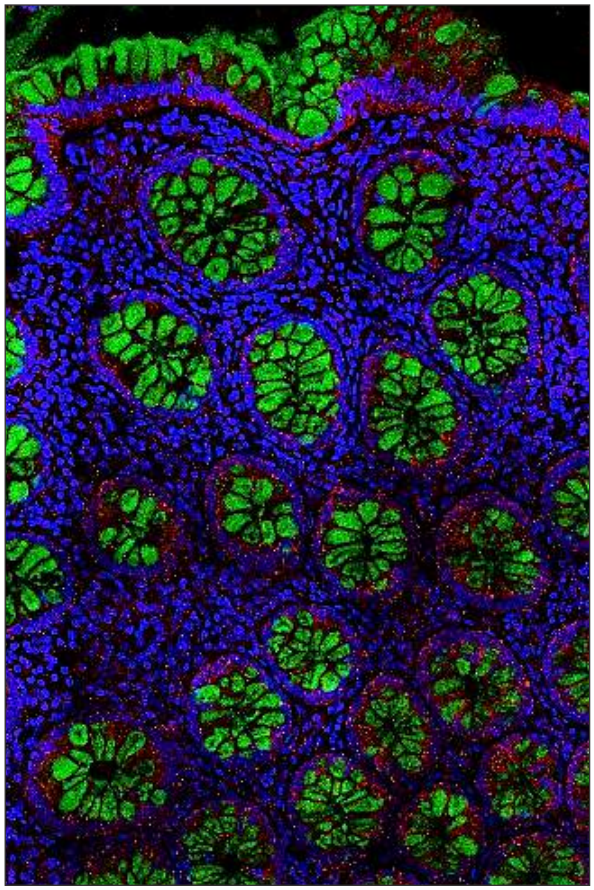
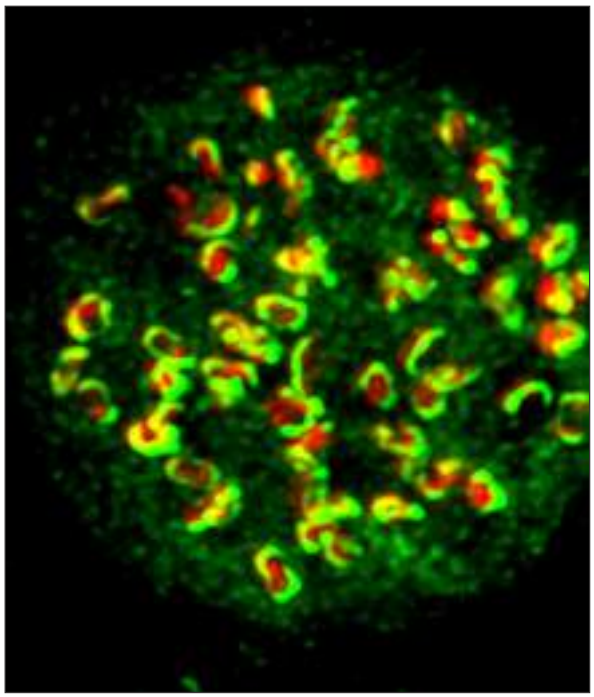
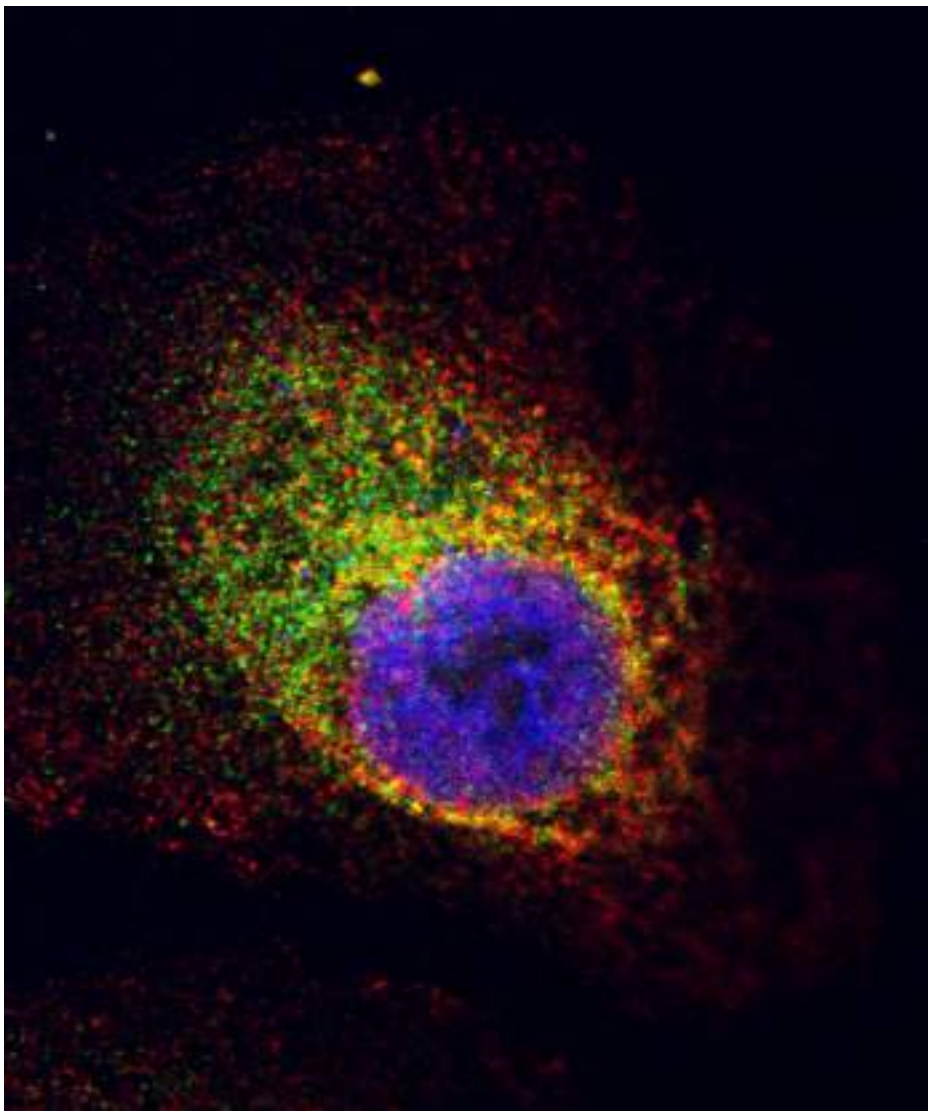




United Nations
Educational, Scientific and
Cultural Organization

क्षेत्रीय जैव प्रौद्योगिकी केन्द्र
Regional Centre
for Biotechnology



ANNUAL REPORT

2021-2022

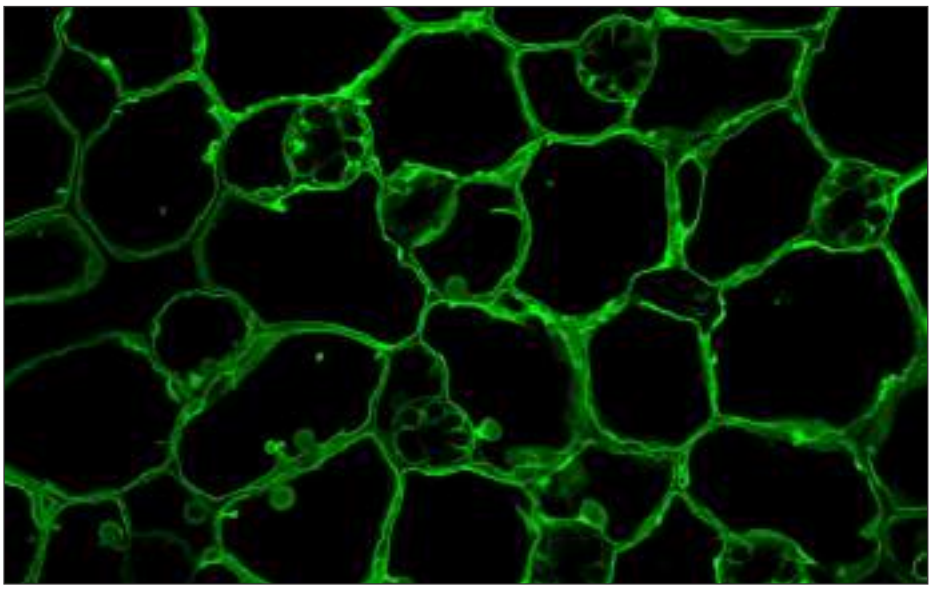


Photo Credit: Shivam Agarwal

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 three key Regional Centre for Biotechnology (RCB) has continued its journey towards achieving its mission and mandate of imparting education and training, and conducting research in the broad area of biotech sciences, and significant progress has been made in these key areas. RCB continues to be a category-2 institution of UNESCO, the linkage providing an international reach to our various programs. A detailed account of each of the RCB activities is provided in different sections of this annual report with a summary in the following paragraphs.

RCB academic programs provide the students an opportunity to work closely with researchers in our laboratories housing the most modern equipment and technologies. Research-based learning is the hallmark of the RCB's education and training programs that include structured degree programs as well as short-term training programs in highly specialized areas of biotechnology and life science research. RCB offers doctoral degree programs in Biotechnology, Bioinformatics, and Biostatistics, and over 100 students were working in the RCB laboratories towards their PhD degrees during the reporting period. The integrated MS-PhD program has now matured and attracts high-quality students from different parts of the country. In the reporting period, 04 students graduated with a Master's degree and 03 students chose to continue with their doctoral research program. The RCB Act 2016 also 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 ESIC Medical College & Hospital, Faridabad and Institute of Bioresources and Sustainable Development (IBSD), Imphal thus bringing the total number of the recognized centers to twelve. A total of 72 students from these recognized centers were registered for their Master's degree and 286 for the PhD degree with RCB.

RCB offers short-term innovative training programs for young scientists to fulfill its mandate on human resource development in the advanced areas of life sciences and biotech sciences. In this direction, UNESCO-sponsored training workshops were conducted in areas of Mass Spectroscopy, Electron Microscopy and Confocal Microscopy introducing to the participants the latest methodology and instrumentation in these important areas of modern bioscience research. Participants for these training workshops included research scholars, doctoral students, and postdoctoral fellows selected from various institutions across India and overseas countries like UAE, Srilanka, Nepal, Ghana, Nigeria, Mauritius and China. 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: 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. Provided below are some of the research highlights of this year.

Pancreatic cancer (PC) is one of the most lethal forms of cancer with a 5-year mean survival rate of less than 10% wherein most of the deaths are associated with secondary metastasis. Studies in Dr. Rajender Motiani's lab have shown that Orai3 expression is inversely associated with the mean survival time of PC patients. The in vitro functional assays showed that Orai3 regulated PC cell cycle progression, apoptosis, and migration. Most importantly, our in vivo xenograft studies

demonstrated a critical role of Orai3 in PC tumor growth and secondary metastasis. Mechanistically, Orai3 was shown to control G_1 phase progression, matrix metalloproteinase expression, and epithelial-mesenchymal transition in PC cells. Taken together, this study for the first-time reports that Orai3 drives aggressive phenotypes of PC cells, i.e., migration in vitro and metastasis in vivo. Considering that Orai3 overexpression leads to poor prognosis in PC patients, it appears to be a highly attractive therapeutic target.

The high toxicity of most cancer drugs remains a major challenge. Dr. Avinash Bajaj's lab engineered a supramolecular nanomicellar system (LCA-DTX-PEG) composed of self-assembled units of the PEGylated lithocholic acid (LCA)-docetaxel (DTX) conjugate, which were safer in comparison with their parent FDA-approved drug formulation (Taxotere® or DTX-TS). The LCA-DTX-PEG nanomicells effectively reduced the tumor volume and increased the survival of 4T1 tumor-bearing mice with improved blood circulation time of the drug and its higher accumulation in tumor tissues. This study highlights the potential of PEGylated bile acid-drug conjugate-based nanomicells for the development of next-generation cancer therapeutics.

Flagella-mediated motility is critical to chemotaxis, biofilm formation, colonization, and virulence in bacteria. Dr. Deepti Jain's group determined the high-resolution crystal structure of the AAA+ domain of FleQ, a transcription activator that regulates flagella and biofilm formation in *Pseudomonas aeruginosa*. The structure of FleQ was determined in complex with its anti-activator FleN which demonstrated a novel allosteric mechanism employed by the anti-activator to regulate flagellar gene expression. Disruption of the conserved protein-protein interface, by mutation, showed motility and transcription defects in bacteria. The study has implications for the design of anti-biofilm strategies against *P. aeruginosa.*

Microglial cells, the resident macrophages in the brain, play a vital role in Japanese encephalitis virus (JEV) pathogenesis. The deregulated activity of microglia can be lethal for the brain. Therefore, it is important to understand the regulators that drive microglia phenotype changes and induce inflammation in the brain. Interferon regulatory factor 8 (IRF8) is a myeloid lineage transcription factor involved in microglial activation. Dr. Arup Banerjee's group demonstrated that lack of IRF8 affected immune cell abundance in the brains of infected mice, restricted IFN-gamma response, and augmented JEV replication.

Xanthomonas Oryzae pv. oryzae (Xoo) causes bacterial blight and *Rhizoctonia solani (R. solani)* causes sheath blight in rice accounting for >75% of crop losses. In a collaborative effort with Dr. Avinsah Bajaj, Dr. Ramu Vemanna's group developed Cholic Acid-Glycine Conjugates (CAGCs) and showed CAGC C6 to be a broad-spectrum antimicrobial able to degrade biofilms. Exogenous application of C6 on pre-infection or post-infection of Xoo on rice susceptible genotype *Taichung native (TN1)* could mitigate the bacterial load and improve resistance through the upregulation of plant defense genes. CAGC C6 induced plant defense responses when seeds were primed with it. This study, thus, demonstrates the potential of CAGCs as effective antimicrobials for crop protection that may be explored for field applications.

RCB continues 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 few drug-like molecules showing antiviral activity against the Chikungunya virus in the cell culture. Their antiviral activity is being further studied in the mouse model of virus infection.

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-two 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, Govt. of India. Details of these activities are provided in the Research & Innovation Infrastructure section of the report.

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, and I look forward to their continued support in further advancing the RCB programs.

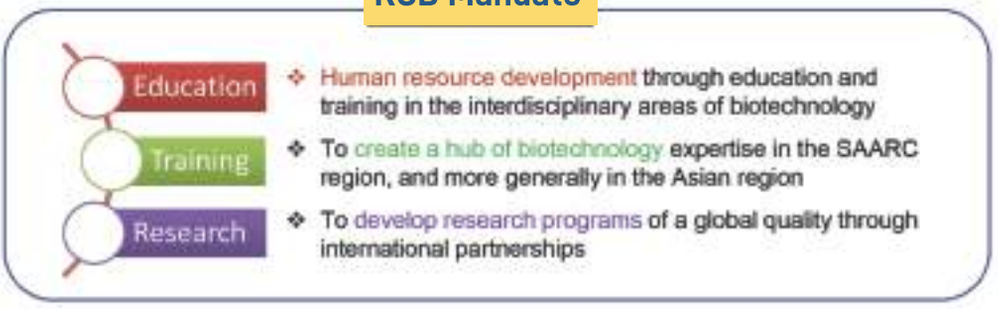
Jai Hind !

Sudhanshu Vrati

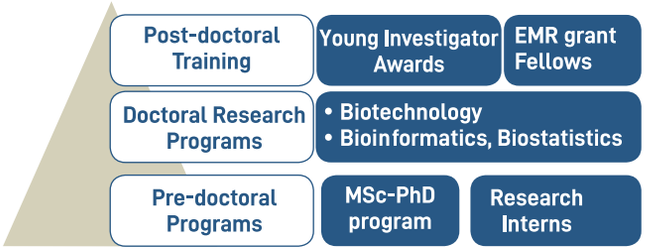
Executive Director

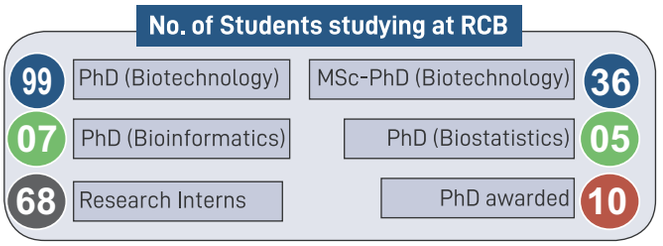
EXECUTIVE SUMMARY

RCB Mandate

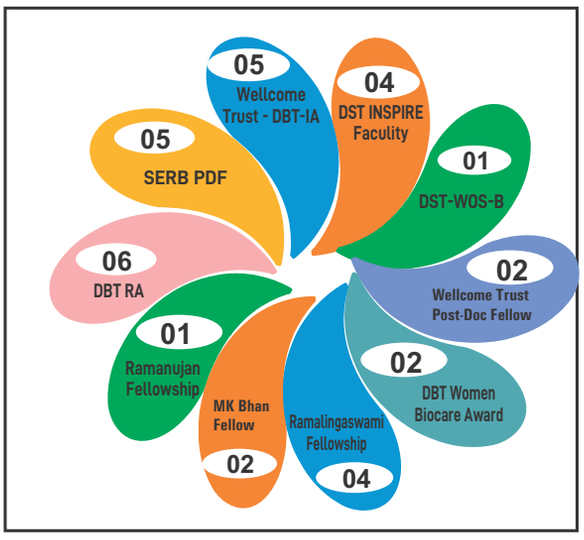


Academic and Training Activities

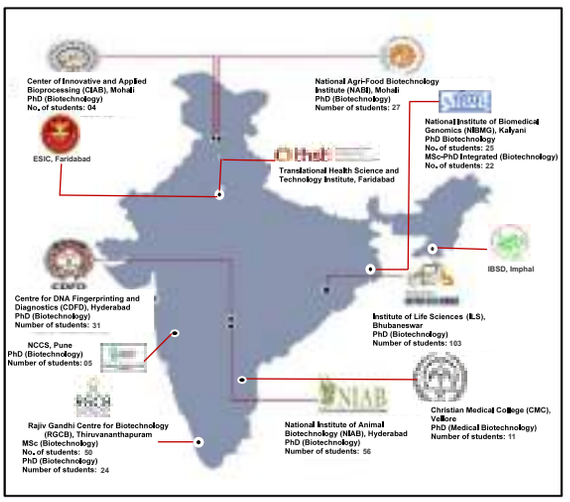




Awards and Fellowships



RCB Recognized Centres

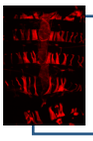


Total number of students registered at RCB: 358

Date	Event Organized
1-15 May, 2021	Swachhata Pakhwada
1-14 September, 2021	Hindi Pakhwada
5-6 October, 2021	Cloud-based Hands-on Workshop: Computational Structure-based Screening and Explicity Molecular Dynamics
12-13 October, 2021	UNESCO sponsored Online Workshop on 'Mass Spectroscopy Based Proteomics'
20 October, 2021	UNESCO sponsored Online Workshop on 'Basics of Electron Microscopy'
22 October, 2021	UNESCO sponsored Online Workshop on 'Confocal microscope-based drug screening (High Content Imaging)'
10 December, 2021	Vigyan Pradarshini
28 February, 2022	National Science Day
1 March, 2022	RCB Foundation Day

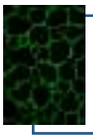
Research Areas


Structural Biology


Molecular Medicine


Infectious Disease Biology


Cancer & Cell Biology


Agricultural Biotechnology


Systems & Synthetic Biology

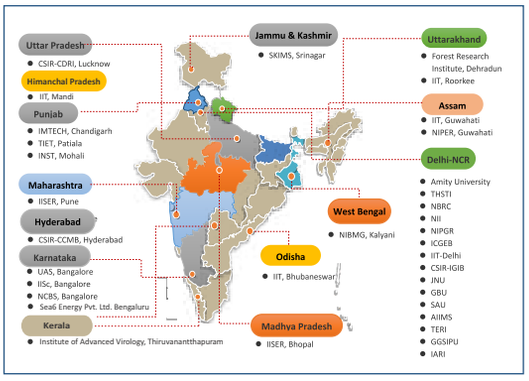
Publications : 105
Patent Filed : 03

Research Highlights

- The candidate genes which can provide resistance against bacterial leaf blight causing Xanthomonas oryzae pv. oryzae have been identified from contrasting genotypes comparative transcriptome analysis.
- Cholic acid-glycine conjugates can protect rice from bacterial leaf blight disease by disrupting the microbial membranes and activating plant defence genes, which can be used as agrochemicals by seed priming or by foliar application.
- A simple screening method for rice to identify the small chemical molecules which can enhance oxidative stress tolerance has been developed; molecules which inhibit DREB2A transcription factor activity have been identified.
- Optimization of dose and treatment regimen of two commercial seaweed extracts was shown to enhance salicylic acid-driven antibacterial resistance in arabidopsis and rice.
- Identified the roles of selective inositol polyphosphates as negative regulators of basal anti-bacterial defenses and balancing phosphate homeostasis in plants.
- Demonstrated that a class of rapidly evolving bacterial effector interfere with nonsense mediated decay (NMD) processes that regulate defense gene expression during plant immunity.
- Elucidated contrasting functions of diverse Arabidopsis SUMO isoforms in maintenance of host SUMOylome and its adjustment during plant defenses.
- The anti-fungal role of the phytoalexin medicarpin was elucidated, providing new insights into the metabolic and signaling pathways required for powdery mildew resistance in legumes.
- A comprehensive analysis of cellular proteome changes induced by Japanese encephalitis virus was performed, and it gave novel insights into infection induced activation of innate immune responses and downregulation of sterol and lipid metabolic pathways.
- TLE4 as a regulator of muscle stem cell function has been identified. TLE4 is expressed in dormant muscle stem cells and its transient downregulation is required for differentiation of stem cells during regeneration.
- Pilus subunits from gut autochthonous (indigenous) commensal *Ligilactobacillus ruminis* have been recombinantly produced, crystallized, and analyzed by X-ray diffraction to provide structural insights into the assembly, anchoring, and functional mechanisms of sortase-dependent LrpCBA pili.
- A non-immunogenic topical hydrogel that can maintain sustained delivery of steroids, and can mitigate the psoriasis in murine model has been engineered.
- A fluorescent based molecular probe that can specifically detect the mycobacteria, and is able to differentiate between gastrointestinal tuberculosis and Crohn's disease patients has been engineered.
- Cholic acid based topical hydrogel can deliver the antibiotics, and mitigate the wound infections more effectively than clinically approved formulation.

