of Rs.45000 per month for the first two years and Rs.50000 for the next three years. Presently, 11 students are registered with RCB for PhD in these programmes.

3. MS-PhD Programme in Biotechnology

RCB introduced a MS-PhD Programme in Biotechnology in 2018-19 with focus on research-based learning. The programme provides extensive learning opportunities in the broad field of life sciences and biotechnology through rigorous classroom study and hands-on laboratory experiments. In the second year, the students work under the supervision of a faculty at RCB, in an area of mutual scientific interest, and submit a dissertation by the end of the fourth semester.

A student may exit the programme with a Master's degree or continue in the programme for pursuing PhD. The students admitted to the programme receive the RCB Ramachandran-DBT fellowship of Rs. 16000 per month for the first two years, after which, the Indian students continue in the PhD component with a fellowship from a national funding agency while the foreign students receive the RCB-DBT International Doctoral fellowship. At present, 48 students are registered in the programme. During the reporting period 05 students quit the programme with M.Sc. degree

4. Research & Training Programme at RCB

RCB offers research training to post-graduate students of biotechnology related areas from various universities/ institutions/ colleges of repute to carry out their project work towards partial fulfilment of their post-graduate degrees.

Short-term summer trainings/ internships are also offered to students interested in research areas of specialization in RCB. Selection is based on the strength of resume and evaluation of write-up on their research interests. Selected candidates undergo research training under the mentorship of RCB faculty. They learn to carry out their own research projects in collaboration with other group members. Trainees get a realistic experience of several facets of conducting modern biological research and embarking on a research career. The training programmes range from two to six months' duration. During 2022-23, 61 research trainees joined for six months' duration at RCB.

5. Academic Programmes at RCB's Recognized Centers

RCB has granted academic recognition to the various institutions of excellence, as per Clause 10(1) f of the RCB Act and RCB Ordinance, for their academic programmes. Students admitted to these programmes are registered at RCB for their degrees. At present, following institutions and their academic programmes are recognized by RCB. During the reporting period, 09 students were awarded PhD degree in the affiliated disciplines. The number of students registered under the various programmes are provided below:

Name of Recognized Centre	Courses Recognized	Students Registered	Adjunct faculty
Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad	PhD (Biotechnology)	32	23
Center of Innovative and Applied Bioprocessing (CIAB), Mohali	PhD (Biotechnology)	4	7
National Institute of Animal Biotechnology (NIAB), Hyderabad	PhD (Biotechnology)	72	20
National Agri-Food Biotechnology Institute (NABI), Mohali	PhD (Biotechnology)	31	11
Institute of Life Sciences (ILS), Bhubaneswar	PhD (Biotechnology)	114	28
Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram	MSc (Biotechnology)	80	37
	PhD (Biotechnology)	31	
Translational Health Science and Technology Institute (THSTI), Faridabad	PhD (Biomedical Sciences)	0	15
National Institute of Biomedical Genomics (NIBMG), Kalyani	MS-PhD (Integrated) (Biotechnology; Specialization: Biomedical Genomics)	30	20
	PhD (Biotechnology; Specialization: Biomedical Genomics)	41	
Christian Medical College (CMC), Vellore	PhD (Medical Biotechnology; Specialization: Haematology)	13	9
	PhD (Medical Biotechnology; Specialization:	4	
National Centre for Cell Science (NCCS), Pune	PhD (Biotechnology)	32	23
ESIC Medical College & Hospital, Faridabad	PhD (Biomedical Sciences)	6	31
Institute of Bioresources and Sustainable Development (IBSD), Imphal	PhD (Biotechnology)	0	13
Institute for Stem Cell Science and	PhD (Life Sciences)	21	11
Total		**490**	**248**

Our Alumni

Name	Passing Year	Current Affiliation
Shreyasi Das	2022	Postdoctoral Associate, Yale School of Medicine
Manisha Kumari	2022	PostDoc, Johns Hopkins Medicine Baltimore, United States
Priyanka Verma	2022	–
Arunima Gupta	2022	–
Shraddha Kantilal Dahale	2022	–
Krishnendu Goswami	2023	–
Shrimali Nishith Maheshbhai	2022	Postdoctoral Research Fellow at BWH, Harvard Medical School, Boston, Massachusetts, United States
Anushka Das	2022	RTG2550 RELOC PhD candidate, Rugarli lab, CECAD, University of Cologne, Germany
M.Sc		
Chhavi Dua	2022	Project Associate, CSIR-IGIB
Biplab Ghosh	2022	Doctoral Researcher, German Cancer Research Centre (DKFZ); European Centre for Angioscience, Heidelberg, Germany.
Harish	2022	–
Anirban Adhikary	2022	–

Webinars/ Seminars

Date & Time	Speaker	Title
24 March, 2023	**Prof. Sanjeev Kumar Mahato Associate Professor** *IIT, BHU*	Regenerative Implants for Tissue Engineering
20 March, 2023	**Prof. Arun Kumar Shukla Professor** *IIT, Kanpur*	Structure, function and Modulation of G Protein-Coupled Receptors
17 February, 2023	**Prof. Benu Brata Das Professor** *Indian Association for the Cultivation of Science, Kolkata*	Insight into the DNA Breaks-Induced Genomic Instability and the Underpinning Cause of Human Diseases
11 January, 2023	**Dr. Rahul Bhosale,** *School of Bioscience, University of Nottingham, UK*	Root Angle is Controlled by EGT1 in Cereal Crops Employing an Anti- Gravitropic Mechanism
25 November, 2022	**Dr. Lipi Thukral,** *Institute of Genomics and Integrative Biology*	How multiscale stimulations are getting better in painting more accurate picture of biology
07 November, 2022	**Prof. Stanton B. Gelvin** *Purdue University, USA*	Understanding and Manipulating Agrobacterium T-DNA Integration into Plant the Genome.
29 September, 2022	**Dr. Varun Aggarwal** *Mount Sinai Hospital, USA*	Precise Quantification of Bacterial Strains after Fecal Microbiota Transplantation Explains outcome and Provides Candidate Strains for Live Biotherapeutics
22 August, 2022	**Dr. Srini Subramaniam Associate Professor** *Department of Neuroscience, UF Scripps Biomedical Research, USA*	Striatal Induction and Spread of the Huntington's Disease Protein: Novel Rhes Route
02 August, 2022	**Dr. Nidhi Rawat** *University of Maryland, College Park, USA.*	Fighting the Fungal Foes of Wheat
05 July, 2022	**Prof. Siddhartha S. Jana Professor** *School of Biological Sciences, Indian Association for the Cultivation of Science, Kolkata*	Nonmuscle Myosin II Activity Controls Membrane Protrusive Activities
01 June, 2022	**Prof. Jorge D Paola** *Washington University School of Medicine, St Louis, USA*	Genomics of Bleeding, Platelets and Von Willebrand Factor
20 May, 2022	**Prof. Perumal Thiagarajan** *Baylor College of Medicine, USA*	Beta2-glycoprotein I and Antiphospholipid Syndrome
20 May, 2022	**Prof. Josef T Prchal** *University of Utah Huntsman Cancer Institute, Salt Lake City, USA*	Genetic Basis of Molecular Response to Hypoxia
12 May, 2022	**Ms. Kanupriya** *Founder of Curative Mind*	Mental Health and Well-Being
22 April, 2022	**Dr. Shri Ram Yadav** *IIT Roorkee*	Species-Specific Function of Conserved Cell Fate Determinants in Orchestrating Rice Root Architecture

ID-75 Seminars

Date & Time	Speaker	Title
24 May, 2022	Dr. Gaurav Chopra Purdue University, USA	How do glial cells become dysfunctional in chronic inflammation: Tools to Molecules
08 April, 2022	Dr. Mahak Sharma IISER Mohali	Mechanisms regulating subcellular location and function of lysosome (online)
18 April, 2022	Dr. Oishee Chakrabarti Saha Institute of Nuclear Physics, Kolkatta	Organellar dynamics regulate cellular surveillance (online)

Events Organised

1st Convocation Ceremony 2022

Regional Centre for Biotechnology organised its First Convocation Ceremony on 30th June, 2022 at the M K Bhan Auditorium. The degrees were conferred to the students of PhD and Master's programmes, who passed out in academic sessions till 2021-22 by the Chief guest Dr. V. K. Saraswat, Hon'ble Member, NITI Aayog.

The Convocation was declared 'Open' by Dr. Rajesh Gokhale, the Secretary, DBT and Chairperson, Board of Governors, RCB. The Director's Report was presented by Prof. Sudhanshu Vrati, the Executive Director, RCB. A total of 51 students were graduated. 1 PhD in Biotechnology and 50 Master of Science in Biotechnology degrees were awarded to the students.

Dr. V. K. Saraswat, Hon'ble Member, NITI Aayog addressed the Convocation. The Convocation was declared 'Closed' by Dr. Rajesh Gokhale, Secretary, Department of Biotechnology and Chairperson, Board of Governors, RCB.

Summer Research Internship Programme Facilitated By Gujarat State Biotechnology Mission (GSBTM)

Regional Centre for Biotechnology organised a Summer Research Internship Programme facilitated by Gujarat State Biotechnology Mission (GSBTM), Department of Science and Technology, Govt. of Gujarat was from 18.07.2022 to 17.08.2022. The main objective of the Programme was to provide early exposure to the students pursuing MSc/BE (Biotech) in Biotechnology and allied areas of Biotechnology about the research environment and mechanism that can help them take better career decisions. A total number of ten interns were allotted for the Programme who successfully completed their internship with hands-on exposure in the areas of Biotechnology like Cell Biology, Stem Cells, Agricultural Biotechnology, Industrial Biotechnology, Structural Biology, Virology, Animal Models and Cancer Biology in order to help them build an interest and enthusiasm to pursue higher education and instil a sense of aspiration to do future research in places of repute like RCB.

A Biotechnology Career Counselling session was also setup to help them decide on their future career path in the biotechnology industry/research. A visit to the Advanced Technology Platform Centre (ATPC) and BSc BioNEST Bioincubator (BBB) was also organised to enable them to understand the nuances of biotechnology research, and the research possibilities available at RCB.

A Memorandum of Understanding (MoU) between Regional Centre for Biotechnology (RCB), Faridabad and Gujarat State Biotechnology Mission (GSBTM), Gandhinagar for the Collaborative on Summer Research Internship Programme has also been executed on 13th March, 2023.

India EMBO 2022

The Regional Centre for Biotechnology (RCB), Faridabad, organised the prestigious international conference India EMBO lecture course on 'Functional Nucleic Acids: Recent Landscapes and Therapeutic Applications' from 16th - 19th August, 2022. Around 150 participants across the world participated in this intellectual meet. The hybrid mode meeting was organized in partnership with European Molecular Biology Organisation (EMBO) and DBT India alliance, at the MK Bhan auditorium of RCB campus where, 25 eminent scientists including Professors Stephen Neidle,

Jean-Louis Mergny, Naoki Sugimoto, Janez Plavec, Eriks Rozners, and Valerie Gabelica delivered talks on diverse aspects of nucleic acids. The conference was attended by more than 150 research scholars, faculties, and students. The research students enthusiastically participated in 80 posters and 15 flash talk presentations. The four-day India EMBO lecture course concluded with a panel discussion where students and faculty members from RCB conversed with the foreign and Indian delegates on a variety of opportunities in science careers world-wide.

Hindi Pakhwada 2022

Hindi Pakhwada (Fortnight) is celebrated every year during the month of September and Hindi Diwas on 14th September to promote the progressive use of official language, Hindi, in government offices in compliance with the Official Language Policy of the Government of India. In this sequence, Hindi Pakhwada was organized from 14th to 27th September, 2022 at the Regional Centre for Biotechnology.
The closing ceremony of the fortnight was held on 29th September, 2022 under the chairmanship of the Executive Director, RCB at M. K. Bhan Auditorium. On this occasion Prof. Sudhanshu Vrati, the Executive Director, RCB, Dr. R.P. Roy, Dean (Academics), RCB and Dr. Nidhi Sharma, the Hindi Nodal Officer, RCB, apprised the personnel about the importance of Hindi and its history. A total of seven competitions were organized during the fortnight in which the personnel and research students participated enthusiastically. The Executive Director and the Dean (Academics), jointly gave cash awards and certificates to the winning employees during the event.

IUBMB Focused Meeting On Biochemistry & Molecular Biology of RNA viruses

Regional Centre for Biotechnology with the support of IUBMB organized 'IUBMB Focused Meeting on Biochemistry & Molecular Biology of RNA Viruses' during 15-18 November, 2022 in RCB. Eminent researchers from across the globe participated in the meeting along with young researchers and students.

The goal of this meeting was to encourage a productive discussion and to disseminate knowledge about new advances in this area. Discussions were concentric on the latest research advancements in different parts of the world to identify critical intervention points in the life cycle of the RNA viruses and ways to exploit this knowledge to develop effective therapeutic and prophylactic strategies. Moreover, the research avenues emerging out of the inherent complexity of viruses were also discussed in depth.

This conference therefore provided an invaluable opportunity for Indian students, postdocs and young faculty members to interact with, and gain knowledge from, international experts in this field. We attracted participants at all levels (PIs, postdocs and graduate students) from research groups located all over the country and from 9 countries. This conference provided a unique opportunity for these Indian researchers to interact in a relatively informal setting with the pioneers in these important research areas. Altogether, the meeting was attended by around 175 young researchers, 30 domain experts and this provided an excellent opportunity for young researchers to present posters and give oral presentations. This meeting was highly interactive and appreciated by both the participants and the speakers.

India International Science Festival (IISF) 2022

The 8th edition of IISF was held in the city of Lakes, Bhopal from January 21-24, 2023. The Ministry of Science and Technology (MoS&T), Ministry of Earth Sciences (MoES), Department of Atomic Energy (DAE), Department of Space (DoS), Government of India and Government of Madhya Pradesh jointly organised the IISF 2022 on the theme 'Marching towards Amrit Kaal with Science, Technology and Innovation'. The Department of Biotechnology, Ministry of Science & Technology is the nodal coordinating department for organising IISF-2022.The Madhya Pradesh Council of Science and Technology (MPCOST) is the local partner and Vijnana Bharati (VIBHA) as Knowledge Partner for IISF 2022.

Maulana Azad National Institute of Technology (MANIT), Bhopal, Madhya Pradesh was the venue for the IISF 2022. The festival had fifteen programs including the Mega Science and Technology Exhibition show casing the theme of the festival. The nodal agency to organise the IISF 2022 was Regional Center for Biotechnology, Faridabad, Department of Biotechnology.

IISF is a festival to celebrate the achievements of India's scientific and technological advancements with students, innovators, craftsmen, farmers, scientists and technocrats from India and abroad, in simpler words it is the celebration of science cherished by all. Celebrating IISF 2022 during India's presidency of the G20 Summit gives an additional edge to showcase Indian scientific accomplishments at global level. The activities held during the festival will foster the global theme of G20 – "One Earth, One Family, One Future".

National Science Day 2023

The National Science Day was celebrated at Regional Centre for Biotechnology on 28th February, 2023. Prof. Sudhanshu Vrati, the Executive Director of the Regional Centre for Biotechnology, gave a welcome address to start off the National Science Day. The students of RCB gave Pitch Talks and presented Posters after the Science Day Programme.

RCB Foundation Day 2023

In 2016, RCB was ordained with the status of an "Institution of National Importance" through an Act of the Parliament. It was brought into effect by a Gazette notification on 1st March, 2017. To commemorate this momentous occasion, 1st March has been adopted as the RCB Day.
The Foundation Day started on 01st March, 2023 with mini-symposium presentations made before the panel of judges by the final year PhD students and the award for the best scientific presentation was distributed to the winners. After lunch, Prof. Sudhanshu Vrati, the Executive Director, gave a welcome speech to start off the programme. The day's guest of honour, Prof. Raghavendra Gadagkar of the Indian Institute of Science, Bengaluru, visited RCB and delivered the RCB Day Oration.

International Women's Day 2023

On 08th March, 2023, the Regional Centre for Biotechnology observed the International Women's Day. Two eminent women scientists from India, Prof. Asima Chatterjee and Dr. Janki Ammal, were honoured at the ceremony for their contributions to science.

Swachhata Pakhwada

RCB observed Swachhta Pakhwada 2023 during 15 September - 2 October 2023. On this occasion Swachhta Shapath (Swachhta Pledge) was taken by all RCB employees to fulfill India's mission of "Clean India" and to make this massive mass movement a success.

Responding to the Hon'ble Prime Minister's appeal for citizen's participation in Swachhata Movement, RCB has taken the following steps:

1. Ban Single use plastic
2. Recycling of scrap materials as stationary products.

As a step towards stopping the use of single use plastic, RCB has issued instructions to stop the entry as well as use of single use plastics and have suggested alternate materials like cloth, paper and corrugated cartons to pack and carry materials in and out of the campus of NCR Biotech Science Cluster.

One Nukkad Natak directed and written by Mr. Sudhir Kumar (Section Officer, RCB) was performed by RCB along with THSTI at Government Girls Primary School, Bhankri to aware them how we can clean our surroundings.

Outreach Programmes

Regional Centre for Biotechnology organised various outreach programmes as a part of the Scientific Social Responsibility (SSR) activity under SERB to imbibe a culture of social commitment among SERB Grantees. The following Programmes were organised:

- Visit of 55 senior school students and 15 teachers from Manav Rachna International School, Faridabad on 02.09.2022 – Prof Sivaram Mylavarapu.

- Visit of students from DAV Public School, Sainik Colony, Faridabad on 15.09.2022 – Prof. Vengadesan Krishnan.

- Visit of 35 students and 5 teachers from Government College, Faridabad on 11.11.2022 – Prof. Avinash Bajaj.

- Visit of undergraduate students from Ramjas College, New Delhi on 12.01.2023 – Dr. Sam J Mathew and Dr. Anil Thakur.

- Regional Centre for Biotechnology also organised a visit for 57 BTech (Biotechnology) students of IMS Engineering College, Ghaziabad on 21.11.2022.

Scientific and Other Events Conducted

Prof. Deepak T Nair

1. Co-organizer: IUBMB focussed meeting on biochemistry and Molecular Biology of RNA viruses at RCB, Faridabad 15-18 November 2022.
2. Indian International Science Festival (IISF-2022) held during 21st-24th January, 2023 at MANIT, Bhopal.

Prof. Vengadesan Krishnan

1. Conducted one-day scientific expedition for students from DAV Public School, Sector-49, Faridabad, as part of the Scientific Social Responsibility (SSR) Policy at the Regional Centre for Biotechnology, Faridabad, on September 15, 2022.
2. Organized an online workshop on Improving research writing using Grammarly in association with BridgePeople, Bangalore, on July 1, 2022.
3. Organized an online User awareness on Plagiarism and training session for using Turnitin in association with TurnitIndia, India, on July 28, 2022.

Dr. Deepti Jain

1. Co-organizer of Science Day celebrations at RCB on 28th February, 2023
2. Co-organizer of RCB day celebrated on 1st March, 2023
3. Co-organizer of Women's Day celebrations at Regional Centre for Biotechnology on 8th March, 2023

Prof. Chittur Srikanth

1. Coordinated RCB's Contemporary Webinar Series

Dr. Manjula Kalia

1. Co-organizer: IUBMB focussed meeting on biochemistry and Molecular Biology of RNA viruses at RCB, Faridabad 15-18 November 2022.

Dr. Arup Banerjee

1. Co-organizer: IUBMB focussed meeting on biochemistry and Molecular Biology of RNA viruses at RCB, Faridabad 15-18 November 2022.

Dr. Anil Thakur

1. Participated in "India International Science Festival (IISF) at MANIT Bhopal, India" from January 21-24, 2023.
2. Coordinated and participated in Mentoring and Counselling Session (Scientific Discussion) at "India International Science Festival (IISF) at MANIT Bhopal, India" from January 22-24, 2023.

Dr. Sam Mathew

1. Hosted Bachelors students from Ramjas College, New Delhi, on 12th January 2023 at RCB, giving them an introduction to and demonstration of the research carried out at RCB.

Prof. Sivaram V S Mylavarapu

1. Coordinated the first RCB-GSBTM undergraduate summer internship programme for visiting undergraduate students from Gujarat from July 18-August 17, 2022 at RCB, organized by RCB in partnership with the Gujarat State Biotechnology Mission (GSBTM).
2. Hosted high school biology students of standard XI and XII from Manav Rachna International School, Sector 14, Faridabad for a one-day research orientation visit on September 1, 2022.

Dr. Karthigeyan Dhanasekaran

1. Organized a one-day introductory training on super-resolution microscopy along with Carl Zeiss, India team at the ATPC on September 6, 2022.

Dr. Ambadas B Rode

1. Organized an international conference India EMBO lecture course on 'Functional Nucleic Acids: Recent Landscapes and Therapeutic Applications' at RCB, Faridabad from August 16-19, 2022.

Prof. Rajendra P Roy

1. Organizing Committee: IIT-UB Conclave on Nanomaterials, Photonics, Sensors, AI and their Applications in Security, Healthcare, and Smart Living, IIT Delhi, Nov 28-30, 2022.

Membership of Professional/Academic bodies/Editorial boards

Prof. Deepak T. Nair

1. Member, Monitoring Committee Meeting to review Niche Creating High Science/ High Technology Projects (NCP) and Focused Basic Research (FBR) projects under Healthcare (HTC) Theme of CSIR
2. Member, Academic Management Committee, Regional Centre for Biotechnology
3. Member, IT Committee, Regional Centre for Biotechnology
4. Acting Head, Advanced Technology Platform Centre of the Regional Centre for Biotechnology
5. Chairman, Internal Works Committee, Regional Centre for Biotechnology
6. Member, Technical Committee to review proposals submitted to the European Synchrotron Radiation Facility Access Program of the Regional Centre for Biotechnology
7. Life Member, Indian Crystallographic Association
8. Life Member, Indian Biophysical Society
9. Life Member, Society of Biological Chemists
10. Member, Guha Research Conference
11. Fellow, Indian National Science Academy

Prof. Vengadesan Krishnan

1. Member, Indian Crystallographic Association (ICA)
2. Member, Indian Biophysical Society (IBS)
3. Member, International Union of Crystallography (IUCr)
4. Member, Electron Microscopy Society of India (EMSI)
5. Member, Probiotic Association of India (PAI)
6. Member, Association of Microbiologists of India (AMI)
7. Member, Board of Studies, Regional Centre for Biotechnology

Dr. Deepti Jain

1. Member, Travel Grant & Symposia Management Committee, CSIR
2. Member, National Committee of International Union of Crystallography, INSA
3. Member, Selection committee of MK Bhan Fellows
4. Member, Indian Crystallography Association (ICA)
5. Member, Society of Biological Chemists (SBC)
6. Member, Electron Microscopy Society of India (EMSI)
7. Member, Protein Society of India (PS)

Dr. Prem S. Kaushal

1. Member, Indian Crystallography Association (ICA)
2. Member, Electron Microscopy Society of India (EMSI)

Prof. Prasenjit Guchhait

1. Member of the Editorial Board for the journals, *Frontiers in Hematology*; *Annals of Clinical and Experimental Immunology*; *Austin Hematology; Cardiology; Journal of Hypertension and Cardiology*; *World Journal of Hypertension,* 2012-present.
2. Member of the selection committee for Aegis Graham Bell Awards 2023 in Life Science, Govt. of India. 2023
3. Member of the Special Committee of Special Centre for Molecular Medicine, JNU, New Delhi, 2022-2025.
4. Member of the Board of Study of the Apeejay Stya University, Gurugram. 2019-present.
5. Steering Committee member of the Good Clinical Practice Professional Certification Scheme (GCPPCS), CDSA, THSTI, Faridabad. 2020-present.
6. Member of the Academic Committee of ESIC Hospital and Medical College, Faridabad, 2022-present.

7. Registrar in-charge of Regional Centre for Biotechnology (RCB), Faridabad, Dec' 2020 – present.
8. Member of Executive Committee of RCB, Dec 2020 - present.
9. Member of Academic Committee of RCB, May 2017 - present.
10. Member of Board of Study of RCB, 2017-present.
11. Member Secretary of the Institutional Ethics Committee (Human Research),RCB, 2012 - present.
12. Chairperson of the Institutional Biosafety Committee, RCB, 2012 – present.
13. Chairperson of the Institutional Animal Ethics Committee, RCB, 2018 – present.
14. Member Secretary of Institutional Committee for Stem Cell Research, RCB, 2019- present.
15. Co-Chairperson of Infectious disease research facility of NCR Biotech Science Cluster, 2017-present.
16. DBT nominee for Institutional Biosafety Committee, THSTI, Faridabad, 2019-present.

Prof. Tushar K. Maiti

1. Executive Council Member, Proteomics Society of India
2. Editorial Board Member, Scientific Reports

Dr. Sam Mathew

1. Member, Institutional Stem Cell Research Committee, THSTI, Faridabad
2. Member, Indian Society for Developmental Biology (InSDB)
3. Member Secretary of the RCB Institutional Animal Ethics Committee (IAEC)
4. Member of the RCB Institutional Biosafety Committee (IBSC)

Dr. Geetanjali Chawla

1. Member, American Medical Writers Association (AMWA)
2. Associate Editor, Journal of Experimental Research on Human Growth and Aging (JERHA)
3. Review editor on the editorial board of Metabolic Physiology (specialty section of Frontiers in Physiology)

Prof. Chittur Srikanth

1. Member, American Society for Microbiology
2. Editorial advisory board member, Journal of gastrointestinal Infections
3. Member, Technical Evaluation Committee of Infectious Disease Biology of DBT
4. Member of the MoE STARS grant subcommittee on Cancer Biology

Dr. Manjula Kalia

1. DBT Nominee of the Institutional Biosafety Committee, NBRC, Manesar, 2021-Present
2. External Expert of the Institutional Biosafety Committee, Jaypee Institute of Information Technology, Noida, 2021-Present
3. Member, American Society for Microbiology
4. Editor, Microbiology Spectrum

Dr. Arup Banerjee

1. Contributing member of the F1000 Faculty Infectious Diseases of the Nervous System Section in F1000Prime (https://f1000.com/prime)
2. Editorial Board member (Infectious Diseases) of Scientific Reports

Dr. Prasad Abnave

1. Member, Institutional Stem Cell Research Committee, THSTI, Faridabad.
2. Guest editor for journal "Journal of Visualized Experiments" (JoVE).

Prof. Avinash Bajaj

1. Invited Member, Biomedical and Health Science, Program Advisory Committee, SERB.

Prof. Sivaram Mylavarapu

1. Member, Institutional Ethics Committee, RCB
2. Member, Institutional Stem Cell Research Committee, THSTI Faridabad
3. Life Member, Indian Society for Cell Biology (ISCB)
4. Member of a faculty probation review committee at RCB
5. External expert for the PhD selection interviews at CSIR-IGIB on June 22-23, 2022.

Dr. Karthigeyan Dhanasekaran
1. Member, Indian Society of Cell Biology.
2. Member, Indian Society of Chemical Biology.
3. Member, Indian veterinary council.
4. Member, Tamil Nadu state veterinary council.
5. Member, SAC for Mr. Nishant Pandey

Dr. Saikat Bhattacharjee
1. Member, International Society-Plant Molecular Microbe Interactions (IS-MPMI)

Dr. Divya Chandran
1. Member, DBT Technical Expert Committee (TEC) of Plant Biotechnology
2. Invited Member, SERB PAC, January 2023
3. Invited Member, SERB PAC OEB- Plant Science, September 2022
4. Associate Editor, Plant Molecular Biology Reporter
5. Member, Fulbright-Nehru Doctoral Research Fellowship Selection Committee, October 2022
6. Member, International Society for Molecular Plant-Microbe Interactions (IS-MPMI)
7. Member, British Society for Plant Pathology (BSPP)

Dr. Ramu S Vemanna
1. Life member, Indian Society of Plant Physiology (ISPP)
2. Life member, Indian Society for Plant Biochemistry and Biotechnology (ISPBB)

Dr. Ambadas B Rode
1. Member, Indian Biophysical Society
2. Member, Society of Biological Chemists
3. Member, Indian JSPS (The Japan Society for the Promotion of Science) Alumni Association

Dr. Nidhi Adlakha
1. Review Editor, Frontiers in Bioengineering and Biotechnology

Dr. Rajendra P Roy
1. Member, Governing Body, NCCS, Pune
2. Member, Research Area Panel – Scientific Advisory Committee, NCCS, Pune
3. Member, American Peptide Society
4. Member, Guha Research Conference
5. Member, Association of Microbiologists of India

Distinctions, Honours and Awards

Prof. Deepak T Nair
1. Elected Fellow of the Indian National Science Academy, New Delhi

Dr. Prasad Abnave
1. INSPIRE Faculty Fellowship, DST

Dr. Anil Thakur
1. Ramalingaswami Fellowship from DBT, India

Dr. Sam Mathew
1. Invited Chair of the session on "Metabolism" at the 4th BIO Group meeting held at the Indian Institute of Science Education and Research (IISER), Thiruvananthapuram, on August 19-20, 2022.

Dr. Pinky Kain
1. Received First prize for best image award in Cell-Fie Cell photography contest organized by Spinco Biotech (31st October, 2022).

Dr. Geetanjali Chawla
1. India Alliance DBT/Wellcome Intermediate Fellowship (2018-2022)
2. Ramalingaswami Fellowship (2016-2017) (Relinquished)

Dr. Rajender K Motiani

1. India Alliance DBT/Wellcome Trust Intermediate Fellowship (2020-2025)

Dr. Prashant Pawar

1. INSPIRE Faculty Fellowship, DST

Dr. Rajendra P Roy

1. Elected Fellow, National Academy of Sciences, India
2. Elected Fellow, Indian National Science Academy
3. Elected Fellow, Indian Academy of Science
4. JC Bose National Fellowship

Lectures delivered/ Conferences attended/ Visits abroad/ Outreach

Prof. Deepak T Nair

1. Delivered a talk titled "New answers for old questions regarding DNA synthesis by DNA polymerases" at Guha Research Conference 2021 held during April 22nd-26th at Bhimtal, Uttarakhand.
2. Represented RCB in the Networking Session of the PDF Meeting 2021 organized by IndiaBioscience on May 9, 2022.
3. Session Chair in India EMBO Lecture Course titled "Functional nucleic acids: recent landscape and therapeutics" held during August 16-19, 2022 at the Regional Centre for Biotechnology.
4. Delivered an invited talk titled "Structural and Functional aspects of monoclonal antibodies." at the workshop titled "Monoclonal antibodies, an emerging era in biologicals: Principles of production, applications in immunodiagnostics and therapeutics" held at Institute of Advanced Virology, Thiruvananthapuram from December 8-9, 2022.
5. Attended the 88th Anniversary General Meeting of the Indian National Science Academy hosted by CSIR-National Institute of Oceanography, Vishakhapatnam during December 14-16, 2022.
6. Attend the Indian International Science Festival (IISF-2022) held during January 21-24, 2023 at MANIT, Bhopal as part of the IISF-2022-RFP committee of RCB.
7. Delivered the Prof. G. N. Ramachandran memorial and birth centenary lecture titled "Structure, Mechanism and Function of Polymerases" at the 35th Kerala Science Congress that was held during February 10-14, 2023 at Mar Baselios Christian College of Engineering and Technology, Kuttikkanam.
8. Delivered an invited talk titled "Structural mechanisms utilized by DinB and HP0593 to combat environmental stress in bacteria." at the conference titled "Bacterial Pathogenesis: The role of stress" held at MCARS, Jamia Milia Islamia, New Delhi on February 16, 2023.
9. Participate in the panel discussion titled "Building the Indian Biological Data Centre" (IBDC) in "Accelerating Biology 2023: *Discovery to Delivery*" organised by Bioinformatics Group of C-DAC during 28th Feb- Mar 2, 2023.
10. Attended Vigyan Chintan Shivir organized by Ministry of Science and Technology and Ministry of Earth Sciences during 3-4 March 2023 at Indian Institute of Public Administration, New Delhi.
11. Participated in discussions on central facilities held at IIT-Delhi on March 27, 2023

Prof. Vengadesan Krishnan

1. Attended 'Three-day symposium on Towards end TB: achievements, challenges and future directions' organized by Translational Health Science and Technology Institute, Faridabad, during March 23-25, 2023.
2. Attended a conference on 'Human Microbiome in Health and Disease' organized by Translational Health Science and Technology Institute, Faridabad, during February 15-17, 2023.
3. Participated and delivered an invited talk on 'Purification and visualization of pili from a probiotic *Lacticaseibacillus rhamnosus* GG' at the International Conference on Electron Microscopy & XLI Annual Meeting of Electron Microscope Society of India (EMSI-2023) held

at University of Delhi, Delhi, during February 8-10, 2023.

4. Participated in the 2-day webinar on 'Fermentation: Interplay of Microbes, Immunity and Nutrition' organized by North-Eastern Hill University in association with BIRAC during February 3-4, 2023.
5. Provided support for the Demonstration of Biomolecules and crystals in 3D for IISF held at Bhopal during January 21-24, 2023.
6. Participated in Three days online national workshop on 'Building Institutional Repository and Content Management System through DSpace and Joomla' organized by Central Library, Poornima Institute of Engineering & Technology, Jaipur, during December 28-30, 2022.
7. Attended the GSK online workshop on 'The latest developments in the field of bioinformatics aligned to the needs of the biopharma sector' conducted by GSK as part of RCB-GSK collaboration on December 16, 2022.
8. Attended 'IISF Curtain Raiser event' held at National Media Centre, New Delhi, on December 12, 2022.
9. Attended online '6th Biennial PAi Conference & International Symposium' on "Psychobiotics and Gut: Potential in Neurological Disorders" organized by Probiotic Association of India in association with ICAR-National Dairy Research Institute, Karnal during December 5-6, 2022.
10. Participated and delivered an invited talk on 'Targeting pili-mediated interactions for controlling dental biofilm development and combating infections' at the 49th National Seminar on Crystallography (NSC49) organized at the University of Jammu, Jammu during November 28-30, 2022.
11. Attended the IUBMB-focused meeting on 'Biochemistry and Molecular Biology of RNA Viruses' organized by the Regional Centre for Biotechnology, Faridabad, in association with IUBMB during November 15-18, 2022.
12. Participated and delivered a talk on 'Structural insights into pili-mediated interactions in dental biofilm, plaque' at the 62nd Annual International Conference of the Association of Microbiologists of India (AMI) on the theme, Microbes and Society: Current Trends and Future Prospects (MSCTFP-2022) organized at University of Mysore, Mysuru during September 21-23, 2022.
13. Attended the India EMBO Lecture Course 2022 (IELC2022) on the theme, 'Functional nucleic acids: recent landscape and therapeutics' organized by Regional Centre for Biotechnology, Faridabad, in association with EMBO during August 16-19, 2022.
14. Attended the Biotech Startup Expo-2022 organized by DBT and BIRAC at Pragati Maidan, New Delhi, during June 9-10, 2022.
15. Attended Elsevier webinar on 'Empowering knowledge on ethical publishing: Mastering the art of identifying predatory, fake and cloned journals' on June 8, 2022.
16. Attended the DeLCON 41st Steering Cum Negotiation virtual Meeting on meeting' on April 20, 2022.

Dr. Deepti Jain

1. Invited talk titled "Advanced Technology Platform Centre, RCB" at the I-STEM Tech Management Conclave for Women, ITMC-W from February 21-22, 2023.
2. Invited talk titled "Regulation of flagellar gene expression in *Pseudomonas aeruginosa*" at the conference titled Microbe Matters held at Indian Institute of Science from November 29-30, 2022.
3. Invited talk titled "Structural basis of transcription anti-activation in bacterial motility" at the international conference with the theme "Protein RNA interaction in cellular regulations" held at ICGEB from November 22-24, 2022.
4. Conducted one day hands on structural biology workshop for 35 students of XI and XII visiting RCB from Manav Rachna International School on September 5, 2022.
5. Invited talk titled "Targeting nucleotide binding proteins for anti-biofilm strategies" at the INDIA-EMBO lecture course with the theme "Functional nucleic acids: recent landscape and therapeutics" held at RCB from August 16-19, 2022.
6. Conducted one day hands on structural biology workshop for Biotechnology undergraduate students visiting RCB from various Universities in Gujrat (sponsored by Gujrat State Biotechnology Mission) on August 8, 2022.
7. Invited online lecture titled "Structural Biology approach to understand regulation of gene

expression" at the refresher course in synthetic biology organized by University of Burdwan from June 16-29, 2022.

8. Invited online talk on "Science and Society" organized by Haryana State Council for Science and Technology and DST for celebration of Vigyan Utsav held online on April 18, 2022.

Dr. Prem S. Kaushal

1. Attended, the group monitoring workshop of SERB Early Career Research Awardees-life Science at KIIT University, Bhubaneswar, on May 9-10, 2022.
2. Science outreach activity, visited Govt Primary School, Barshanghar of Distt Kullu, HP and Govt Centre Primary School, Shanghar, Distt Kullu HP. Delivered talks titled "The Importance of Education" on June 1-3, 2022.
3. Attended, Biotech-Startup 2022, organized by the Department of Biotechnology at Pragati Maidan on June 9-10, 2022.
4. Delivered an invited talk (virtual mode), titled "Recent advances in single-particle cryo-electron microscopy (cryo-EM) to determine the structure of biological macromolecules" at "International Seminar on Recent Trends in Omics, Regenerative and Precision Medicine" organized by the University of Kerala & the Kerala Academy of Sciences on July 22-24, 2022.
5. Attended the Annual Convention 2022 on RTI of Central Information Commission at Vigyan Bhawan, New Delhi, on November 9, 2022.
6. Delivered an invited talk, titled "Cryo- EM structure of the mycobacterial ribosome in complex with ribosome hibernation factor, RafH" at the 49th National Seminar on Crystallography organized by the University of Jammu, Jammu, on November 28-30, 2022.
7. Attended, the Curtain Raiser Ceremony of the 8th India International Science Festival (IISF-2022) at the National Media Centre, New Delhi, on December 12, 2022.
8. Delivered an invited talk, titled "Dealing structural heterogeneity in cryo- EM data" at the CEM3DIP meeting at IISER Pune on December 17, 2022.
9. Delivered an invited talk, titled "*Cryo- electron microscopy (cryo- EM): a modern technique for the structure visualization of biomolecules in the atomic details*" at the international conference on Exploring New Horizons in Biotechnology, NEB, 2023, organized by the School of Biotechnology, Banaras Hindu University on February 10–12, 2023.
10. Delivered an invited talk, titled "*The unique strategy of mycobacterial ribosome hibernation revealed by cryo- EM*" at 1st symposium on Cryo- Electron Microscopy of Biological Systems (CEMBioS Symposium) organized by the National Institute of Science Education and Research, NISER, Bhubaneswar, on February 13–14, 2023.
11. Attended, a three-day symposium on "Towards END TB: Achievements, Challenges, and Future Directions" organized by THSTI Faridabad, on March 23-35, 2023.

Prof. Prasenjit Guchhait

1. Teaching "one-day course work on Immunology" at the Indian immunological Society meeting, Chandigarh, India, during November, 2022.
2. "Dietary αKG inhibits SARS-CoV-2 replication and rescues lung pathogenesis to restore O_2 saturation by inhibiting pAkt", Bio analytical Methods and application international workshop of IISER-Kolkata at Ooty, India, June 2022.
3. "Monocytes with Tibetan specific PHD2D4E;C127S mutation display protection against viral infection under hypoxia, but are susceptible to infection under normoxia", International Symposium on Hypoxia at Leh, India, May' 2022.

Prof. Tushar K. Maiti

1. Delivered an invited talk entitled Understanding the intercellular signaling landscape through mass spectrometry-based proteomics at Workshop on Proteomics and Data Analysis, held at Translational Health Science and Technology Institute in association with the Proteomics Society of India from February 9-10, 2023.
2. Participated and chaired a session at Annual Meeting of the Proteomics Society, India and International Conference on Proteins & Proteomics (PSI-ICPP 2022) held at IICB Kolkata from November 3-5, 2022.
3. Delivered an invited talk entitled Application of proteomics technology for management of future pandemics at CEP course on Preparedness and Technological solutions for

Management of Future Pandemics: Lessons Lerarnt from COVID19 held at DRDE, Gwalior 'from September 26– 30, 2022.

Dr. Sam Mathew

1. Delivered the talk "Signals that regulate adult stem cell function" as part of the Science Setu lecture series commemorating the 75th Year of Independence at the Regional Centre for Biotechnology, on April 22, 2022.
2. Hosted 10 undergraduate students sponsored by the Gujarat State Biotechnology Mission (GSBTM) on 11th August 2022, as part of their month-long visit to RCB, giving the talk "Animal models in research" and conducting practical sessions.
3. Invited participant at the 4th BIO Group meeting held at the Indian Institute of Science Education and Research (IISER), Thiruvananthapuram, on August 19-20, 2022.
4. Conducted a demonstration session on using animal models in research to Class XI and XII students visiting RCB from Manav Rachna International school on September 2, 2022.

Dr. Pinky Kain

1. Delivered an invited talk titled "Role of circadian clocks and sleep in mediating metabolism" at Aligarh Muslim University on January 5, 2023.
2. Delivered an invited talk title "Understanding gustatory processing using *Drosophila* as a model system" at Aligarh Muslim University November 7, 2022.
3. Delivered an invited talk titled "Understanding gustatory processing using *Drosophila* as a model system" at IISER Thiruvananthapuram May 26, 2022.
4. Online mentoring of students at Freedom Academy of employability (Delhi and Lucknow)

Dr. Geetanjali Chawla

1. Presented talk titled "Molecular dissection of a conserved cluster of microRNAs", at the 11th RNA Group meeting, organized by NCCS, Pune, December 1, 2022.
2. Serving as a volunteer in the Evidence synthesis team of the Lancet Commission for Reimaging healthcare in India, since February, 2021.
3. Served as a mentor in the Freedom Employability academy since 2018.

Prof. Chittur Srikanth

1. Delivered an online invited talk titled, "*Salmonella* mediated host epigenetic modifications and their possible long-term consequences", a part of IIN talks supported by EMBO on December 8, 2022.
2. Delivered an invited talk titled "Rab7 dependent secretory function of intestinal cells in colitis (IBD)", at the 'Mini symposium on Latest in Autophagy and Lysosomal Biology' organised by CSIR-IGIB, Delhi on January 12, 2023.
3. Delivered an invited talk titled '*The tale of SUMO wrestling in Salmonella pathogenesis: much to learn*' at the international conference on Microbial technologies for sustainable Biosphere at MDU, Rohtak on February 3, 2023.
4. Participated in the one day meeting on Health Research @NCR - from bench-to-bedside at Ashoka University, Sonipat, on February 4, 2023.
5. Participated in the Chintan Shivir on S&T organised by Ministry of Science and Technology and Ministry of Earth Science at IIPA, New Delhi during March 3-4, 2023.

Dr. Manjula Kalia

1. Delivered an invited talk titles 'Pharmacological modulation of autophagy as a potential therapeutic for Japanese encephalitis' at NBRC, Manesar '27th meeting of Society of NeuroImmune Pharmacology' March 15-18, 2023.
2. Delivered an invited talk titled 'Antiviral and neuroprotective effects of phenothiazines in Japanese encephalitis virus infection' at IISC, Bangalore 'Biological Transactions: From molecules to organisms' January 18-21, 2023.
3. Delivered an invited talk titled 'Antiviral and neuroprotective effects of phenothiazines in Japanese encephalitis virus infection' at CSIR-IGIB Mini Symposium 'Latest in Autophagy and Lysosome Biology' on January 12, 2023.

Academic & Training Activities |

4. Delivered an invited talk titled 'Pharmacological modulation of autophagy as a potential therapeutic for Japanese Encephalitis Virus' at the IIT Mandi & SPARC sponsored INDO-US symposium on Molecular Virology -2022 held online from February 15-17, 2022.
5. RCB Science Setu seminar titled 'Targeting cellular stress responses as an anti-viral strategy for Japanese encephalitis' on March 25 2022.

Dr. Arup Banerjee

1. Delivered an invited talk titled 'Next Generation Sequencing & Exosomal RNA profiling' at the 'ExoTECH – 2022 Exosomes: A Platform for Novel Therapy and Diagnostics' organized by AIIMS, New Delhi' October 10-12, 2022.

Dr. Prasad Abnave

1. Participated in the Group Monitoring Workshop of SERB Startup Research Grant - Life Sciences (SRG-LS) at IIT, Indore during July 4-5, 2022.
2. Participated in the Inflammation Symposium organized by the Translational Health Science and Technology Institute (THSTI), Faridabad held on July 14, 2022.
3. Participated and chaired a session in India EMBO conference on "Functional nucleic acids: recent landscape and therapeutics" at RCB during August 16-19, 2022.

Dr. Anil Thakur

1. Attended Yeast India conference 2023 (Fundamentals to applications of yeast and fungi) at Indian Institute of Sciences Education and Research Mohali (IISERM) from March 10-13, 2023.
2. Hosted students from Ramjas College, New Delhi to showcase ongoing research of RCB as a part of the SERB Scientific Social Responsibility (SSR) on January 12, 2023
3. Hosted students from Ladakh to showcase ongoing research of RCB on January 27, 2023.
4. Presented poster in 13th DBT-Ramalingaswami fellowship Conclave at Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvanthapuram from November 30 - December 3, 2022.
5. Presented and participated in the Group Monitoring Workshop of SERB Startup Research Grant - Life Sciences (SRG-LS) at IIT, Indore from July 4-5, 2022.

Prof. Avinash Bajaj

1. Delivered an invited talk entitled Localized Drug-Loaded Hydrogel Implant can Reduce Distant Tumor Growth via Activation of Systemic Immune Response at 16th International Cancer Symposium on "Translational Chemoprevention and Brainstorming" being organized by Special Centre for Systems Medicine & School of Life Sciences Jawaharlal Nehru University (JNU), New Delhi, India on November 18 -19, 2022.
2. Delivered an invited talk entitled Unlocking the Chemistry of Bile Acids for Biomedical Needs at Government College, Faridabad on October 19, 2022.
3. Delivered an invited talk Unlocking the Potential of Nanomaterials to Address the Unmet Biomedical Needs at International Conference on Nanotechnology; Opportunities and Challenges (ICNOC 2022) organized in virtual mode by Department of Applied Sciences & Humanities, Jamia Millia Islamia (Central University), New Delhi, India during November 28-30, 2022.
4. Delivered an invited talk Engineering of Chimeric Nanomicelles for Temporal Targeting of Tumor Microenvironment at International conference on Biomaterials, Regenerative Medicine and Devices, BIO-Remedi 2022 organized by Indian Institute of Technology Guwahati (IITG), Assam, India during 14th –18th, December 2022.
5. Delivered an invited talk Strengthening the Pillars of Nanomedicine to Combat Cancer at 42nd Annual Convention of the Indian Association of Cancer Research held at the Advanced Centre for Treatment Research and Education in Cancer (ACTREC), Tata Memorial Centre, during January 12- 15, 2023.
6. Delivered an invited talk Membrane-Specific Probe can Detect *Mycobacteria* in Human Gastrointestinal Tissues at two-day Symposium on "End TB: Achievements, Challenges and Future Directions" organized by THSTI, Faridabad during March 24-25, 2023.

Prof. Sivaram Mylavarapu

1. Delivered an invited research talk titled "Faithfully promiscuous: a twist in the tail for dynein function during mitosis" at the Interdisciplinary Approach to Biological Sciences (IABS) 2023 conference held at the Indian Association for the Cultivation of Science (IACS) Kolkata, from

February 1-3, 2023.