Intra-institutional collaborations

National Collaborations



International Collaborations

Infrastructure and Support Services

Advanced Technology Platform Centre

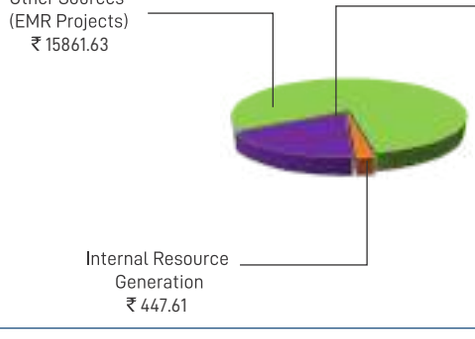
Biosafety Support Unit

BSC BioNEST BioIncubator

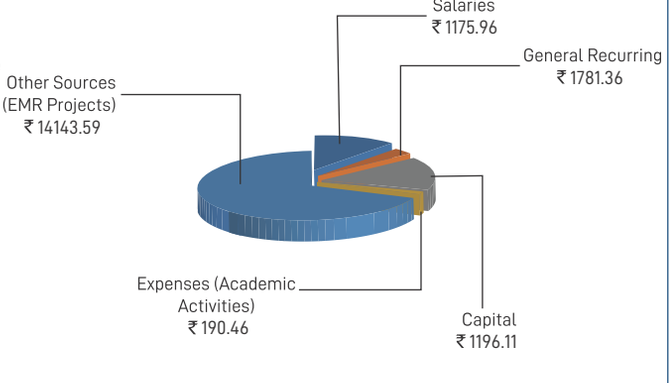
IBDC & DBT HRD-PMU

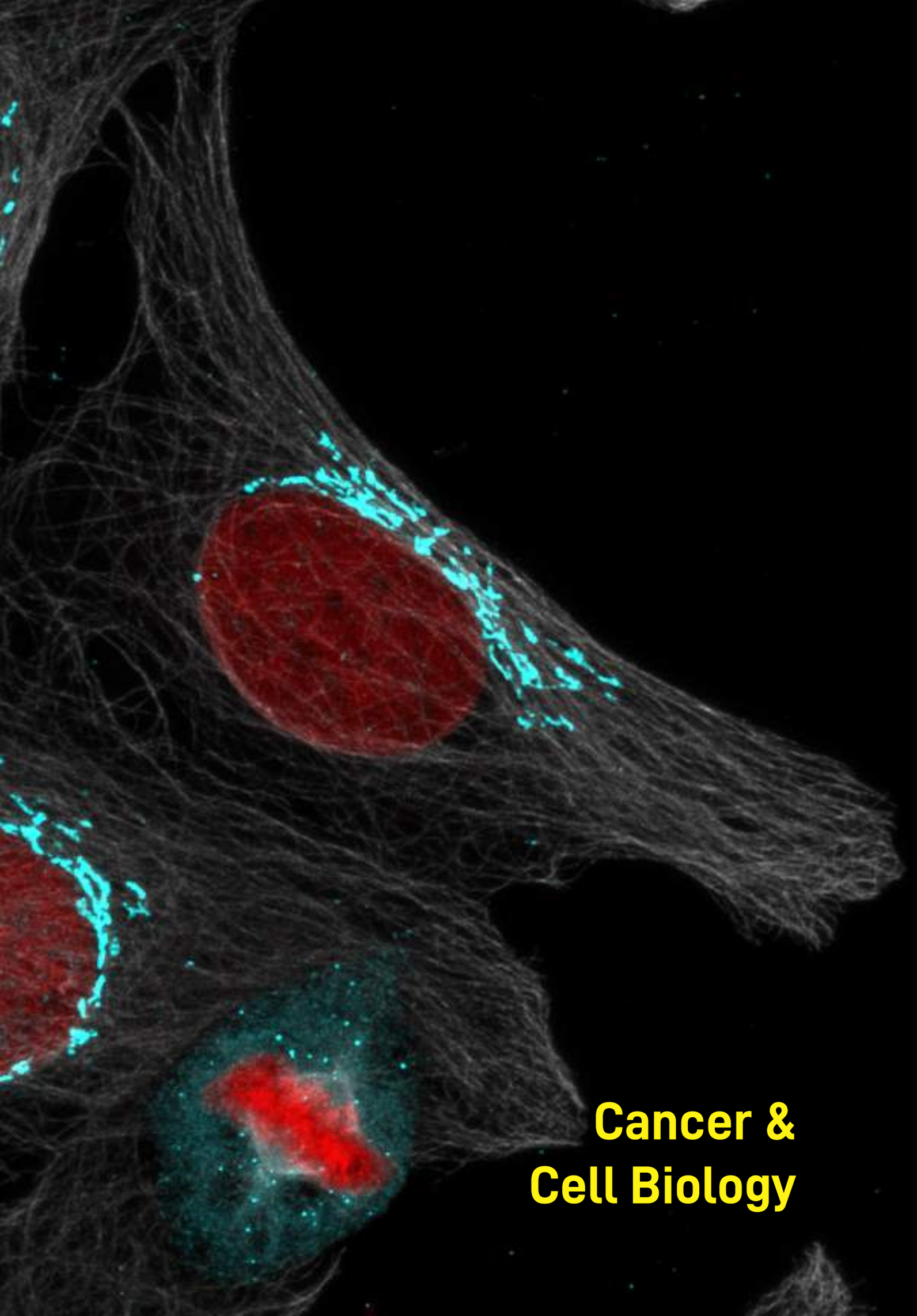
Financial Figures

Total Income (Rs. In lakhs) 2021-2022



Total Expenses (Rs. In lakhs) 2021-2022





Cancer & Cell Biology

Avinash Bajaj
Principal Investigator

Lab Members

Ruchira Chakraborty
Animesh Kar
Priyanka Verma
Poonam Yadav
Kajal Rana
Dolly Jain
Varsha Saini
Somesh K Jha
Nishant Pandey
Bharti Agarwal
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 synthesized four molecular probes (P1-P4) where C24 carboxyl terminal of CA was conjugated with a fluorophore and three charged head groups were appended to three hydroxyl terminals of CA (Fig. 30A). The probes were tested using *Mycobacterium bovis* (*M. bovis*) as a model mycobacterium where 10^5 CFU/mL of bacteria were incubated with different concentrations of probes P1-P4 for 10 min. Flow cytometry analysis revealed that P4 probe was able to stain >95% of mycobacteria at 0.5-10 µM. We observed >80% staining of mycobacteria with only 0.2 µM of the probe (Fig. 30B). In contrast, probes P1, P2 and P3 could not stain the mycobacteria at any of the tested concentrations. With these results, we identified P4 as the most suitable probe and tested its ability to stain gram-negative, gram-positive and other mycobacterial species using flow cytometry and microscopy. The flow cytometry data suggested that P4 has a very poor affinity for all the tested gram-positive and gram-negative bacteria as it could stain only < 5% of gram-positive and gram-negative bacteria, while > 95% of mycobacteria species (*M. smegmatis*, *M. bovis* or *M. tuberculosis*) can be easily stained by P4. These results confirm the specificity of P4 for mycobacterial species. Fig. 30C shows the confocal micrographs of *M. bovis*, *M. smegmatis*, *M. tuberculosis*, *E. coli, S. typhimurium* and *S. aureus* after labelling with P4 (10 nM). We observed that P4 was able to stain only the mycobacteria species and none of the other bacteria gets labelled with P4, thereby confirming the flow cytometry results. Next, we ascertained the specificity and sensitivity of P4 probe in detecting mycobacteria in mixed populations like mixture of *M. smegmatis* and *E. coli* or mixture of *M. smegmatis* and *S. aureus* in different ratios. On staining the polymicrobial cultures, we observed that P4 can stain the mycobacteria with high specificity even when mixed in a ratio of 1:10000 (*M. smegmatis : E. coli*). P4 didn't stain closely existing gram-negative bacteria and a similar selectively was witnessed with the polymicrobial cultures of *M. smegmatis* and *S. aureus*.

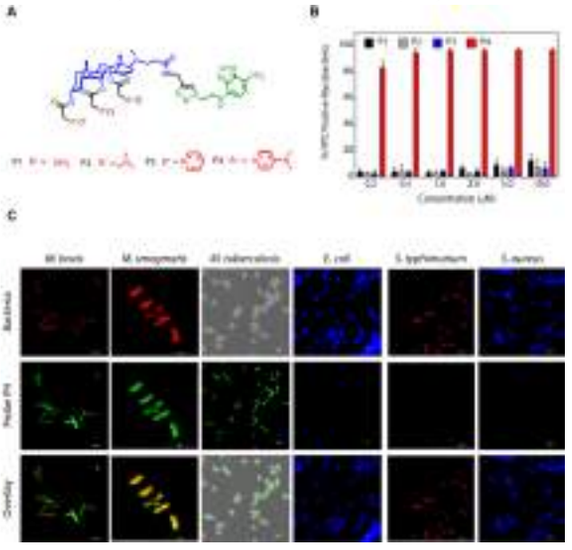


Figure 30. *A) Molecular structures of the probes P1-P4 where NBD fluorophore was conjugated at C24-carboxyl terminal of cholic acid and different charged groups were attached to hydroxyl groups. B) Percentage of FITC-positive mycobacterial cells after staining of M. bovis with different concentrations of probes P1-P4 confirm the ability of P4 to stain the mycobacteria. C) Confocal micrographs of different bacterial species after staining with P4 confirm the selectivity of the P4 for mycobacterial strains.*

To test the efficacy of P4 probe to permeate the mammalian cells and detect the intracellular mycobacteria, we infected RAW macrophages with mCherry expressing *M. smegmatis* and stained the infected cells with P4. CLSM images showed a clear colocalization of probe's fluorescence (FITC) with mCherry expressing *M. smegmatis*. Next, we infected macrophages simultaneously using with pCypet expressing *E. coli* and mCherry expressing *M. smegmatis* and stained the infected cells with P4. P4 showed colocalization with only mycobacteria confirming its selective binding to intracellular mycobacteria and P4 does not bind with *E. coli*. The same specificity of detection was also witnessed in case of coinfection by *M. smegmatis* and *S. aureus*.

To explore the selectivity of P4 in labelling the mycobacteria in polymicrobial biofilms, we first tested the ability of P4 to stain the mycobacterial biofilms. Biofilms of mCherry-*M. smegmatis*, pCypet-*E. coli* and pCypet-*S. aureus* were prepared and stained with P4. It was observed that P4 could stain only mycobacterial biofilms in spite of their dense extracellular matrix. Biofilms formed by pCypet-*E. coli* and pCypet-*S. aureus* remain unstained. We then tested the efficacy of P4 in detection and differentiation of mycobacteria in polymicrobial biofilms where we prepared polymicrobial biofilms from combination of mCherry-*M. smegmatis* and pCypet-*E. coli* and from combination of mCherry-*M. smegmatis* and pCypet-*S. aureus*. These two different sets of biofilms were then stained with P4. Imaging data confirmed that fluorescence of P4 is colocalized only with mCherry fluorescence of *M. smegmatis* and P4 was unable to stain other bacteria in the polymicrobial biofilms, thereby confirming the selective staining of mycobacteria even in dense polymicrobial biofilms.

To assess the ability of P4 to detect the mycobacteria in human tissues, we probed human tissue sections with P4. Suspected mycobacteria infected tissue sections were obtained from All India Institute of Medical Sciences, New Delhi after due human ethical clearance. These sections were stained with P4 and mycobacteria specific antibody followed by TRITC-labelled secondary antibody. We observed clear co-localization of green fluorescence of P4 with red fluorescence of antibody in tissues of colon, gall bladder, lymph node and bone tissues (Fig. 31). We also tested the probe in tissue sections obtained from patients suffering from Crohn's disease and P4 was unable to find any mycobacteria in those tissues. These results confirm the ability of probe P4 to detect mycobacteria in complex gastrointestinal tissues and its ability to differentiate between gastrointestinal tuberculosis and Crohn's disease.

In summary, cholic acid-derived amphiphile having dimethylamino pyridine head group showed selective binding with mycobacteria and can detect mycobacteria in gastrointestinal tissues.

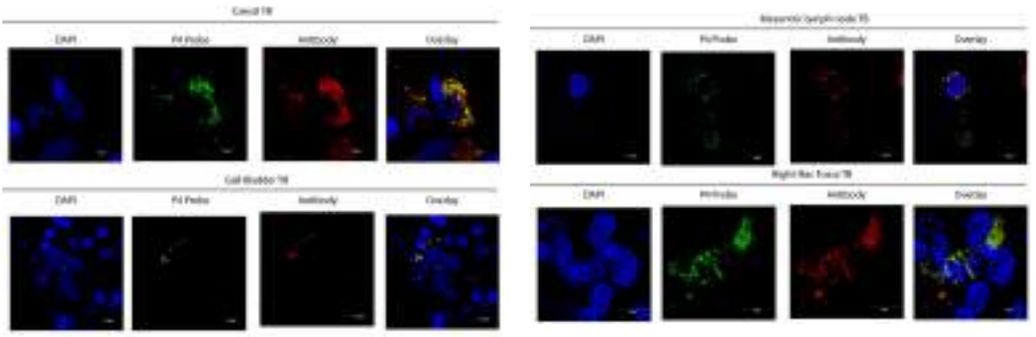


Figure 31. Confocal micrographs of tissue sections obtained from different TB patients after staining with P4 probe and anti-mycobacteria antibody (Ab905) followed by secondary antibody. *Nuclei were stained by Hoechst 33258. Colocalization of two fluorescent signals confirm the presence of mycobacteria.*

Sivaram V S Mylavarapu
Principal Investigator

Lab Members

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Diksha Pathak
Neeraj Wasnik
Harsh Oza
Mahendra Singh
Mahima Singhal
Anushka Das

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 cell division and intercellular communication through multi-disciplinary approaches. Knowledge gained from these studies could be exploited towards strategies for the amelioration of disease conditions.

Mitotic phosphorylation and Pin1 binding to the LIC1 subunit selectively regulate dynein functions

The microtubule cytoskeleton supports both positive-end directed transport through kinesin motors, and negative end-directed transport primarily through the dynein motor. Vertebrate cells contain mainly one dynein, but nearly fifty kinds of kinesins. Dynein's remarkable cargo-binding diversity is therefore essential for its multiple essential functions during interphase and mitosis. Dynein's light intermediate chain subunits (LICs) are pivotal for directly engaging diverse cargo adaptors, of which spindly and Hook2 function exclusively during mitosis. Dynein's dramatic interphase-to-mitosis cargo-switching is strongly correlated with cdk1-cyclinB-mediated LIC phosphorylation at conserved cdk1-cyclin B phosphorylation sites, S389, S405 and T408 in the LIC1-CTD exclusively during mitosis. Importantly, these three clustered LIC1-CTD sites lie upstream of helix-1 (H1, residues 440-455), which binds directly to various cargo-binding adaptor NTDs. Conformational regulation of phosphorylated proteins can be achieved through the peptidyl prolyl isomerase Pin1, which binds to phosphorylated Ser/Thr residues in "Ser-Pro/Thr-Pro (SP/TP)" sites and isomerizes the adjacent proline, thereby regulating a wide variety of cellular functions. While the LIC1-CTD cdk1 phosphosites present potential targets for Pin1 binding and regulation, no dynein subunit had been reported to be a Pin1 substrate.

Conserved LIC1-CTD phosphorylation is required for normal mitotic progression and recruits Pin1 to mitotic dynein

We first confirmed the mitotic phosphorylation of hLIC1. We cloned the single, double and triple combinatorial hLIC1-MTAP phospho-deficient CTD mutants (S398A, S405A and T408A), and generated stably expressing U2OS cell lines. Both the SST (wild type) and AAA (triple mutant) LIC1 proteins could efficiently integrate into the dynein complex. We simultaneously achieved efficient endogenous hLIC1 depletion and exogenous LIC1-MTAP expression for rescue experiments in stable cell lines. SST and the single site mutants could efficiently rescue hLIC1 depletion-induced delays in anaphase onset; however, the double mutants showed compromised function, and AAA was the least capable (Fig. 32). Mitotic index measurements confirmed the requirement of the LIC1-CTD phosphosites for timely mitotic progression.

Immobilized glutathione-S-transferase tagged Pin1 (GST-Pin1) was able to pull down LIC1 and HC from mitotic, but not interphase lysates, suggesting a mitotic dynein-Pin1

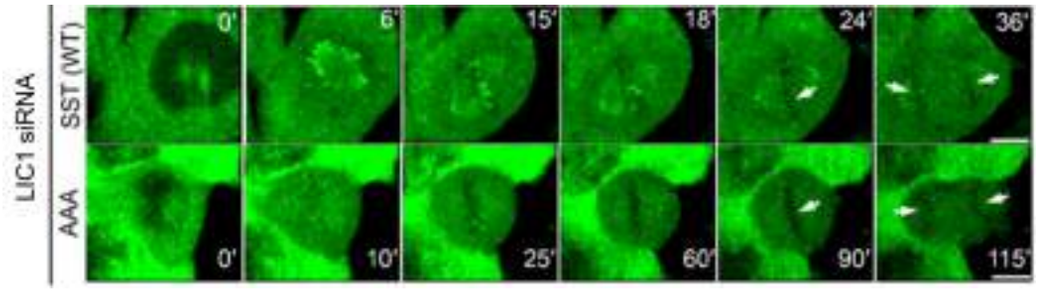

Figure 32: *Stills from representative time-lapse videos of U2OS cells [mock, LIC1 KD (knockdown) – DIC] or the respective U2OS stable cell lines (green = YFP fluorescence from the MTAP tag) as indicated, from cell rounding (mitotic entry) to anaphase onset. Time-stamps (min) included, arrows depict chromosomes.*

interaction. We observed that only cdk1-cyclin B phosphorylated hLIC1 and rLIC1 could bind directly to GST-Pin1, specifically through the LIC1-CTD. Further experiments revealed that no single LIC1-CTD phosphorylation was sufficient for Pin1 binding, but abrogating phosphorylation altogether completely abolished the Pin1 interaction.

Pin1 preferentially binds to and regulates selective mitotic dynein complexes

LIC1-CTD is required for engaging directly with activating adaptors of dynein. GST-Pin1 (bait) was able to robustly pull down dynein subunits from mitotic lysates but surprisingly, not the spindly-dynactin-dynein mitotic kinetochore complex, suggesting that the spindly-occupied fraction of dynein is unlikely to be regulated by Pin1. Literature surveys revealed that dynactin-free dynein can contain the cofactors Nde1 and Lis1, and mediates high load-bearing functions. Indeed, we found that mitotic Nde1 and Lis1 bound to GST-Pin1, as did CENPF, and the mitotic dynein adaptor Hook2, which interacts with the late G2/prophase Nde1-Lis1-CENPF-dynein complex (Fig. 33A, B). Thus, Pin1 binds preferentially to Hook2-bound dynein, but not to spindly-bound dynein in mitosis. Pin1's binding to LIC1, IC and Hook2 was drastically reduced upon making the phospho-deficient AAA mutation (Fig. 33B-D), suggesting compromised Pin1 binding with the whole dynein complex. We observed clear localization of both Pin1 and SST/AAA LIC1 at G2/prophase centrosomes and metaphase spindles, but no substantial Pin1 localization at prometaphase kinetochores (Fig. 33E). Overall, these results highlighted Pin1's ability to differentiate between dynein complexes containing distinct mitotic adaptors.

Functional experiments revealed that abrogating LIC1-CTD phosphorylation disengages Pin1 from dynein and causes prophase centrosome-nuclear envelope (NE) detachment and chromosome miscongression, suggesting compromised Nde1-Lis1-Hook2-dynein function. Interestingly, we observed that phosphorylation of a corresponding conserved SP site in zebrafish LIC1-CTD is essential for normal embryonic development. Our work reveals that LIC1-CTD phosphorylation differentially regulates distinct mitotic dynein pools, and suggests the evolutionary conservation of this phospho-regulation.

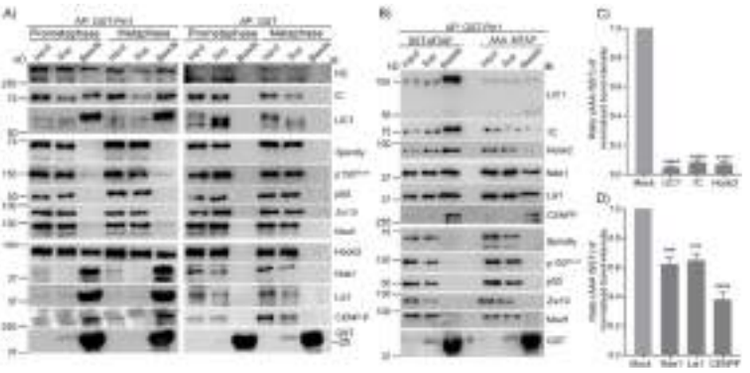

Figure 33: *A, B) Immunoblots showing affinity precipitates of GST-Pin1/GST from prometaphase and metaphase HeLa cell lysates (A) and GST-Pin1 from SST-MTAP and AAA-MTAP prometaphase U2OS stable cell lysates (B), probed for the indicated antigens. C, D) Ratios (AAA-MTAP/SST-MTAP) of eluate (beads) fraction band intensities for each indicated antigen over 3 independent AP experiments.*

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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+} dynamics and functional relevance of intracellular Ca^{2+} handling proteins remains unappreciated. Our preliminary data suggest that indeed organellar Ca^{2+} signaling plays an important role in regulating pigmentation. Another projects under the ambit of this program is focused on understanding the role of inter-organellar crosstalk especially ER-Mitochondrial and Mitochondrial-Melanosome communication in regulating pigmentation.

This year, we report role of Mitofusin-2 (MFN2), one of the key regulator of inter-organellar communication in pigmentation. MFN2 mediates Mitochondrial-Melanosome crosstalk. However, role of MFN2 in melanogenesis remains poorly understood. Using B16 cell line and primary human melanocytes, we demonstrated that MFN2 negatively regulates melanogenesis. Both transient and stable knockdown of MFN2 resulted in enhanced melanogenesis, which is associated with increased melanosome maturation and augmented expression of key melanogenic enzymes. Further, ectopic expression of MFN2 in MFN2 silenced cells led to complete rescue of the phenotype at cellular as well as molecular levels. Mechanistically, MFN2 silencing elevated mitochondrial reactive oxygen species (ROS) levels and that in turn increases melanogenesis. ROS quenching with antioxidant N-acetyl cysteine (NAC) reversed MFN2 knockdown mediated increase in melanogenesis. Importantly, MFN2 expression is significantly lower in the darkly pigmented primary human melanocytes in comparison to lightly pigmented melanocytes highlighting a potential contribution of lower MFN2 levels to higher physiological pigmentation. Taken

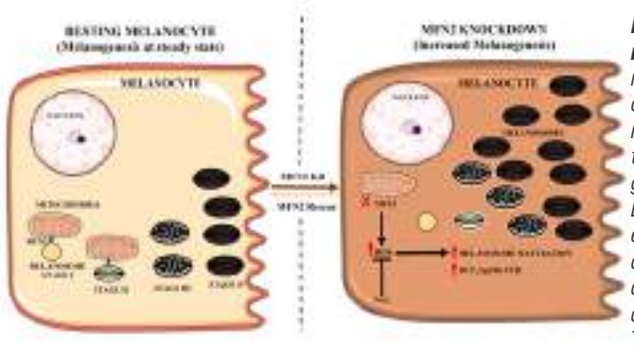

Figure 34: MFN2 negatively regulates melanogenesis. *MFN2 plays a critical role in mitochondria-melanosome crosstalk and in maintaining melanocyte redox homeostasis. MFN2 silencing leads to increase in mitochondrial ROS generation and melanosome maturation. Both molecular rescue of MFN2 expression or quenching of ROS via anti-oxidant NAC reverts the phenotype associated with MFN2 silencing. Figure adopted from our recent publication Tanwar et al., Cells Feb. 2022.*

together, our work established MFN2 as a novel negative regulator of melanogenesis (Fig. 34).

Targeting calcium signaling for curtailing tumor growth and metastasis

Pancreatic Cancer (PC) is one of the deadliest cancers that causes around 40 lakh deaths annually and has mean survival time of less than 5 years. Most of the PC deaths are associated with secondary metastasis. For developing effective treatment strategies, it is necessary to understand the molecular mechanisms that drive PC progression and metastasis. 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 such as immune cells, endothelial cells, airway and vascular smooth muscle cells. 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).

Notably, we recently reported a critical role of Orai3 in PC progression and metastasis (Fig 35). We performed extensive bioinformatic analysis of publicly available datasets and observed that high Orai3 expression is associated with poor prognosis. We then carried out detailed Ca^{2+} imaging experiments in several PC cell lines and noticed that Orai3 forms a functional SOCE channel in PC cells. Our *in vitro* functional assays show that Orai3 regulates PC cell cycle progression, apoptosis and migration. Importantly, our *in vivo* xenograft studies demonstrate a crucial role of Orai3 in PC tumor growth and secondary metastasis. Mechanistically, we observed that Orai3 controls G1 phase progression, matrix metalloproteinase expression and epithelial-mesenchymal transition in PC cells. Taken together, our study for the first time reported that Orai3 drives aggressive phenotypes of PC cells i.e. migration *in vitro* and metastasis *in vivo*. Considering that Orai3 overexpression leads to poor prognosis in PC patients, it appears to be a highly attractive therapeutic target. Taken together, we have identified and characterized a novel therapeutically relevant regulator of PC progression.

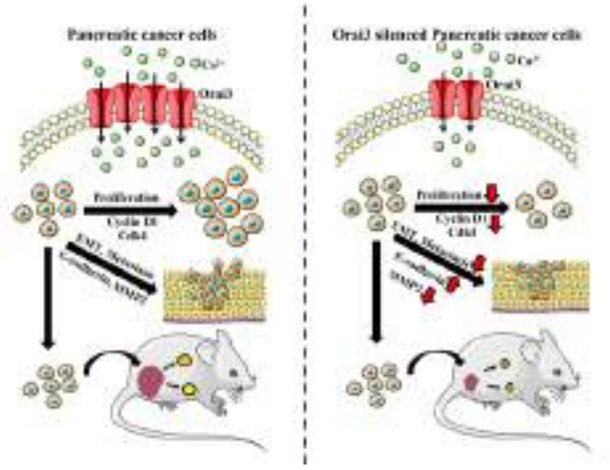

Figure 35: Orai3 is upregulated in pancreatic cancers and regulates metastasis. *In pancreatic cancer cells, Orai3 is overexpressed and that leads to its functional activation i.e. higher Orai3 mediated Ca^{2+} entry. Orai3 silencing in pancreatic cancer cells results in decreased Ca^{2+} influx, cell cycle arrest and reduced migration in vitro. Further, in vivo mice studies demonstrated that Orai3 regulates PC progression and metastasis. Figure adopted from our recently published study Arora et al., Cancers Nov. 2021.*

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Understanding the Structure and Function of Centriole Based Organelles

Centrosomes are one of the oldest membrane less organelle discovered more than a century earlier. The major role being microtubule nucleation, often appreciated as spindle fibres in dividing cells and as ciliary axoneme in the post-mitotic cells. Basically this allows them to function as a microtubule organising centre in most of the animal cell types with few exceptions. Centrosome biology over the years have revealed a lot about their duplication, segregation, maturation and their functioning in process like mitosis and organelle trafficking. Beyond this we have also seen a lot more signalling events involving centrosomes both in the physiological and pathological context. Our lab is majorly focused towards the centrosome and ciliary functional aspects regulating these signalling events revolving around centriole based structures like centrosome, centriolar satellites and ciliary basal bodies. Currently we study the proteomic composition of these organelle in a define setting of DNA damage response (DDR). The focus of our team is as follows.

Centrosome and cilia during DNA damage response

DNA damage is well documented event at the cellular and molecular level. A substantial number of factors and their mechanism of sensing the damage or aiding in its repair process are well known. We also understand that a perturbation of this DDR could lead to several pathological consequences like Cancer, Xeroderma Pigmentosum, Ataxia-Telangiectasia, Bloom's and Werner's syndromes, Li-Fraumeni-syndrome and many other disorders. The basic functional consequence of any DNA damage is a direct derangement of the involved organism's genomic integrity. It this is not sensed and corrected within the appropriate spatiotemporal window then the damage turns on the checkpoint system to put the cells either into a halted or arrested state or further direct them towards senescence and cell death in worst case. It is known that centrosomes also react to DNA damage and as a consequence it invokes the cellular checkpoint factors to tame the damaged and to establish normalcy by either repairing the dysfunction or by totally eliminating these damaged cells. This may happen immediately or in the subsequent rounds of cell division based on the checkpoint activity. It is well appreciated in terms of the events related to such checkpoint activation yet the early response evinced upstream of these checkpoints are not well established. Our team is now attempting to understand the centriolar and DNA damage related factors participating and communicating certain signals between damage sensing, repair, rescue and elimination related events (Fig. 36).

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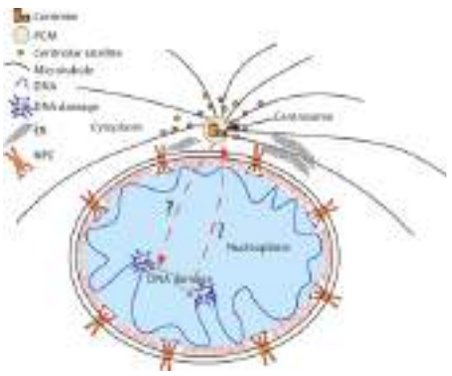


Figure 36: *Cartoon representing signal integration between centrosome and DNA damage associated machinery in the nucleus.*

To identify the centriolar signal integration during the DNA damage response we are currently inducing these damages using two major approaches. One is by means of small molecule drugs and the other is by means of a CRISPR/Cas9 tool that is capable of inducing the specified DNA break in a given cell. On the other hand, we are trying to unambiguously interrogate the centriolar components by purifying these organelles from the cytoplasmic fraction past damage and analyse their composition using LC/MS based proteomic profiling. So far we have successfully standardized these methods to purify centrosome and some of the damage induction procedures using bleomycin. At present we are trying to develop the tool for inducing CRISPR/Cas9 based double and single stranded DNA breaks (Fig. 37). Right now we are trying to induce a regulated amount of DNA damage that is close to the physiological and pathological doses and subsequently assess the involvement of centrosomes under both these instances of single and double stranded breaks. Based on

the outcome of the proteomic profiles we would next look into the putative sensor and transducers originating in and around the centriolar structures that could possibly communicate between the nucleus and cytoplasmic DNA damage response / repair events.

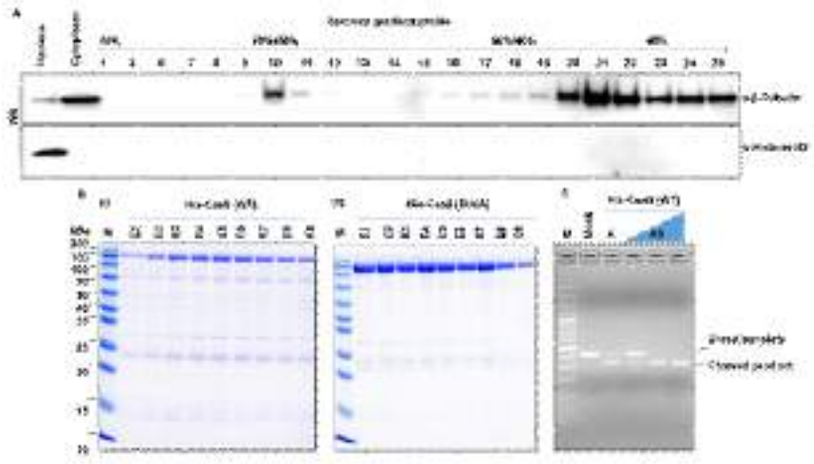
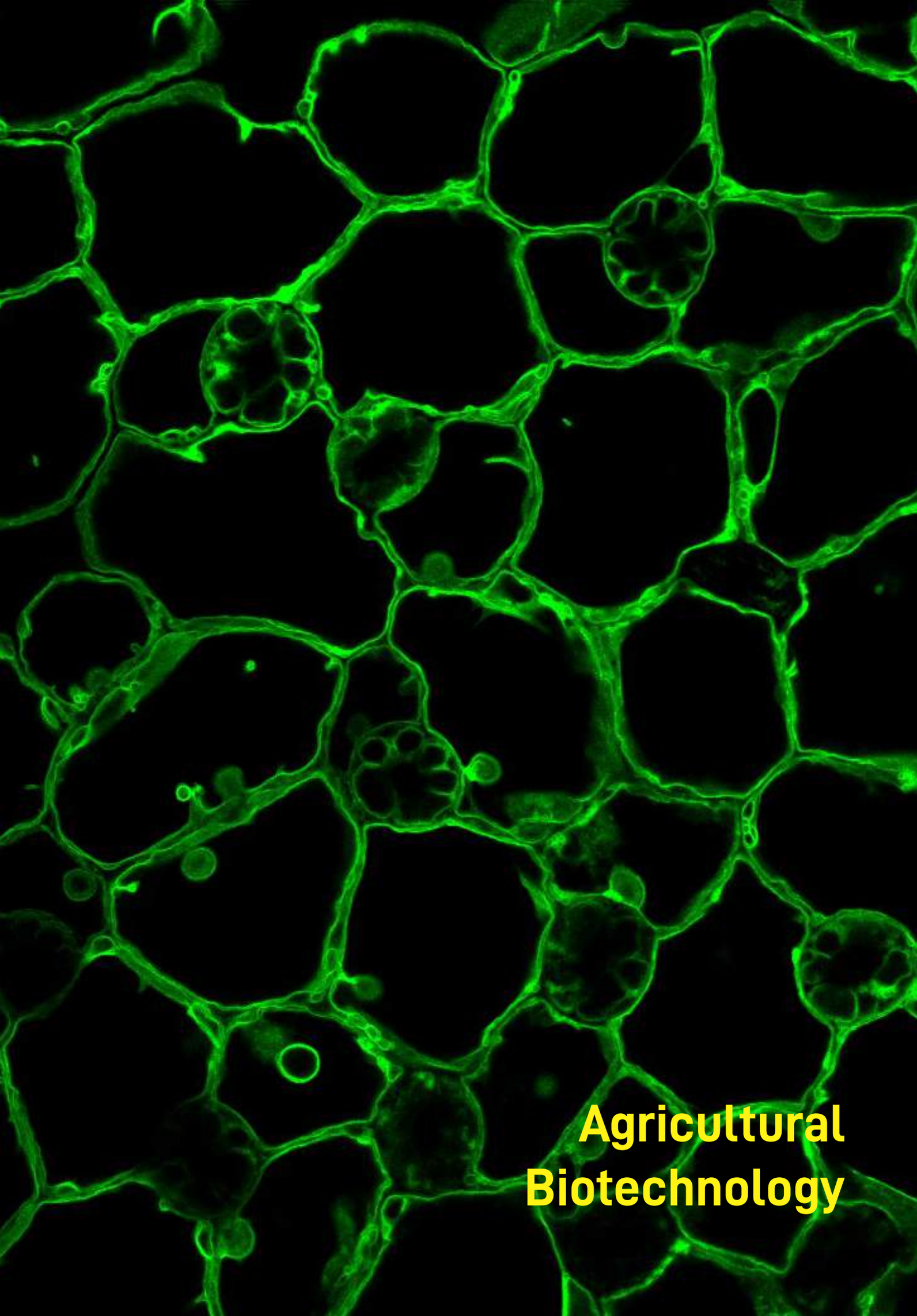


Figure 37: Top: Centrosome enrichment profile (A). *Western-blot analysis using -Tubulin antibody to demarcate the fraction enriched for centrosomes and Histone H3 antibody to show the purity of the nucleus and cytoplasmic fractionation. Bottom: Purification and activity profile of Cas9 protein (B) CCB staining of affinity purified His-Cas9 wild type (I) and nickase (II) endonucleases (M: marker; E1 to E9 represent the eluate fractions). (C) In vitro cleavage activity of Cas9 (WT) protein purified by one step (A-affinity) and two step purification (AS- affinity followed by size exclusion) using a ~450 bp template.*

Presently we know the composition of centrosomes under most common circumstances and the list seems to be growing with more tools being invented are readily available to investigate them today. We also do not understand the extent to which this DDR is dependent on the centrosomal machinery and if so is this organelle being involved directly or indirectly. To address this our team is investigating the damage repair and response in cell either totally lacking centrosomes or instances where they are inactivated upon terminal differentiation to examine the dependence.

Also, understanding the cell biology related to supernumerary centrosomes a commonly observed defect in DDR will have implications in instances like cancer and ciliopathies involving centrosome dysfunction. Understanding the crosstalk between DDR and centriolar structures in a dynamic setup in the backdrop of such disease and disorders will reveal the amount of contribution by these organelles in establishing such disease pathology. We will be employing cell biology, biochemical, proteomic and super-resolution imaging based assays to investigate the centriolar biology involved in a variety of physiology and pathological situations. We are currently using cell line based models to begin with and later intend to move into the appropriate *in vivo* model based on the outcome and the requirements needed to test our hypothesis established *ex vivo*.



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Molecular Mechanisms of Signal Transduction in Innate Immune Responses of Plants

Intracellular innate immunity in plants is orchestrated by key immune sentinels deployed at strategic cellular locations. Their coupling to downstream signaling messengers upon activation and subsequently to gene expression networks although result in immune elicitation, the molecular mechanistic of the processes remain largely unknown. With versatile activities as signaling messengers, we are exploring the roles of selective inositol phosphates (InsPs) in transduction of these responses. Evasion of host immunity is a constant challenge in biotechnological efforts to improve plant resistance. Using a class of rapidly evolving effectors from *Pseudomonas syringae* (*Ps*) pathovars that are differentially sensed in *Arabidopsis thaliana*, we are identifying defense modulators that trigger immunity. Lastly, as a part of an ongoing national biotechnological effort, we are characterizing defense promoting functions of natural, bio-safe and commercialized seaweed extracts (SWEs) on plants.

SWEs potentiate plant defences

Plant pathogens and pests are responsible for massive agricultural losses worldwide. The constant risk to flora and fauna posed with the application of bio-pollutant pesticides warrants alternative environmental-friendly approaches. Seaweed extracts (SWEs) with reported antiviral, antibacterial or antifungal properties present promising ecologically-safe substitutes for improving broad-spectrum defences in plants. However, underlying immune signalling pathways modulated by these SWEs remain mostly understudied. Using the well-characterized pathosystem of immunity elicited in *Arabidopsis thaliana* against the *Pseudomonas syringae* pv *tomato* (*PstDC3000*) strain, we optimized dose efficacies and treatment regimen of two *Kappaphycus alvarezii* extract formulations, Tomatough® (LBD3) and AgFort® (LBD12) developed and commercialized for farmer use by Sea6 Energy Pvt Ltd. These formulations comprise of different molecular weight fractions of sulphated galactooligosaccharides of < 5 KDa and < 1KDa, respectively.

We showed that the formulations are not directly bactericidal. Instead, their foliar application either at pre- or post-infection phase heightens *in-planta* anti-bacterial defenses in comparison to the mock-treated plants (Fig. 38). To maintain economic feasibility, most formulations are applied by the farmers at the first onset of visible disease symptoms, i.e., curative rather than as a prophylactic (preventive) measure. Our data identified the optimal dose and treatment regimen required to reduce disease manifestation in the infected plants. Treated plants accumulated higher levels of the defensive hormone salicylic acid (SA) and displayed increased expression of immune-associated genes such as *PATHOGENESIS-RELATED PROTEIN 1* (*PR1*), *FLG22-INDUCED RECEPTOR LIKE KINASE 1* (*FRK1*) or *FLAVIN-DEPENDENT OXIDOREDUCTASE* (*FOX*), among others (Fig. 38). We also identified that SA-biosynthesis or signaling mutants were unresponsive to formulation-induced defences. The well-characterized mutants such as *eds1-2*, *sid2-1*, or *npr1-1* that fall under this categorization remained hypersusceptible to

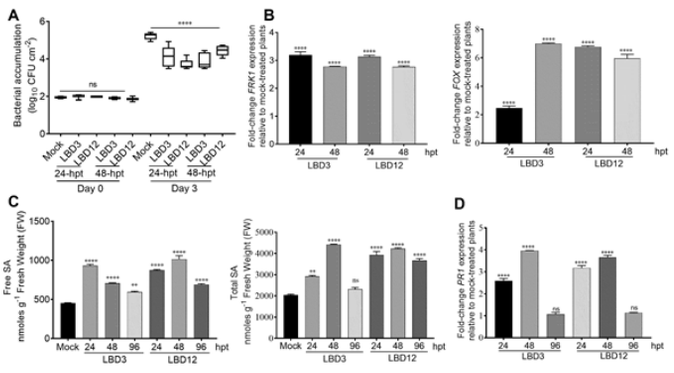

Figure 38: Primed-defenses in formulation-treated plants. *(A) PstDC3000 accumulation in mock or formulation treated plants (hpt, hours post-treatment). ANOVA (Tukey) analysis was performed for statistical differences ($p < 0.001$) between samples. (B) FRK1, or FOX, and (D) PR1a transcripts, or (C) Free and total SA levels in the indicated plants. Data is mean ± SD (n=3). Student's t-test denote statistical significance relative to mock-treated plants; ** = $p < 0.01$; **** = $p < 0.0001$; ns = not significant*

PstDC3000 and were recalcitrant in inducing immune-associated gene expression upon formulation treatments. Further, a gradual increase in free SA levels at progressive time-points was only detected in the formulation treated wild-type but not in any of the above mutants. Overall, our results suggested that downstream activation of SA-signaling routes in plants plays a critical role in the elicitation of defense responses upon formulation application.

Extensive crosstalk between SA networks to other phytohormone pathways is increasingly evident in the orchestration of plant defensive responses. To probe this, we analyzed via high performance liquid chromatography (HPLC) the levels of jasmonic acid (JA), abscisic acid (ABA), the cytokinins (CKs) Kinetin, t-Zeatin, and auxin (indole acetic acid; IAA) in extracts from formulation-treated plants. We detected a prominent increase in endogenous JA and CK levels in the formulation-treated plants. Small but statistically significant upregulation in IAA levels was also detected in the formulation treatments than untreated plants. These results were further validated by measuring the expression changes in the cognate phytohormone-responsive marker genes. Our data revealed that indeed multiple phytohormone signaling networks are modulated by foliar application of the formulations. These observations raised a promising possibility to test the immune-potentiation functions of the formulation in different plant systems against diverse lifestyle pathogens.

To test the proficiency and underlying molecular aspects of the above formulation on an economically relevant crop pathosystem, we selected the Xanthomonas oryzae pv. oryzae (Xoo) pathogen that causes devastating bacterial blight disease on rice. Disease incidence of Xoo on rice was significantly reduced upon AgFort® (LBD12) application at the post-infection stage (Fig. 39). Marked reduction in disease symptoms and *Xoo* -induced lesion sizes on the AgFort®-treated leaf blades were evident in comparison to the mock controls. At the molecular level, defense-associated gene expressions were more pronounced in the formulation-treated samples relative to the uninfected plants (Fig. 39). Interestingly, expression of *SWEET14*, a sucrose transporter upregulated by *Xoo* effectors reflecting the pathogen's attempts to manipulate host physiology to obtain nutrients, was lower in the formulation-treated samples than in the mock controls. These results suggested that enhanced defenses induced by formulation were more efficient in countering the pathogen's efforts to exploit the host. Overall, with our investigations, we not only demonstrated the broad-spectrum propensities of the tested SWE formulations across various pathosystems but also provided valuable insights into its application window for

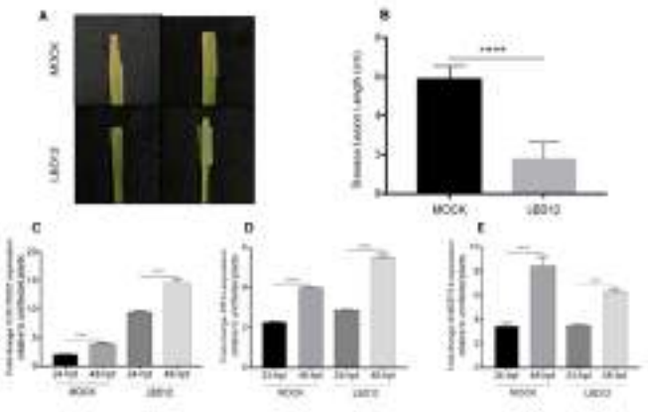

Figure 39: AgFort® (LBD12) applications reduces Xanthomonas oryzae pv oryzae (Xoo) infections on rice. *(A) Images of Xoo-infected leaf blades of mock- and AgFort®-treated rice plants. (B) Disease lesion-lengths as in A. Relative expressions of (C) ICS1, (D) PR1a, and (E) SWEET14 at 24- or 48-hpt (hours post-treatment). Values shown are mean ± SD (n=3). Statistical analysis is by Student's t-test relative to mock- or uninfected plants ***=p<0.001; ****=p<0.0001, ns= not significant.*

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Investigations into the Molecular Mechanisms Underlying Legume-Powdery Mildew Interactions

Powdery mildews (PM) are biotrophic fungal pathogens that cause substantial yield losses in grain legumes, such as pea, lentil, and mung bean. The broad goal of our research program is 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 pea, to identify host resistance/susceptibility factors and pathogen virulence determinants that significantly impact disease development.

The isoflavonoid phytoalexin medicarpin confers PM resistance in M. truncatula

Isoflavonoids are a subclass of the flavonoid group of phenylpropanoid secondary metabolites that are almost exclusively synthesized by plants belonging to the Leguminosae family. They possess antimicrobial properties but their role in PM resistance was not explored. Here, we leveraged the inherent genetic variability in the *M. truncatula* germplasm to elucidate the role of isoflavonoids in PM resistance.