2. Delivered an invited research talk titled "Faithfully promiscuous: a twist in the tail for dynein function during mitosis" at the Autophagy India Network (AIN) 2023 meeting held at the CSIR-Institute of Microbial Technology (CSIR-IMTECH), Chandigarh from February 17-19, 2023.
3. Moderator for a panel discussion on the topic "Careers for Research Scholars: The Conventional and the Contemporary" at the EMBO Lecture course 2022 titled "Functional nucleic acids: recent landscape and therapeutics", held at RCB Faridabad from September 17-19, 2022.

Dr. Rajender K Motiani

1. Delivered an invited talk titled "Basic Science for Atmanirbharatha" at Vigyan Utsav as a part of Azadi Ka Amrit Mahotsav organized by Haryana State Council for Science, Innovation & Technology, Panchkula on June 15, 2022.
2. Delivered an invited talk titled "Calcium dynamics is a critical determinant of human skin pigmentation" at India Investigator Network (IIN) Webinar Series on June 23, 2022.
3. Delivered lecture to Masters students undergoing training at RCB as part of Gujarat State Biotechnology Mission (GSBTM) titled "Keeping peace with peace keeper to curtail pancreatic cancer" on August 12th 2022. These students further did one day rotation in our laboratory.
4. Delivered an invited talk titled "Calcium dynamics: a critical determinant of human skin pigmentation" at 12th Indo-Japan Scientific Conclave (ICFAST-2022), University of Hyderabad on September 10th2022.
5. Delivered an invited talk titled "Zebrafish: Rearing, Breeding, Microinjections and Model System" at 4th Workshop on Basic Training in Animal Handling and Experimentation, Institute of Liver and Biliary Sciences (ILBS), New Delhi on November 5, 2022.
6. Delivered an invited talk titled "Zebrafish as an in vivo model system: From basics of rearing to applications in biomedical research" at Certificate Course on Laboratory Animal Science, National Brian Research Centre (NBRC), Manesar on February 16th 2023.

Dr. Karthigeyan Dhanasekaran

1. Centrosome in viral pathobiology, RCB-PAC meeting, Oct, 2022.
2. Presented poster in IUBMB Focused meeting on the Biochemistry and Molecular biology of RNA viruses during November 15-18, 2022.
3. Attended India | EMBO Lecture course on Functional nucleic acids, August 16-19 2022.
4. Mentored short term trainee Ms. Neha Sharma from January-April 2022.
5. Mentored dissertation trainee Mr. Shankar Jan-June from 2023 and Mr. Sampathkumar from January-April 2023.

Dr. Saikat Bhattacharjee

1. Delivered an invited Seminar titled '*Inositol polyphoshphate-kinases regulate functional dynamics of a central cellular hub in maintenance of phosphate homeostasis in plants'* at the 'Inositol Phosphates: Cellular messengers at the interface of metabolism and signaling' Meeting Indian Institute of Science, Bengaluru, India, November 25-26, 2022.
2. Delivered an invited Seminar titled *'Dynamics of a central macromolecular complex in defense signaling of plants Cause and consequences?*' at the 'International Conference on Plant Genetic Engineering and Genome Editing', Central University of Kerala, Kasargod, India, October 27-29, 2022.
3. Delivered an invited virtual Seminar titled '*Inositol polyphosphates regulate dynamics of COP9 signalosome activities on Cullin RING ligase functions'* at the International Inositol Phosphates: the MORE, the MERRIER, 2023' Meeting January 9-11, 2023.

Dr. Divya Chandran

1. Delivered an invited lecture entitled "Exploiting pathogen effectors for fungal disease management in crops" as part of the International Conference on Current Technologies and Opportunities in Bio-Science organized by College of Agriculture, Hassan, University of Agricultural Sciences, Bangalore and COMBETT Institute, Bangalore, on March 28, 2023.

2. Delivered an invited lecture entitled "A secondary metabolic pathway conferring powdery mildew resistance in legumes" as part of the International Conference on Food and Nutritional Security organized by NABI-CIAB, Mohali, on January 09, 2023.
3. Delivered an invited lecture entitled "Using the model legume *Medicago truncatula* to identify molecular targets for powdery mildew resistance in crop legumes" as part of the Technical Symposium on Basic Science and Technology for Sustainable Development organized by INYAS and BARC, Mumbai on September 17, 2022.
4. Co-organized an educational visit for high school students and teachers from Manav Rachna International School, Faridabad, on September 01, 2022.
5. Delivered an invited lecture entitled "Using functional genomics to elucidate the mechanisms underlying legume-powdery mildew interactions" as part of the Kosambi International Webinar Series on Plant Genomics organized by Savitribai Phule Pune University, Pune and Plaksha University, Punjab on August 01, 2022.
6. Delivered an invited lecture entitled 'Uncovering the role of isoflavonoids in powdery mildew resistance in legumes' as part of the International Symposium On Advances In Plant Biotechnology And Nutritional Security-2022 organized by the Plant Tissue Culture Association (India), NASC Complex, New Delhi on April 29, 2022.
7. Co-organized a monthly Science Setu lecture series to showcase the ongoing research programs at RCB as part of the DBT 75th year of Indian independence celebratory event, April-August 2022.

Dr. Ramu S Vemanna

1. Delivered an invited talk titled "Ribosomal proteins role in improving protein synthesis under drought stress" at the conference 'Biotechnology trends and future prospects' organized by Department of Plant Biotechnology, University of Agricultural Sciences, GKVK. September 13-15, 2022.
2. Delivered an invited virtual talk titled " Small molecules and gene editing approaches to improve crop protection" at "Current trends in rapid diagnosis and management of emerging diseases and insect pests in horticultural crops", a workshop organized by the Division of Crop Protection, ICAR- Indian Institute of Horticulture Research, Bangalore, July 11-23, 2022.
3. Delivered an invited virtual talk titled "Improving drought stress adaptation of crops using gene editing approaches" at "capacity building programme on Genomics of abiotic stress in crop plants" organized by Full bright Specialist: Dr. Kalapalatha Melmaie, Assoc. Prof., Delaware State University, Dover, Delaware, USA at Centre for Plant Breeding and Genetics, TNAU, Coimbatore, July 11, 2022.
4. Delivered an invited talk titled "Creating genetic variability to improve agronomic traits in rice" at "International Conference on Food and Nutritional Security" (iFANS-2023). Organized by National Agri-Food Biotechnology Institute (NABI), Mohali, Punjab, India January 6-9, 2023.

Dr. Prashant Pawar

1. Attended and presented at SERB-SRG Group Monitoring Workshop at IIT-Indore, July 4-5, 2022.
2. Attended Kosambi International Webinar Series organized by the Department of Botany, Savitribai Phule Pune University, July 31-August 01, 2022.
3. Attended the conference titled Functional nucleic acids: recent landscape and therapeutics at the Regional Centre for Biotechnology, Faridabad, August 16-19, 2022.
4. Attended Plant Cell Webinar on Plant Responses to Abiotic Stresses, February 7, 2023.

Dr. Ambadas B. Rode

1. Delivered an invited talk entitled "Role of alternate RNA conformations in human health and disease" in Karyashala (workshop) on Advanced Bio-analytical methods and applications at Ooty Organised by IISER Kolkata between June 14-19, 2022.
2. Delivered an invited talk entitled "Role of alternate RNA conformations in human health and disease" in SERB- Innovative Inclinations and Sustainable Technologies in Chemical Sciences (IISTCS) national symposium at Deogiri College, Aurangabad on February 24, 2023.
3. Delivered a talk entitled 'Role of Alternate RNA Conformations in Human Health and Disease' in an International conference India EMBO lecture course on 'Functional Nucleic

Acids: Recent Landscapes and Therapeutic Applications' at RCB, Faridabad from August 16-19, 2022.

Dr. Nidhi Adlakha

1. Delivered an invited talk titled 'Path to Product-Development of microbial cell factories for innovative bioproduction' organised by Shaheed Rajguru College of Applied Sciences for Women, University of Delhi, on February 23, 2023.
2. Attended IISF Mega Expo (IISF2022) held in MANIT, Bhopal from January 21- 24, 2023.
3. Mentored an educational visit of students and teachers from Daulat Ram College, University of Delhi on Industrial Biotechnology, held on March 23, 2023.

Prof. Rajendra P Roy

1. Delivered a talk entitled "Breaking and Making Peptide Bonds", ID75 Science Setu Webinar at RCB, Aug 5, 2022

Reviewer of proposals/thesis/research articles

Prof. Deepak T Nair

1. Reviewer of research proposals and progress reports submitted to the SERB Program Advisory Committee for Interdisciplinary Biological Sciences
2. Reviewer for the journals *Nucleic Acids Research, Nature Communications, FEBS Journal Chembiochem & Biochemistry.*
3. Reviewer of proposals submitted for synchrotron beamtime to the European Synchrotron Radiation Facility Access Program of the Regional Centre for Biotechnology
4. Review of research programs and promotion applications
5. Examiner for PhD theses from IIT, IISc and AcSIR

Dr. Vengadesan Krishnan

1. Viva-voce examiner and reviewer for PhD thesis from Academy of Scientific and Innovative Research (AcSIR), New Delhi.
2. Reviewer for PhD thesis from Jawaharlal Nehru University (JNU), New Delhi.
3. Reviewer for *Microbial Pathogenesis, Biophysical Chemistry, Vaccines, International Journal of Biological Macromolecules, Journal of Biomolecular Structure and Dynamics*, *Protein & Peptide Letters*, *Frontiers in Cellular and Infection Microbiology,* and *Frontiers in Microbiology.*

Dr. Deepti Jain

1. Review Editor of Frontiers in Bioengineering and Biotechnology
2. Reviewer for PhD thesis from IISER-Pune, JNU, CDRI
3. Reviewer for *FASEBJ, International Journal of Biological Macromolecules*

Dr. Prem S. Kaushal

1. Reviewer for research grants of DST-SERB
2. Reviewer for Ph.D. thesis from Osmania University, Hyderabad

Prof. Prasenjit Guchhait

1. Reviewer of the *DBT/Wellcome* Trust India *Alliance* (India *Alliance*) grants 2023.
2. Reviewer for research proposals for BIRAC, DBT, Govt. of India, 2019-present.
3. Reviewer for Scientific Journals: *Blood*, *Frontiers in Immunology*, *Frontiers in Medicine, Frontiers in Hematology* 2022-2023
4. PhD thesis reviewer for 2 students of other University in India

Prof. Tushar K Maiti

1. Reviewer for *Biochemical J, Biomacromolecules, J Proteomics, Bioscience Report, Int J Biol. Macromol*
2. Reviewer for DST-CRG grant proposal
3. Reviewer for PhD thesis from Tezpur University, Assam and NIPER Ahmedabad

Dr. Sam Mathew

1. Reviewer for research proposals for DBT, CSIR, SERB, Israel Science Foundation, Medical

Research Council (UK), and INSERM-CNRS (France).

2. Reviewer for PhD thesis from AcSIR, Indian Institute of Science, Jawaharlal Nehru University, Manipal University, and Sastra University.
3. Reviewer for *Cell Death and Disease*, *Developmental Biology*, EMBO Molecular Medicine, *FASEB Journal*, *Journal of Cell Science*, *FEBS Letters*, *Molecular Therapy*, *Molecular Therapy-Nucleic Acids*, *IUBMB Life, Frontiers in Immunology* and *Scientific Reports.*

Dr. Pinky Kain

1. Reviewer for Scientific reports
2. Reviewer for PloS One
3. Reviewer for Neural Regeneration Research
4. Reviewer for Science Progress
5. Reviewer for Neuroscience insights
6. Reviewer for Annals of the Entomological Society of America
7. Reviewer for Journal of Biosciences
8. Reviewer for International journal of Gastronomy and food science
9. Reviewer for International journal of Autism and related disabilities

Dr. Geetanjali Chawla

1. Reviewer for *PLOS Genetics, PLOS One, Insect Science, Journal of Bioscience*
2. Reviewer for DBT proposals

Dr. Manjula Kalia

1. Review Editor for Frontiers in Cellular & Infection Microbiology
2. Review Editor for Frontiers in Neurology
3. Reviewer for *Autophagy, Journal of Virology, mBio, Science Signalling, Cell Stress & Chaperones, Vet. Microbiology, Scientific Reports, Plos one.*
4. Reviewer for PhD thesis from ICGEB, KIIT, CSIR-IMTECH, Cochin University, Savitribai Phule Pune University.

Dr. Arup Banerjee

1. Review editor, Virology section, Frontiers in Microbiology
2. Reviewer for Ph.D. thesis from BHU

Dr. Prasad Abnave

1. Reviewer for journal "Nature Communications"
2. Review Editor for journal "Frontiers in Cellular & Infection Microbiology"
3. Review Editor for journal "Frontiers in Cell and Developmental Biology"
4. Reviewer for journal "Pathogens"

Dr. Anil Thakur

1. Reviewer for *Scientific reports*
2. Reviewer for research proposal/grants for SERB, DST
3. Reviewer of Journal of Pharmaceutical Research International

Prof. Avinash Bajaj

1. Reviewer, American Chemical Society.
2. Reviewer, Royal Chemical Society

Dr. Rajender K Motiani

1. Reviewer of research proposals submitted to SERB, DST: Core Research Grants.
2. Reviewer for the Journals: Journal of Biological Chemistry, Mitochondrion, Pigment Cell & Melanoma Research, Cells, International Journal of Molecular Sciences and Cell Calcium.
3. Ph.D. Thesis Examiner of Mr. Hemang Brahmbhatt, Institute of Genomics and Integrative Biology (IGIB), New Delhi and Ms. Sunanda, Institute of Genomics and Integrative Biology (IGIB), New Delhi.
4. Ph.D. Viva Examiner of Mr. Hemang Brahmbhatt, Institute of Genomics and Integrative Biology (IGIB), New Delhi.

Dr. Karthigeyan Dhanasekaran

1. Reviewer for IEEE Access
2. Reviewer for Cell Biology

Dr. Saikat Bhattacharjee

1. Expert for Plant and Molecular Biology, Question Paper Settling, JNU Entrance Examination, National Testing Agency (NTA)
2. Reviewer for *Plant Cell Reports* and *Planta*
3. Expert Reviewer for SERB-CRG proposal
4. Reviewer of Ph.D. thesis from CSIR-IHBT

Dr. Divya Chandran

1. Reviewer for *Plant Communications, Journal of Experimental Botany, Plant Physiology and Biochemistry*, *Genomics*, *Frontiers in Plant Science*
2. Reviewer of Ph.D. thesis from IISER Mohali and JNU
3. Expert Reviewer for SERB-CRG proposal

Dr. Ramu S Vemanna

1. Expert Reviewer for SERB-CRG and DBT proposals
2. Reviewer of Ph.D. thesis from IARI, New Delhi
3. Reviewer for *Plant Physiology*, *Frontiers in Plant Sciences, Journal of Soil Science and Plant Nutrition*, *Plant Molecular Biology Reporter*, *Tissue and Organ Culture*, *Plant Physiology Reports*, *Molecular Biotechnology*, *Cells*, *Agronomy*, *IJMS*

Dr. Prashant Pawar

1. Reviewer for *Frontiers in Bioengineering and Biotechnology*, *Frontiers in Energy Research*, *Plant Physiology and Biochemistry*.

Dr. Ambadas B. Rode

1. Expert Reviewer for DST research proposals
2. Reviewer for *Journal of Applied Biochemistry and Biotechnology*, *Process Biochemistry*, *Genes*, and *Biomolecules*.

Dr. Nidhi Adlakha

1. Expert Reviewer for DBT and CSIR research proposals
2. Reviewer for *Applied and Microbial Technology and Infections* and *Biotechnology for Biofuel*
3. Reviewer of Ph.D. thesis from ICT Mumbai and IIT Mandi

EXTRAMURAL ACTIVITIES & NETWORKING

Courtesy: Dr. Nidhi Sharma

ESRF Access Program

Regional Centre for Biotechnology (RCB) and European Synchrotron Radiation Facility (ESRF) have entered into an agreement concerning the medium-term use of synchrotron for non-propriety research for the benefit of the Indian scientific community as a whole, and notably the structural biology research groups. The program provides access to Indian investigators to experimental stations for macromolecular crystallography, small angle X-ray scattering and Cryo-Electron Microscopy located in ESRF.

The DBT-supported ESRF access program of the RCB helps Indian researchers to carry out experiments at this unique facility located in Grenoble, France. The program, in its current form, was initially flagged off in June, 2017 by the Honourable Minister for Science & Technology, Dr. Harsh Vardhan in the presence of Prof. Sudhanshu Vrati and the then DBT Secretary, Prof. K. VijayRaghavan. The initial agreement was renewed by Prof. Vrati and Dr. Francesco Sette (Director General, ESRF) for another three years till January, 2023. At present, discussions are on with DBT to renew access for another three to five years.

In the last six years, researchers from 30 different institutes from all over India have obtained X-ray diffraction, small angle X-ray scattering or Electron Microscopy data for different macromolecules and macromolecular assemblies. The list of institutions are as follows: - All India Institute of Medical Sciences (New Delhi), CSIR-Central Drug Research Institute (Lucknow), CSIR-Central Leather Research Institute (Chennai), CSIR-Institute of Genomics & Integrative Biology (New Delhi), CSIR- Institute of Microbial Technology (Chandigarh), Indian Institute of Science (Bangalore), Indian Institute of Science Education & Research-Bhopal, Indian Institute of Science Education & Research-Pune, Indian Institute of Science Education & Research-Thiruvananthapuram, Indian Institute of Science Education & Research-Tirupathi, Indian Institute of Technology-Bombay (Mumbai), Indian Institute of Technology-Delhi, Indian Institute of Technology-Kharagpur, Indian Institute of Technology-Roorkee, Institute of Life Sciences (Bhubhaneswar), Institute of Stem Cell & Regenerative Medicine (Bangalore), International Centre for Genetic Engineering and Biotechnology (New Delhi), Jawaharlal Nehru University (New Delhi), National Centre for Cell Sciences (Pune), National Chemical Laboratories (Pune), National Institute of Immunology (New Delhi), National Institute of Mental Health & Neurosciences (Bangalore), National Institute of Plant Genome Research (New Delhi), National Institute of Science Education & Research (Bhubhaneswar), Poornaprajna Institute of Scientific Research (Bangalore), Regional Centre for Biotechnology (Faridabad), Saha Institute of Nuclear Physics (Kolkata), St. Xaviers College (Kolkata), Translational Health Science and Technology Institute (Faridabad), and University of Madras (Chennai).

The ESRF access program has enabled Indian researchers to publish more than 200 research papers involving basic and applied research in the last six years, in international peer-reviewed journals. Due to this program, more than 100 researchers, largely PhD students, have been trained in cutting-edge methods in Structural Biology. The program has helped Indian scientists to obtain data that will aid formulation of innovative solutions to problems faced by the nation in the areas of health, agriculture and environment.

Indian Biological Data Centre (IBDC)

The Indian Biological Data Centre (IBDC) is the first national digital data repository mandated to archive all life science data generated from publicly funded research in India. It is supported by the Government of India (GOI) through the Department of Biotechnology (DBT). It enables the implementation of the "Biotech-Pride Guidelines" (Promotion of Research and Innovation through Data Exchange). The computational infrastructure including a High Performance.

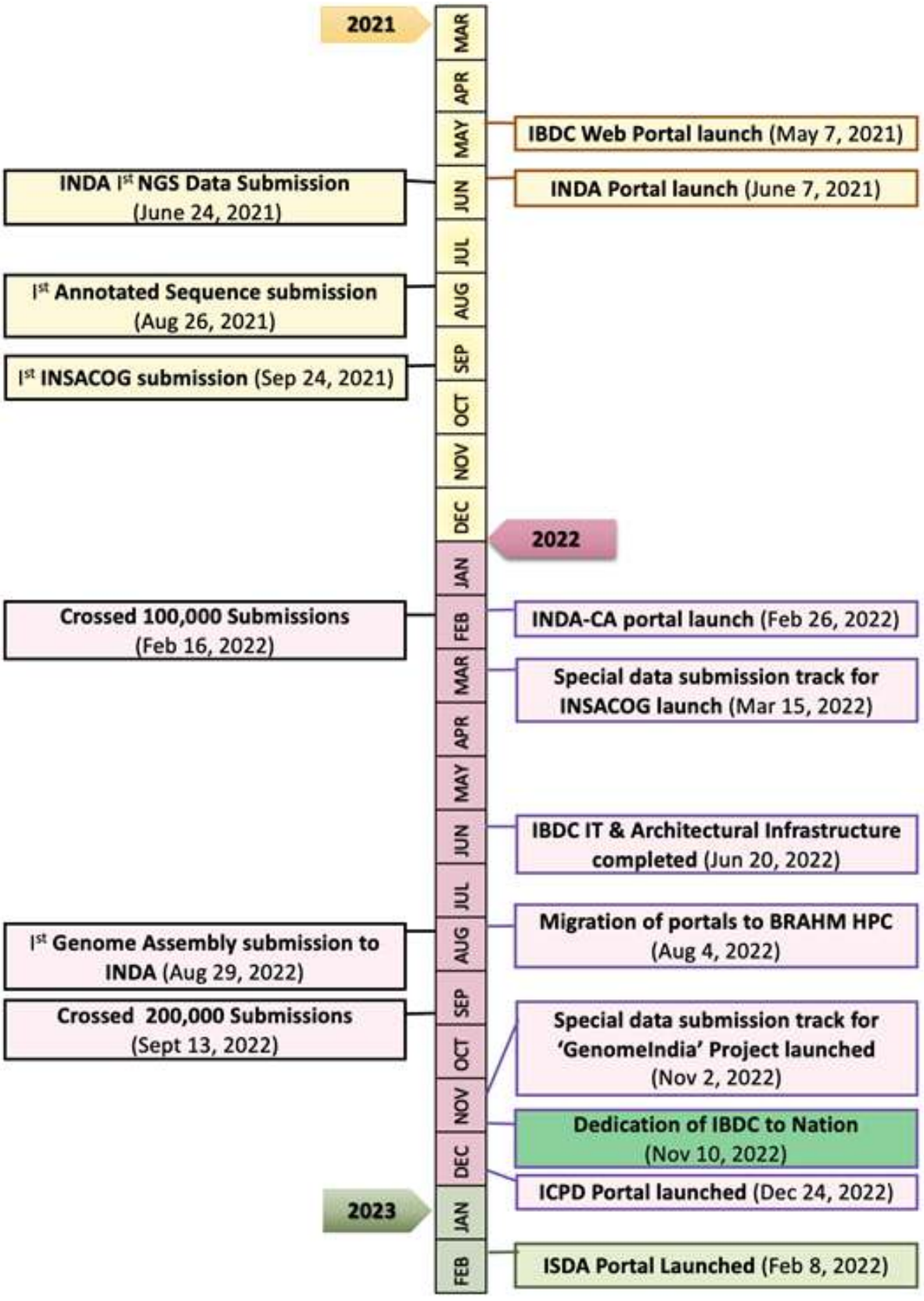


Figure 1. *Milestones during the development of the Indian Biological Data Center (IBDC).*

Computation (HPC) cluster and archival data storage is hosted at RCB and NIC, Bhubaneswar. RCB house a compute power of about 800 Tera Flops (AI mixed precision) alongwith a 3.2 PB (PetaByte) of storage, while NIC (Bhubaneswar) has data storage capacity of about 900 Tb. The two sites are connected by high band-with internet connectivity through NKN. The biological data generated by researchers in India is being archived and curated at RCB.
Owing to the magnitude and complexity of the expected data, IBDC is being developed in a modular nature. Currently, IBDC operates through four specialized data portals dedicated to the management of diverse biological data types (Figure 2).