Targeted gene expression and metabolite analyses revealed an early induction of isoflavonoid biosynthesis in the resistant (R) *M. truncatula* genotype A17 compared to the moderately susceptible (S) genotype R108 in response to PM infection (Fig. 40). Medicarpin, the pterocarpan end-product of this pathway, localized to the infection site and was induced earlier in A17 compared to R108 on PM infection. Transient overexpression of a putative positive regulator of the isoflavonoid pathway enhanced medicarpin accumulation and PM resistance of R108 whereas RNA interference-based silencing of a key pathway gene compromised PM penetration resistance of A17. Exogenous application of medicarpin or the intermediate metabolites leading to its synthesis resulted in a significant reduction in fungal load in R108 leaves (Fig. 40). Fungal growth was mainly arrested at the appressorium stage in medicarpin-treated leaves. Medicarpin treatment also enhanced hydrogen peroxide accumulation at fungal penetration sites, which is a plant response to pathogen attack that is generally associated with host cell inaccessibility and hypersensitive response (HR)-associated cell death. Our findings suggest that medicarpin may contribute to penetration resistance and post-penetration HR in *M. truncatula* by triggering infection-localized H_2O_2 production.

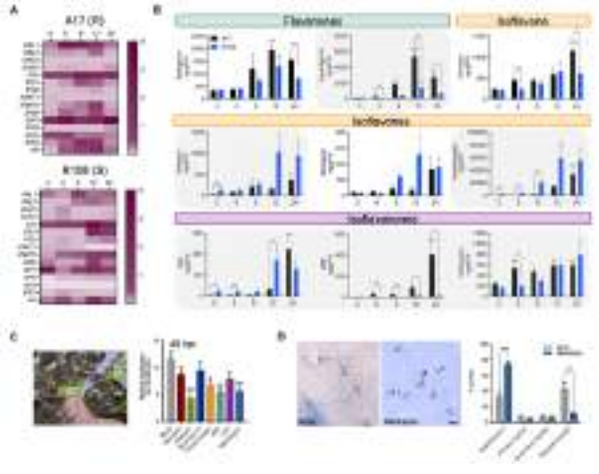

Figure 40: *Medicarpin confers PM resistance in M. truncatula. (A) Expression heat map of isoflavonoid biosynthetic genes relative to that of ubiquitin and (B) isoflavonoid levels in resistant and susceptible genotypes at different hours postinoculation (hpi) with PM (C) E. pisi 18S rRNA abundance after exogenous application of isoflavonoids in R108 leaves (D) PM growth quantification after medicarpin treatment; c, conidium; a, appressorium. Bar, 50 µm; *p<0.05, ** p<0.01, ***p<0.001, ****p<0.0001*

Medicarpin treatment activates salicylic acid synthesis and signaling in *M. truncatula*

Exogenous application of medicarpin in R108 leaves enhanced PM infection-induced levels of the defense phytohormone salicylic acid (SA) and the expression of SA signaling markers such as the *pathogenesis-related* (*PR*) genes. However, medicarpin treatment had no significant effect on basal or PM infection-induced levels of the defense phytohormone, jasmonic acid (JA). SA is synthesized in plants via the ICS and/or PAL pathways. Our gene expression analysis suggests that medicarpin treatment positively regulates SA

biosynthesis in *M. truncatula* primarily through transcriptional activation of the PAL pathway whereas both ICS and PAL pathways may contribute to SA accumulation during PM infection. SA treatment, in turn, induced medicarpin accumulation in R108 leaves but only in response to PM infection. Collectively, our study suggests a synergism between the isoflavonoid and SA biosynthetic pathways that may be crucial for early PM resistance (Fig. 41). This has important implications for agriculture, as the use of medicarpin can enhance crop protection against PMs and potentially reduce the use of harmful pesticides.

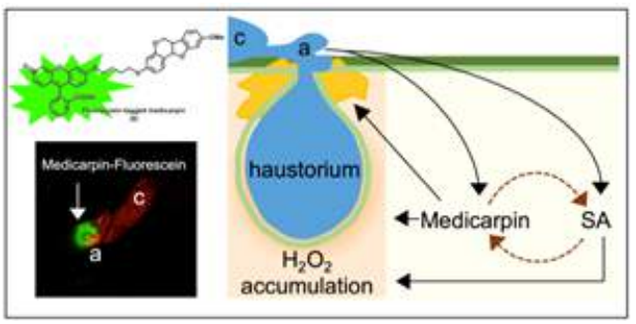

Figure 41: Proposed model showing the contribution of medicarpin and SA in PM resistance in M. truncatula. *PM infection stimulates the biosynthesis of medicarpin, SA and JA. Medicarpin and SA act in concert, perhaps in a regulatory loop, triggering the localized accumulation of medicarpin and H_2O_2 at fungal penetration sites that leads to HR and PM resistance.*

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 on this signal to master regulators, which in turn, bring about changes in downstream components, leading to changes in gene expression. One of these master regulators is the HY5 transcription factor. We have identified three orthologs in rice based on the presence of COP1-binding and bZIP domains. We previously functionally characterized one of the orthologs, OsbZIP48. We are now investigating how these three genes work in tandem as well as independent of each other. OsbZIP48 is known to form heterodimers with other bZIPs. Therefore, in-silico analysis was done to identify potential interacting bZIP partners of OsbZIP48. They have been cloned and their in-vivo interaction with OsbZIP48 is being studied through BiFC and CO-IP.

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 limits water loss through stomatal regulation and induces the synthesis of osmoprotectants and ROS scavengers. Dehydration control by stomatal regulation usually limits CO2 uptake, 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. We target rice genes encoding anion channels ALMT12 (Aluminium-activated malate transporter) and SLAC1 (Slow anion channel-associated 1) using CRISPR-Cas9 and chemical genomics. Genome-edited rice plants targeting ALMT12 and SLAC1 were developed through tissue culture and their validation for stomatal regulation is in progress. The molecules targeting these genes improved the phenotype and stomatal opening in Arabidopsis and rice. The broad-spectrum effect of these molecules on cowpea and green gram improved growth and yield parameters. Transcriptome analysis identified 41 F-box genes with 23 up and 18 downregulated upon ABA treatment.

Dr. Babitha K.C.
DBT Women BioCARe Awardee

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Functional Genomics and Crop Improvement for Stress Adaptation

Rice plants are exposed to multiple stresses in field conditions, such as drought and bacterial infection by *Xanthomonas oryzae* pv. *oryzae (Xoo)* that affect productivity. Pathogen *Xoo* causes bacterial blight in rice resulting in >25% crop loss. In this context, our emphasis is on the identification of stress-responsive ribosomal protein-encoding genes and plant E3 ligases in Arabidopsis and rice. We aim to characterize their functional relevance to improve plant health under diverse stress conditions to sustain the nutritional quality and yield.

Studying the functional relevance of ribosomal proteins in responses to different stress conditions

Ribosomes are an essential component of life and play a vital role in cell growth and survival. If ribosomes are not functional, protein translation decreases, resulting in reduced cell growth or cell death. It was believed that mutations in ribosomal proteins would result in lethality, surprisingly this is not always the case and in the last few decades, multiple rare, genetic diseases have been attributed to defects in ribosome function in humans and other mammals. The function of ribosomal proteins other than protein synthesis has not been explored in detail in plant or mammalian systems. In this context, our emphasis is on the Identification of stress-responsive ribosomal protein-encoding genes in rice and characterising their relevance with regard to plant health under diverse stress conditions in rice.

Rice plants are exposed to multiple stresses in field conditions, such as drought and bacterial infection by *Xanthomonas oryzae* pv. *oryzae* that affect productivity. Over the years significant overlapping mechanisms have been identified in response to pathogen and drought. Under these conditions protein structure and function are affected, and to sustain this, continuous synthesis of proteins is required with the help of ribosomal proteins. In this context, the emphasis of the study is on the identification of differentially expressed ribosomal proteins to understand their mechanisms and manipulate them using genome-editing technology.

To identify differentially expressed genes under drought, pathogen and combined stress, the contrasting rice resistant genotype BPT5204 and sensitive TN-1 were exposed to stress to generate RNA seq data (Fig. 42a). The RNA seq data is generated in rice when infected with *Xoo* or drought. The results suggested that unique sets of genes are differentially regulated in each stress in both genotypes. Several combinations of analysis were made to identify the common and unique genes from both up and downregulated genes for further characterization (Fig. 42b). Since the focus was on ribosomal protein-encoding genes, the genes and their expression values were filtered. Based on the analysis several ribosomal protein-encoding genes were differentially responsive to stress (Fig. 42c). Several genes show shared responses between combined stress and a few of them are unique to individual stresses. Interestingly, time-dependent gene expression analysis suggested that in the resistant genotype the ribosomal protein-encoding genes were upregulated in early time points compared to susceptible genotype TN1 (Fig. 42d-f).

A novel role of salt and drought-induced RING 1 protein in modulating plant defense

Plants are constantly threatened by microbial infections throughout their life cycle. Phytopathogenic bacteria have the ability to deliver effector molecules into host cells through the type III secretion system (T3SS) to suppress plant defense responses and favor the establishment of disease. Following their translocation into plant cells, type III effectors (T3Es) target a range of subcellular compartments to promote virulence. One of the host defense systems that has emerged as a common target of bacterial effectors is the ubiquitination system in which substrate proteins are post-translationally modified by covalent conjugation with the small protein ubiquitin. We identified the interaction of *P. syringae* pv tomato (DC3000) bacterial helper effector protein HopP1 with Arabidopsis salt and drought-induced resistance (SDIR1), an E3 ligase and further studies are in progress.

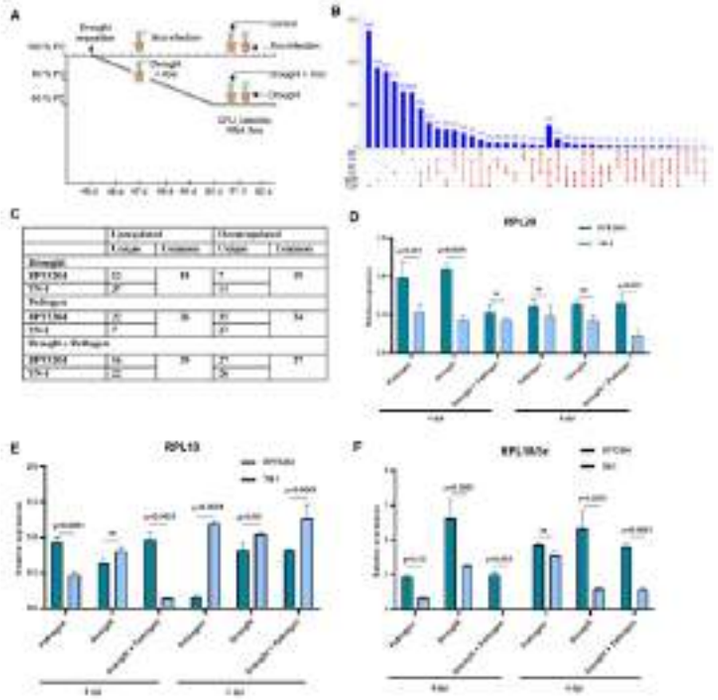

Figure 42: Combined stress response of contrasting rice genotypes. *(A) Scheme showing combined and individual drought and pathogen stress imposition method (B) Differentially expressed genes under combined and individual Xoo and drought stress (C) Differential expression of ribosomal protein-encoding genes from RNA sequencing data (D-F) Expression of ribosomal protein-encoding genes at 4 and 6 d after drought stress, Xoo pathogen stress, and combined stress.*

Pathogens target the ubiquitin systems of plants to suppress their innate immunity. We report a novel role of E3 ligase SALT- AND DROUGHT-INDUCED RING FINGER1 (SDIR1) in plant immunity. The silencing of SDIR1 in *N. benthamiana* reduced the multiplication of the virulent pathogen *Pseudomonas syringae pv*. tabaci. The Arabidopsis *sdir1* mutant is resistant to virulent pathogens, whereas *SDIR1* overexpression lines are susceptible to both host and nonhost hemibiotrophic bacterial pathogens.

The molecular interactors of SDIR1 during pathogen infection are not known. SDIR1 interacting Jasmonate ZIM-domain (JAZ) proteins were identified through a yeast two-hybrid (Y2H) screen. JAZ9 interacts with SDIR1 only in the presence of coronatine, a bacteria secreted toxin, or jasmonic acid (JA) in Y2H assay. The bi-molecular fluorescence complementation and co-immunoprecipitation assays confirmed the *in planta* interaction of these proteins. JAZ9 protein, a negative regulator of the JA-mediated plant defense, was degraded during pathogen infection by SDIR1 through a proteasomal pathway leading to disease susceptibility against hemibiotrophic pathogens (Fig. 43).

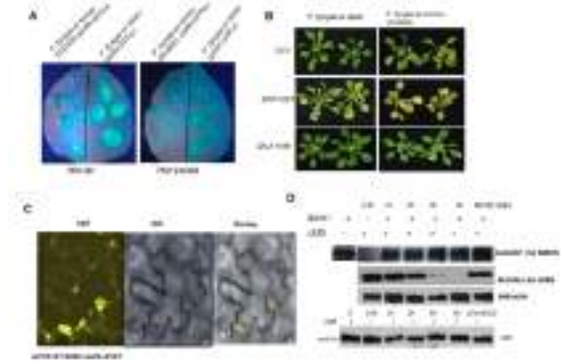

Figure 43: Functional Characterization of E3 ligase SDIR1. *(A) Silencing of 24D08 cDNA clone encoding SDIR1 gene in N. benthamiana reduces multiplication of both host and nonhost pathogens. (B) Overexpression of AtSDIR1 in Arabidopsis compromises nonhost disease resistance and sdir1 mutant lines show tolerance to host pathogen. (C) Bi-FC assay confirming the interaction of AtSDIR1 with AtJAZ9. (D) Protein gel blot analysis showing SDIR1 degrading JAZ9. MG132 inhibit proteasome degradation.*

Prashant Mohan Pawar
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Understanding the Role of the 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 critical factor which plays 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 those to redesign cell walls for different bioenergy applications.

Glucuronoacetylated xylan (GAcX) is one of the most abundant polysaccharides present on earth. The GAcX backbone consists of (1,4) linked xylose residues substituted with glucuronic acid and acetyl groups. These groups allow limited hydrolysis of xylan by xylan-degrading enzymes. Moreover, xylan itself or through these groups interacts with cellulose and lignin, which are the main components of the cell wall. Disrupting 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.

Using a bioinformatics study, we identified a few putative candidate genes that might show polysaccharide esterase activity. Our transient expression studies in *Nicotiana benthamina* suggested that *At*GELP7/AtAXE1 might be involved in polysaccharide de-esterification. Therefore, we checked the acetyl content in the homozygous Arabidopsis *ataxe1* mutant and found an elevated level of stem cell wall acetyl content (Fig. 44).

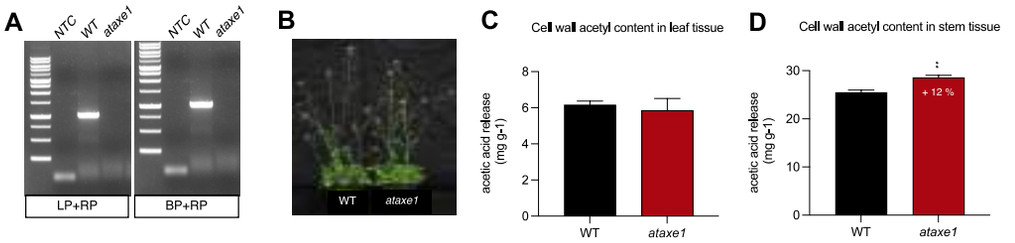


Figure 44: Characterisation of gelp7 or atxe1 Arabidopsis mutant. *(A) Agarose gel showing homozygous line confirmed by Left Primer (LP), Right Primer (RP), and Border Primer (BP). (B) Picture of 6 weeks old Arabidopsis wild type and ataxe1 mutant. (C) Leaf and (D) stem alcohol insoluble residues saponified and acetyl content analysed by acetic acid kit (K-ACET) from Megazyme. Data represents mean ± SE, n = 3-4 biological replicates, Student's t-test at **p ≤ 0.05, *p ≤ 0.1*

To further validate this, we generated independent transgenic lines overexpressing *At*AXE1. We found that these lines showed an elevated level of acetyl xylan esterase activity. Therefore, we tested polysaccharide acetylation in different polysaccharide fractions, i.e., pectin, xyloglucan and xylan. We found only xylan acetylation was decreased in transgenic lines (2b, 3b, 5b) compared to wild type. The results were further confirmed by digesting the cell wall with xylanases and performing xylooligosaccharide (XOS) profiling. We found more release of shorter chains and less release of longer XOS in transgenic lines than wild type. This further confirmed that deacetylation in transgenic lines increases the digestion of xylan by xylanases. We further tested the effect of deacetylated xylan on cellulose digestibility with and without pretreatment. The highly expressed transgenic line 5b showed a 27% increase in cellulose digestibility as compared to the wild type.

Furthermore, the cell wall of both wild type and transgenic lines were pre-treated with 1M NaOH that solubilises hemicellulosic components and cleaves acetyl groups. The remaining

pellet enriched in cellulose was digested by cellulases, and all AtAXE1 transgenic lines showed an increase in its digestibility (Fig. 45). This suggests that deacetylation has also positively changed the extractability of cell walls. In conclusion, we have identified the first plasma membrane localised acetyl xylan esterase, and its overexpression enhances both xylan and cellulose digestibility and extractability without affecting plant growth and development.

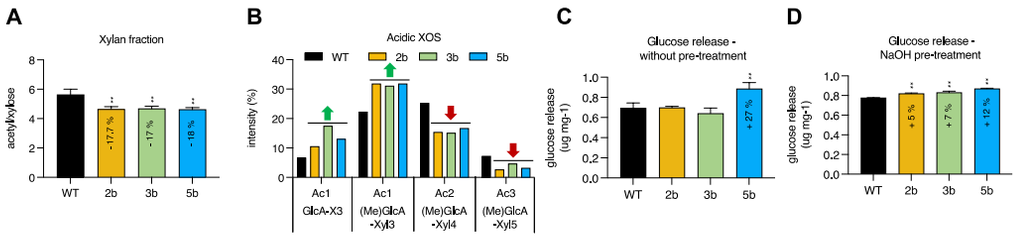
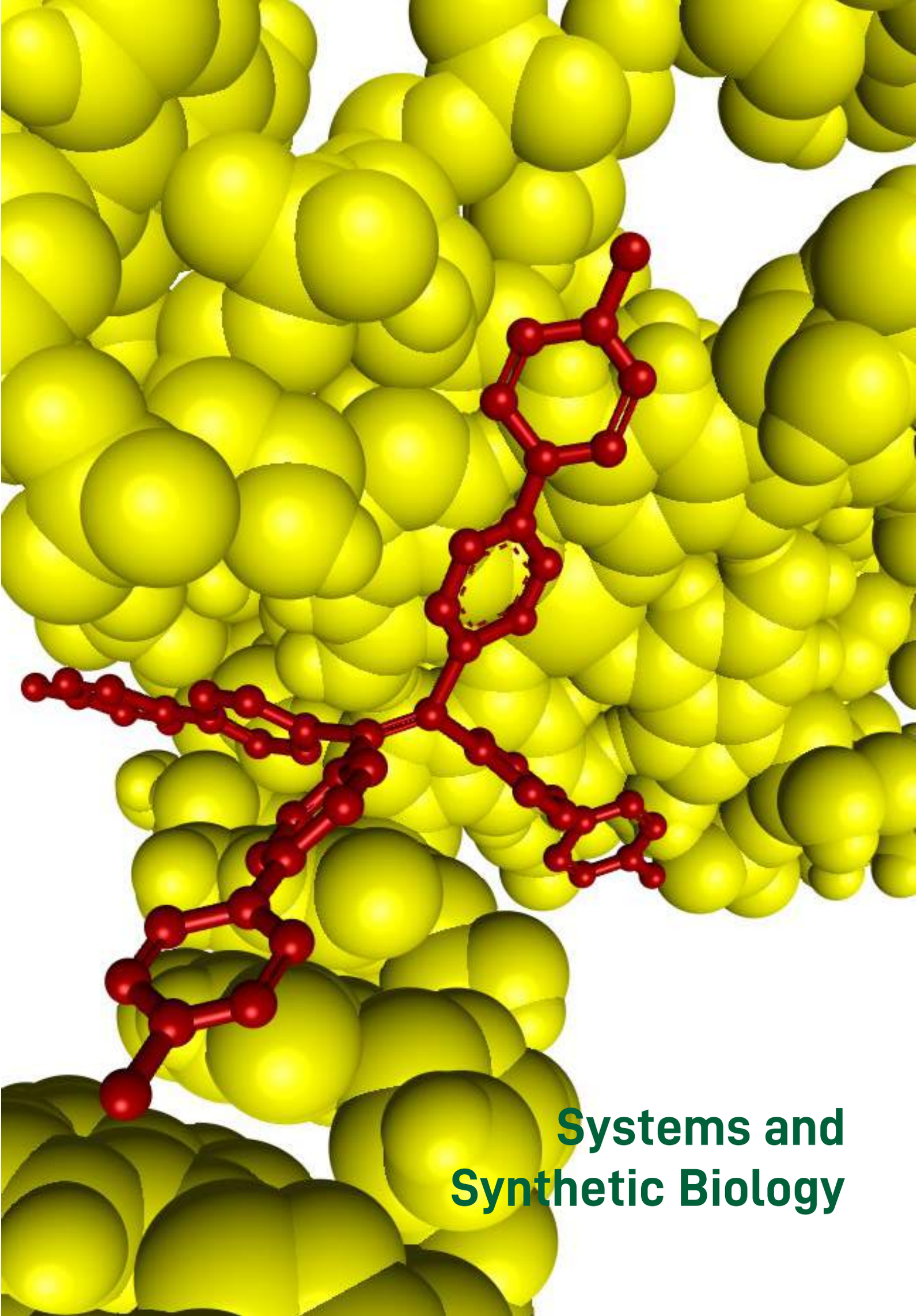


Figure 45: Characterisation of transgenic lines overexpressing AtAXE1. *(A) Acetyl content analysis in xylan-rich fraction. (B) Xylan oligosaccharide analysis in acidic Xylo-OligoSaccharide (XOS) fraction, released by GH11 xylanase and analysed by MALDI-TOF-MS (C) without pretreatment, and (D) after NaOH pretreatment. 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 belonging to the Fabaceae. It has a diploid chromosome number of 2n=2x=22 and is native to India and Central Asia. The adaptive traits like flowering time, seed size and plant cell wall composition vary with changing climates and diverse environmental factors. However, these traits follow a quantitative inheritance pattern. Therefore, it is necessary to decipher these traits' complex genetic inheritance patterns. Genome-wide association study has been performed to analyse the genetic inheritance pattern and identify genes/alleles/QTLs regulating seed size and plant cell wall composition in mungbean. It led to identifying some potential candidate genes regulating seed size in mungbean. Further, functional characterisation of these genes is in progress. To identify mungbean cell wall regulation genes, we will be performing high throughput wall composition by Fourier Transform Infrared spectroscopy (FTIR) in the mungbean mapping population containing several mungbean genotypes, which will be used QTL analysis.



Systems and Synthetic Biology

Rajendra P Roy
Principal Investigator

Lab Member

Sumit Murmu
Shalini Sharma

Peptide Ligation and Protein Semisynthesis

We are interested in developing chemoenzymatic approaches for protein semi-synthesis, labeling and bioconjugation. Our efforts are geared towards creating synergy in protein engineering by fusing recombinant expression with chemical synthesis and enzymatic peptide ligation for potential applications in mechanistic biology and biotechnology. In recent years, the transpeptidase sortase of *Staphylococcus aureus* (SrtA) has been found extremely useful in this endeavor.

Sortase enzymes are membrane-anchored transpeptidases universally present in Gram-positive bacteria. These enzymes recognize a LPXTG type of sequence present near the C-terminus of substrate proteins, cleave the scissile T-G peptide bond and transfer protein-LPXT to the peptidoglycan glycine (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

Eukaryotic organisms store genetic information in a complex protein-DNA assemblage, referred to as chromatin. The highly basic histones (H2A, H2B, H3, H4) serve as building blocks to package DNA into repetitive nucleosome units in which two copies of each histone (histone octamer) are wrapped around approximately 146 base pairs of DNA. Histone proteins at the core of the nucleosomes are subjected to a variety of epigenetic (posttranslational) modifications (PTMs) . The installation and erasure of epigenetic marks on chromatin serves as a fascinating regulatory mechanism for cellular processes emanating from chromatin. Biochemical interrogation of histone PTMs is often stymied by the non-availability of chemically well-defined modified histones, and sometimes complicated by functional redundancy of erasers–. Much of our knowledge about the specificity of erasers for disparate chemical marks in histones has been gleaned from heterogeneously modified mixture of endogenous histones. Therefore, chemically 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 histones is quite wide-spread and scattered across more than fifty lysine residues of the four core histones. The acetyl marks on specific Lys residues installed by the action of histone acetyl transferases (HATs) are erased by histone deacetylases (HDACs). There are 18 human HDACs (including Sirtuins) capable of erasing acetyl groups from histones and other acetylated proteins (Fig. 46). The site-specific eraser action of HDACs in 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* results thus far have enabled the identity of specific HDACs for H2BK5Ac and H3K4Ac. Studies are currently in progress to validate these results *in vivo*.

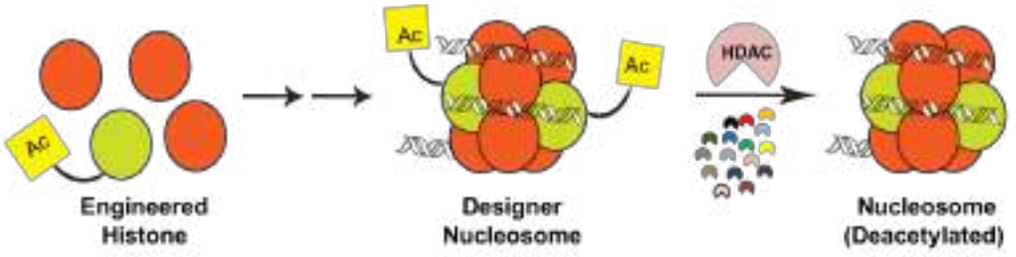


Figure 46: Mark and Erase: *Assembly of designer nucleosomes embedded with well-defined acetyl marks in histones to delineate their site-specific erasers among 18 human HDACs.*

Probing the altered specificity of a new class E sortase

The class E (SrtE) and F (SrtF) sortases are usually present in actinomycetes. While SrtE in these organisms performs the housekeeping roles akin to SrtA, the function of SrtF remains obscure. Previous work emanating from this laboratory demonstrated that SrtE from *Streptomyces avermitillis* (SavSrtE) preferred the LAXTG pentapeptide as against LPXTG, which is generally the substrate of choice for archetypal SaSrtA. The altered substrate specificity of SavSrtE was ascribed to the presence of a critical Tyr residue in the vicinity of the binding cleft, which appears to be conserved in Class E sortases including the *Thermobifida fusca* SrtE (TfSrtE) recently characterized in this laboratory (Prity Yadav, unpublished). Curiously, TfSrtE was observed to act on both peptide substrates (LAXTG and LPXTG) equally well.

Site-directed mutagenesis of Tyr128 was carried out and two single mutants of 64TfSrtE carrying a substitution of Tyr128 to Phe or Ala were created to evaluate their respective abilities to modulate LPXTG/LAXTG peptide substrate recognition propensity. Interestingly, the preference for LAXTG substrate observed in the transpeptidation reactions of the wild type enzyme was compromised in the Tyr128Phe mutant, but its intrinsic activity toward the LPXTG peptide substrate was retained. In contrast, the Tyr128Ala mutant displayed high proteolytic activity against the peptide substrates (LAXTG, LPXTG and GGGKY) and lost its transpeptidation potential. The above result of the Tyr128Phe mutant is reminiscent of the behavior of an analogous Tyr to Phe mutant in SavSrtE. However, the Tyr to Ala mutant of SavSrtE was found to be devoid of any transpeptidation or proteolytic activity.

Attempts to crystallize wild type and mutants of Δ64TfSrtE were unsuccessful. However, a newer construct (Δ90TfSrtE), obtained by further deletion of 26 residues from the N-terminal of Δ64TfSrtE, produced diffraction quality crystals. Curiously, the transpeptidation profile of both mutants (Tyr128Phe/Ala) of Δ90TfSrtE was found to be similar and akin to the Tyr128Phe mutant of Δ64TfSrtE. The disparate effects of Ala substitution in the two truncated constructs of TfSrtE raises the possibility of remote communication of the Tyr128 residue with the N-terminal region of TfSrtE (Fig. 47). Further studies of structural aspects in conjunction with modelling and molecular dynamics simulation of wild type and mutant TfSrtE are likely to shed more light on the substrate specificity and tolerance of TfSrtE.

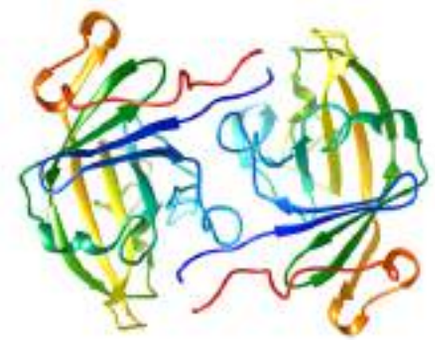


Figure 47: Crystal structure of TfSrtE.

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Molecular Engineering of Functional Nucleic Acids for Biomedical and Biotechnological Applications

Our research focuses on harnessing the nucleic acids structure-mediated gene regulation in human 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, 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 a therapeutic target. 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.

Targeting Hairpin-G-quadruplex conformational equilibria for anticancer therapy

Nucleic acids (DNA and RNA) have been shown to form non-canonical nucleic acid structures in the guanine rich regions widely known as G-quadruplexes (GQ). The human genome is believed to possess more than 3,00,000 guanine-rich regions capable of forming GQ conformations. The RNA G-quadruplexes (RGQs) adopt parallel conformations (Fig. 48A). The RGQs are commonly found in the exons, introns, 5' and 3' UTRs and ORFs where they regulate alternative splicing, translation, and mRNA transport. The involvement of RGQs in a plethora of biological processes makes it a promising therapeutic target for the treatment of several deadly genetic diseases such as cancer and neurodegenerative diseases as well as those diseases caused by viruses and bacteria.

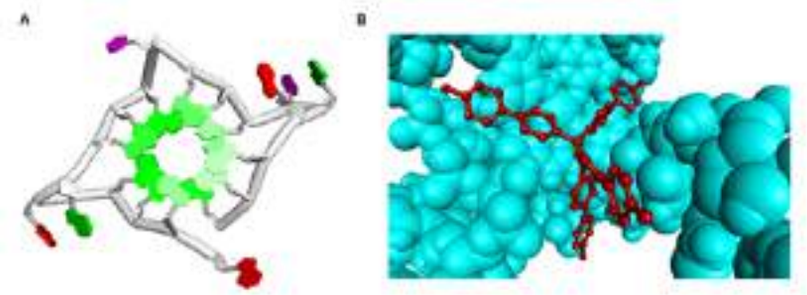

Figure 48: *(A) Crystal structure of RNA G-quadruplex (B) Docked structure of representative small molecule with RNA G-quadruplex*

In human cells, the RGQ formation depends on various inherent factors such as the existence of flanking sequences near G-rich regions. The flanking sequences adjacent to G-quadruplex forming sequences can potentially form alternative hairpin structures, which are in conformational equilibrium with the G-quadruplex. RGQ sequence in 5' UTRs of certain proto-oncogenes colocalize with the hairpin (Hp) forming sequence resulting in intramolecular Hp-GQ conformational equilibria which is suggested to regulate cancer development and progression. Thus, we envision that the regulation of Hp-GQ equilibria with small molecules is an attractive but less explored therapeutic approach and can serve as a promising target for the discovery of new leads for anticancer therapy. The representative binding of small molecule to RGQ is shown in Fig. 48B.

Developed small molecules to modulate the RNA Hairpin-G-quadruplex conformational equilibria in Proto-Oncogenes

We have synthesized a library of Tetraphenylethene (TPE) derivatives and investigated their role on Hp-GQ conformational shift. An HpGQ model sequence which can adopt mutually exclusive hairpin and GQ structures was used for the initial screening and the change in conformational equilibrium was studied using Fluorescence resonance energy transfer (FRET) technique. The result shows increase in FRET signals in presence of certain TPE

derivatives indicating the conformational shift towards GQ (Fig. 49A). Also, in the presence of TPE derivatives the observed rate constant values for the first and second folding step were found to be increased up to 14.6 and 2.6-fold, respectively. We further used FRET melting assay to get an insight about the stability of HpGQ, mediated by TPE derivatives, and the result shows strong stabilizing ability as it increased the Tm by 4.36 C (Fig. 49B). This result was further validated through circular dichroism spectroscopy (Fig. 49C).

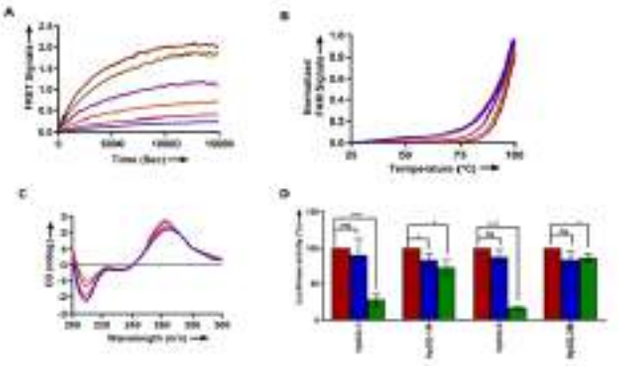

Figure 49: *(A) FRET signals of HpGQ-1 in presence of TPE derivatives (0 μM-1 μM) (B) Normalized FAM signals of HpGQ-1 in presence of TPE derivatives (0 μM-1 μM) (C) CD signals of TPE derivatives in presence of HpGQ (0 μM-20 μM) (D) CD signals of TPE-MePy (0 μM-20 μM) in presence of HpGQ (D) In vitro translation assay of HpGQ-1 and HpGQ-2 (TRF-2) along with their mutants in absence (0 μM) or presence of 10 μM TPE-Py or TPE-MePy.*

The small molecules that bind to GQ within 5'-UTR of eukaryotic mRNAs can interfere with translation. Thus, we have performed reporter gene assays to evaluate the influence of TPE derivatives on the HpGQ-mediated gene regulation. We have chosen two HpGQ sequences, one is HpGQ-1 which was used in FRET assays and the second is HpGQ-2 derived from the 5′-UTR of the human telomeric repeat binding factor 2 (TRF2) mRNA. We also designed mutants i.e., HpGQ-1 M and HpGQ-2 M for HpGQ-1 and HpGQ-2 sequences, respectively. The HpGQ sequences and its mutants were cloned into the 5′-UTR of the *Renilla* luciferase reporter gene. The translation efficiency of these constructs in the presence of TPE derivatives were evaluated. The results suggests that TPE derivatives decrease the luciferase level of HpGQ-1 construct by 3.7-fold and HpGQ-1 (TRF2) construct by 5.7-fold by shifting the Hp-GQ equilibrium toward GQ conformers in the 5' UTR (Fig. 49D). The mutant constructs (HpGQ-1M and HpGQ-2M) did not show any significant change in luciferase activity in the presence of TPE derivatives (Fig. 49D). Taken together, our results indicate that Hp-GQ conformational equilibria should be considered as a potential therapeutic target for treating cancer.

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Rational Development of Biocatalysts for Production of Value-Added Products

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

Insight into Lytic polysaccharide monooxygenase for biomass degradation

The major goal of our research is to develop superior biocatalyst 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 development of superior biocatalysts for cellulose degradation. The commercial enzyme preparations for cellulose disintegration were found to catalyse mere 60-70% of biomass disintegration, owing to the absence of critical enzyme components or accessory carbohydrate active enzymes (CAZymes). These enzymes are Lytic polysaccharide monooxygenases (LPMO), which belong to Auxiliary Activity (AA) family. So far characterized LPMOs have very low catalytic activity and is thus not suitable for scale-up. For this, we have mined genome of phytopathogenic fungus, Botrytis cinerea (B. cinerea), and identified a CBM containing AA9 LPMO (BcAA9C). The supplementation of full length LPMO (flLPMO) to classical cellulase cocktail led to 1.6 fold increase in glucose released from biomass disintegration highlighting its importance in saccharification of polysaccharide substrate. The enzyme possesses additional linker and CBM domain associated with catalytic domain. To understand role of linker and CBM domain associated with flLPMO, we designed and expressed CBM and linker truncated enzymes in Pichia pastoris. The biochemical assays and biophysical techniques clearly indicated that the linker region facilitate binding and activity towards polymeric substrate (Fig. 50). Furthermore, the presence of linker region was shown to contribute towards thermal stability of flLPMO. Collectively, we have elucidated that the linker region present in flLPMO is crucial for its activity on polymeric substrate (*Srivastava et al, Microbiol Spectr 2022*).

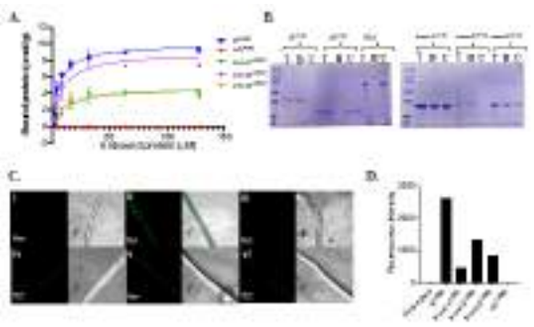


Figure 50: Influence of linker on binding polysaccharide substrate *(A) Binding isotherms for full length (flLPMO), CD-CBM (trunc1LPMO, trunc2LPMO, trunc3LPMO) and CD (cdLPMO) (B) Representation of binding experiment where 120 µM protein was allowed to bind 2mg biomass for 12 h at 4°C in 250 µl reaction and total protein (T), Bound fraction (B) and U (Unbound fraction) was loaded onto SDS-PAGE gel (14 %). BSA was used as negative control (C) The protein bound biomass was analysed for protein binding using confocal microscopy. (D) FITC Fluorescence Intensity averaged for nine images indicates quantitative binding of LPMO constructs*

Mining Plant Growth Promoting Rhizobacterial Biofertilizers for Sustainable Crop Production

Collectively, several modes of action, direct or indirect, are behind the plant growth-promoting ability of microbes. Improved nutrient availability, stimulation of root development via phytohormone release and/or interference with plant's ethylene synthesis and, induced systemic resistance in plants are some of the direct mechanisms by which microbes affect plant growth. While indirect mode involves competition or antagonism towards plant pathogens (reviewed by Olanrewaju et al., 2017). Through these mechanisms, microbes are capable of contributing to plant fitness under physiological conditions as well as under environmental stress. However, there are gaps in our understanding of the molecular basis of beneficial plant-PGPR (plant growth promoting rhizobacteria)

interactions, especially under conditions that interfere with normal functioning of plants. Thus, there is a pressing need to analyze more and more genomes in order to identify novel traits and corresponding genes, for efficient screening of microbes for application in the stressed soils.

We chose two recently isolated microbial strains, Pseudomonas sp. CK-NBRI-02 (or P2; GenBank ID: VSJH00000000) and Bacillus marisflavi CK-NBRI-03 (or P3; GenBank ID: VSJG00000000) for analysis (Gupta et al., 2019; 2020) since our preliminary screening in rice revealed their promising effect on plant growth under stress conditions. We observed several differences between the two strains with respect to known plant-beneficial functions. While assessing their MG detoxification ability, we found P2 to possess enhanced capability to metabolize MG, which indeed was reflected from its ability to tolerate dicarbonyl stress (imposed by MG) better than P3 whereas P3-treated seedlings exhibited elevated tolerance under salinity stress. It is possible that the coordinated regulation of glyoxalase activity in P3 under salinity conditions may be one of the contributing factors for improved salinity tolerance of P3 (Fig. 51).

Further, to unfold the contribution of MG metabolism in mitigation of salt stress, we determined changes in MG levels and consequently, MG detoxification enzyme activities in bacterial cells treated with NaCl. For this purpose, equal number of cells of each strain were subjected to two different concentrations of NaCl viz. 0.5 M and 1 M NaCl during their early logarithmic phase of growth and cells were harvested after 2 h for the assessment of MG levels and glyoxalase activity. We found that NaCl treatment led to an increase in endogenous MG levels in a dose-dependent manner in all the three strains. P2 cells exhibited a 1.6-2.4-fold increase in MG levels in response to NaCl whereas increase was more pronounced in case of P3 and E. coli. In case of P3, MG levels increased from 1.8-fold in the presence of 500 mM NaCl to ~7-fold at 1 M NaCl concentration. Likewise, E. coli cells also exhibited similar increase in MG levels at the two NaCl concentrations. An important point to be noted here is that though the fold increase in MG levels at 1 M NaCl was lowest in P2 but its concentration was marginally higher than in P3. In agreement, we could detect a dose-dependent decline in GLYI activity in P2 cells, from being highest under non-stress conditions to gradually declining in the presence of NaCl. On the contrary, increase in GLYI activity was proportional to NaCl concentration in P3, and attained levels higher than even P2 at 1 M NaCl concentration. We could not however, detect GLYII activity in any of the three strains in response to NaCl treatment. Overall, results suggested that in addition to other known mechanisms, MG homeostasis may also be an important factor contributing towards salt tolerance of microbes, as seen for P3. Overall, our studies suggest that both the strains could confer growth promoting effects in Arabidopsis under physiological as well as stress conditions, albeit via different mechanisms and that the microbial MG metabolism may play an important role towards stress alleviation (*Kaur et al, Environ Microbiol 2021*).

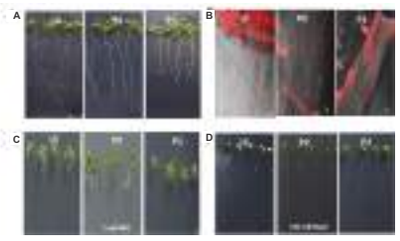


Figure 51: Assessment of growth promotion of Arabidopsis seedlings in response to PGPR strains under control and stress conditions. *(A) Growth assessment under non-stress conditions in response to P2 and P3. (B) Visualization of P2 and P3 association with Arabidopsis roots via confocal microscopy. Growth performance of P2- or P3- treated Arabidopsis seedlings subjected to either (D) 1 mM MG or (E) 150 mM NaCl for inducing stress in plants.*

SARS-CoV-2 related Research and Development

Prof. Deepak T Nair

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 in cell culture and animal models. We have determined the structure of the Fab region of P4A2 with the receptor binding domain (RBD) of the Spike protein. Our studies show that the Spike-RBD epitope for P4A2 binding overlaps with the binding site for the ACE2 receptor. The structural studies and allied computational analysis provide a rationale for the ability of P4A2 to neutralize all known VOCs of SARS-CoV-2 and suggests that this monoclonal antibody may be effective against future variants also.

Prof. Prasenjit Guchhait

We are working on the mechanism of inflammation and clot formation in the lungs resulting into fibrosis and cell death leading to hypoxemia in SARS-CoV-2 infected animals and patients (Agarwal *et al*, 2022). We are also testing anti-inflammatory/anti-thrombotic drugs in SARS-CoV-2 infected animals and investigating immune (innate and adaptive) responses (Shrimali *et al*, 2021). In addition, we are studying cytokine signaling and platelet activation in COVID-19 patients (Kaur *et al*, 2022). We are currently investigating the severity of SARS-CoV-2 infection in mice with diabetic phenotype.