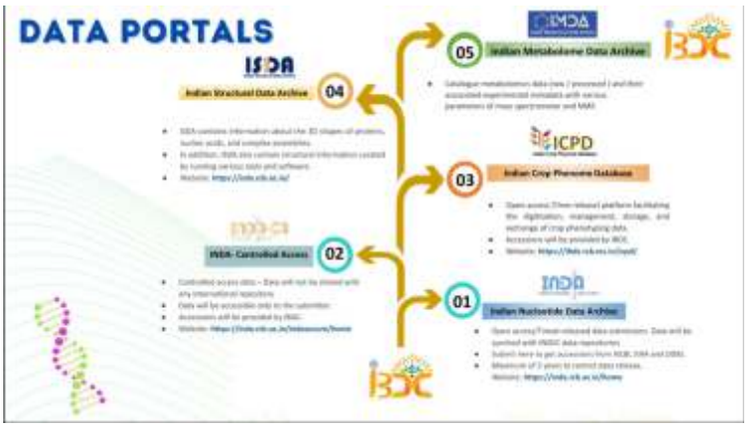


Figure 2. *Overview of various data portals at IBDC.*

Indian Nucleotide Data Archive: INDA is an open-access (Time released) platform for archiving, managing, and sharing diverse types of nucleotide sequencing data generated across India. Data is synched with INSDC (The International Nucleotide Sequence Database Collaboration) repositories like GenBank-NCBI, ENA, and DDBJ. Submission to IBDC automatically generates both IBDC and INSDC (GenBank, ENA-EMBL, and DDBJ) accessions and thus there is no need to re-submit the data to international repositories (Fig. 3).

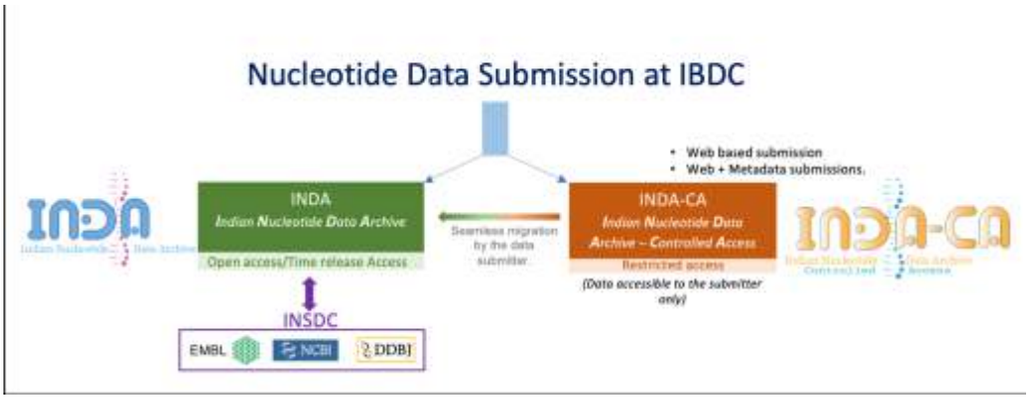


Figure 3. *Nucleotide data submission at IBDC*

Indian Nucleotide Data Archive-Controlled Access: INDA-CA is a controlled access platform for archiving and managing diverse types of nucleotide sequencing data (similar to INDA) generated across India. In contrast to INDA, data submitted to INDA-CA is not shared with any international repository and resides securely on servers in India (IBDC) only. Data submitters can control the access of their data sets in consultation with the data center team. IBDC has also developed special submission tracks for projects of national relevance such as INSACOG, and GENOMEINDIA. Presently 230551 SARS-CoV-2 genomes have been submitted via INSACOG track while 1800 ubam with 1624 gvcf files has been submitted through GenomeIndia track.
In general, currently 2,37,551 nucleotide datasets have been submitted to IBDC (INDA/INDA-CA). Figure 4. shows the organism-wise summary of the nucleotide data submitted to INDA/INDA-CA .

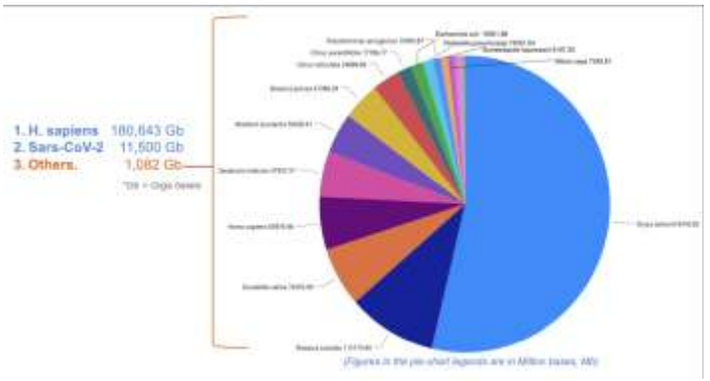
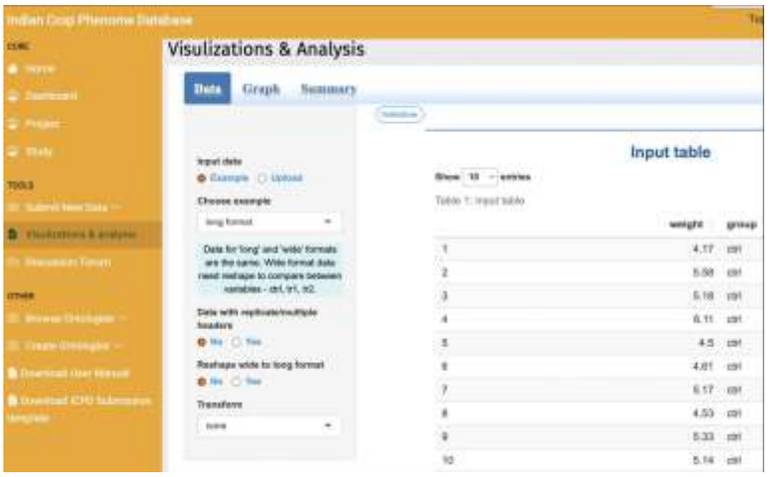


Figure 4. *Organism-wise summary of Nucleotide data submission at IBDC*

Indian Crop Phenome Database: ICPD is an open-access (Time released) platform facilitating the digitization, management, storage and exchange of crop phenotyping data following FAIR data guidelines. The portal provides data formats for submission of phenotyping datasets from 30 different crops (Fig. 5a). Data from 6571 different plant traits using over 7000 different experimental techniques can be submitted. All submissions are provides permanent accessions by IBDC.

(a)



(b)

Figure 5. *Overview of the 'Indian Crop Phenome Database' or ICPD data portal. (a) Snapshot of the ICPD web data portal. (b) Snapshot of the phenotyping data visualization and analysis utility at ICPD.*

The data portal also provides personalized desktops for the users where thay can view and analyze their submitted data sets (Fig. 5b). Tools for graphical visualization and statistical analysis of the submitted data is also provided on the web dashboard.

Indian Structural Data Archive: ISDA is a structural biology archive that contains information about the 3D shapes of proteins, nucleic acids, and complex assemblies. In addition, ISDA also contains structural information curated by running various tools and software.

In addition to data archiving services, IBDC also provides bioinformatics data analysis and access to 'BRAHM-HPC' to research community upon request. Several research groups are already availing the HPC storage service and analysis support from IBDC. To guide and explain the users

to the submission process of data to IBDC portals database-specific SOPs, HPC request form and BRAHM-HPC access guide and video tutorials are made available on IBDC website under tutorials-SOP section (https://ibdc.rcb.res.in/tutorial-sop/). Further IBDC support (support@ibdc.rcb.res.in) dedicatedly handles all user-specific queries and service requests.

Figure 6. *Summarization of various outreach activities of IBDC.*

Team IBDC comprise a blend of experts from diverse disciplines including different domains of biological sciences, bioinformatics, information technology, etc. A total of 27 personnel have been recruited and trained extensively in various IBDC activities.

Academic Program with GlaxoSmithkline Pharmaceuticals India Private Ltd. (GSK)

RCB offers interdisciplinary PhD programmes in Biostatistics and Bioinformatics supported through a collaboration with the global pharmaceutical giant, GSK. These programmes are run as per RCB statutes, ordinances and regulations.

MoU with CDRI

RCB has entered an MoU with CSIR-Central Drug Research Institute, Lucknow to provide cooperation through collaborative research programs, student and faculty exchange programs, sharing of instrumentation facilities and submission of joint projects.

Collaborators of Faculty Members

RCB Principal Investigator	Collaborators
Prof. Deepak T. Nair	Prof. D. N. Rao (IISc, Bangalore), Prof. Pradeep Kumar (IIT-Bombay, Mumbai), Dr. Rajesh Kumar (IIT-Roorkee), Dr. Dinakar M. Salunke (ICGEB, New Delhi), Dr. VG Vaidyanathan (CSIR-CLRI, Chennai), Dr. Shailendra Asthana (THSTI, Faridabad), Prof. Sangeeta Sawant (SPPU, Pune) and Dr. Urmila Kulkarni-Kale (SPPU, Pune)
Prof. Vengadesan Krishnan	Dr. Priti Saxena (SAU, New Delhi), Dr. Amit Kumar Pandey (THSTI, Faridabad), Dr. Airi Palva's group (University of Helsinki, Finland), Dr. RP Roy (RCB, Faridabad)
Dr. Deepti Jain	Prof. Sudhanshu Vrati, Prof. Deepak T Nair, Dr. Divya Chandran, Dr. Ambadas Rode (RCB), Dr. Gopaljee Jha, (NIPGR, New Delhi), Prof. Sunil Kumar Khare (IIT Delhi)
Dr. Prem S. Kaushal	Dr. Rajesh Ringe (IMTECH), Dr. Anil Thakur (RCB), Prof. Nisheeth Agarwal (THSTI), Prof. N. Gourinath (JNU)
Prof. Tushar K Maiti	Dr. Dinakar M Salunke (ICGEB, New Delhi), Dr. Shinjini Bhatnagar, Dr. Bhabatosh Das, Dr. Nitya Wadhwa, Dr. Pallavi Kshetrapal (THSTI, Faridabad), Dr. Partha P Majumder, Dr. Arindam Maitra (NIBMG, Kalyani), Dr. Neel Sarovar Bhavesh (ICGEB, New Delhi)
Dr. Sam J Mathew	Dr. Tushar Maiti (RCB, Faridabad), Dr. Manoj Menon (IIT, New Delhi), Dr. Ramandeep Singh (THSTI, Faridabad), Dr. Janvie Manhas (AIIMS, New Delhi), Dr. Munia Ganguli (IGIB, New Delhi), Dr. Jayanth Kumar (AIIMS, New Delhi), Dr. Gargi Bagchi (Amity University, Gurugram), Dr. Ruchi Tandon (THSTI, Faridabad), Dr. Vivek Natarajan (IGIB, New Delhi)
Dr. Pinky Kain	Prof. Teiichi Tanimura (Nagoya University, Nagoya, Japan), Prof. Axel Brockmann (NCBS-TIFR, Bangalore, India), Prof. S.V.Eshwaran (TERI, Delhi, India), Dr. Nisha Kannan (IISER TVM)
Dr. Geetanjali Chawla	Prof. Pankaj Kapahi (The Buck Institute for Research on Aging, CA, USA), Dr. Nick Sokol (Indiana University)
Prof. Prasenjit Guchhait	Dr. Ashley L St. John (Duke-NUS Medical School, Singapore), Prof. Josef T Prchal (Univs of Utah, Salt lake city, USA), Prof. Perumal Thiagarajan, Prof. Miguel M Cruz, Dr. Andrew Yee (Baylor College of Medicine, Houston, USA), Prof. Jorge Di Paola (Washington Univs, St Louis, USA), Dr. David Scheim (US Public Health service, Blackburg, USA), Prof. Tulika Seth, Prof. Rajesh Khadgawat, Prof. Naval Vikram, Dr. Suman Das (AIIMS, New Delhi), Prof. Parvaiz Kaul (SKIMS, Srinagar), Prof. Anil K Pandey (ESIC Hospital, Faridabad), Prof. Ramandeep Singh, Dr. Shailendra Asthana, Dr. Milan Surjit, Dr. Tripti Srivastava (THSTI, Faridabad), Prof. Anirban Basu (NBRC, Manesar), Dr. Surajit Karmakar (INST, Mohali), Dr. Garima Agarwal (IIT, Mandi), Prof. Sudhanshu Vrati, Dr. Manjula Kalia, Prof. Tushar K Maiti, Dr. Rajender Motiani (RCB, Faridabad)
Prof. Chittur Srikanth	Dr. Vineet Ahuja, Gastroenterology (AIIMS, Delhi), Dr. Girish Ratnaparkhi (IISER, Pune), Dr. Pramod Garg (THSTI, Faridabad), Dr. Sujoy Paul, Gastroenterology (AIIMS, Delhi), Dr. Prasenjit Das, Gastroenterology (AIIMS, Delhi)
Dr. Manjula Kalia	Dr. Dinesh Mahajan (THSTI), Dr. Shailendra Asthana (THSTI), Dr. Krishnan H Harshan (CSIR-CCMB), Dr. Santosh Chauhan (CSIR-CCMB)
Dr. Arup Banerjee	Dr. Sujata Mohanty (AIIMS, New Delhi), Dr. Anirban Basu (NBRC, Manesar), Dr. Prafullakumar B. Tailor (NII, New Delhi), Prof. Jayasri Das Sharma (IISER, Kolkata), Dr. Jayanta Bhattacharyya (IIT, Delhi), Dr. Sweety Samal (THSTI, Faridabad)
Dr. Prasad Abnave	Dr. Santosh Mathapati (THSTI, Faridabad)

RCB Principal Investigator	Collaborators
Dr. Anil Thakur	Dr. Alan G. Hinnebusch (NIH, USA), Dr. Ishaan Gupta (IIT – Delhi), Dr. Rekha Puria (GBU, Greater Noida)
Prof. Avinash Bajaj	Dr. Sagar Sengupta, Dr. Vinay Nandicoori, Dr. Arnab Mukhopadhyay, and Dr. Veena S Patil (NII), Dr. Ujjaini Dasgupta and Dr. Rajendra Prasad (Amity University, Haryana), Dr. Aasheesh Srivastava (IISER, Bhopal), Dr. Prasenjit Das and Dr. Vineet Ahuja (AIIMS), Dr. C. V. Srikanth (RCB)
Prof. Sivaram Mylavarapu	Dr. Sourav Banerjee (NBRC, Manesar), Dr. Anjana Saxena (CUNY, USA), Dr. Megha Kumar (CSIR-CCMB, Hyderaba), Dr. Jayanta Bhattacharya (THSTI-IAVI), Dr. Amitabha Mukhopadhyay (IIT Delhi), Dr. Divya Chandran (RCB Faridabad)
Dr. Rajender K Motiani	Dr. Sridhar Sivasubbu (IGIB, New Delhi) and Dr. Shantanu Chowdhury (IGIB, New Delhi)
Dr. Karthigeyan Dhanasekaran	Dr. Soumik Siddhanta (IIT-Delhi), Prof. Sudhanshu Vrati (RCB, Faridabad), Prof. R. P. Roy (RCB, Faridabad)
Dr. Saikat Bhattacharjee	Dr. Girish TR & Sailaja Nori (Sea6 Energy Pvt. Ltd., Bengaluru), Dr. Souvik Bhattacharjee (JNU, New Delhi), Dr. Nimisha Sharma (GGSIPU, New Delhi), Dr. Ramu Vemanna (RCB, Faridabad), Dr. Debabrata Laha (IISc, Bengaluru), Dr. Sang Hee Kim (GNU, Korea), Dr. Gabriel Schaaf (University of Bonn, Germany)
Dr. Divya Chandran	Dr. Senjuti Sinharoy, Dr. Senthil Kumar Muthappa (NIPGR, New Delhi), Dr. Bonamali Pal (Thapar Institute of Engineering and Technology, Patiala), Dr. Shri Ram Yadav (IIT Roorkee), Dr. Atul Goel (CDRI, Lucknow), Dr. Archana Chugh (IIT Delhi), Dr. Deepti Jain (RCB, Faridabad)
Dr. Ramu S Vemanna	Dr. Kiran Mysore, (Oklahoma State University, USA), Dr. Prasanna Kumar M (University of Agricultural Sciences, Bangalore), Dr. Avinash Bajaj, Dr. Saikat Bhatacharjee (RCB)
Dr. Prashant Pawar	Dr Nidhi Adlakha (RCB), Dr Saikat Bhattacharjee, Dr Yashwant Kumar (THSTI), Dr Gyan Misra (IARI, New Delhi), Dr Harsh Kumar Dixit (IARI, New Delhi), Dr Aline Voxeur (INRA, France), Dr Jeongim Kim (University of Florida, USA)
Dr. Ambadas B. Rode	Prof. Ming-Hon Hou (National Chung Hsing University, Taichung, Taiwan), Prof. Sheshnath Bhosale (Goa University), Dr. Ramandeep Singh (THSTI, Faridabad)
Dr. Nidhi Adlakha	Dr. Syed Shams Yazdani (ICGEB, New Delhi), Dr. Charanpreet (NABI, Mohali), Dr. Tarun Sharma (GBU, Gujarat), Prof. Rakesh Bhatnagar (JNU, New Delhi)
Prof. RP Roy	Dr. Srinivasa-Gopalan Sampathkumar (NII, Delhi), Prof. Vengadesan Krishnan (RCB), Dr Karthigeyan Dhanasekaran (RCB)

Extramural Funding

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
1.	Prof. Deepak T. Nair	Renewal of access to Structural Biology Facilities at ESRF, France	DBT	2639.8 lakh	2021-24
2.	Prof. Deepak T. Nair	Sponsorship for the IUBMB focused meeting titled "Biochemistry and Molecular Biology of RNA viruses"	IUBMB	26.0 lakh	2022
3.	Prof. Deepak T. Nair (co-PI)	Chemical synthesis of adducts induced by 3-nitrobenzanthrone and evaluation of the effect of these adducts on natural DNA synthesis	SERB	15.0 lakh	2022-24
4.	Prof. Vengadesan Krishnan	Elucidating the Structural characteristics of pilus components from *Enterococcus faecalis*, an opportunistic pathogen of the Urinary tract	DBT	49.7 lakh	2022-25
5.	Prof. Vengadesan Krishnan (Co-PI)	Investigating Functional Role of Polyketide Modifying Enzymes in Mycobacterial Biology	SERB	46.7 lakh	2019-22
6.	Prof. Vengadesan Krishnan	Structural studies on pilus proteins from *Streptococcus sanguinis*, a primary colonizer in oral biofilm development (dental plaque)	SERB	45.1 lakh	2020-23
7.	Dr. Deepti Jain	Antibiotic tolerance And Resistance In Biofilm-Associated Infections: A Belgian-Indian Networking Approach to Address a Worldwide Problem - A joint Indo-Belgian Network	Indo-Belgian Networking Grant DBT	35.0 lakh	2022-25
8.	Dr Deepti Jain	Targeting Bacterial Motility and Adherence for Inhibition of Biofilms from *Pseudomonas aeruginosa*	DBT	84.6 lakh	2022-25
9.	Dr. Deepti Jain	Inhibition of *Pseudomonas aeruginosa* biofilms by bioactive molecules derived from halophilic rare actinomycetes *Nocardiposis lucentensis*	RCB-IITD Collaborative Grant Scheme	10.0 lakh	2021-2023
10.	Dr. Prem S. Kaushal	Understanding the translation strategies adopted by *M. tuberculosis*	SERB	46.3 lakh	2019-22
11.	Prof. Prasenjit Guchhait	Identification of small molecule inhibitors of PF4 and CXCR3 to prevent Dengue and JEV infection in	SERB	57.0 lakh	2019-23

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
12.	Prof. Tushar Kanti Maiti	A "bench to bedside" model for clinical and translational science between academic research institutes and hospitals focused on fetal growth restriction and preterm birth."	DBT	23.1 lakh	2018-23
13.	Prof. Tushar Kanti Maiti	Multi-Omics Signatures of Human Placenta: Real time assessment of underlying mechanisms for prediction of birth outcomes and development	DBT	64.7 lakh	2020-23
14.	Prof. Tushar Kanti Maiti	MOMI: Biorepository local analysis- INDIA	BMGF	61.8 lakh	2021-23
15.	Prof. Tushar Kanti Maiti	Inter-Institutional Program for Maternal, Neonatal and Infant Sciences A translational approach-interdisciplinary Group for Advanced Research on BirtH outcomes - DBT INdia Initiative (GARBH-Ini Phase II)	DBT	138.0 lakh	2021-26
16.	Prof. Tushar Kanti Maiti	MOMI Ideas Fund 2021: N-linked glycosylation in GDM	BMGF	57.9 lakh	2023-22
17.	Dr. Sam Mathew	Functional characterization of skeletal muscle myosin heavy chain-embryonic in adult muscle regeneration and disease.	DBT	77.0 lakh	2020-23
18.	Dr. Sam Mathew	The Wnt signaling pathway and its repressor Transducin-like Enhancer of Split 3 (TLE3) as therapeutic targets to treat Rhabdomyosarcoma tumors	ICMR	54.0 lakh	2021-24
19.	Dr. Sam Mathew	Regulation of mammalian growth, homeostasis and differentiation by Transducin-like Enhancer of Split (TLE) proteins.	SERB	53.0 lakh	2022-25
20.	Dr. Sam Mathew and Dr. Manoj Menon	Sensitizing cells to the chemotherapeutic SMAC mimetics and investigating the dependence on cellular differentiation	RCB-IIT Delhi collaborative project proposal scheme	10.0 lakh per year (5 lakh for RCB)	2023-24
21.	Dr. Masum Saini	Role of Sprouty2 as a modulator of MET signaling during mammalian skeletal muscle development, regeneration and disease.	Wellcome Trust/DBT India Alliance Early Career Fellowship	167.0 lakh	2018-22
22.	Dr. Pinky Kain	Understanding taste and its modulation using *Drosophila melanogaster*	India Alliance DBT Wellcome Trust Intermediate grant	350.0 lakh	2016-23

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
23.	Prof. CV Srikanth & Dr. Girish Ratnaparkhi	From the gut SUMO cycles its way into gastrointestinal disorders	MHRD	93.0 lakh	2020-23
24.	Dr. Geetanjali Chawla	Post-transcriptional regulators of aging and dietary restriction	India Alliance DBT-Wellcome Trust	359.0 lakhs	2018-23
25.	Prof. CV Srikanth & Dr Vineet Ahuja	Studying the mechanism of Rab7 based regulation of Goblet cell function in Ulcerative colitis	DBT	86.0 lakh	2023-26
26.	Dr. Manjula Kalia	Pharmacological Modulation of Autophagy as a Potential Therapeutic for Japanese encephalitis	DBT	81.2 lakh	2019-22
27.	Dr. Manjula Kalia	Role of Guanylate-binding proteins and Gasdermin D in the inflammatory response to Japanese encephalitis virus infection and link to pyroptotic cell death	SERB	48.8 lakh	2021-24
28.	Dr. Arup Banerjee	Understanding the therapeutic role of adult stem cell-derived exosome in combating virus-induced neurodegenerative disease	DBT	Total grant: 81.3 Lakh Grant for RCB: 29.0 lakh	2018-22
29.	Dr. Arup Banerjee	Investigating the molecular modulators of microglial activation and their effect on JEV pathogenesis	SERB	41.1 lakh	2018-22
30.	Dr. Prasad Abnave	Investigating molecular mechanisms governing the proliferation-differentiation balance in adult stem cells during chronic infections.	DST	35.0 lakh	2019-24
31.	Dr. Prasad Abnave	Investigating histone methylation changes induced in adult stem cells during bacterial infections.	SERB-SRG	28.3 lakh	2020-22
32.	Dr. Anil Thakur	Translation dynamics govern fungal virulence and drug resistance in Candida species	DBT	42.5 Lakh	2020-25
33.	Dr. Anil Thakur	Characterization of translation initiation codons dynamics to determine pathogenicity of *Candida albicans*	SERB	23.4 Lakh	2020 -23
34.	Dr. Anil Thakur	"Genetic and translational landscape of *Candida glabrata* pathogenesis for identification of novel antifungal drug targets	SERB	44.8 Lakh	2023 -26