Dr. Arup Banerjee

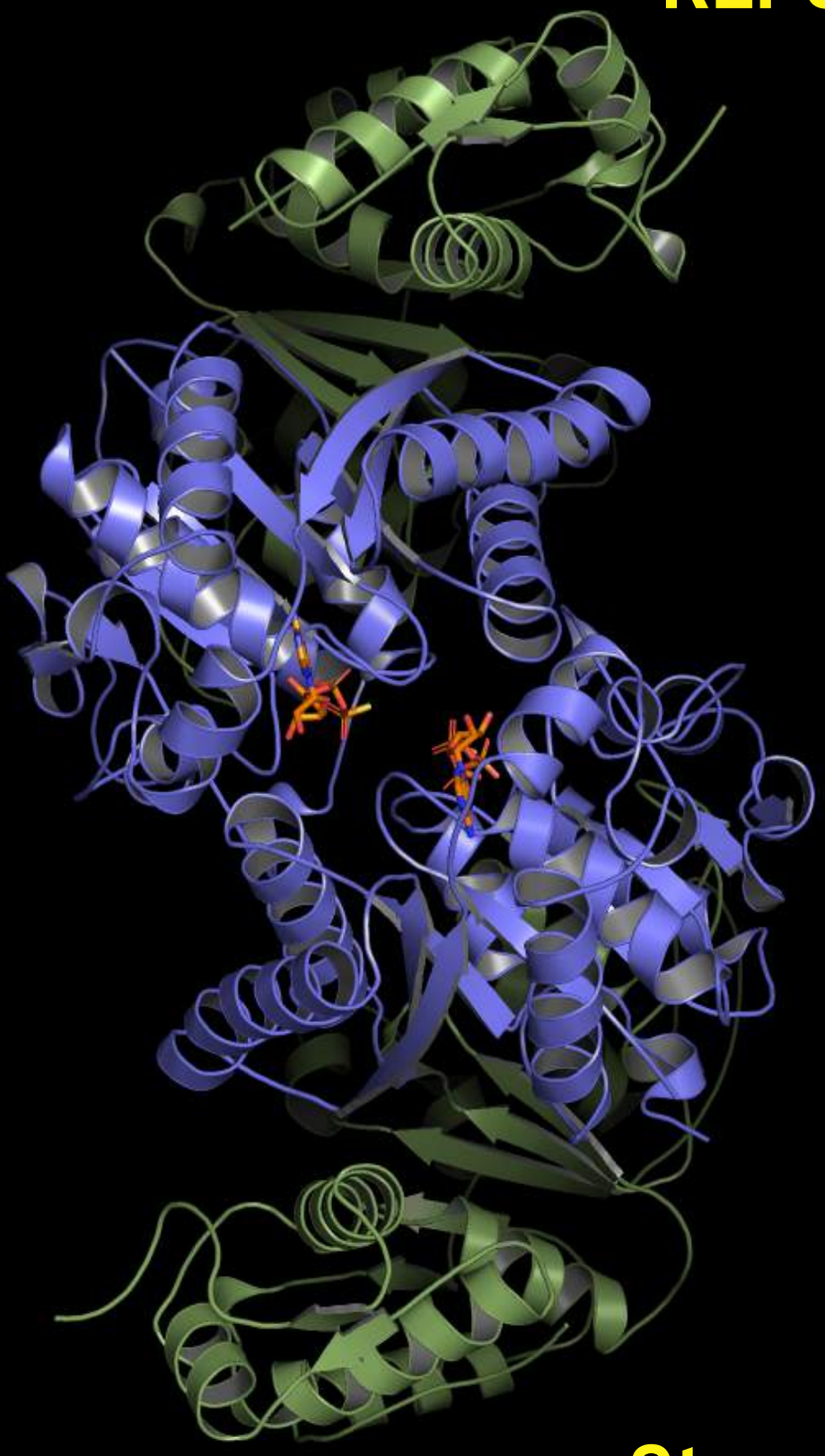
A study was conducted in collaboration with the Centre for Biomedical Engineering, Indian Institute of Technology Delhi, India exploring the possibilities of using exosomes to generate effective neutralizing antibody response and effective CTL response against SARS-CoV-2. We exploited Dendritic cells (DCs) exosomes (DEx) as a tool to tailor neutralizing antibody responses against SARS-CoV 2. Dendritic cells were isolated from murine bone marrow (BM) culture. Mature DCs were generated from immature DCs by culturing them in the presence of maturation cocktails and with or without Spike protein of SARS-CoV2. Finally, exosomes were isolated from the culture of mature DCs using ultracentrifugation techniques. The immunogenicity and efficacy of the Spike activated DEx were tested in mice and compared with free Spike protein. *In vivo* assays demonstrated that subcutaneous administration of both Spike and DEx to mice appeared safe and well-tolerated. DEx can express SARS-CoV-2 specific peptides on the surface and induce a humoral response by producing specific antibodies, which causes virus neutralization *in vitro* assay. Moreover, DEx also induces an adaptive immune response by secreting serum IL-2, IFN-γ, and IL-6 levels and inducing the differentiation of different T-cell subsets, including CD8+ and CD4+ T-cell Tfh cells (CD4+CXCR5+). However, further study is warranted to compare the efficacy of DEx with the commercially available vaccines in terms of antibody production, stability, and capacity to neutralize the virus.

Dr. Ambadas B Rode

Targeting RNA G-quadruplexes conformations in SARS-CoV-2 genome with small molecules for antiviral therapy

The severe acute respiratory syndrome virus (SARS-CoV-2) contains structured RNA elements that are involved in viral replication. Despite diverse structures and crucial functions compared to proteins, RNAs are an under-exploited therapeutic target for antiviral therapy. We have virtually screened a compounds database against four putative RNA G-quadruplexes found in SARS-CoV-2 genome. The ligands were docked against the defined active site of SARS-CoV-2 RNA G-quadruplexes to gauge their binding affinities. The docking results suggested that certain molecules could snugly fit into the active site of RNA G-quadruplexes. We have synthesized the active compounds and are screening them against SARS-CoV-2 in collaboration with Prof. Sudhanshu Vrati.

SCIENTIFIC REPORTS



Structural Biology

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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. A substantial amount of reactive oxygen species (ROS) are generated by the biochemical pathways that operate in the apicoplast and the ROS can oxidize the nucleotide pool. 8oxodGTP represents the most common oxidized nucleotide and is known to lead to transversion mutations in the genome through mispairing with template nucleotide dA. The apicoplast genome is particularly vulnerable to the harmful effects of 8oxodGTP 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. As a result, the presence of these DNA lesions will generally lead to impaired DNA replication which can ultimately lead to the death of the malaria parasite. PfpPol is the only known DNA polymerase that is present in the apicoplast and we tested the ability of this enzyme to synthesize DNA past the 8odG, Tg and 2-OHdA lesions. We observe that the PfpPol enzyme has significant ability to accurately bypass the three DNA lesions and thus neutralize their adverse effects on genome replication (Fig. 1). The residues N505 and Y509 that are unique to PfpPol play a critical role in the lesion bypass activity of this enzyme. Due to its special active site, PfpPol can carry out the generally conflicting activities of high fidelity DNA synthesis and lesion bypass. 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.

Strategies to develop evolutionarily robust therapeutic molecules

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.

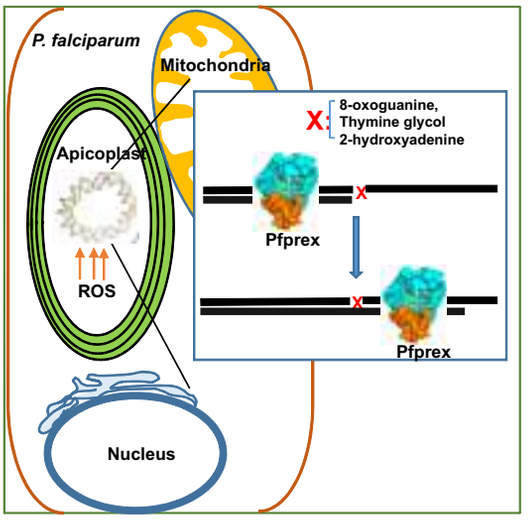

Figure 1: Schematic for the DNA lesion bypass activity of PfpPol. *The apicoplast organelle of Plasmodium falciparum possesses a circular genome which is replicated by the Pfprex enzyme. Reactive oxygen species (ROS) induce DNA lesions in this genome that can block replication. Such lesions are generally bypassed by low-fidelity translesion DNA polymerases which are absent in the apicoplast. Pfprex possesses unique residues in the active site that enable bypass of these lesions to prevent the deleterious effects of ROS on replication.*

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. 2A). The structure shows that the P4A2 Fab binds to regions on the Spike-RBD which are important for binding to the ACE2 receptor (Fig. 2B). 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.

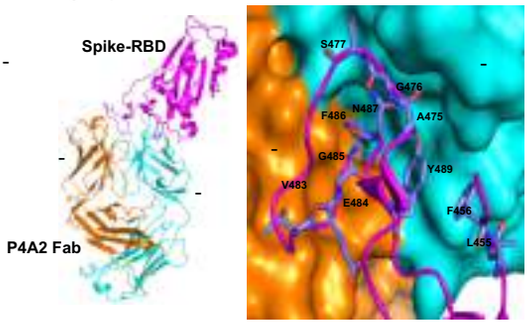

Figure 2: Structure of the P4A2 Fab in complex with Spike-RBD of SARS-CoV-2. *(A) Structure of P4A2 Fab in complex with RBD of Alpha variant. The heavy (H) and light (L) chain of P4A2 Fab are coloured in orange and cyan, respectively and the RBD is coloured magenta. (B) Surface representation of the P4A2 paratope with the RBD epitope is shown. 486Phe from RBD is present in a hydrophobic cavity formed on the paratope. The residues 455Leu, 456Phe, 486Phe, 487Asn, and 489Tyr are also critical for ACE2 binding and hence binding of P4A2 mAb to the Spike-RBD will prevent entry of the SARS-CoV-2 virus into cells.*

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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) that mediate the initial contacts 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

Ligilactobacillus (formerly Lactobacillus) *rhamnosus* GG (LGG), a well-known probiotic strain for its various health-promoting effects, contains two different sortase-mediated pilus operons. The *spaCBA* operon encodes a major pilin (SpaA), two minor pilins (SpaB and SpaC), and a C-type sortase. Similarly, the *spaFED* encodes a major pilin (SpaD), two minor pilins (SpaE and SpaF), and a C-type sortase. While the C-type sortase (SrtC) catalyzes the pilus polymerization, a housekeeping A-type sortase (SrtA) attaches the assembled pilus to the cell wall. The LGG pili play a crucial role in adherence, persistence, and beneficial health effects. We have previously determined the crystal of LGG pilins except for SpaF and revealed new insights about pilus shaft formation and pili-mediated interaction. We have produced SpaF, and its structure determination is in progress. For the first time from a non-pathogenic host, we have solved crystal structures of sortases (Fig. 3), constituting a prototype model for probiotic bacteria.

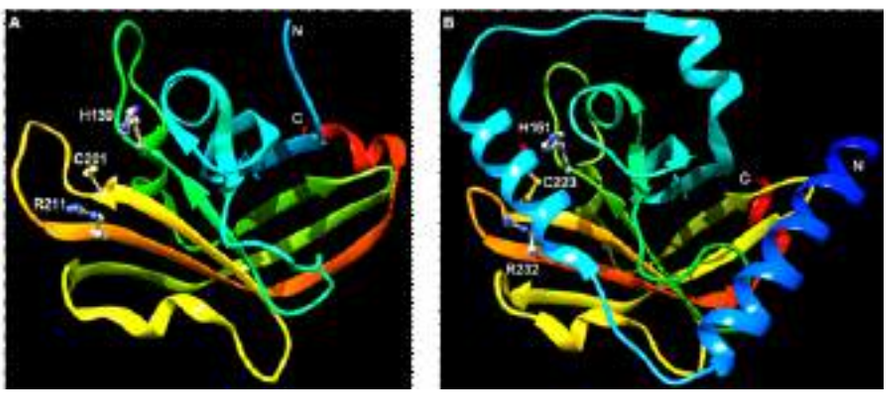

Figure 3: Crystal structure of sortases from Ligilactobacillus rhamnosus GG *(A) Structure of housekeeping sortase (SrtA). (B) Structure of pilus-specific sortase (SrtC). Structures are shown in ribbon representation with a blend through (i.e., blue to red) colors. The catalytic residues (in ball and sticks) and termini are labeled.*

Ligilactobacillus ruminis (LRU) is a member of the indigenous microbiota present in the gut of humans and animals. In addition to its probiotic effects, the LRU is an indispensable agent in the fermentation of foods and feed. 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 seem different from LGG pili, it likely represents a third sortase-mediated pilus type in Ligilactobacillus species. We have produced and crystallized LRU pilins (Fig. 4). We have collected high-resolution X-ray diffraction data from the pilin crystals and developed successful strategies to determine structures. A bifidobacterial strain was included in the structural investigations for comparison.

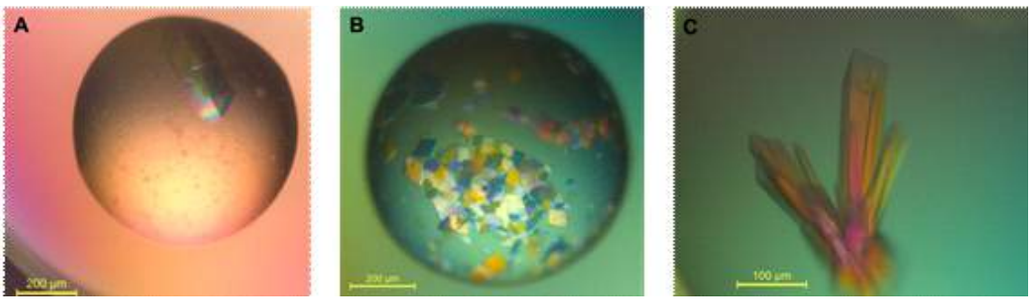

Figure 4: Crystals of Ligilactobacillus ruminis pilus proteins. *(A) LrpA crystal. (B) LrpB crystals. (C) LrpC crystals. The scale bar and its size are indicated in the images.*

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*) 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 sortase-mediated pilus containing three types of pilins (tip, backbone, and basal), the PI-2 pilus in *S. oralis* is a heterodimeric structure with only the tip (PitA) and backbone (PitB) pilins. The PI-2 pilus constituents also possess other unusual attributes (e.g., a noncanonical sorting motif and the absence of a pilin motif). We have determined the crystal structures of PitA and PitB. PitA consists of four immunoglobulin (Ig)-like domains and a von Willebrand Factor A (vWFA) domain, while PitB consists of two extended Ig-like domains. Our initial structural analysis indicates that the adhesive vWFA domain might involve receptor binding. We are now performing both *in vitro* and *in vivo* experiments to examine the role of pili in mediating attachment with host surfaces and other primary colonizers for plaque development.

Collaborative projects

Mycobacterium tuberculosis (Mtb) is the causative agent of tuberculosis (TB), one of the deadliest infectious diseases. The pathogen Mtb can develop a complex relationship with its host and persist in host tissues for decades without causing disease. To enhance our current knowledge of the complex host-pathogen interactions in TB, we have determined the structures of critical molecules (VapB12 and MMAR_2190) from the Mycobacterium genus.

Natural products continue to be an essential source of leads for new medicines. As part of the herbal biotechnology collaborative project, the binding potential of piperine from black pepper extract with targets SMAD1 (mother against decapentaplegic protein homolog 1) and STAT3 (signal transducer and activator of transcription 3) was studied by computational analysis to evaluate the effect of piperine on anemia of inflammation.

Deepti Jain
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Transcription Regulation: Structure and Mechanism

Resistance to antibiotics represents an escalating challenge in the treatment of bacterial infections. Pathogenic bacteria such as *Pseudomonas aeruginosa* are known to switch phenotype to reduce sensitivity towards antimicrobial agents. These phenotypic transitions are 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 in pathogenic bacteria. The mechanistic insights obtained are exploited for the development of novel therapeutic agents.

Regulation of biofilm and flagellar genes in Pseudomonas aeruginosa by FleQ

Pseudomonas aeruginosa is an opportunistic human pathogen with rising cases of antimicrobial resistance. The pathogen is known to transition from a motile to biofilm phenotype to evade antimicrobial agents. This ability is regulated by transcription modulators called bacterial enhancer-binding proteins belonging to AAA+ (ATPase associated with various cellular activities) family of proteins. The activity of these proteins is regulated by anti-activators. Recent studies from our laboratory have delineated the structural mechanism of anti-activation of transcription factor. We have determined the crystal structure of the complex and characterized the interactions between the transcription activator and its anti-activator (Fig. 5). We have shown that the anti-activator inhibits the catalytic activity of the activator and also prevents the formation of the functional form of the activator. The data reveal that FleN allosterically prevents ATP binding to FleQ. Furthermore, FleN remodels the region of FleQ essential for engagement with RNA polymerase for transcription initiation. Disruption of the conserved protein-protein interface, by mutation, shows motility and transcription defects in vivo and multiflagellate phenotype. Our study provides a detailed mechanism utilized by monoflagellate bacteria to fine-tune the expression of flagellar genes to form and maintain a single flagellum.

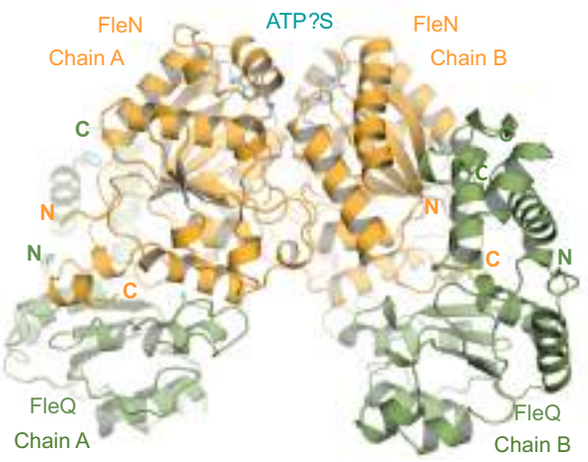
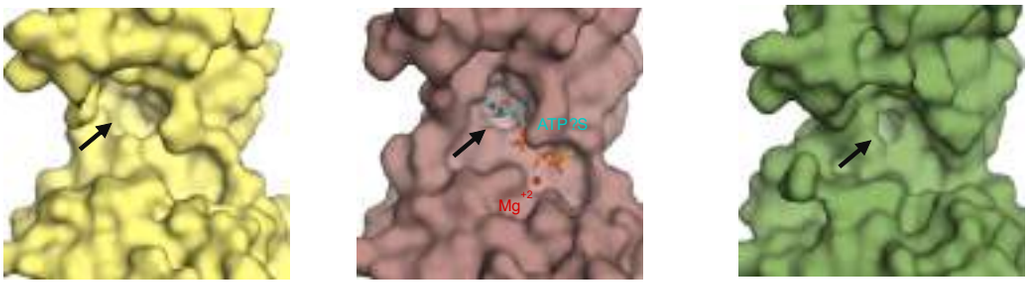


Figure 5: Structure of FleN-ATP S-FleQ$_{AAA+}$ complex. *FleN-ATPγS-FleQ$_{AAA+}$ structure showing FleN dimer (orange) in complex with ATPγS (cyan), interacting with FleQ$_{AAA+}$ domains (green) forming a heterotetrameric complex.*

Compared to the earlier determined structure of FleQAAA+-ATPγS, the conformation of FleQ in the FleN bound structure reveals surprising features. There is rigid body movement of the sub domains, towards the bound FleN to form a more compact structure compared to ATPγS bound form. As a result, the ATP binding site of FleQ becomes too constricted to accommodate the nucleotide triphosphate (Fig. 6). It was hence not surprising that there was no electron density for the nucleotide in the active site. 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 FleQ. These molecules will be further examined for their

ability to bind and inhibit the ATPase activity of FleQ through in vitro assays and eventually for their ability to inhibit biofilm.



FleQ Apo
PDB – 5EXP

FleQ ATP - Mg^{+2} complex
PDB – 6J7E

FleQ from FleQ- FleN
complex structure

Figure 6: Conformational changes in FleQ AAA+ domain. *Surface representation of $FleQ_{AAA+}$ in Apo, in ATPγS and Mg^{+2} bound and in FleN-ATPγS-$FleQ_{AAA+}$ structure (smudge), depicts the conformation of ATP binding pocket (pointed with black arrows)*

Regulation of flagellar genes in Pseudomonas aeruginosa by FleR

FleSR is a two-component signal transduction system which serves as a critical checkpoint in flagellar formation and assembly in *Pseudomonas aeruginosa*. It regulates the expression of 26 flagellar genes. Knockout of FleR renders the bacterium non-motile. The two component signalling (TCS) systems couple the environmental or cellular signals to the alteration in the gene expression profile of the bacterium. TCS are deployed in bacteria as a part of adaptation strategy to various environmental conditions. FleR is the bacterial enhancer-binding protein of the AAA+ ATPase superfamily that undergoes phosphorylation *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. The structural details reveal that FleR, exists predominantly as a monomer in the inactive form and assembles into hexameric discs upon activation. Further, the REC domain positively modulates the assembly of the functional FleR. The structural, biochemical and *in vivo* data provide details of the phosphorylation mediated assembly of functional FleR to regulate the expression of flagellar genes to form and maintain the flagellum. The analysis uncovers the mechanism utilized by the two-component signal transduction to regulate the assembly of AAA+ domains. Through the in vivo experiments we demonstrate that phosphorylated REC domain is required for the transcription activation by FleR. 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.

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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 to identify 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 *M. tuberculosis* (Mtb) under different stresses and how a mega Dalton protein synthesis machinery, the ribosome, assembles inside the cell. We apply structural biology tools: cryo- electron microscopy and X-ray crystallography with molecular biology and biochemistry techniques.

Understanding the translation strategies *M. tuberculosis* adopts in different stresses

Mtb is the causative agent of one of the most deadly bacterial diseases, tuberculosis (TB), which remains a major health threat to the human race. MTb becomes dormant, nonreplicating and phenotypically drug-resistant when it encounters multiple stresses within the host macrophages. This condition is also known as latent tuberculosis infection (LTBI), dormancy. Nearly one third of the world population possesses LTBI, from which ~10% of LTBI infected develops acute Tb infection. The nonreplicating persistent mycobacteria during latent TB infection slow down all cellular processes, including protein synthesis, making the ribosome-targeting antibiotics less effective in treating tuberculosis. Therefore, the latent Mtb infection serves as a reservoir for TB spread.

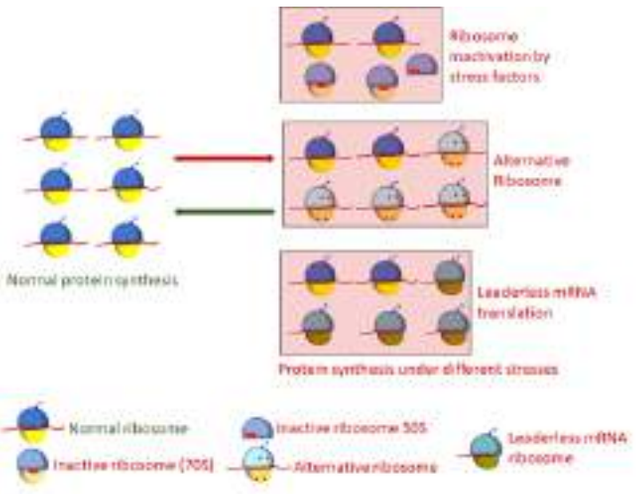


Figure 7: Hypothetical model proposed for M. tuberculosis's strategies to cope with the different environmental stresses. *Normal protein synthesizing ribosomes, ribosomes inhibited by stress factors, alternative ribosomes, and leaderless mRNA translating ribosomes are shown with a different illustration.*

The Mtb has evolved with different mechanisms to survive in the harsh environment inside the macrophages (Fig. 7) and is able to evade the host immune response. Mtb changes its translational landscapes in response to environmental changes. When mycobacteria encounter different stresses, it modulates their protein synthesis. It may adopt the following strategies, as illustrated in Fig. 7. Promoting hibernation and inactivating ribosome in its 70S form, stabilizes its 50S subunit, reprograms its ribosome composition by replacing C- paralogue of r-protein, forming 61S ribosome, switching to leaderless mRNA translation, or inactivating its translation apparatus by toxins. Consequently, total eradication of Mtb remains a challenge, and tuberculosis is still a major health threat to society. A thorough understanding of Mtb's translational strategy for its survival in latent tuberculosis infection and survival under different stresses would provide mechanisms to target dormant and persistent mycobacteria.