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
35.	Prof. Avinash Bajaj	Elucidating the Role of Post-transcriptional Regulation of Sphingolipid Metabolic Genes in Breast Cancer Progression.	SERB	9.0 lakh	2021-24
36.	Prof. Avinash Bajaj	Towards development of a potent antiviral against the SARSCoV2 by targeting interactions between nucleocapsid protein and viral RNA	SERB	9.7 lakh	2020-23
37.	Prof. Avinash Bajaj	Engineering of Membrane Targeting Molecular Probes for Diagnosis of Mycobacterial Infections	SERB	50.5 lakh	2019-22
38.	Prof. Avinash Bajaj	Combating Topical and Medical Device Related Multidrug Resistant Fungal Infections Using Molecularly Engineered Anti-Fungal Hydrogels	DBT	9.7 lakh	2019-22
39.	Prof. Sivaram Mylavarapu	Understanding the role of transgelin-2 in cell division	SERB	57.3 lakh	2022-25
40.	Prof. Sivaram Mylavarapu	Delineating the role of Rab5 GTPase isoforms in mammalian cell cytokinesis	RCB-IITD Collaborative Project Proposal Scheme (MFIRP)	10.0 lakh	2021-23
41.	Dr. Rajender K Motiani	Role of ER and Mitochondria in Pigmentation: Organellar Calcium signaling perspective	India Alliance DBT/ Wellcome Trust	360.0 lakh	2020-25
42.	Dr. Karthigeyan Dhanasekaran	Impact of Flaviviral proteins on centrosome and cilia	SERB-SRG	27.8 lakh	2022-24
43.	Dr. Karthigeyan Dhanasekaran	Centrosome as a target for viral pathogenesis intervention	Ramalingaswami Fellowship: DBT	42.5 lakh	2021-26
44.	Dr. Karthigeyan Dhanasekaran (co-PI)	Tracking protein dynamics in cells using clusteroluminescence	IITD-RCB collaborative grant	10.0 lakh	2023-25
45.	Dr. Saikat Bhattacharjee (Co-PI) Dr. Souvik Bhattacharjee, JNU	Translating the Phylogenetic affinities between a plant pathogenic oomycete *Phytophthora infestans* and a human pathogen *Plasmodium falciparum* to reveal evolutionary convergence in virulence secretion using *In-silico*, proteomic and metabolomics approaches.	SERB	9.9 lakh (RCB)	2021-24

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
46.	Dr. Divya Chandran (PI, RCB) (PI and Project Coordinator: Dr. Senjuti Sinharoy; Co-PI: Dr. Senthil-Kumar Muthappa, National Institute of Plant Genome Research)	Generation of a retrotransposon-based mutant population of chickpea for functional genomics studies	DBT	Total grant: 128.0 lakh Grant for RCB: 39.1 lakh	2022-25
47.	Dr. Divya Chandran (PI: Dr. Bonamali Pal, Thapar Institute of Engineering and Technology)	Nanocarriers for topical delivery of pathogen-specific RNAi molecules for sustained protection of pea crop against powdery mildew	DBT	Total grant: 63.5 lakh Grant for RCB: 38.3 lakh	2021-24
48.	Dr. Divya Chandran (Co-PI: Dr. Deepti Jain, RCB)	Elucidation of the functional interactome of legumes with the fungal pathogen *Erysiphe pisi* as keys to powdery mildew disease resistance	SERB	43.9 lakh	2020-23
49.	Dr. Naini Burman (mentor Dr. Divya Chandran)	Functional characterization of HY5 homolog in rice	DST(INSPIRE faculty)	35.0 lakh	2018-23
50.	Dr. Babitha K.C. (mentor Dr. Divya Chandran)	Modulation of stomatal aperture regulating genes to improve carbon gain and crop yield	DBT (BioCARe)	52.9 lakh	2019-22
51.	Dr. Ramu S Vemanna	Influence of drought stress on ribosomes and protein synthesis and understanding the functional relevance of Ribosomal Protein L10 in rice	SERB	28.0 lakh	2020-23
52.	Dr. Ramu S Vemanna (PI) Dr. Saikat Bhattacharjee (Co-PI) Dr. Prashant Pawar (Co-PI) Dr. Avinash Bajaj (Co-PI)	Nanogel-mediated gene editing (CRISPR/Cas9) technologies to improve crop protection against bacterial leaf blight in rice	DBT	118.0 lakhs	2022-25
53.	Dr Prashant Pawar (PI)	Understanding plant cell wall biosynthesis to optimise lignocellulosic biomass	DST (INSPIRE)	35.0 lakh	2018-23

54.	Dr Prashant Pawar	Investigating GDSL lipase/esterase family to understand the mechanism and role of polysaccharide O-acetylation in plants for bioenergy applications	SERB	26.7 lakh	2020-22
55.	Dr Shouvik Das (Mentor: Dr Prashant Pawar)	An integrated molecular genomics approach to unveil genomic and epigenetic complexity of adaptive traits, like flowering time, seeds size and plant cell wall	MK Bhan Fellowship	87.0 lakh	2021-2024
56.	Dr Ambadas B Rode	Rationally targeting & tuning riboswitch mediated gene regulation for therapeutic and synthetic biology application	DBT	88.0 lakh	2018-23
57.	Dr Ambadas B Rode	Targeting riboswitches with synthetic small molecules for development of anti-tubercular drugs	SERB	46.1 lakh	2023-2026
58.	Dr Ambadas B Rode	India EMBO lecture course grant as an organizer on 'Functional Nucleic Acids: Recent Landscapes and Therapeutic Applications'	EMBO & DBT India Alliance	40.1 lakh	2022
59.	Dr. Nidhi Adlakha	Development of *Paenibacillus polymyxa* as a platform for the production of branched chain alcohols	DBT-Mission Innovation- IC4 grant	Total grant: 89.5 lakh Grant for RCB: 0 lakh	2019-22
60.	Dr. Nidhi Adlakha	Unravelling transcriptional regulation of cellulase gene overexpression in Talaromyces sp. NA01	Intracluster grant	20.0 lakh	2020-22
61.	Dr. Nidhi Adlakha	Aptamer-nanoparticles conjugate: a next generation theranostic agent for phytopathogenic fungi	DBT	Total grant: 57.0 lakh Grant for RCB: 19.3 lakh	2022-25
62.	Dr. Nidhi Adlakha	Development of stable enzyme preparation for generating diet for PKU patients	RCB-IITD grant	Total grant: 20.0 lakh Grant for RCB: 10.0 lakh	2021-2023
63.	Prof. RP Roy	Semisynthetic histones with defined chemical marks for interrogation of eraser specificity	SERB	40.7 lakh	2020-23
64.	Prof Sudhanshu Vrati (Co-ordinator) Prof. Deepak T Nair Dr. Deepti Jain	Development of small molecule antivirals against Chikungunya and Japanese Encephalitis virus	DBT	480.7 lakh	2020-23

65.	Prof Sudhanshu Vrati (Co-ordinator) Prof. Deepak T Nair	Setting up of the Indian biological Data Centre- Phase 1	DBT	7578.8 lakh	2020-23
66.	Prof. Deepak T Nair Dr. Vengadesan Krishnan Dr. Deepti Jain Dr. Prem Singh Kaushal	Bioinformatics Centre for Computational Drug Discovery- BIC at Regional Centre for Biotechnology, Faridabad	DBT	197.3 lakh	2021-26
67.	Prof. Deepak T Nair	Identification of lead molecules for development of novel therapeutic strategies against viruses	DBT	242.7 lakh	2022-27
68.	Dr Deepti Jain	Bioinformatics Centre for Computational Drug Discovery at Regional Centre for Biotechnology- BIC at Regional Centre for Biotechnology, Faridabad	DBT	197.3 lakh	2021-26

RESEARCH & INNOVATION INFRASTRUCTURE

Courtesy: Himanshu Rathour

BSC BioNEST Bio-Incubator (BBB)

BSC BioNEST Bio-Incubator (BBB), a BIRAC's Associate Partner, continues to foster Bioentrepreneurship as a leading startup ecosystem enabler in the National Capital Region. It has been providing support in terms of infrastructure (lab and office space), central instrumentation facility, funding, mentorship, networking and Intellectual Property. The year was eventful with BBB, securing the funds under Startup India Seed Fund Scheme (SISFS) from DPIIT, Government of India, to further support entrepreneurial ecosystem. In its sprawling 35,000 Sq. Ft incubation space, new startups have been on boarded and existing incubatees continue to support 'Make in India' initiative through development of innovative indigenous products across thrust domains of Biopharmaceuticals, Nutraceuticals, Diagnostics, Industrial Biotechnology, Medical Devices and Anti-infectives. Selected accomplishments made during this year include InnoDx Solutions Pvt Ltd securing a patent for their COVID-19 LAMP assay test for sensitive and specific detection of COVID-19 virus; Translational Research & Innovations releasing the Bio-fermented Fish Feed; Peptomer Therapeutics Pvt. Ltd securing funding under NIDHI-PRAYAS scheme; Vanguard Diagnostics Pvt. Ltd. winning the Startup of the Year award in the Medical Devices sector; Entrepreneur from BBB being featured in the Compendium of 75 Women Biotech Entrepreneurs, released by BIRAC, DBT, Government of India.

BBB participated in the Biotech Startup Expo - 2022 during June and Government's flagship event of India International Science Festival (IISF) at MANIT, Bhopal, during January, disseminating its growing impact and attracting young minds towards Bioentrepreneurship and its promise in solving public health issues, in an innovative manner. Outreach activities continue to happen through release of quarterly newsletter, effective use of social media platforms and engagement with young students of colleges and universities. BBB continues to impart training to UG and PG students from colleges / universities located in NCR, through a series of workshops designed to enhance skill set in Biotechnology and related domains. SPARK Innovation Challenge, a unique ideathon competition, was conducted by BBB with aim to promote entrepreneurial thinking among UG and PG student community.

Recently, BBB executed MoU with Manav Rachna International Institute of Research and Studies (MRIIRS), Faridabad and Haryana State Council for Science, Innovation & Technology (HSCSIT) to enable collaborations in diversified areas of entrepreneurship. BBB also conducted CXO level B2B meeting among incubatees to catalyse innovative thinking and collaborations.

Startups Supported till date:

S.No	Company	Area	Type of Incubatee
1	SHC Shine Biotech Pvt. Ltd	Diagnostic	Residential
2	QbD BioSciences Pvt. Ltd.	Bio-Pharma	Residential
3	Bioheaven 360 Genotec Pvt. Ltd.	Molecular Diagnostic	Residential
4	NextGen InVitro Diagnostics Pvt. Ltd.	Diagnostic	Residential
5	VaxFarm Life Sciences LLP	Bio-Pharma	Residential
6	AIGen Therapeutics Pvt. Ltd.	Anti-infective	Residential
7	InnoDx Solutions Pvt. Ltd.	Diagnostic	Residential
8	BioDva Life Sciences Pvt. Ltd.	Bio-Pharma	Residential
9	Stellar Diagnostics India Pvt. Ltd.	Diagnostic	Residential
10	Vanguard Diagnostics Pvt. Ltd.	Diagnostic	Residential
11	Incredible Devices Pvt. Ltd.	Medical Device	Residential
12	BioCredence	Nutraceuticals	Residential
13	AptaBharat Innovation Pvt. Ltd.	Diagnostic	Residential
14	Sunny Corporation Pvt. Ltd.	Diagnostic	Residential
15	Biotide Solutions LLP	Anti-infective	Residential
16	Organic 121 Scientific Pvt. Ltd.	Industrial	Residential
17	Dharaksha Ecosolutions Pvt. Ltd.	Environmental	Residential
18	Peptomer Therapeutics Pvt. Ltd.	Anti-infective	Residential
19	Sleepiz India Pvt. Ltd.	Medical Device	Residential
20	Inte-e-Labs Pvt. Ltd.	Bio-Pharma	Residential
21	Genvynn Biologics Pvt. Ltd.	Bio-Pharma	Residential
22	Kantech Research Solutions	Anti-infective	Residential
23	3CR Bioscience Ltd.	Diagnostic	Non-Residential
24	TechInvention Lifecare Pvt. Ltd.	Bio-Pharma	Residential
25	Anziam Bio Pvt. Ltd.	Bio-Pharma	Residential
26	Celleome Biosciences LLP	Diagnostic	Residential
27	PriDignity Pvt. Ltd.	Sanitation	Residential
28	Valetude Primus Healthcare Pvt. Ltd	Diagnostic	Residential
29	Ruhvenile Biomedical OPC Pvt. Ltd	Anti-infective	Residential
30	Mr. Sharad Rai	Nutraceuticals	Residential
31	Advinogen Innovations Pvt. Ltd.	Diagnostic	Residential
32	Biotrends India Pvt. Ltd.	Industrial Biotech	Residential
33	Micronic Analytical Device Pvt. Ltd.	Diagnostic	Residential
34	Meraki Herbzz	Nutraceutical	Non-Residential
35	Florecer Services Pvt. Ltd.	Industrial Biotech	Residential
36	Tritek innovation Pvt. Ltd.	Diagnostic	Residential

S.No	Company	Area	Type of Incubatee
37	Translational Research Innovations Pvt. Ltd	Industrial Biotech	Residential
38	Biolytics Research & Innovation Pvt. Ltd.	Diagnostic	Residential
39	Dr. Suman Das	Diagnostic	Residential
40	Mr. Nidhin Murali	Bio-Pharma	Residential
41	Tropical Animal Genetics Pvt. Ltd.	Bio-Pharma	Residential
42	East Ocyon Bio Pvt. Ltd.	Bio-Pharma	Residential
43	Cellogen Therapeutics Pvt. Ltd.	Bio-Pharma	Residential

Incubatee Companies by BBB

Grants/Awards secured by startups in FY 2022-23

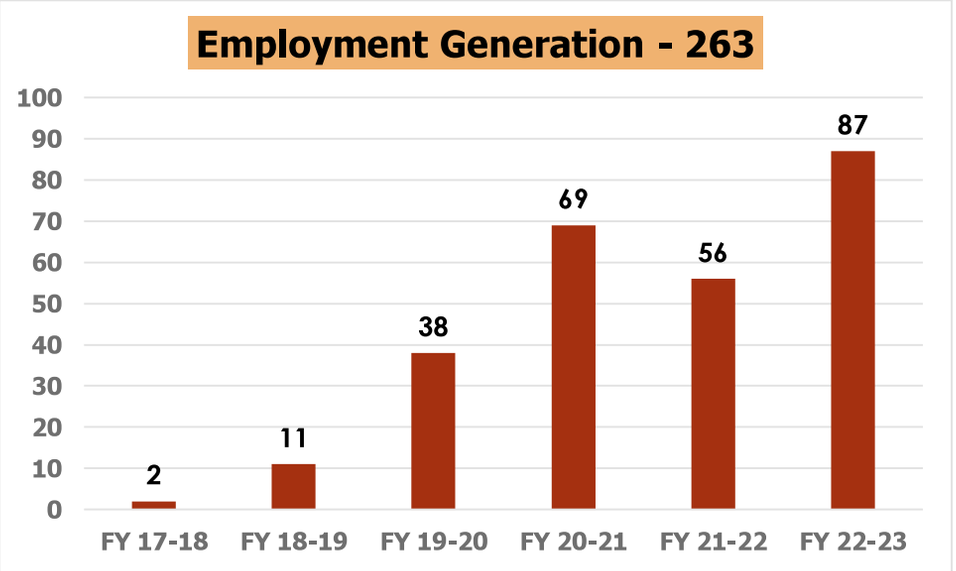
S.No	Name of Incubatee Company	Grant & Awards
1	InnoDx Solutions Pvt. Ltd.	BIG
2	Peptomer Therapeutics Pvt. Ltd.	BIG, NIDHI PRAYAS

Startups onboarded during FY 2022-23

07 new startups were onboarded during FY 2022-23.

S.No	**Company**	**Area**
1	Translational Research Innovations Pvt. Ltd	Industrial Biotech
2	Biolytics Research & Innovation Pvt. Ltd.	Diagnostic
3	Dr. Suman Das	Diagnostic/AI-ML
4	Mr. Nidhin Murali	Bio-Pharma
5	Tropical Animal Genetics Pvt. Ltd.	Bio-Pharma
6	East Ocyon Bio Pvt. Ltd.	Bio-Pharma
7	Cellogen Therapeutics Pvt. Ltd.	Bio-Pharma

Employment generated by BBB Incubatee startups:



Events conducted during FY 2022-23

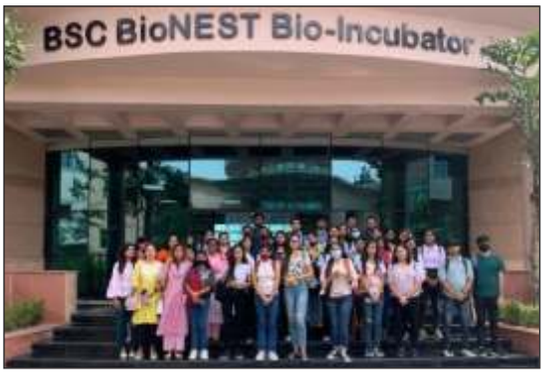
BBB is actively promoting the entrepreneurial aptitude among young innovators through its strategic programs & outreach activities. It also regularly conducts workshops, seminars and facilitates the interaction between entrepreneurs & mentors. 32 events were conducted in FY22-23.

S.No	Event Name	Category	Month
1	RT-PCR Training/workshop	Workshop /Training	April' 22
2	Talk for G. D. Goenka University students	Awareness Session on Entrepreneurship Development	April' 22
3	Talk on "Research Innovation & Incubation Ecosystem to Enable Start-up Culture" at Guru Gobind Singh Indraprastha University	Awareness Session on Entrepreneurship Development	May'22
4	Talks and panel discussion on theme " bio innovation in health technology" at iCEN-03 organized by Ministry of science & technology	Awareness Session	May'22
5	Outreach activity at Biotech startup expo 2022 organized by Department of Biotechnology (DBT)	Networking	June'22
6	Hands-on Workshop on Microbial Techniques	Workshop	June'22
7	Workshop on Advancement in medium pressure chromatography for protein purification	Workshop	June'22
8	Workshop on real time PCR	Workshop /Training	July'22
9	Awareness Session on BIG Call by BIRAC	Awareness Session	July'22
10	Awareness session on Finance for startups	Awareness Session	July'22
11	Awareness Session on BIG Call by BIRAC	Awareness Session on BIG	July'22
12	Awareness Session on Entrepreneurship Development & IP for students from Gujrat	Awareness Session	July'22
13	Awareness Session on BIG Call by BIRAC	Awareness Session on BIG	July'22

S.No	Event Name	Category	Month
14	Talk at VIGYAN UTSAV on Theme: "Intellectual Property Rights" conducted by Haryana State Council for Science, Innovation and Technology	Awareness Session on IP	Aug'22
15	Panel Discussion in an event on "Venture Capital – Biotech Startup Connect" - WHALE TANK, organized by Federation of Asian Biotech Associations (FABA)	Networking	Aug'22
16	Incubator visit by students from RLA College	Awareness Session	Aug'22
17	Panel discussion at ForeCytDX 2022 - the premier India Healthcare and Diagnostics Business Summit.	Networking	Oct'22
18	Workshop on "New Age Diagnostics"	Workshop	Oct'22
19	Incubator visit by students from IMS Engineering College	Awareness Session	Nov'22
20	Business to business connect series for startup founders	Networking	Nov'22
21	Awareness Session on BIG Call by BIRAC	Awareness Session	Jan'23
22	Ideathon Competition for students- SPARK	Innovation Challenge	Jan'23
23	Outreach booth at India International Science Festival -IISF Bhopal	Networking	Jan'23
24	Awareness Session on BIG Call by BIRAC	Awareness Session on BIG	Jan'23
25	Awareness Session on BIG Call by BIRAC	Awareness Session on BIG	Jan'23
26	A talk on Bio-entrepreneurship skills at the J.C. Bose University of Science and Technology, YMCA	Awareness Session on Entrepreneurship Development	Feb'23
27	Talk at SGT University, Gurugram	Awareness Session on Entrepreneurship Development	Feb'23
28	Ideathon evaluation at YMCA	Innovation Challenge	Feb'23
29	Visit of Biotech Delegation from Estonia	Networking	Feb'23
30	Workshop on "The Basics of Bioprocessing: Upstream & Downstream"	Workshop	Feb'23
31	Talk at Shaheed Rajguru college of Applied Sciences for women	Awareness Session on Entrepreneurship Development	Feb'23
32	Educational Tour for the students of Daulat Ram College, University of Delhi	Awareness Session	Mar'23

Pictures of Events @ BBB

Awareness Session & Visits



RT PCR Workshop

Hands on workshop on Microbial Technique

New Age Diagnostic Workshop

Workshop on The Basics of Bioprocessing: Upstream & Downstream



Biotech Startup Expo


India International Science Festival (IISF) - Bhopal



Business to Business Connect @ BBB


SPARK – Innovation Challenge Organized by BBB and RCB

Biosafety Support Unit (BSU)

Biosafety Support unit (BSU) is a unit established by Department of Biotechnology, Government of India as a part of the reforms to strengthen biosafety regulatory system in partnership with Regional Centre for Biotechnology (RCB).

A. Major activities undertaken by BSU during the year 2022-23 include:

1. Provided assistance to RCGM/GEAC (Statutory bodies established under Rules 1989 of EPA 1986) in the scrutiny of all the applications received for conducting research in biotechnology, product development and monitoring field trials. The activities of BSU includes desk review of all applications to ensure the completeness of the data requirements, compliance of the approved protocols/procedures to be followed at the time of field trials (Event selection, BRL-I and BRL-II) and preclinical toxicology (PCT) data and other regulatory compliances.
2. Developed and updated a number of guidelines, Standard Operating Procedures and policy documents.
3. Assisted the RCGM Secretariat in developing revised guidelines and protocols for generating biosafety data to address the challenges raised by the emerging new areas of Biotechnology such as Genome Editing.
4. BSU team is also fulfilling the training needs of the personnel engaged in Biosafety regulations and developing e-learning modules for IBSCs and other stakeholders working in the regulatory science.
5. BSU is fully engaged in providing a communication platform for scientific community and other stakeholders through Indian Biosafety Knowledge Portal, an online portal for all transaction and submission and tracking of applications.
6. BSU provided all necessary services to RCGM and assisted RCGM Secretariat in organizing scheduled meetings of the RCGM, various sub-committees and monitoring teams, etc.

B. Major accomplishments

B.1. RCGM/GEAC Related Activities:

1. **Review of applications:** BSU evaluated a total of 1653 applications in the field of Biopharma and Agri-Biotechnology submitted to Review Committee on Genetic Manipulation (RCGM), of which 643 applications were considered in RCGM meetings (230th to 254th Meetings) during year 2022-23. BSU extended its support towards conducting all the meetings of RCGM by preparing Agenda notes and draft Recommendations. Further, in-depth desk review was carried out for each of the application/reports submitted by the applicants on confined field trials (CFTs) and pre-clinical trials (PCT).

2. **Certification of BSL-3 facilities Nation-wide**: To ensure compliance with biosafety for high containment facilities, '*Guidelines for the Establishment of containment facilities: Biosafety Level 2 (BSL-2) & -3 (BSL-3) and certification of BSL-3 facility, 2020*' defining specifications and SOPs for these facilities have been notified. Further, a mechanism for certification of such facility based on review of documents was also devised and now being followed with ongoing review of the applications. BSU assists in preliminary examination of applications for Certification of BSL-3 facility and has assessed 49 applications so far. Of these, 29 facilities have been recommended by the Interministerial committee for BSL-3 certification and approved by RCGM.

3. **Biosafety Protocols and Guidelines: New/Revised/Updated:** BSU has undertaken a major activity of drafting/revising/updating of various guidelines related to biosafety of recombinant DNA research.