Translation regulation in hypoxia induced dormancy

To mimic the host macrophage stress environment, different models have been developed, and most widely accepted models are: (1) Wayne hypoxia model, (2) Lobel nutrient starvation model and (3) Multi stresses condition model in which mycobacteria are grown in low

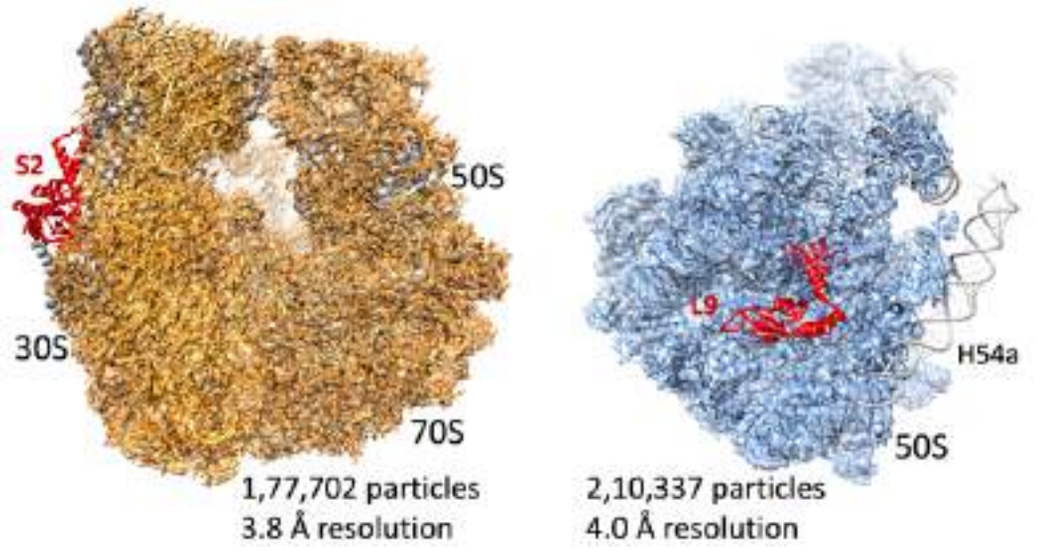
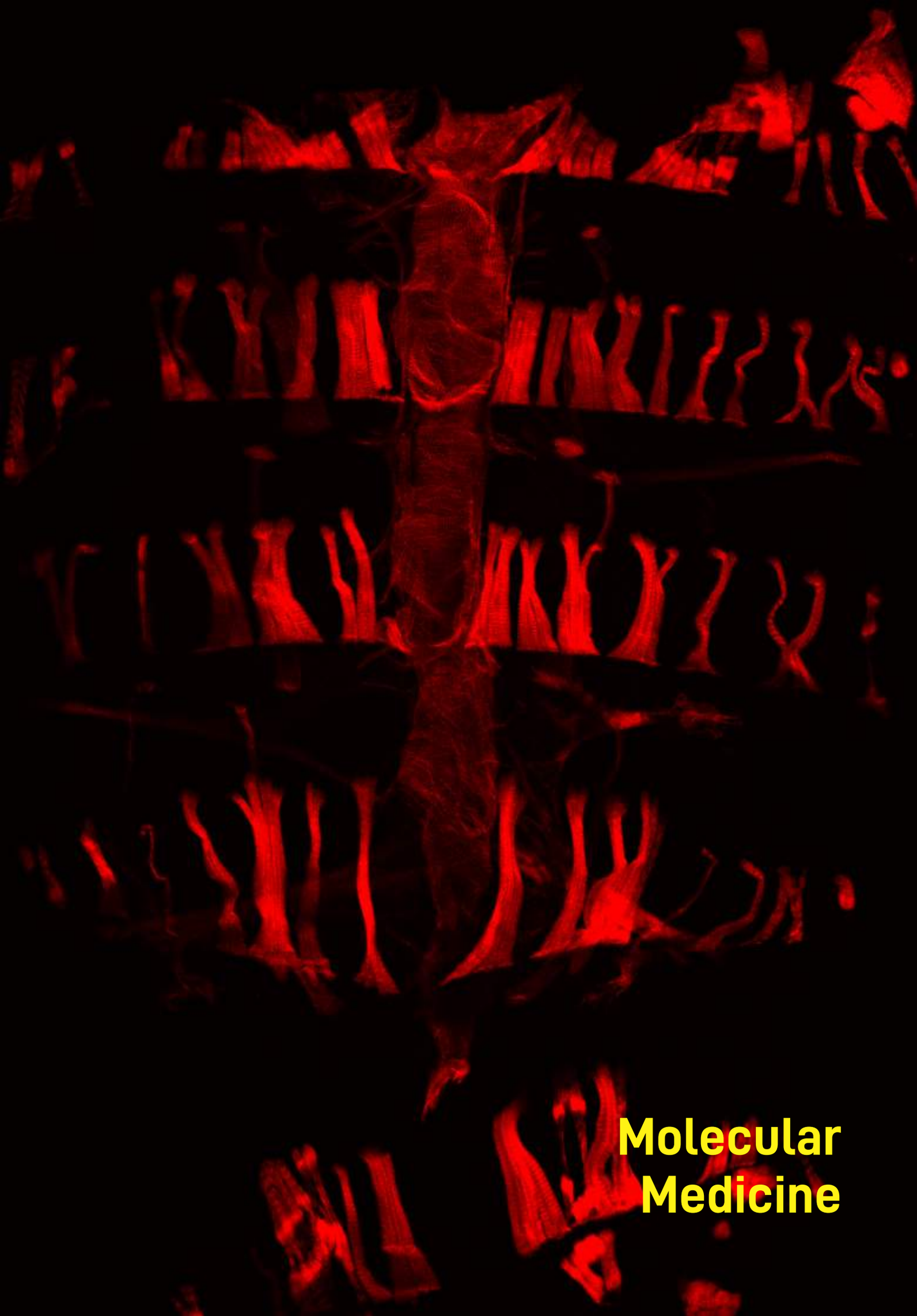


Figure 8: Cryo- EM structure of M. smegmatis 70S and 50S ribosome. Final 3.8 Å resolution 70S ribosome map (orange) with coordinates of the normal 70S docked (grey), missing density for S2 protein (red) shown in the left panel. *A final 4.0 Å resolution 50S ribosome map (blue), with the coordinate of the normal 50S docked (grey) missing electron density for L9 (red), are shown in the right panel. The initial optimization of cryo- EM data collections were carried out in JEOL 2200FS microscope with K2 submit camera at ATPC, RCB, Faridabad. The high resolution images were collected in Titan Krios with Falcon 3 camera at National Facility for electron cryo microscopy, InStem, NCBS, Bangalore.*

oxygen content, low nutrient conditions and different stresses conditions, respectively. We grew the *M. smegmatis* under hypoxia by following the Wayne hypoxia model. The cells were grown at 37°C in airtight flasks, and methylene blue dye was added as an indicator for oxygen concentration. The ribosomes were isolated and purified, and single particle cryo- EM data were collected in move mode. For the hypoxia 70S and 50S ribosomes, we have obtained 3,815 and 3,723 movie stacks from the National Electron cryo- EM facility, NCBS, Bangalore. The single-particle reconstruction was performed using RELION 3.1, and data were processed to 3.8 Å and 4.0 Å resolution, respectively. The docking coordinates of normal ribosomes show some unique features associated with hypoxic ribosomes. The ribosomal proteins S2 and L9 appear to be missing (Fig. 8). The helix H54a adopts a different conformation in its 50S ribosome (Fig. 8).

Further analysis is in progress, and we aim to find unique features of hypoxia stressed ribosomes that could be a potential target for developing antituberculosis drugs.



Molecular Medicine

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Thrombosis, Thrombophilia, Inflammation and Immune Response in Human Diseases

This research program is designed to understand the molecular mechanism of **1)** thrombosis, thrombophilia and inflammation in the lung leading to hypoxemia, and host immune responses in COVID-19 infected animal and human. **2)** Host inflammatory immune responses in Dengue and JEV infected animals and human. **3)** How the gain-of-function PHD2 mutations in Tibetans protects the native highlanders from hypoxia-induced anomalies. Implementation of this lesson for developing therapeutics for mountain travelers against acute mountain sickness (AMS) and high-altitude pulmonary edema (HAPE). **4)** Hyperglycemia-mediated thrombosis, thrombophilia, inflammation and immune responses in mice model of type-2 and type-1 diabetes, and patients. **Finally**, identifying biomarkers and molecular targets to develop potential therapeutics for the above diseases.

COVID-19: COVID-19: We investigated the mechanism, how SARS-CoV-2 induces 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) rescues the inflamed lungs and restores oxygen pressure saturation (SpO_2) in circulation of the SARS CoV-2 infected hamsters and mice by increasing PHD2-mediated inhibition of Akt phosphorylation (pAkt), without affecting anti-viral response of T cells and IgG, Figure-1 (Shrimali et al, 2021, Agarwal et al, 2022). Currently, we are investigating the severity of SARS-CoV-2 infection in mice with diabetic phenotype. In another work, we investigated an elevated plasma level of pro-inflammatory cytokines including IL6 and TNFα in conjunction with increased platelet activation in patients with severe form of COVID-19 infection compared to asymptomatic counterparts. Using whole transcriptome data, we show that an upregulation of pathways including IL6 and TNFα signalling pathways along with hyperactivation of coagulation and thrombotic pathways in the platelets of severe patients compared to asymtomatic, thus highlighting the cytokine-mediated

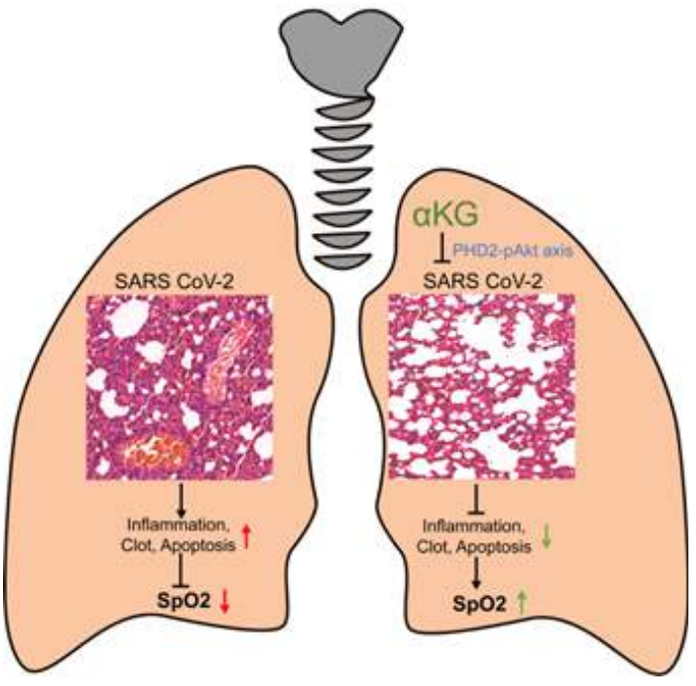

Figure 9: Schematic describes an elevated inflammation, thrombosis and apoptotic tissue damage in the lungs of SARS CoV-2 infected animals leading to a condition called hypoxemia or decreased oxygen pressure saturation (SpO_2) in circulation. *In contrast, γKG supplementation rescues animals from SARS CoV-2 mediated above clinical events by increasing PHD2-mediated inhibition of pAkt, resulting in a restoration of normal SpO_2. γKG does not affect the anti-viral response of IFNγ+CD4 and IFNγ+CD8 T cells, and IgG. Agarwal S et al, 2022, BIORXIV/2022/486853*

Dengue and JEV: Recently we reported that platelet factor 4 (PF4) is pro-viral for both Dengue virus (DV) and Japanese Encephalitis virus (JEV). PF4 inhibits interferon (IFN) - and promotes viral replication (Ojha *et al*, 2019). Further our unpublished data confirm the above observation in PF4-knockout mice showing less infection of both viruses in immune cells. Our unpublished data also show that a small-molecule antagonist to CXCR3, receptor of PF4, significantly inhibited PF4-induced virus replication and rescued the disease phenotypes for both viruses. Both unpublished works are in final stage.

AMS and HAPE: Recently, we have shown that the Tibetan specific variant of Prolyl hydroxylase-2 (PHD2), known as $PHD2^{D4E/C127S}$ protects these highlander individuals form hypoxia-triggered elevated inflammatory response by downmodulating several transcription factors including HIF1α and p65. We found that the cofactor of PHD2, common metabolite α-Ketoglutarate (αKG) augments $PHD2^{WT}$ activity and protects mice from hypoxia-induced exaggerated lungs inflammation (Bhattacharya S *et al*, 2021). Thus, suggesting the use of αKG in the prophylaxis of systemic as well as lungs inflammation, commonly observed in AMS and HAPE. Further, our unpublished data show that monocytes from $PHD2^{D4E/C127S}$ individuals are susceptible for infection under normoxic environment but are protected from viral infection under hypoxia.

Diabetes: Our unpublished data show a parallel correlation among hyperglycemia, thrombosis/thrombophilia and inflammation in db/db mice or patients with type-2 diabetes (T2D). Our data also show that glycosylation of platelet glycoproteins is associated with hyperactivation of platelets in T2D patients. Another work shows that mice with type-1 diabetes (T1D) are susceptible to viral infections alongside significant alteration in both innate and adaptive immune responses of the mice. We are currently exploring these observations. proof to our above concept of pro-viral role of PF4, we observed a decreased propagation of JEV *ex vivo* in monocytes from PF4-deficient mice. Contrastingly, monocytes from PF4-overexpressed mice shows more expression of viral NS1 protein .

Figure 10: Schematic showing mechanism of platelet activation in severely ill COVID-19 patients. *An elevated plasma IL-6 and TNFα coexisted with the upregulated pathways like IL-6 and TNF signalling, pro-coagulation and thrombosis, inflammation and ROS metabolism in platelets of ICU patients. Thus, suggesting that these cytokines may be the risk factor for platelet activation and related malady like thrombophilia in these patients. Kaur S et al. 2022, Blood Cells Molecules and Diseases, 94:102653.*

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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.

Mechanistic insight into α-synuclein mediated neuroinflammation in Parkinson's disease

Parkinson's disease (PD) is one of the most common neurodegenerative disorders worldwide, which affects almost 2% of the world population, over age of 60. The pathological hallmarks of PD are progressive loss of dopaminergic neurons in the substantia nigra along with chronic inflammation, mitochondrial dysfunction and accumulation of α-synuclein rich protein aggregates in form of Lewy body. α-Synuclein is a small intrinsically disorder protein that plays a crucial role in synaptic vesicle formation and its trafficking. Recent studies have shown that type 2 diabetes mellitus is one of the risk factors for PD. Individuals with diabetes mellitus have 35% risk of developing cognitive and motor impairment and finally Parkinson's disease. In fact, hyperglycaemic state in an individual produces more methylglyoxal (MGO) due to altered carbohydrate metabolism or impairment of glyoxalase system. MGO is a di-carbonyl compound that spontaneously modifies Lysine, Arginine and Cysteine residues of proteins and generates advance glycation end products (AGEs). Proteins with AGEs have been shown at the periphery of Lewy bodies and their levels are increased in the brain of PD patients. Here, we show that glycation of α-synuclein perturbs the aggregation kinetics and prevents fibrilization through the alteration of surface charges of N-terminal domain residues (Fig. 11).

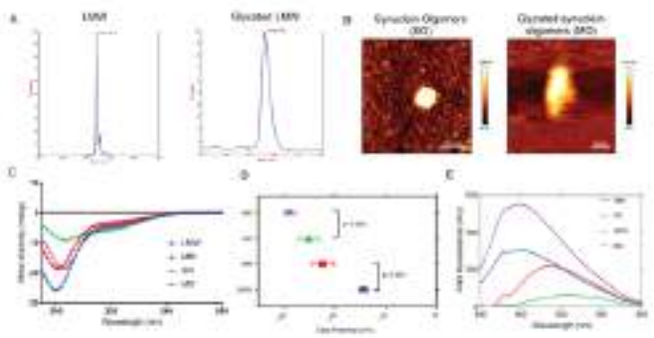

Figure 11: Glycation of α-synuclein alters the morphology and topology of synuclein oligomers. *(A) Intact mass analysis using MALDI mass spectrometry demonstrating increase of mass of low molecular weight (LMW) species of α-synuclein upon modification with glycation (MM). (B) High resolution AFM showed distinct morphology synuclein oligomers (SO) and Modified oligomers (MO), respectively. (C) CD spectroscopy revealed differences in secondary structure of SO and MO. (D) Zeta potential analysis revealed the overall surface charges of synuclein species. MO and MM showed more negative potential than SO and LMW, respectively. (E) ANS fluorescence revealed that MO and MM expose greater hydrophobic surface to solvent than SO and LMW.*

Proteomic analysis of microglial cells treated with glycated oligomers provides evidence of alterations in endocytic mechanism, mitochondrial dysfunction, and inflammatory cascades. The microglial activation leads to chronic neuroinflammation and is also one of the hallmarks of PD. An activated microglial signature has been observed in the post-mortem PD brain. Microglia tirelessly survey the micro-environment and are able to recognize any minute changes. During neuronal transmission of α-synuclein, microglia sense, engulf and clear the extracellular α-synuclein to maintain homeostasis in brain. The

uptake of α-synuclein oligomeric species is dependent on TLR2 receptor of microglia. TLR2 mediated microglia activation is conformation specific such that monomeric and fibrillar species fail to act as TLR2 agonist. Recently, NLRP3 inflammasome activation has been reported in post-mortem PD brains. Interestingly, α-synuclein fibrils have also been shown to activate the NLRP3 inflammasome. α-Synuclein produces large number of structural ensembles and produces diverse oligomeric intermediates. This brings up a question that how do these diversified α-synuclein species and strains modulate microglial inflammatory processes. In this study, we employed various biophysical and biochemical methods to demonstrate the conformational differences between glycated synuclein oligomers (MO) and wild type synuclein oligomers (SO), along with their conformation driven microglia activation pathways. Our results show that glycation of α-synuclein generates oligomers of different morphologies and exhibit reduced membrane binding. Surface charge alteration in the N-terminal domain inhibits seed amplification for further fibrilization of α-synuclein. Our findings also reveal that MO choose clathrin-dependent endocytic pathway and activate microglia, preferably via. inflammasome pathway (Fig. 12). Holistically, this study addresses the link between diversity of synuclein oligomeric strains and the modulation of neuroinflammation

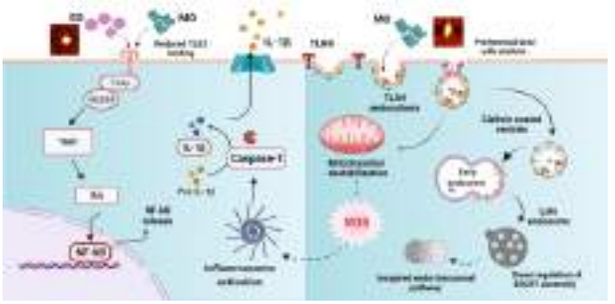

Figure 12: Glycation contributes to conformational heterogenicity of α-synuclein oligomers and modulates microglia activation. *α-Synuclein oligomers possess doughnut shape morphology with specific topology. The α-synuclein oligomers activate microglia by binding with TLR2 leading to the release of NF-αB, which further enhances the inflammasome mediated-IL-1α pro-inflammatory cytokines release. However, glycated oligomers show lesser binding to TLR2 and induce the endocytosis of TLR4 followed by its degradation. The glycated synuclein oligomers preferably activate inflammasome assembly by destabilizing the mitochondria and ROS production.*

Development of prenyltransferase-based labelling technology for imaging applications

Protein tagging is critical for studying dynamic biological processes. Although fluorescent protein tags are commonly used for visualisation of the protein of interest, their large size, weak fluorescence, and rapid photobleaching limit the utility. Chemical fluorophores, on the contrary, are smaller, brighter, and more photostable. However, site-specific labelling is challenging in complex cellular environment. We hypothesise that site-specific combination of a short genetically encoded peptide tag with a small-detection reagent will aid in the development of a technology for understanding various biological processes. In this effort, we aim to develop a novel enzyme-based protein/peptide labelling technique relying on PagF, a prenyltransferase, that can recognises short-peptide motifs and labels it with isoprenoid moiety. We have effectively generated and evaluated peptide tags that are selective to PagF using peptide-protein interaction studies. Unique fluorophore-conjugated isoprenoid analogues are being synthesised chemically. We believe that our work will lead to development of 'Peptide-dependent Prenyltransferase-mediated Probe Incorporation (PPPIn)' labelling-system for varied applications.

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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. The skeletal muscle can get injured in accidents, during physical activity such as sports, or due to congenital diseases such as muscular dystrophy. A tissue resident pool of stem cells known as satellite cells, present in the skeletal muscle, help in its repair and regeneration. We are studying how skeletal muscle regeneration occurs, specifically looking at the genes that regulate satellite cell function. We are also studying the signaling events that result in a cancer type called rhabdomyosarcoma, where the tumor cells exhibit properties of muscle cells.

TLE4 regulates muscle stem cell function

Satellite cells or the skeletal muscle stem cells mediate skeletal muscle regeneration following muscle injury or disease. Satellite cells occupy their niche between the muscle fiber plasma membrane and the basal lamina, where they remain quiescent under normal conditions. Pax7 is a homeobox transcription factor expressed by satellite cells, which is crucial for satellite cell identity and function. Upon muscle injury, satellite cells perceive signals from the damaged muscle fibers and undergo a process known as activation, wherein they start expressing proteins such as Myf5, which promote differentiation. Activated satellite cells exit their niche, proliferate rapidly, migrate to the injury site, fuse to the damaged muscle fibers to repair and regenerate the fibers. While most satellite cells fuse to damaged fibers and differentiate, some undergo self-renewal whereby they repopulate the niche. One of the key questions in the field is how satellite cells decide between differentiation and self-renewal fates following activation. Identifying such regulators would be vital to understanding stem cell function and associated therapeutic strategies.

The Transducin-like Enhancer of Split (TLE) proteins are a family of corepressors with wide ranging functions in animal development, tissue differentiation and regeneration. We found that one family member, TLE4, is expressed by satellite cells in the muscle (Fig. 13). Studying TLE4 expression carefully in the satellite cells of isolated muscle fibers, we observed that a proportion of satellite cells downregulate TLE4 during the early stages of satellite cell activation (Fig. 13). Thus, we were able to identify Pax7+TLE4+ and Pax7+TLE4- satellite cells during muscle fiber culture, where the Pax7+TLE4- satellite cells were seen only until 24 hours. This suggested that TLE4 expression is transiently downregulated in satellite cells during early stages of activation, associated with muscle regeneration.