The following guidelines have been notified:

Guidelines for Safety Assessment of Genome Edited Plants, **2022**
DBT notified the **Guidelines for Safety Assessment of Genome Edited Plants, 2022**, vide OM dated 17.05.2022. The Guidelines provide a road map for the development and sustainable use of Genome Editing Technologies for plants in India, specifying the biosafety concerns, and describing the regulatory pathways to be adopted while undertaking genome editing of plants.

Standard Operating Procedures for Regulatory Review of Genome Edited Plants under SDN-1 and SDN-2 Categories, **2022**

DBT notified the **Standard Operating Procedures for Regulatory Review of Genome Edited Plants under SDN-1 and SDN-2 Categories, 2022**, vide OM dated 04.10.2022. The SOPs have been notified to facilitate regulatory review for research and development of genome edited plants falling under the categories of SDN-1 and/or SDN-2 until free from exogenous introduced DNA. These SOPs are applicable only for research and development under contained conditions.

In addition, the following guidelines are under preparation:

- **Guidelines and SOPs for research on Genetically Engineered insects, 2023**: To harness the wide application of genetic engineering in insects with the proper appraisal of biosafety concerns, to ensure safety for the organisms and environment, final draft of this guidelines have been prepared after extensive deliberations by the expert committee constituted for this purpose. RCGM, in its 252nd meeting, held on 22.02.2023, approved and recommended the Guidelines and Standard Operating Procedures for Research on Genetically Engineered Insects, 2023, the document for further notification by Department of Biotechnology. BSU assisted in drafting of these Guidelines.
- **Guidelines on CAR-T Cell Therapy**: RCGM in its 228th meeting held on 17.03.2022 deliberated on the draft checklist on tentative data requirements for CAR-T trials till preclinical stage. RCGM in its 231st meeting held on 28.04.2022 deliberated that the valuable inputs from the experts has been incorporated in the draft document and hence RCGM recommended to adopt the checklist on tentative data requirements for CAR-T trials till preclinical stage for maintaining the uniformity in assessing the applications from academia and industry. The same will be shared with the GTAEC for incorporation in the final Guidance document on specific modalities of CAR-T Cell Therapy guidelines under preparation by joint collaboration of ICMR-DBT-CDSCO. BSU assisted in drafting of Checklist and modifying it in view of Expert member's deliberations and comments.
- **Guidelines for Notified Field Trial Sites (NFTS)**: Guidelines for Notified Field Trial Sites (NFTS) To Conduct Confined Field Trials of GE Crops: Draft Guidelines have been submitted to MoEFCC vide DBT letter dated 19.02.2020 and were considered in the 139th GEAC meeting held on 19.05.2020. The committee requested the GEAC Secretariat to examine the proposal which will be discussed in the subsequent meeting of GEAC for taking appropriate decision. In the meantime, the members were also requested to provide written comments on the above proposal.

Further the revision/drafting of following guidelines is under consideration:

- Updation of Guidelines on Similar Biologics.
- Updation of Regulations & Guidelines for Recombinant DNA Research and Biocontainment.

4. Commissioning of Indian Biosafety Knowledge Portal (IBKP):

The Portal facilitates registration of Institutional biosafety committees and uploading of new applications through portal. It is the nodal point for IBSC registration and monitoring, in addition to submission of respective applications for RCGM consideration and notification of the appropriate decision to the applicant. BSU evaluated the following, since commencement of the Portal:

Number of organization registrations approved	1004
Number of IBSCs registered	628

5. Monitoring of IBSCs and Assessment of compliance documents:

DBT-RCGM has taken several reforms including empowering of IBSCs, hence stringent mechanism to monitoring the IBSCs through their Minutes, Annual Compliance Reports and medical Surveillance Reports has been started with IBKP portal. BSU is facilitating the RCGM is the monitoring of IBSCs and assessment of compliance documents.

6. Biological Research Regulatory Approval Portal (BioRRAP) Launch: In keeping with the spirit of "One Nation, One Portal", Union Minister Dr. Jitendra Singh launched Single National Portal for Biotech researchers on May 21, 2022. BioRRAP will cater to all

regulatory approvals required for biological research and development activity in the country, thereby emphasizing on the "Ease of Science as well as Ease of Business". BSU assisted in the development and launch related activities for BioRRAP.

BSU Team along with DBT Officers

7. **Interactive sessions for awareness raising of Researchers**: DBT along with BSU scientists provided training sessions to Researchers (Principal Investigators, Scientists, Post-doctoral researchers) from Academia, Start-ups and Industry. 20 sessions were conducted during this financial year, which were attended by approximately 900 participants.

8. **Training and Capacity Building:**
   - CSO, BSU delivered Presentation entitled "*Role of RCGM in Regulation of GE crops*" on 19.07.2022 for Training Programme on Genetically Engineered (GE) Plants: Biosafety Considerations, Policies, Challenges and Detection Strategies (Hybrid Mode: July 19-25, 2022) at ICAR-NBPGR, Delhi.
   - CSO, BSU delivered presentation on "*India - Genome Editing Technologies Regulation*" on 15.11.2022, for Global Biotechnology Regulators Meeting, held on Nov 15-16, 2022, at Belgium.
   - Scientist, BSU attended 21-days Training course on New crop breeding Technologies, ICRISAT, Hyderabad (Nov 21-Dec 11, 2022).
   - CSO and Scientists (03), BSU attended International Meet on Preparedness for Future Epidemics, THSTI, Faridabad (Dec 05-06, 2022).

B.2. Other activities:

1. BSU has supported RCGM/GEAC for drafting affidavits/ replies for in matters related to Parliamentary Standing Committee, Court Cases, Parliament questions etc.

2. Providing background information to various Sub-Committees (eg. GE Mosquito, BGIII

RRF, Risk group updation, engineering controls, Gene therapy).

C. Admin. & Finance

C.1. Manpower:

- The Project titled "Establishment of Biosafety Support Unit (BSU), Phase-II" has been sanctioned (dated 19.10.2022) at a total cost of Rs 1921.57 Lakhs to RCB, Faridabad and commenced from 03.01.2023. The advertisements for the positions of Chief Scientific Officer, Project Scientist III/II/I, Senior Project Associate, Project Associate-II, Project Associate-I, Executive (Admin, Fin. & Services), Website Administrator, Executive (IPR), Executive (Legal) were published and five (5) Project Scientists-III, three (3) Project Scientist-II, one (1) Senior Project Associate and one (1) Project Associate-II have been selected for the project.
- RCB has awarded the outsourcing contract to M/s. Bedi & Bedi Associates w.e.f 03.01.2023 and the agency has deployed four (4) supporting staff in the project BSU, Phase-II with Senior Administrative Assistants (2), Senior Accounts Assistant (1) and Data Entry Operator (1).

C.2. Infrastructure

- An office space has been hired for BSU at NPC Building w.e.f. 1.9.2015. The lease agreement for office space (3678 sq. ft.) at NPC for BSU has been renewed for 3 years w.e.f. 01.09.2017 at enhanced rental by 5% and a provision for enhancement of rent by 5% every year. The proportionate maintenance charges were to be paid extra.
- RCB requested NPC for reduced space (part-only half of right side portion) of lease period extension for the project BSU. NPC agreed for extension of lease agreement of first floor (part only half of the right side portion) of NPC premises for the period from 01.03.2022 to 31.03.2022 at reduced monthly rent of Rs. 7,46,483/- including GST for BSU. Earlier the duration of the project BSU was up to 31.03.2022 accordingly the lease agreement was extended till 31.03.2022 at reduced rental of Rs. 7,46,483/- (all inclusive).
- Department of Biotechnology (DBT) sent letters to various DBT's Autonomous Institutes in Delhi for availability of space for BSU. In response, DST informed regarding availability of space for BSU at Technology Bhawan. Accordingly, RCB extended the agreement with NPC till 30.04.2022 as per existing conditions with reduced rental for the half portion only and also informed that there is a direction from the funding agency for moving the BSU to an identified office premises in the Dept. of Science & Technology (DST) w.e.f. 01.05.2022.
- Since then, the project BSU is housed at Ground Floor, Block-2, Technology Bhawan, DST. The proportionate Maintenance charges (including electricity and water bill) are being paid for the acco**BSU Team (Coordinator, Scientists & Admin staff)**mmodated area.

BSU Team (Coordinator, Scientists & Admin staff)

Advanced Technology Platform Centre

The mission of the centre is to act as a catalyst for multidisciplinary basic and translational research and development by providing relevant state-of-the-art instrumentation and professional services for research laboratories in industry and academia, training personnel in the use of these technologies, and developing new technologies in collaboration with academia and industry.

The Centre plugs a massive lacuna in the innovation pipeline that has previously attenuated the ability of Indian researchers to realize their true potential. At present the ATPC has six operational platform facilities equipped with the various high-end technologies for aiding biotechnology researchers and start-ups.

1. Protein Purification and Molecular Interactions Facility

This facility houses state-of-the-art technologies for protein production and downstream purification and studying biomolecular interactions. Molecular interaction platform is currently providing scientific and technical support for diverse range of projects involving following state of art equipment:

- Production of recombinant proteins in 7-litre and 14-litre Bioreactors (New Brunswick™_Bioflo® 415 - 7L, 14L).
- Protein purification by affinity and size-exclusion chromatography using AKTA prime and AKTA pure FPLC systems (Acta Pure M from Wipro GE Health care).
- Molecular interaction studies using BioLayer Interferometry – BLI (Pall ForteBio) and MicroScale Thermophoresis -MST (Nanotemper tech.)

2. Mass Spectrometry Facility

Mass spectrometry houses a suite of leading edge instrumentation for proteomics and metabolomics. Highly sensitive and accurate mass spectrometry services that are being provided include the following:

- Identification and quantitation (labelled, TMT /iTRAQ/SILAC/label free) and intact mass analysis of proteins by high resolution liquid chromatography ESI Q TOF (SCIEX 5600 Plus Triple–TOF) system and a high throughput SCIEX 5800 Plus matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-TOF-MS) system with EKSpot MALDI spotter.
- Peptide enzymatic digests analysis (In-gel/In-sol) for protein identification and post-translational modifications (PTMs) determination.
- Ultra-low-level identification and MRM based targeted and untargeted, absolute and relative quantitation of both small and large molecules, secondary metabolites, lipids and proteins by triple quadrupole linear ion trap spectrometer SCIEX QTRAP® LCMS/MS 6500+ system.
- Fractionation and separation of TMT/iTRAQ/SILAC labelled peptides for deeper coverage of whole proteome and PTM analysis by a high flow Perkin Elmer Flexar™ HPLC.

Recently, a high-resolution mass spectrometry solution ZenoTOF 7600 system that combines powerful MS/MS sensitivity, fragmentation technology and a step-change in data independent acquisition (DIA) to deliver a high depth of coverage, particularly on low abundance species, quickly and robustly.

3. Electron Microscopy Facility

The electron microscopy facility at ATPC is furnished with state of the art instruments. The electron microscopy facility consists of:

- Cryo-electron microscope (200kV JEM 2200FS)
- Transmission electron microscope (120kV JEM-1400 Flash)
- Field emission scanning electron microscope (Apreo Volume Scope)

The JEM-2200FS is a field emission electron microscope with a 200 kV field emission gun (FEG), piezo-controlled goniometer, holders for cryo-observation, and tomography, in-column energy filter (Omega filter), and Gatan direct detection camera (K2 summit). This instrument is capable of high-resolution cryo-electron microscopy, zero-loss imaging, energy-filtered imaging, and tomography. JEM1400 Flash is 120 kV TEM equipped with tungsten filament and a highly-sensitive sCMOS camera. It can achieve high contrast imaging of samples from biological and material science. FESEM provides novel serial block-face (SBF) imaging that enables excellent z-resolution from multi-energy deconvolution SEM combined with the efficiency of in situ sectioning. The instrument is equipped with in-lens and in-column detectors for HiVac, and LoVac analysis of samples and energy-dispersive X-ray spectroscopy (EDS) detectors for elemental analysis. The facility is furnished with accessory equipment e.g. Cryo-plunger, glow discharge, plasma ion cleaner, carbon coater, critical point dryer, sputter coater, and an ultramicrotome.

4. Genomics Facility

Genomics Facility caters to the needs of researchers especially from Biotech Science Cluster institutes in NCR from the standpoint of their requirement for DNA - based services. This facility currently provides scientific and technical support for various research projects through usage of following state of the art equipment:

- Automated DNA Sequencing using AB3500 Genetic Analyzer
- Droplet Digital PCR (ddPCR) using BioRad QX200

Human Cell Line Authentication (CLA) and Mycoplasma Contamination Testing has also been initiated recently. Beneficiary institutes of the Genomics Facility include THSTI-

Faridabad, NBRC-Manesar, NIPB-New Delhi, National Institute of Cancer Prevention and Research-Noida, in addition to RCB. This AB3500 Genetic Analyzer equipment has been used for STR typing based Human CLA as well, ensuring best use of this high-end equipment for scientific advancement.

5. Optical Microscopy facility

The optical microscopy centre is equipped with state-of-the-art research facilities, skilled personnel and world-class infrastructure. With an intent to make a significant contribution to the global research pool, the facility is ever vigilant towards generating reproducible and reliable data complying with international research standards.

The optical Microscopy facility hosts following state-of-the-art fluorescence based imaging instruments:

- Super Resolution Microscope; Elyra PS1, Carl Zeiss
- Laser Scanning Confocal Microscope; LSM 880, Carl Zeiss
- High Content Imaging System; ImageXpress, Molecular Devices

The scientists and researchers that avail facilities are from both academics and industries, mainly from RCB and Clusters institutes

6. Flow Cytometry

Flow Cytometry Facility is aiding scientist fraternity in addressing key cell biology and immunological research questions by providing services, with scientific and technical inputs through deployment of following technologically advanced equipment, which includes 3 Analyzers and 1 Cell Sorter:

- BD FACSVerse (3-lasers and 8-colours analyzer)
- BD Accuri C6 (2-lasers and 4-colours analyzers)
- Beckman Coulter's Gallios (3-lasers and 10-colours analyzer)
- Cell Sorter, BD Influx (5 laser system supporting high speed sorting with BD FACS Accudrop Technology enabling study of 16 parameters simultaneously and 6-way sorting).

Use of ATPC Facilities

The details on how to access the facilities at ATPC are available at the website https://atpc.rcb.res.in. During the period extending from April, 2022 to March, 2023, more than 300 different users from 52 different user institutions (Research Institutes, Universities, Hospitals and Commercial organizations) have utilized different facilities of the ATPC. A cumulative revenue of Rs. 115 lakhs was generated during the reporting period by different facilities of the ATPC.

High Performance Computing Cluster & IT Infrastructure

In terms of IT Infrastructure & Computing Facilities hosted & managed by RCB, A high performance computing (HPC) cluster with 8 nodes and a total of 128 processors & a Schrodinger suite server with 3 clients, and workstations are placed at **Graphics Lab** for research in computational biology and structure-based drug design. The Information and Communication facilities at RCB are continuously evolving with state-of-the-art facilities. All the computers at RCB are provided with the latest updated software and hardware. Internet, printing and scanning facilities are also available throughout the network.

An impressive array of information technologies and resources have been deployed with a harmonious blend of old and new, notable among these are:

Computing Facilities

The Institute has three state of the art Computer facilities. All the computers facility in the Institute are provided with the latest updated software and hardware. Internet, printing and scanning facilities are also available through network. Desktops/ Laptops, multifunction printers have been provided to the staff with internet connectivity. There are about 250+ client machines with windows 10, Linux (CentOS, Red Hat Enterprise Linux) and Mac OS X. There are common Personal Computer in each research lab and MSc lab for students to access various commercial off-the-shelf software such as Adobe Premium & Standard Suite, Systat, Sigma Plot, PyMol, Graphpad Prism, SPSS, Turnitin, Endnote, and Corel Draw Graphics Suite for preparing manuscripts, various reports and presentations. Face Recognition Biometric Attendance System has also been enabled for the staff, to register attendance by simply presenting his/her biometric. In addition, online resources are available for scholars for research, case studies and for preparation of their projects.

Internet Connectivity

RCB has 1 Gbps shared internet leased line from National Knowledge Network offering high-speed Internet connectivity in the campus. Additionally, a 125 Mbps fiber connectivity has been provisioned from an alternate service provider as a backup. The internet connection is distributed to users and facilities through RCB's network infrastructure comprises about 1000 metres of fibre, with a 10Gbps backbone, 115+ wireless access points, and 45+ network switches that provide on-campus wireless & wired connectivity. The RCB has implemented a security policy to ensure the highest levels of network health and security. The Centre has been functioning in conformity with the guidelines of the Government of India with regard to guidelines on IPV6 implementation and has also been an active participant in the Government initiatives of the "Digital India Campaign". The campus is fully covered by Wi-Fi into all the administrative buildings, labs, advanced platform technology centre (ATPC), associated centres, and hostels. Wi-Fi access is provided to internal users by Captive portal & media access control (MAC) address authentication and to visitors by separate guest accounts.

E-mail and Website

The e-mail system at RCB, offers a user-friendly web-based e-mail allowing users to access mails, both from inside the campus and outside. A very competent & experienced IT service support team has been put in place and the Centre is also in the process of developing & implementing a highly attractive, user-friendly and dynamic web-site. All major information about the institute, academic research, infrastructure, people, job portal, news and announcements is being regularly updated on the website.

Internet Security

The Campus Network is protected using Shopos XG310 - where Unified Threat Management as a primary network gateway defense solution has been implemented with traditional firewall built into an all-inclusive security product able to perform multiple security functions: network firewalling, network intrusion detection/prevention (IDS/IPS), gateway antivirus (AV), gateway anti-spam, content filtering, load balancing, data loss prevention, and on-appliance reporting. Quick heal Seqrite end point security total edition 18.0 has been implemented as protection from viruses, adware, spyware etc.

Telephone Connectivity

The Campus has a PRI connectivity from Bharat Sanchar Nigam Limited and a distribution of about 300+ extensions for ease of communication within the campus and connecting with the outside world.

Audio Visual and Video Conferencing Facility

Auditorium, conference and seminar halls are equipped with a hi-tech sound and projection system, digital podium and Internet connectivity. These facilities are actively used for regular seminar series, colloquia and distinguished lectures, hands-on workshops and symposiums/ conferences. In addition, projection facility has been setup in classrooms and discussion rooms for regular teaching, lab meetings and scientific discussions. RCB has an Internet-based Video Conferencing Facility setup in the Seminar Hall. In addition to this, RCB has enrolled subscriptions for various virtual conference meeting rooms for holding virtual seminars or conferences. Classrooms, meeting rooms and conference halls are furnished with the latest digital technology i.e. digital podium, LCD projection system with audio/ video facility and video conferencing systems in the Institute.

Digital Library

RCB has a small but fully functional library with several copies of standard international textbooks spanning various areas of biotechnology practiced by its researchers and taught in its coursework. The RCB library houses over 1400 books including scientific textbooks, administrative, engineering and Hindi books in multiple copies. Web-based Online Public Access Catalogue (WebOPAC) has been set up through KOHA Open Source Library Management Software at RCB Library to provide online access to RCB library catalogues. In addition, an electronic library provides access to a vast range of primary literature in the form of peer-reviewed journals and reviews, through the DBT electronic library consortium (DeLCON). The RCB library provides access to online resources to users 24 X 7 via Intranet/Internet. Library also contains common Personal Computer systems for browsing online resources (e.g. journals and books) and checking for plagiarism.

Office Automation

RCB is moving towards adapting a paperless work environment in which the use of paper is eliminated or greatly reduced. This is done by converting documents and other papers into digital form and development of various online applications (services or facilities) through the intranet portal named eRCB. All the faculty and students have access to this customised online software package being used for administrative applications. The major modules in eRCB are online leave management, user management, vehicle booking, vendor management, HR, visitor management, bill claim portal, purchase workflow etc. In continuation of paperless work environment using office automation, IT has to implement the ERP System in the upcoming year. This system will provide paperless centralised automation mechanism to complete any task faster with the better traceability & reporting. This system will have centralized cover of all the major activities for five sections i.e. Finance, HR, Purchase, Academics & General Administration. In addition to this, many other online services are available over internet accessible from outside Institute. The majors are:

- Implemented GeM for all kind of purchases at RCB
- An online system of APAR (Annual Performance Appraisal System) be made more consultative and transparent. The full APAR including the overall grade shall be communicated to the concerned officer after the report is complete with the remarks of the reviewing officer.
- Central e-Procurement Portal)eWizard(for online tendering of any value
- PhD and Integrated PhD Admission portal with integration of payment gateway
- Job Portal with integration of payment gateway
- Google forms are being used for various online application to reduce paper usages
- Online Class Attendance for all programs
- Google Classroom / Zoom Meeting are available for conducting Online Classes
- Micro websites for various research workshops & conferences and facility for online registrations.

- Online Payment Gateway for collecting Student Fee, any conference registration fee etc.
- Vendor Registration portal etc.

Further, the RCB has recently implemented Academic and Payroll portals. The RCB Academic portal gives a centralize repository of Student's Academic records and their research progress for RCB and its affiliated centres. At present date, approx. 650 students have been registered for their course and research work of RCB and affiliated Centres both. Also, the RCB has recently implemented Online Payroll system for RCB officials and students for their online leave approval workflow and other payroll features like TDS declaration, leave records, daily IN/OUT punching details, salary slip etc.

In addition to the above core activities, the IT department of RCB will also play a critical role in the development of the following two centres:

Indian Biological Data Center (IBDC): The IBDC has deployed & start functioning soon by RCB, NII, ICGEB and NIC with support from Department of Biotechnology, Govt. of India. The computational infrastructure of IBDC will include High Performance Computation (HPC) cluster and High capacity archival data storage. The data will be curated at RCB and will be hosted by NIC, Bhubaneswar. The RCB IT-department is providing technical support for the development and day-to-day operations of the RCB component of IBDC. Detailed information on the kind of infrastructure developing under IBDC project is provided into separate section of this annual report.

Bioinformatics Center: The DBT has sanctioned the development of a Bioinformatics centre for computational drug discovery at RCB. The centre will have personnel and equipment to help researchers carry out structure based drug design to identify potential drugs against different pathogens. The RCB IT-department will provide technical support for the development of this centre.

DBT-HRD Project Management Unit (DBT-HRD PMU) at RCB

Human resource development in Biotechnology and its allied areas is of utmost importance to the Department of Biotechnology (DBT), Ministry of Science and Technology, Government of India.Recognizing the need for nurturing large pool of skilled and dynamic human capital which are critical for success of the Indian Biotechnology sector, DBT supports several human resource development programmes for the capacity-building as well as competency-building of students, research scholars, faculty, scientists, entrepreneurs, etc.

Since the year 2020, DBT has initially entrusted RCB as the Nodal Implementation Agency for management of three (3) key human resource development programmes through establishment of DBT-HRD Project Management Unit (DBT-HRD PMU) at RCB. Thereafter, DBT has assigned four (4) additional HRD programs to RCB for implementation on a national scale.

Currently, the programmes being managed by the DBT-HRD PMU are as follows:

1. Ramalingaswami Re-entry Fellowship Programme (RRF)
2. Junior Research Fellowship Programme (JRF)
3. Post-Graduate Teaching Programme (PG Program)
4. DBT Research Associate ship (RA) Program
5. Biotech Industrial Training Program (BITP)
6. DBT – TWAS Fellowship Program (TWAS)
7. DBT Bio-Care Program (Bio-Care)

Summary of the activities undertaken and the progress made in the year 2022-2023 are given below.

1. Ramalingaswami Re-entry Fellowship Programme (DBT RRF):

Ramalingaswami Re-entry Fellowship supports Indian Nationals who are working overseas in various fields of biotechnology and life sciences and are interested in taking up scientific research positions in India. In the year 2022-2023, a total of 26 Indian researchers working abroad joined the Ramalingaswami Re-entry Fellowship programme against the call for applications initiated in 2021-2022 by DBT-HRD PMU.

DBT-HRD PMU has disbursed total grant of Rs. 44.23 crores to 274 Ramalingaswami fellows working in different universities/institutions across the country in the previous year.

The 13th Ramalingaswami Conclave of mentors and fellows was organized by DBT-HRD PMU on 30th November – 2nd December, 2022. This year a joint conclave for Ramalinga swami Re-entry Fellowship and MK Bhan Fellowship was organized in physical mode in RGCB Trivandrum. Dr. Rajesh Gokhale, Secretary, Department of Biotechnology, Government of India attended the inaugural session as the Chief Guest. The Inaugural Session was attended by several DBT officials, DST Officials, Eminent academicians and scientists as mentors, ongoing and alumni Ramalingaswami fellows, MK Bhan Fellowship fellows and students. A total of 12 area-specific technical sessions were organized with the participation of 136 Ramalingaswami fellows, 30 MK Bhan fellows and 28 senior scientists/faculty as mentors. The conclave concluded successfully with exchange of ideas, evaluation of progress achieved by the fellows in their research work, interaction & guidance provided by the mentors.

The call for applications for the year 2022-2023 was initiated by DBT-HRD PMU through the online portal https://rrfdbtindia.in/ wherein several applications have been received for this prestigious fellowship.

2. Junior Resarch Fellowship Programme (DBT JRF):

The DBT -Junior Research Fellowship Programme support students to pursue doctoral

studies in the discipline of Biotechnology and Life-sciences across any recognised universities/ institutions in India.

Biotechnology Eligibility Test (BET) is the qualifying examination for issuance of fellowship award under the programme. BET 2022 was conducted on 23rd April, 2022. A total of 13,699 applications were received out of which 11,771 candidates appeared for the examination conducted at 101centres in 56 cities across the country. A total of 434 category I and 193 Category II candidates were shortlisted. Subsequently, 352 candidates under category-I and 104 candidates under category-II have availed their award letters under DBT JRF program. A total of 270 research scholars joined the programme as DBT JRF fellows, with the joining/ activation processed by DBT- HRD PMU.

DBT HRD-PMU has disbursed fellowship grant of Rs. 42.41 crores for 1067 fellows in the year 2021-22. This includes disbursals performed for DBT BINC programme as it has been merged with DBT JRF Programme.

DBT JRF Programme is managed by an online Program Management Software. During the year 2022-23 new feature added to the portal was for eliciting the publication data. Also, to capture the program outcomes, a form had been created and hosted on the program portal for eliciting the placement details from alumni of the programme.

3. Post-Graduate Teaching Programme (DBT PG Program):

In FY 2022-23, DBT HRD PMU managed DBT supported Post Graduate (DBT PG) Programme in Biotechnology (63 program) for around 1538 students across India. DBT HRD PMU at RCB has disbursed Rs. 32.33 crores in FY: 2022-23 to host universities/institutions under the DBT PG program. Besides routine programme management activities, DBT HRD PMU organised the annual national entrance examination, Graduate Aptitude Test – Biotechnology (GAT-B) on 23rd April, 2022 for close to 9500 applicants. Subsequently, the list of 1837 qualified candidates were announced and admission guidelines to the participating institutions/universities were issued to ensure uniform implementation of the program across India. DBT HRD PMU had also organized the DBT Steering Committee Meeting for evaluation of old programs approved under 14th FC on behalf of Department of Biotechnology wherein the progress of 70 programs across India was evaluated for final recommendation for their account settlement. In the FY: 2022-23; DBT had announced a fresh call proposals under the DBT PG teaching program. 59 proposals were received against the call and DBT HRD PMU had organized the DBT Steering Committee Meeting for HRD programs for evaluation and selection of programs for DBT support. A total of 23 programs were recommended by the committee and was approved by DBT for support under the program.

4. Biotech Industrial Training Programme (BITP):

Biotech Industrial Training Programme (BITP) is a scheme to provide six months industrial hands- on training to fresh B.E./B.Tech./M.Sc. /M.Tech Biotechnology students. The objective of this program is to impart skill based training to students for their holistic development so that their employability increases in relevant industries.

DBT has adopted apprenticeship model for implementation of DBT-BITP Programme, and linkages have been developed with Life Science Sector Skill Development Council (LSSSDC), New Delhi for selection of partnering industries for providing apprenticeship in Biotechnology sectors. A stipend of Rs. 10,000/- per month is paid to all selected candidates for six months' period and companies are also providing apprenticeship to all trainees.

During the FY: 2022-23, linkages have also been established with Food Industry Capacity & Skill Initiative (FICSI) to increase number of requisitions from companies. For 2022-23 session, call for training requisition from companies has been published and in response a total 393 requisition have been received from 36 companies.

DBT HRD PMU had engaged NSEIT Pvt. Ltd. to execute exam related activities an dBITP exam was successfully held on 26th February 2023 across the country at 40 centres of 36 cities. Total 3344 candidates have registered for the exam, of which 2975 candidates have appeared.

BITP Expert Committee has reviewed the requisitions received from companies and

approved 198 requisitions for 30 companies and had shortlisted 205 candidates accordingly. The process of matchmaking and placement of trainees through HRD PMU has been started.

5. **DBT-Research Associateship (DBT-RA) programme:**

In April 2022-2023, DBT transferred the implementation of DBT-Research Associateship (DBT-RA) programme from the Indian Institute of Science, Bengaluru to RCB, Faridabad. DBT Research Associateship programme was initiated in the year 2001 with the objective to train post-doctoral students in frontier areas of research in life sciences and biotechnology at premier institutions in country as well as enhance the post-doctoral culture in the country.

There is a provision for award of 100 fellowships through two call for applications per year.RCB had announced call for applications under 2022-23/ Call-I in July, 2022 with receipt of 1033 applications.Publicity of the call for applications was created with advertisement in newspapers, journals, etc. for widespread dissemination and outreach of the programme.RCB had organized meetings of DBT-RA Screening Committee and DBT-RA Selection Committee for review of applications towards award of fellowship to 47 candidates in September &October, 2022. Similarly, RCB had announced call for applications under 2022-23/ Call-II in February, 2023 with receipt of 733 applications. The process of final selection of awardees is underway.

For the evaluation of ongoing fellows, RCB had organized 4 meetings of DBT-RA Evaluation Committee by organizing review presentations of the fellows.

A grant of Rs. 6.3 crores was disbursed to 104 ongoing fellows and 34 newly joined fellows during 2022-2023 under DBT-RA programme.

6. **DBT - Biotechnology Career Advancement & Re-orientation Programme (BioCARe) programme**

In January 2022-2023, DBT transferred the implementation DBT - Biotechnology Career Advancement & Re-orientation Programme (BioCARe) from the International Centre for Genetic Engineering and Biotechnology, New Delhi to RCB, Faridabad. BioCARe Programme is a very important human resource development programme of DBT for supporting women scientists towards career development and re-join research / academia.

The programme implementation activities were kick-started with RCB organizing the Women's Day event at DBT on 6th March, 2023 with active participation of Dr. Rajesh S. Gokhale, Secretary, DBT and senior officials from DBT. Dr.SudhanshuVrati, Executive Director, RCB delivered the Inaugural Address and Dr.ChandrimaShaha, J. C. Bose Chair Distinguished Professor, Indian Institute of Chemical Biology, Kolkata delivered the Keynote Address during the programme. Several BioCARe awardees shared their professional achievements n receipt of BioCARe award during the event.

RCB had organized 5 meetings of Letter of Intent Screening Committees for shortlisting of Letter of Intents received under 6th Call of BioCARe programme. Currently, the process of submission of full applications by the shortlisted applicants is underway.

7. DBT-TWAS Fellowship Programme:

The Department of Biotechnology (DBT), Ministry of Science and Technology, Government of India and The World Academy of Sciences (TWAS), Trieste, Italy have jointly supported the "DBT-TWAS Fellowship programme" to foster Science and Technology (S&T) for scientists in developing countries of the South through research collaborations and capacity building. The DBTHRD Project Management Unit (DBT HRD PMU) established at the UNESCO Regional Centre for Biotechnology, Faridabad is coordinating the DBT-TWAS Fellowship Programmew.e.f 1st April 2022.

The DBT-TWAS program address the societal challenges through S&T application in emerging areas of biotechnology such as agriculture sciences, biological systems and organisms, chemical sciences, medical and health sciences, structural and molecular biology for scientists from developing countries who wish to pursue research in India.

During the tenure from 1st April 2022 to 31st March 2023, the DBT HRD PMU has made

remarkable progress in the program development by conducting proactive program management, liaising with the program partners and fellowsand disbursement of funds to the ongoing fellows and new joining through their Indian Host institution.

Over Rs. 93 lakhs have been disbursed in FY: 2022-23 to 18 fellows under the program including Post Graduate and Post-Doctoral fellows. The disbursement of funds included a rigorous task of compilation of joining information and review of the document on the provided banking details of the host institution and the process includes a rigorous work flow for on boarding the international fellows in India.

A total of 96 applications (PG-38 and PD -58) were received under 2022 program call. The DBT HRD PMU conducted preliminary review of the submitted applications and organised the Selection Committee Meeting held on 9th February 2023 at CDFD, Hyderabad. 25 candidates (PG: 10 and PD: 15) have been selected for availing the fellowship in India subject to completion of the procedural formalities.

In addition, the DBT HRD PMU also made the program presentation for the Sixteenth General Conference of The World Academy of Sciences (TWAS) convened in hybrid mode from November 21-24, 2022 by collating research experiences and feedback from the DBT TWAS fellows which included the talk by the Honourable Minister of Science and Technology, Dr. Jitendra Singh. The presentation was highly appreciated and captured the program output in an impressive manner.

Given that the DBT-TWAS fellowship is a prestigious program offering research and international exposure to the researchers and scientists from developing countries, the DBT HRD PMU has taken program initiatives with full dedication and extended support to the fellows in-time.

FINANCIAL STATEMENTS

Courtesy: Patterson Clement

REGIONAL CENTRE FOR BIOTECHNOLOGY, FARIDABAD

BALANCE SHEET AS AT 31st MARCH, 2023

Amt (₹)

LIABILITIES	Schedule	31.03.2023	31.03.2022
Corpus / Capital Fund	1	7,77,54,578	5,76,91,500
Reserves and Surplus	2	83,47,57,667	69,15,63,146
Earmarked/Endowment Funds	3	-	-
Secured Loans and Borrowings	4	-	-
Unsecured Loans and Borrowings	5	-	-
Deferred Credit Liabilities	6	-	-
Current Liabilities and Provisions	7	1,55,89,48,476	2,58,49,09,735
TOTAL		**2,47,14,60,721**	**3,33,41,64,381**
ASSETS			
Fixed Assets (Net Block)	8	64,56,39,703	49,46,47,815
Investment From Earmarked/Endowment Funds	9	-	-
Investment-Others	10	37,18,11,366	94,60,81,097
Current Assets, Loans, Advances etc.	11	54,66,75,055	54,12,62,757
Biotech Science Cluster (BSC)	8	90,73,34,597	1,35,21,72,712
TOTAL		**2,47,14,60,721**	**3,33,41,64,381**
Significant Accounting Policies and Notes on Accounts	24		
Contingent Liabilities		NIL	NIL

Schedules 1 to 24 form an integral parts of Balance Sheet

(SANJEEV KUMAR GOYAL)
FINANCE OFFICER
संजीव कुमार गोयल, वित्त अधिकारी
Sanjeev Kumar Goyal, Finance Officer
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
भूतेल्वे के प्रावधान में जैवप्रौद्योगिकी विभाग, भारत सरकार द्वारा स्थापित
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana-121 001

(Dr. SUDEEP BHAR)
CONTROLLER of ADMINISTRATION

(Dr. Arvind K. Sahu)
EXECUTIVE DIRECTOR
डॉ. अरविंद के. साहू / Dr. Arvind K. Sahu
कार्यपालक निदेशक / Executive Director
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र / Regional Centre for Biotechnology
फरीदाबाद - 121 001 (हरियाणा), भारत / Faridabad-121 001 (Haryana), India

REGIONAL CENTRE FOR BIOTECHNOLOGY,FARIDABAD

INCOME & EXPENDITURE ACCOUNT FOR YEAR ENDED 31st MARCH, 2023

Amt (₹)

INCOME	Schedule	31.03.2023	31.03.2022
Income from Sales/ Services	12	2,28,47,186	2,64,24,139
Grants/Subsides	13	34,23,12,648	29,36,23,802
Fees/Subscriptions	14	55,28,372	77,03,500
Income from Investments	15	-	-
Income from Royalty, Publication etc.	16	-	-
Interest Earned	17	1,81,61,839	44,370
Other Income	18	13,03,348	25,93,590
Increase/(Decrease) in stock of Finished goods and works in progress	19	-	-
Deferred Income-Fixed Assets		8,01,05,479	6,56,52,594
TOTAL (A)		**47,02,58,872**	**39,60,41,995**
EXPENDITURE			
Establishment Expenses	20	14,46,07,236	14,33,70,421
Other Administrative Expenses etc.	21	22,54,83,079	17,81,35,330
Expenditure on Grants , Subsidies etc.	22	-	-
Interest	23	-	-
Depreciation (Net Total at the year-end-corresponding to Schedule 8)		8,01,05,479	6,56,52,594
Prior period Adjustment A/c (ANN-A)			-
TOTAL(B)		**45,01,95,794**	**38,71,58,345**
Balance being excess of Income Over Expenditure (A-B)		**2,00,63,078**	**88,83,650**
Transfer to special Reserve(Specify each)			-
Transfer to /from General Reserve		2,00,63,078	88,83,650
BALANCE BEING SURPLUS /DEFICIT CARRIED TO CORPUS/CAPITAL FUND		-	-
Significant Accounting Policies and Notes on Accounts	24		
Contingent Liabilities		NIL	NIL

Schedules 1 to 24 form an integral parts of Balance Sheet

(SANJEEV KUMAR GOYAL)
FINANCE OFFICER
संजीव कुमार गोयल/Sanjeev Kumar Goyal, Finance Officer
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
पूनेस्को के तत्वावधान में जैवप्रौद्योगिकी विभाग, भारत सरकार द्वारा स्थापित
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा/Faridabad, Haryana-121 001

(Dr. SUDEEP BHAR)
CONTROLLER of ADMINISTRATION

(Dr. Arvind K. Sahu)
EXECUTIVE DIRECTOR
डॉ. अरविंद के. साहू/Dr. Arvind K. Sahu
कार्यकारी निदेशक/Executive Director
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र/Regional Centre for Biotechnology
फरीदाबाद-121 001 (हरियाणा), भारत/Faridabad-121 001 (Haryana), India

Regional Centre for Biotechnology

Schedule 24: Accounting Policies and Notes Forming Parts of the Balance Sheet and Income & Expenditure Account for the Year Ended at 31st March, 2023.

1. The annual accounts have been broadly prepared in the revised format of accrual system of accounting, **except for extramural funds and other project grants**.

2. The liability on account of terminal benefits to employees like leave encashment & gratuity have been accounted for in accordance with Accounting Stanbdard-15 on actuarial valuation basis.

3. (a) Recurring Grants have been recognised in the Income & Expenditure account and Non-Recurring Grants have been shown as part of Capital reserve.

(b) Grant of core funds relating to depreciable fixed assets are treated as deferred income and recognised in the Income and Expenditure Account on a systematic and rational basis over the useful life of such assets i.e. such grants are allocated to income over the periods and in the proportions in which depreciation in charged (As per Accounting Standard-12 title Accounting for Government Grants). During the year income recognised in respect of such Grants amounts to **Rs.8.01 crores.**

4. (a) The depreciation has been provided w.e.f. the date of installation/put to use of fixed assets as per the rates prescribed as per section 32 of Income Tax Act 1961.

(b) Depreciation has been charged during the year of acquisition and no depreciation is provided during the year of assets sold / discarded. In respect of additions to/deductions from fixed assets during the year, depreciation is considered on pro-rata basis.

5. (a) Fixed assets have been created with core grants received from the Department of Biotechnology. No equipment procured out of project funds have yet been capitalized.

(b) Fixed Assets are stated at cost acquisition inclusive of custom duty (non-recoverable) and taxes, inward freight, incidental and direct expenses related to acquisition.

6. All purchases of chemicals, glassware, consumables and stationary have been charged to consumption at the time of purchase without working out closing stock at the end of the year.

7. Further all entries relating to purchase of consumables /equipments or other fixed assets in accounts are being passed only after submission of satisfactory Bill/Invoice, inspection/installation report irrespective of the date of actual receipt of the supplies /equipments.

8. Transactions denominated in foreign currency are accounted at the exchange rate prevailing at the date of transaction.

9. The institute has a policy of incurring expenditure on various projects in accordance with the sanctioned budget under various heads of accounts irrespective of the actual releases during a financial year. Since the actual release of money by the sponsoring agency is subject to various factors, the expenditure on approved heads of accounts is incurred within the overall sanction budget of the project.

डॉ. अरविंद के. साहू / Dr. Arvind K. Sahu
कार्यकारी निदेशक / Executive Director
क्षेत्रीय जैवप्रौद्योगिकी केंद्र / Regional Centre for Biotechnology
फरीदाबाद - 121001 (हरियाणा) भारत / Faridabad-121001 (Haryana) India

10. The balances of the previous year have been rearranged/regrouped as per requirement and shown in Balance Sheet against the relevant heads.

11. Expenses and Overheads incidental to construction building of institute as well as other buildings in the NCR BSC, as reported by the Project Monitoring Unit are added to the capital work in progress to be capitalized along with the building only on submission of final accounts.

13. The Capital Work-in-progress booked in the accounts includes the construction of laboratory buildings of ATPC, Bio-incubator and hostels & faculty housing, common facilities, BSL-3 laboratory, Office of Connectivity Building, etc. under Phase-I Extension and Phase II. The expenditure under Phase-I was transferred to the respective stakeholders as per their contribution and area wise expenditure. Expenditure under phase-I was capitalised during the FY 2019-20 and expenditure under Phase-I Extension is under process of settlement and WIP under Phase-II has been settled during FY 2022-23.

14. Interest earned on saving bank account and fixed deposits during the financial year 2022-23 amounting to Rs.99.44 Lakhs has been allocated to the respective projects on pro-rata basis.

15. No income tax or GST scrutiny is pending for any of the years.

Schedule 25: Contingent Liabilities

NIL

(SANJEEV KUMAR GOYAL)
FINANCE OFFICER

(Dr. SUDEEP BHAR)
CONTROLLER of ADMINISTRATION

(Dr. ARVIND K. SAHU)
EXECUTIVE DIRECTOR

डॉ. अरविंद के. साहू / Dr. Arvind K. Sahu
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फरीदाबाद - 121 001 (हरियाणा), भारत / Faridabad 121 001 (Haryana), India

सत्यमेव जयते

कार्यालय महानिदेशक लेखापरीक्षा,
पर्यावरण एवं वैज्ञानिक विभाग
नई दिल्ली-110 002
OFFICE OF THE DIRECTOR GENERAL OF AUDIT,
ENVIRONMENT & SCIENTIFIC DEPARTMENTS,
A.G.C.R. BUILDING, I.P. ESTATE
NEW DELHI-110 002

स.म.नि.ले.प.(पर्या.एवं वै.वि)/नि./4(48)/RCB/SAR/2023-24/ 393 दिनांकः 18-10-2023

सेवा में,

डा. अरविंद के. साहू
कार्यपालक निदेशक
क्षेत्रीय जैव प्रौधोगिकी केन्द्र
तृतीय मील पत्थर, फरीदाबाद-गुड़गांव एक्सप्रेसवे,
फरीदाबाद-121001

विषयः क्षेत्रीय जैव प्रौधोगिकी केन्द्र वर्ष 2022-23 के लेखों पर पृथक ऑडिट रिपोर्ट।

महोदय,

मुझे क्षेत्रीय जैव प्रौधोगिकी केन्द्र के वर्ष 2022-23 के लेखों पर पृथक ऑडिट रिपोर्ट अग्रेषित करने का निर्देश हुआ है।

संसद के दोनों सदनों में प्रस्तुत करने से पहले वर्ष 2022-23 के वार्षिक लेखों को क्षेत्रीय जैव प्रौधोगिकी केन्द्र, फरीदाबाद द्वारा अपनाया जाए। प्रत्येक दस्तावेज जो संसद में प्रस्तुत किया जाए उसकी तीन प्रतियां इस कार्यालय तथा दो प्रतियां भारत के नियंत्रक एवम महालेखापरीक्षक को अग्रेषित की जाए। संसद के दोनों सदनों में प्रस्तुत करने की तिथि (या) भी इस कार्यालय को सूचित की जाए।

आपसे अनुरोध है कि पृथक ऑडिट रिपोर्ट का हिन्दी अनुवाद अपने कार्यालय में कराने के पश्चात सॉफ्ट कॉपी तथा हार्ड कापी दोनों में हमें भेज दें ताकि हिन्दी प्रति को शीघ्र अग्रेषित किया जा सके।

यह महानिदेशक द्वारा अनुमोदित है।

भवदीय,

संलग्नकः यथोपरि।

उप-निदेशक (निरीक्षण)

Draft Separate Audit Report of Comptroller and Auditor General of India on the accounts of Regional Centre for Biotechnology, Faridabad for the year ended 31 March 2023

We have audited the attached Balance Sheet of Regional Centre for Biotechnology (RCB), Faridabad as at 31 March 2023 and the Income and Expenditure Account/ Receipts and Payments Account for the year ended on that date under Section 19 (2) of the Comptroller and Auditor General's (Duties, Powers and Conditions of Service) Act, 1971 read with section 32 (1) of RCB Act, 2016. These financial statements are the responsibility of the RCB's management. Our responsibility is to express an opinion on these financial statements based on our audit.

2. This Separate Audit Report contains the comments of the Comptroller and Auditor General of India on the accounting treatment only with regard to classification, conformity with the best accounting practices, accounting standards and disclosure norms, etc. Audit observations on financial transactions with regard to compliance with the Laws, Rules & Regulations (Propriety and Regularity) and efficiency-cum-performance aspects, etc., if any, are reported through Inspection Reports/ Comptroller and Auditor General's Audit Reports separately.

3. We have conducted our audit in accordance with auditing standards generally accepted in India. These standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free from material misstatements. An audit includes examining, on a test basis, evidences supporting the amounts and disclosure in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of financial statements. We believe that our audit provides a reasonable basis for our opinion.

4. Based on our audit, we report that –

(i) We have obtained all the information and explanations except those stated in the report, which to the best of our knowledge and belief were necessary for the purpose of our audit;

(ii) The Balance Sheet and Income and Expenditure Account dealt with by this report have been drawn up in the format approved by the Government of India. However, the Receipts and Payments Account dealt with by this report has not been drawn up in the format approved by the Government of India;

(iii) In our opinion, proper books of accounts and other relevant records have been maintained by RCB, except those stated in this audit report.

(iv) We further report that –

A. LIABILITIES

A.1 Current Liabilities & Provisions

A.1.1 Project Grant/ Fellowship [Schedule 7 : Rs 5575 lakh]

A balance of Rs 5575 lakh reported as 'Project Grant/ Fellowships' was a net figure consisting of credit balance of Rs 5648.33 lakh and debit balance of Rs 73.33 lakh under 80 sponsored projects, which were set-off against each other while representing the amount in the Balance Sheet.

As the debit balances were nothing but the excess expenditure incurred against amount available with RCB which was to be received from the project sponsoring agencies, netting of excess expenditure by RCB led it to understate its current liabilities (Project Grant/ Fellowship) as well as current assets (Excess expenditure incurred on projects – Receivable) each by Rs 73.33 lakh.

A.2 Provisions [Schedule 7 : Rs 615.03 lakh]

(a) RCB did not make any provision for wages amounting to Rs. 13.24 lakh for the month of March 2023 payable to contractual staff which were actually paid in 2023-24. As a result, it understated its current liabilities and expenditure each by Rs 13.24 lakh.

(b) RCB did not maky any provision for audit fee for certification audit of its accounts. As a result, it understated its current liabilities and expenditure by the amount payble for audit.

B. ASSETS

B.1. Fixed Assets

Biotech Science Cluster (Capital work in progress) [Schedule 8 : 9073.35 lakh]

It was reported in previous year's Audit Report that although works amounting to Rs 12146.73 lakh had been completed long ago in 2015 and 2021 and were also put to use, yet the same were shown under Capital Work in Progress (CWIP). RCB assured (August 2022) that the same will be capitalised during the year 2022-23. However, RCB capitalized an amount of Rs. 450.98 lakh only during 2022-23. Thus, works amounting to Rs. 11695.75 lakh[1] were yet to be capitalized. As a result, RCB could not charge depreciation amounting to Rs. 5017.61 lakh [2] on such buildings. Hence, RCB understated its expenditure (depreciation) and overstated the Fixed Assets each by Rs. 5017.61 lakh.

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[1] Amount to be capitalized (Rs. 12146.73 lakh) – Amount capitalized (Rs. 450.98 lakh)

[2] Depreciation till 2021-22 (Rs. 4250.54 lakh) + Depreciation for 2022-23 (Rs. 789.62 lakh) – Depreciation actually charged during 2022-23 (Rs. 22.55 lakh)

B.2 Current Assets, Loans and Advances [Schedule 11 : Rs. 5466.75 lakh]

Above included an amount of Rs. 3565.13 lakh shown as balance of Deposit Accounts. However, the bank balance as confirmed by relevant bank was Rs. Nil as on 31.03.2023. Hence, Current Assets as well as Current liability were overstated by Rs. 3565.11 lakh.

C. INCOME AND EXPENDITURE ACCOUNT

C.1 Income

C.1.1 Deferred Income – Fixed Assets [Rs 801.05 lakh]

It was reported in previous year's Audit Reports that expenditure on account of depreciation charged on Fixed Assets was set off by booking as Deferred Income in Income and Expenditure Account, which was against the Uniform Format of Accounts prescribed by Government of India for Autonomous Bodies as it allows booking of deferred income only in case of grant received for specific fixed assets.

However, RCB again adopted same practice and an expenditure of Rs 801.05 lakh booked towards depreciation on Fixed Assets was set off by booking as Deferred Income in Income and Expenditure Account for 2022-23. This resulted in overstatement of income as well as of liabilities by Rs. 801.05 lakh.

C.2 Expenditure

C.2.1 Other Administrative expenses etc. [Schedule 21 : Rs 2254.83 lakh]

(a) Accounting policy adopted by RCB for chemicals, glassware, consumables and stationary was not in conformity with generally accepted accounting principles, as all purchases of chemicals, glassware, consumables and stationary were charged to consumption at the time of purchase without working out closing stock at the end of the year.

D. RECEIPTS AND PAYMENTS ACCOUNT

(a) Receipts and Payments Account was not as per Uniform Format of Accounts prescribed by Government of India for Autonomous Bodies as it contained various heads like 'Current liablities', 'Current Assets', Fixed Assets'; which are not part of Receipt and Payment Account as per Uniform Format.

E. GRANTS-IN-AID

On 01 April 2022, RCB had carry forward grant of Rs 12.31 lakh. During 2022-23, Department of Biotechnology issued sanctions for release of core Grants-in-aid of Rs 5245 lakh to RCB through account opened with Reserve Bank of India under TSA system. An expenditure of Rs 5235.44 lakh was incurred by RCB during 2022-23 and Rs. 21.87 lakh were refunded/lapsed to DBT, leaving no unspent balance as on 31 March 2023.

Audit noticed that during 2022-23, RCB transferred a total amount of Rs 1991.02 lakh from TSA account to it's other commercial bank accounts for various purposes, including for Salary, Fellowship, Medical expenses, which was not permissible as per instructions. RCB utilized the transferred core grants-in-aid alongwith other funds (grants-in-aid received from other departments and income generated from internal resources) already available in commercial bank account. Hence, the possibility of parking of unspent amount of grant under this account cannot be ruled out.

(v) Subject to our observations in the preceeding paragraphs, we report that the Balance Sheet, Income and Expenditure Account and Receipts and Payment Account dealt with by this report are in agreement with the books of accounts.

(vi) In our opinion and to the best of our information and according to the explanations given to us, the said financial statements read together with the Accounting Policies and Notes on Accounts, subject to the significant matters stated above and other matters mentioned in Annexure to this Audit Report give a true and fair view in conformity with accounting principles generally accepted in India:

(a) *In so far as it relates to the balance sheet, of state of affairs of the Regional Centre for Biotechnology, Faridabad as at 31 March 2023; and*

(b) *In so far as it relates to Income and Expenditure Account, of the surplus for the year ended on that date.*

For and on behalf of C&AG of India

Director General of Audit
(Environment and Scientific Departments)

Dated:
Place: New Delhi

Annexure to Separate Audit Report

1. Adequacy of Internal Audit System

Internal Audit of the Regional Centre for Biotechnology (RCB) was required to be conducted annually by the internal audit wing of Principal Pay and Accounts Office of the Ministry of Science and Technology, New Delhi which was completed up to March 2021. A total number of 9 paras pertained to the period 2019-21 were outstanding till date. Internal Audit of RCB is pending since March 2021.

2. Adequacy of Internal control system

Internal control mechanism in RCB needs strengthening in following areas :

Improper maintenance of Assets Register

As per provisions contained in General Financial Rules, separate accounts/registers were required to be maintained for fixed assets viz. Plant and Machinery, equipment furniture and fixture in the form GFR-22. The register was required to be closed at the end of the financial year and the value of fixed assets shown in it should tally with the value of assets shown in the Annual Account.

However, the Assets Register maintained by RCB did not reflect all the assets as some of its assets (examples given below) were shown in Stock Register instead of Assets Register:

Sl. No.	Description of Asset	Purchase value (in lakh Rs.)
1	Air Handling Unit	37.40
2	Air Handling Unit	41.22
3	Air Handling Unit	64.85
4	Car	6.89

3. System of physical verification of fixed assets

(a) Physical verification of fixed assets

Latest physical verification of fixed Assets was conducted up to 31 March 2022.

(b) Physical verification of library

Latest physical verification of library was conducted up to 31 March 2022.

4. System of physical verification of inventories

Latest physical verification of library was conducted up to 31 March 2022.

5. Regularity in payment of statutory dues

There was no outstanding statutory dues against RCB.

Deputy Director (Inspection)

Annexure to Circular letter No. 173-Rep. (AB)/27-84(I) dated10.01.1999

PROFORMA

(Referred in Paragraph 4.11 of the Manual of Instruction for Audit of Autonomous Bodies)

Proforma on progress of Audit to be sent to the Office of the Comptroller and Auditor General of India along with the audited accounts and Audit Report

Name of the Autonomous Body: Regional Centre for Biotechnology, Faridabad

1.	Date of submission of the account to the Audit by the Autonomous Body	27.06.2023		
2.	Where applicable reasons for returning the accounts for revision indication why the accounts could not be certified with qualification	Not applicable		
3.	Date of submission of revised accounts to Audit where revision was considered essential	Not applicable		
4.	Dates on which audit was taken up and completed	05.07.2023 to 18.07.2023		
5.	Date of issue of draft SAR to autonomous Body for replies/ comments	04.08.2023		
6.	Date of receipt of replies/comments from autonomous body	17.08.2023		
7.	Date of issue of draft SAR including replies/comments of autonomous body along with an Aid memoire to CAG's office for approval	10.10.2023		
8.	(a) Date of CAG's office letter communicating approval to SAR	16.10.2023		
	(b) Date of receipt of letter and approval at 8(a)			
9.	Date of issue of final Audit Report to Government of India/ State Government/CAG's office English version/Hindi version			
10.	Reasons for delay, if any at various stages			
11	Dates of presentation of the previous Audit Reports before Parliament/Legislature (Where the Audit Report for previous years have not been placed, years to which these pertain, may also be indicated)	Year	Lok Sabha	Rajya Sabha
		2020-21	02.02.2022	16.12.2021
		2021-22	21.12.2022	22.12.2022

Director General of Audit
(Environment and Scientific Departments)

Reply to CAG Office annotation on the SAR of Regional Centre for Biotechnology, Faridabad for the year 2022-23

S. No.	Heading	Hq Remarks	Action taken
1	A.1 Current Liabilities & Provisions [Schedule 7: Rs 5575 lakh]	Netting is not good practice, it should be avoided.it may be retained in SAR.	Retained please.
2	A.2 Provisions [Schedule 7: Rs 615.03 lakh]	(a)Liability was noy provided, it may be retained. (b)Liability was noy provided, it may be retained.	Retained please.
3	B.1. Fixed Assets Biotech Science Cluster (Capital work in progress) [Schedule: 9073.35 lakh]	Work was completed were not capitalized; it may be retained in SAR.	Retained please.
4	B.2 Current Assets, Loans and Advances [Schedule 11: Rs. 5466.75 lakh]	This should be reconciled; it may be retained in SAR.	Retained please.
5	C.1 Income Deferred Income – Fixed Assets [Rs 801.05 lakh]	Repeat comment, no action was taken, it may be retained in SAR.	Retained please.
6	C.2 Expenditure Other Administrative expenses etc. [Schedule 21: Rs 2254.83 lakh]	Account is not correct; it may be retained in SAR. Amount is not material; it may be shifted in ML.	Retained please. Shifted to ML as suggested.
7	D. RECEIPTS AND PAYMENTS ACCOUNT	Format is not followed; it may be retained.	Retained please.
8	E. GRANTS-IN-AID	Factual it may be retained. It may also be examined in TA.	Noted in Important Point Register.
9	Annexure to Separate Audit Report	May be retained in SAR.	Retained please.

Sr. Audit Officer (Inspection)

INSTITUTIONAL GOVERNANCE

Courtesy: Rushikesh M. Khadake

Board of Governors (BOG)

- **Dr. Rajesh Gokhale (Chairperson)**
  Secretary
  Department of Biotechnology, GOI
  New Delhi - 110 003
- **Director (Ex-officio Member)**
  Rajiv Gandhi Centre for Biotechnology
  Thiruvananthapuram - 695 014, Kerala
- **Director (Ex-officio Member)**
  National Institute of Immunology,
  Delhi 110 067
- **Director (Ex-officio Member)**
  NIMHANS, Bangalore 560 029
  Karnataka
- **Director (Ex-officio Member)**
  UNESCO Delhi Office,
  New Delhi - 110 021
- **Chairperson, RCB PAC (Permanent Invitee)**
- **Dr. Alka Sharma (Special Invitee)**
  RCB Coordinator
  Scientist-H, Department of Biotechnology,
  GOI, New Delhi
- **Dr. Nitin K Jain (Ex-officio Member)**
  RCB Nodal Officer
  Scientist-F, Department of Biotechnology,
  GOI, New Delhi
- **Prof. Sudhanshu Vrati (Convenor)**
  Executive Director
  Regional Centre for Biotechnology,
  Faridabad - 121 001

Programme Advisory Committee (PAC)

- **Dr. Umesh Varshney (Chairperson)**
  Professor, IISc-Bangalore
- **Dr. Joel Sussman (Member)**
  Professor, Dept. of Structural Biology
  The Weizmann Institute of Science,
  Israel
- **Prof. Angelo Azzi (Member)**
  Tufts University, Medford, USA
- **Dr. Mohan Wani (Member)**
  Director, NCCS-Pune
- **Dr. Saumitra Das (Member)**
  Professor, IISc-Bengaluru
- **Dr. Krishnaveni Mishra (Member)**
  Professor, University of Hyderabad
- **Dr. Sabhyata Bhatia (Member)**
  Staff Scientist, NIPGR, New Delhi
- **Mr. Shrikumar Suryanarayan**
  Chairman, Sea6 Energy,
  Bengaluru
- **Dr. Vinay K. Nandicoori**
  Director, CCMB, Hyderabad
- **Dr. Alka Sharma (Member)**
  Scientist-H, Dept. of Biotechnology,
  New Delhi
- **Dr. Rakesh Mishra (Member)**
  Director, TIGS, Bengaluru
- **Dr. Nitin K Jain (Special Invitee)**
  Scientist-F, Dept. of Biotechnology,
  New Delhi
- **Prof. Sudhanhsu Vrati (Ex-officio Member Secretary)**
  Executive Director, Regional Centre for Biotechnology
  Faridabad 121 001

Executive Committee (EC)

- **Prof. Sudhanshu Vrati (Chairman, Ex-officio)**
  Executive Director, RCB, Faridabad 121 001
- **Dean (Member, Ex-officio)**
  Regional Centre for Biotechnology
  Faridabad 121 001
- **Joint Secretary (Administration) (Member, Ex-officio)**
  Department of Biotechnology, GOI
  New Delhi 110 003
- **Director (Member, Ex-officio)**
  UNESCO Office,
  New Delhi 110 021
- **Dr. Alka Sharma (Special Invitee)**
  RCB Coordinator
  Scientist-H, Department of Biotechnology
  GOI, New Delhi
- **Dr. Nitin K. Jain (Ex-officio Member)**
  RCB Nodal Officer,
  Scientist-F, Department of Biotechnology
  GOI, New Delhi
- **Joint Secretary (ICC) (Member, Ex-officio)**
  Ministry of Human Resource Development
  GOI, New Delhi 110 066
- **Joint Secretary (Member, Ex-officio)**
  UNES Division,
  Ministry Of External Affairs,
  GOI, New Delhi 110 001
- **Registrar (Permanent Invitee)**
  Regional Centre for Biotechnology,
  Faridabad 121 001
- **Finance Officer (Permanent Invitee)**
  Regional Centre for Biotechnology,
  Faridabad 121 001
- **Controller of Administration (Member Secretary, Ex-officio)**
  Regional Centre for Biotechnology,
  Faridabad 121 001

Finance Committee (FC)

- **Prof. Sudhanshu Vrati (Chairman, Ex-officio)**
  Executive Director,
  Regional Centre for Biotechnology
  Faridabad 121 001
- **Additional Secretary & Financial Advisor (Member, Ex-officio)**
  Department of Biotechnology
  GOI, New Delhi 110 003
- **Dr. Alka Sharma (Member, Ex-officio)**
  RCB Coordinator
  Scientist-H, Department of Biotechnology
  GOI, New Delhi
- **Dr. Nitin K Jain (Member, Ex-officio)**
  RCB Nodal Officer
  Scientist-F, Department of Biotechnology,
  GOI, New Delhi
- **Executive Director (Member, Ex-officio)**
  Translational Health Science &Technology Institute, Faridabad 121 001
- **Shri PS Rawat (Member, Ex-officio)**
  National Institute of Immunology,
  New Delhi
- **Shri Pitambar Behera (Member)**
  Deputy Finance Officer,
  Indian Institute of Foreign Trade
  New Delhi 110 016
- **Controller of Administration (Member, Ex-officio)**
  Regional Centre for Biotechnology,
  Faridabad 121 001
- **Finance Officer (Member Secretary, Ex-officio)**
  Regional Centre for Biotechnology,
  Faridabad 121 001

Scientific Personnel

Faculty

Executive Director and Professor
Prof. Sudhanshu Vrati

Dean
Dr. Rajendra Prasad Roy

Professor
Dr. Prasenjit Guchhait
Dr. Deepak T. Nair
Dr. Avinash Bajaj
Dr. Sivaram V. S. Mylavarapu
Dr. C. V. Srikanth
Dr. Vengadesan Krishnan
Dr. Tushar Kanti Maiti

Associate Professor
Dr. Manjula Kalia
Dr. Arup Banerjee
Dr. Deepti Jain
Dr. Sam Jacob Mathew
Dr. Divya Chandran
Dr. Saikat Bhattacharjee

Assistant Professor
Dr. Ambadas B. Rode
Dr. Nidhi Adlakha
Dr. Prem Singh Kaushal
Dr. Ramu S Vemanna
Dr. Rajender K Motiani
Dr. Prashant Pawar
Dr. Prasad Abnave
Dr. Anil Thakur
Dr. Karthigeyan Dhanasekaran

JC Bose Fellow
Prof. Sudhanshu Vrati
Dr. R.P. Roy

Wellcome Trust-DBT IA Intermediate Fellowships
Dr. Geetanjali Chawla
Dr. Pinky Kain Sharma
Dr. Rajender Kumar Motiani

Wellcome Trust -DBT IA Early Career Fellowship
Dr. Masum Saini

DST INSPIRE Faculty
Dr. Naini Burman
Dr. Prashant M. Pawar
Dr. Prasad Abnave

DBT Woman BioCARe awardee
Dr. Babitha Chandrashekhar

Ramalingaswami Fellowship
Dr. Ambadas B. Rode
Dr. Anil Thakur
Dr. Karthigeyan Dhanasekaran

Ramanujan Fellowship
Dr. Ramu S. Vemanna

DST SERB-NPDF
Dr. Eira Choudhary
Dr. Ruchira Chakraborty

MK Bhan Fellow
Dr. Shouvik Das
Dr. Nitu Singh

Wellcome Trust Post-Doc Fellow
Dr. Farina Sultan
Dr. Akshay Sharma
Dr. Jyoti

DBT-RA
Dr. Vineet Kumar
Dr. Archana Prasad
Dr. Yashika Walia Dhir
Dr. Arundhati Tiwari
Dr. Kesiraju Karthik

ICMR-SRF
Mr. Pankaj Kumar
Ms. Akashi
Mr. Pharvendra Kumar
Ms. Naina Soni
Ms. Shreyasi Das
Mr. Chandan Kumar
Mr. Animesh Kar
Mr. Devashish Mehta
Ms. Anushree
Ms. Sandhini Saha

Project Associate
Mr. Sathish Dorairaj
Ms. Sandhini Saha
Mr. Jaidev Sharma
Mr. Murlidhar Madhukar
Mr. Biswambhar Biswas
Ms. Khashpatika Ganesh
Ms. Shilpi Nagpal
Mr. Nitin Kumar
Ms. Apurva Gangal
Mr. Pankaj Kumar Sahoo
Mr. Shouri K A

Management

Office of the Executive Director

Executive Director
Prof. Sudhanshu Vrati

Staff Officer to Executive Director
Dr. Nidhi Sharma

Technical Assistant
Mr. Ramesh Chandiramouli

Administration, Finance and Purchase

Controller of Administration
Dr. Sudeep Bhar

Registrar
Prof. Prasenjit Guchhait (Acting Registrar)
Dr. Deepika Bhaskar (On Deputation)

Finance Officer
Mr. Sanjeev Goyal

Administrative Officers
Mr. V.M.S. Gandhi
Mr. C.B. Yadav
Mr. Rakesh Yadav

Section Officers
Mr. Sanjeev Kumar Rana
Mr. Sudhir Kumar
Mr. Chakrawan Singh Chahar

Management Assistants
Mr. Sumit Sharma
Mr. Vinod Kumar
Mr. Praveen Kumar V.
Mr. Amit Naryal

Technical
Executive Engineer
Mr. R.K. Rathore

System Administrator
Mr. Naveen Kumar

Instrumentation Engineer
Mr. Pankaj

Senior Technical Officer
Mr. Mahfooz Alam
Mr. Deepak Kumar (On deputation)
Mr. Vijay Kumar Jha

Technical Officers
Mr. Atin Jaiswal
Mr. Suraj Tewari
Ms. Vishakha Chaudhary
Mr. Madhav Rao M.

Technical Assistants
Mr. Nagavara Prasad G.
Dr. Shaminder Singh
Mr. Dharmender Gupta
Mr. Manoj Kumar Soni
Dr. Reena Rani

Documentation Assistant
Mr. Priyanshu Joshi
Mr. Amit Kumar Yadav

Consultant (Rajbhasha)
Mr. Maharam Tanwar

Advanced Technology Platform Centre (ATPC)

Application Scientists
Dr. Neha Sharma

Technical Officers
Mr. Ghanshyam Sharma
Ms. Meena Kapasiya

Instrument Engineer
Mr. Rajesh Kumar

Software Engineer
Mr. Mohit Kumar Vats

BSC BioNEST Bio-incubator (BBB)
Chief Operating Officer
Ms. Suman Gupta

Intellectual Property Manager
Ms. Malvika Garg

Technical Assistants
Ms. Sapna Rani
Ms. Kanchan Rawat

Office of Connectivity

Chief Executive Officer
Dr. Feroz Khan Suri

Service Coordinator
Mr. Akshay Bhardwaj

Management Assistants
Ms. Mahua Das
Mr. Yashpal
Mr. Naveen Swaroop

DBT-HRD-PMU
Project Manager
Dr. Feroz Khan Suri

Senior Liaison Assistant
Mr. Nirmal Kumar Jha

Grants Advisors
Ms. Elsy Samuel
Ms. Shreya Malik
Mr. Dilip Joy T
Dr. Harmeet Kaur
Ms. Aasita Apoorva

Project/Grants Executives
Mr. Anupam Saxena
Ms. Anuradha Pathania
Mr. Akshay Bhardwaj

Senior Accounts Assistant
Mr. Raman Kumar Nimesh
Mr. Sachin Kumar Mogha

Accounts Assistant
Mr. Nimesh Kumar Singh
Mr. Kuldeep Singh
Mr. Prashant

Data Entry Operator
Mr. Sher Bahadur
Ms. Deepika Kumari
Mr. Vipul Kumar

Secretarial Assistant
Mr. Navin Kumar Yadav

Front Office Assistant
Mr. Puneet Sharma

Multi-Tasking Staff
Mr. Vishal

Indian Biological Data Center

Project Head
Dr. Saurabh Raghuvanshi

Scientists
Dr. Nidhi Batra
Dr. Arun Sharma
Dr. Sonia Balyan
Dr. Dibyabhaba Pradhan

Administrative Officers
Ms. Sanjana Singh
Mr. Dikshant Sharma

Technical Assistants-A
Mr. Vipul Adhana
Mr. Gautam Kanwal
Mr. Rajesh Kumar

Technical Assistants-B
Mr. Mayank Mamgain

Data Curators
Mr. Murari Uthayakumar
Mr. Sanjay Deshpande
Mr. Navajeet Chakravartty
Mr. Pawan Kumar
Ms. Isha Saini
Dr. Nivedita
Ms. Indu Kumari
Dr. Shivani Sharma
Ms. Himanshu Bhusan Samal

Dr. Abhisek Kumar Behera

Database Engineers/ Software Developers

Mr. Manish Namdeo Alone
Mr. Kalpanath Paswan
Mr. Ankit Tomar
Mr. Abhay Shankar Pandey
Mr. Midhun Kumar A
Dr. Vibha Oberoi
Mr. Mayank Chauhan
Ms. Mayuri Jain
Mr. Mohit Kumar Vats

Programmer
Ms. Neetu Kumari

BSU, Phase II

Chief Scientific Officer
Dr. Sangeeta Agarwal

Project Scientists-III
Dr. Manpreet Kaur
Dr. Poonam Vishwakarma
Dr. Pranjali Vishwakarma
Dr. Shipra Shahi
Dr. Govind Rai

Project Scientists-II
Dr. Renu Arora
Dr. Bhawna Yadav
Dr. Subhasish Dutta

Project Associate-II
Dr. Shubhi Sharma

Senior Project Associate
Dr. Virendra Kumar

United Nations
Educational, Scientific and
Cultural Organization

क्षेत्रीय जैव प्रौद्योगिकी केन्द्र
Regional Centre
for Biotechnology

REGIONAL CENTRE FOR BIOTECHNOLOGY
an Institution of National Importance for Education, Training and Research
Established by the Dept. of Biotechnology, Govt. of India
Under the Auspices of UNESCO
2nd Milestone, Faridabad-Gurgaon Expressway
Faridabad-121001, Haryana, India
http://www.rcb.res.in