Next, we characterized the in vivo function of TLE4 during skeletal muscle regeneration by siRNA-mediated knockdown of TLE4 in the tibialis anterior (TA) muscle of the hind limb,

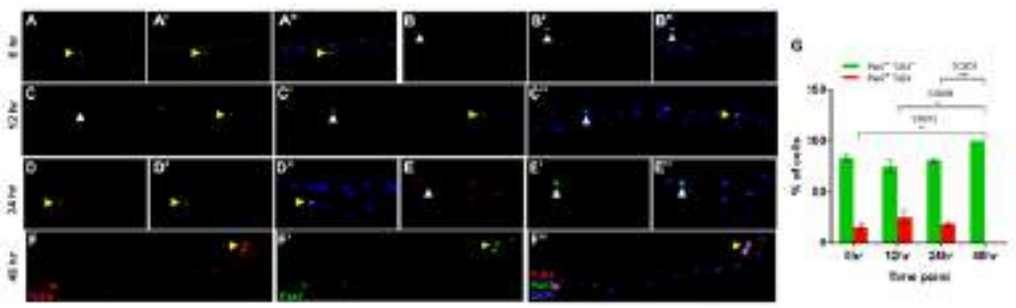

Figure 13: TLE4 is expressed by muscle stem cells. *(A-F") Muscle stem cells on isolated mouse muscle fibers labeled for TLE4 (red), Pax7 (green) and DAPI (blue), at 0 hours (A-B"), 12 hours (C-C"), 24 hours (D-E") and 48 hours (F-F") after fiber isolation and culture; yellow arrowheads indicate Pax7+TLE4+ stem cells and white arrowheads indicate Pax7+TLE4- stem cells. (G) Quantification of Pax7+TLE4+ and Pax7+TLE4- stem cells.*

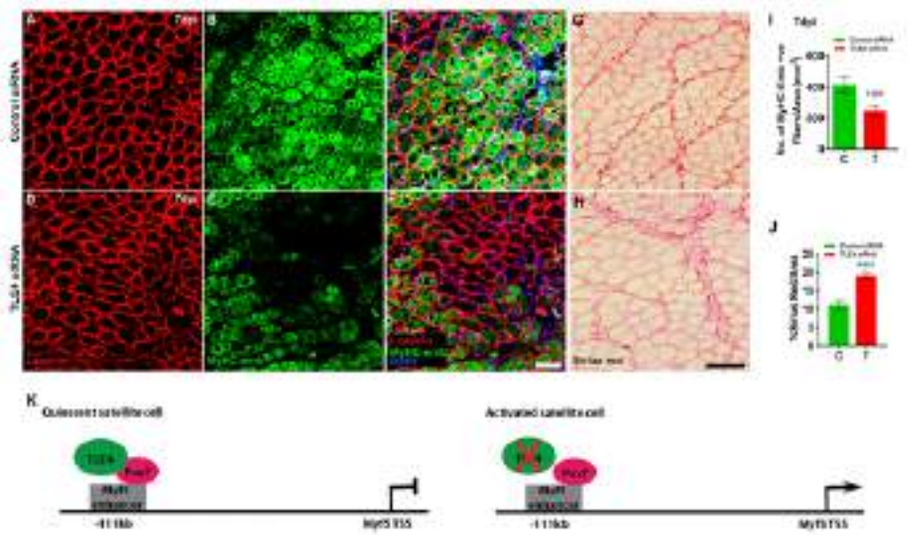

Figure 14: TLE4 is required for proper skeletal muscle regeneration. *(A-H) Cross sections through control siRNA (A-C, G) and TLE4 siRNA (D-F, H) electroporated mouse TA muscle 7 days post-injury, labelled for laminin (red), MyHC-emb (green), and DAPI (blue) (A-F) or Sirius red (G-H). (I-J) Quantification of the MyHC-emb+ and Sirius red+ area in control siRNA and TLE4 siRNA electroporated TA muscle. (K) Model detailing the role of TLE4 in regulating Myf5 expression during muscle regeneration.*

which was subjected to injury. We found that TLE4 knockdown led to reduced expression of the differentiation marker myosin heavy chain-embryonic in the injured TA (Fig. 14). In addition, increased fibrosis was observed in the regenerating TA upon knockdown of TLE4 (Fig. 14). These results indicate that TLE4 is essential for proper muscle regeneration and its knockdown results in impaired regeneration. Thus, we have identified a novel function of the co-repressor TLE4 in skeletal muscle differentiation and regeneration, which could be of importance in developing therapies to treat muscle injury and diseases.

Modulation of MET signaling and its role in myogenesis

Cell signaling by receptor tyrosine kinases/RTKs is vital to biological processes, and its dysregulation underlies numerous diseases. Signaling from Met, a RTK, is crucial to migration of muscle precursors during muscle formation/myogenesis in the embryo and in post-injury muscle regeneration. Deranged MET signaling is implicated in rhabdomyosarcoma (a pediatric cancer) where tumor cells resemble muscle precursors but fail to differentiate. Therefore, MET signaling is a shared feature between muscle development, regeneration and disease, and to ascertain its role in myogenesis I am using mouse genetics to ablate/knockout MET in muscle precursors. Animals lacking MET in embryonic/early stages do not survive to birth but are alive until embryonic day-E16.5. Contrarily, MET ablation in fetal/later stages has no impact on survival, suggesting that the embryos have crossed the critical developmental stage. I am trying to identify the stage of in utero lethality and understand the underlying mechanism. This work will provide context to understand the diverse physio-pathological roles of MET signaling.

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Understanding Taste and its Modulation using *Drosophila Melanogaster*

Taste is an essential sensory modality that influences food intake and allows animals to evaluate palatability, nutritional content of food sources and avoid consumption of toxic food. Nutrient homeostasis and its tight regulation is critical for overall health. 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 and causal relationship between taste identities and behavior, we are using genetic model system *Drosophila melanogaster* that can sense the same taste stimuli as mammals (sweet, sour, water, salt, umami and bitter). My lab is interested in understanding how the fruit flies make feeding decisions? Specifically, we are interested in understanding how the taste information is wired in the brain and how it gets modulated by physiological state, intrinsic and extrinsic factors. Understanding how taste preference reshapes 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 as well. Answering these questions may open up avenues to reduce diet-related diseases and other neurological disorders and ultimately, how neural pathways can be targeted for better drug treatment.

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 allow 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 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. 15) 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.

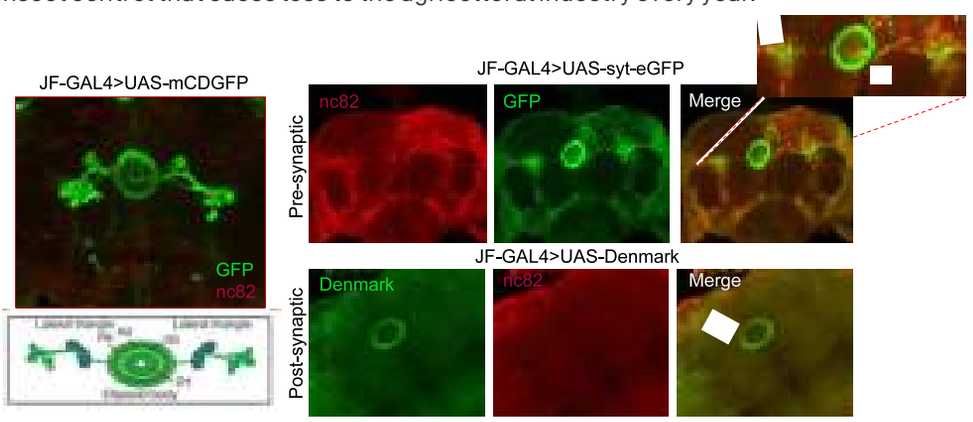


Figure 15: Newly identified Foraging-feeding circuit in adult fly brain. *A. JF-GAL4 (JF-GAL4>UAS-mCD8GFP) line marking ring neurons of Drosophila central complex (visualized with anti-GFP- green). Structure of ring circuit shown below. For all brain images, neuropil is stained with anti-nc82 (red). B. Pre-synaptic terminals marked syt-eGFP (B' is a zoomed image of GFP expressing region). C. Post synaptic areas marked with genetic construct UAS-Denmark (m-cherry).*

Understanding post-ingestive gut brain circuitry using Drosophila melanogaster

In animals including flies, 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. Over consumption of sugar is an important contributor to increase in obesity rates.

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 for their functions never studied before in gut particularly to dissect the neural basis for sweet taste preference. We have already performed a screen and have identified potential GRs that are present in the gut and play a key role in modulating taste behaviour. We are now looking at the mechanism by which these taste circuit 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 affords 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.

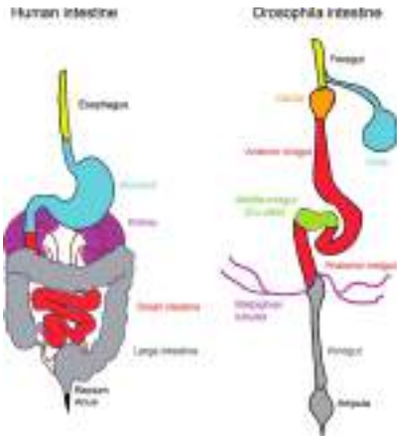
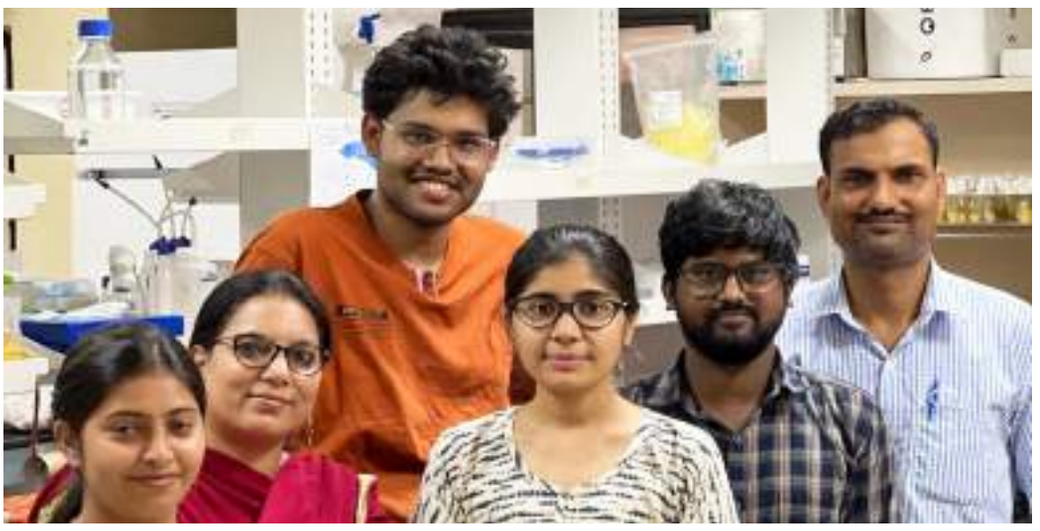


Figure 16: Comparison between human and Drosophila gut. *Organs with similar functions are coded with same colors. Drosophila contains many tissues/organs that functionally resemble to most essential human gastrointestinal system: Esophagus (foregut), midgut (small intestine) and large intestine (hindgut), stomach (crop), kidneys (malpighian tubules).*



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RNA Biology of Aging and Dietary Restriction

Aging is characterized by a progressive decline in physiological function, which leads to an increased risk of chronic degenerative diseases. Deregulated nutrient signaling is one of the key hallmarks of aging, and restricting nutrient intake or dietary restriction (DR) has been shown to enhance health and longevity most species. More significantly, DR delays age-related pathologies associated with diabetes, cardiovascular diseases, cancer, and neurodegenerative disorders. Emerging evidence from diverse model systems has implicated micro-ribonucleic acids (miRNAs) as critical components of signaling pathways that modulate lifespan by regulating mRNA turnover and translation. These small noncoding RNAs direct effector complexes to target mRNAs and silence the target mRNA. Since the interaction of a miRNA and its target occurs by imperfect base-pairing interactions, a single miRNA can target several mRNAs in a given context. Thus, these dosage-sensitive effectors possess the key attributes to facilitate the complex metabolic reprogramming that occurs during DR.

MiRNA networks in aging and dietary restriction

Dietary restriction (DR) extends healthy lifespan in diverse species. Age and nutrient-related changes in the abundance of miRNAs and their processing factors have been linked to organismal longevity. However, the mechanisms by which they modulate lifespan and the tissue-specific role of miRNA-mediated networks in DR-dependent enhancement of lifespan remains largely unexplored.

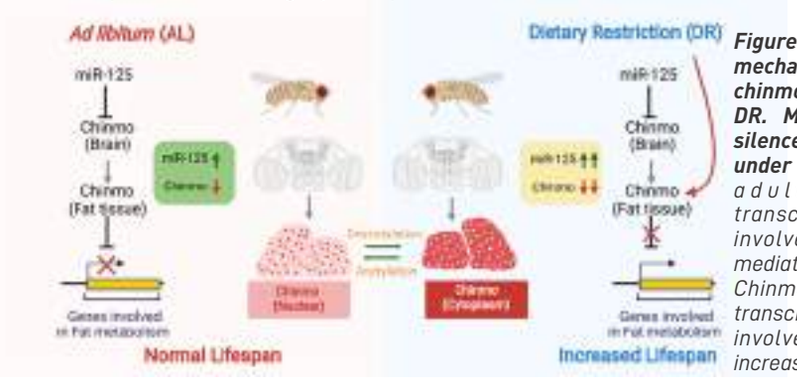


Figure 17. Model summarizing the mechanism by which miR-125 and chinmo regulate lifespan extension by DR. MiR-125 post-transcriptionally silences chinmo mRNA in the brain under AL and DR conditions. *In the adult fat tissue, Chinmo transcriptionally represses genes involved in fat metabolism. DR-mediated cytoplasmic relocalization of Chinmo in the fat tissue relieves transcriptional repression of genes involved in fat metabolism, thus increasing lifespan.*

In our recent study we have shown that nutrient restriction in *D. melanogaster* upregulates *miR-100*, *let-7*, and *miR-125* (*Pandey et al., Elife 2021*). Furthermore, *let-7* and *miR-125* loss of function mutations dampen the DR-dependent lifespan extension. The DR phenotype associated with loss of *miR-125* is due to the derepression of its target, *Chronologically Inappropriate Morphogenesis (chinmo)*. Our analysis reveals that *chinmo* codes for a nutrient-regulated transcription factor and its upregulation in the nervous system results in altered fat metabolism. Our analysis has also uncovered a previously unknown mechanism of nutrient-dependent post-translational control of Chinmo that may be linked to a novel nutrient-dependent non-nuclear role for this protein (Fig. 17). Consistent with the *miR-125* loss of function DR phenotype, increasing the dosage of human *miR-125* in the fat body increased longevity. Taken together, we have identified a conserved miRNA that mediates the effects of DR by promoting tissue-tissue communication demonstrating its potential as an RNA-based therapeutic that can mimic the beneficial effects of DR.

Dietary interventions that promote healthy lifespan

Advances in aging research in model organisms indicate that dietary manipulations based on nutrient restriction and few antioxidants promote healthy aging. The free radical theory of aging proposes that aging results from accumulation of oxidative damage to cells and tissues of the body due to aerobic metabolism. Hence, a major focus of research has been to test the potential of antioxidant compounds to delay aging and prevent age-related diseases. However, the evidence that supports this theory has only been able to correlate aging with oxidative damage and many of the experiments involving manipulations have produced variable effects. Clinical studies with single antioxidant supplements such as

beta carotene and vitamins (A, C and E) have demonstrated that single antioxidants do not protect against chronic diseases including heart disease and cancer. In contrast to the above-described studies, there is substantial evidence to suggest that intake of antioxidant-rich fruits, vegetables and whole grains consumed in their natural context is associated with a lower risk for chronic oxidative stress-related diseases like cardiovascular diseases. Whether the protection mediated by plant-based diets is due to the antioxidants and/or other substances in the diet is unclear. Thus, assessment of the natural whole foods' rich in networks of antioxidants and the helper substances is needed to gain an understanding of the aging pathways that are modulated by these interventions. Anthocyanins are one class of natural dietary phytochemicals that function as antioxidants and are responsible for the black, blue, purple, red and orange colors of many fruits and vegetables. Thus, evaluation of plant-based diets and an understanding of the mechanisms underlying the beneficial effects can provide an acceptable solution for enhancing healthy lifespan and delaying age-related diseases. In our recently published work, we report that anthocyanin rich, high yielding crossbred blue wheat prolongs lifespan of *Drosophila melanogaster* in different dietary contexts (*Pandey et al., Experimental Gerontology, 2022*). In addition to functioning as an antioxidant rich intervention, the biofortified blue wheat also works through modulating expression of DR pathway genes including *AMPK alpha, SREBP*, *PEPCK* and *Cry*. Supplementation with blue- or purple-colored

wheat provided better protection against paraquat-induced oxidative stress than control diet and increased survivability of flies in which superoxide dismutase 2 was knocked down conditionally in adults (Fig. 18). Lastly, our findings indicate that supplementing biofortified blue wheat formulated diet prevented the decrease in lifespan and cardiac structural pathologies associated with intake of high fat diet. Overall, our findings indicate that plant-based diets formulated with biofortified cereal crops promote healthy aging and delay progression of diseases that are exacerbated by accumulation of oxidative damage.

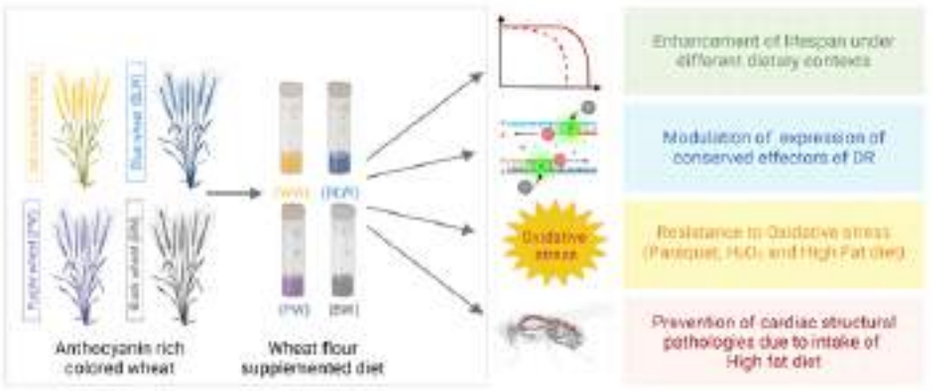
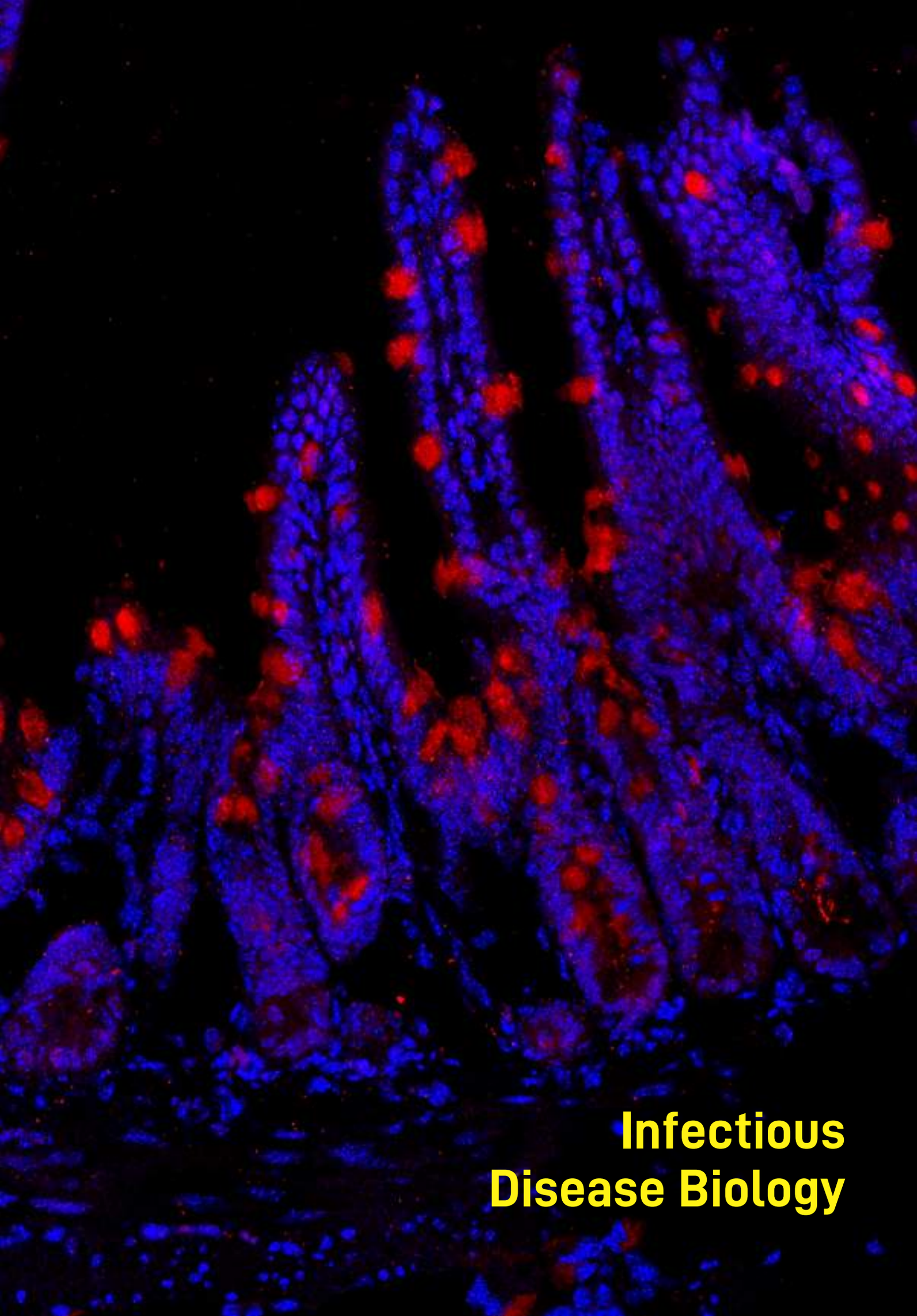


Figure 18. Evaluation of lifespan promoting effects of biofortified wheat in Drosophila melanogaster. *Biofortified anthocyanin-rich wheat prolongs lifespan under ad libitum and dietary restriction, promotes expression of conserved effectors of dietary restriction, enhances resistance to oxidative stress and prevents structural defects in the adult heart under high fat diet.*



Infectious Disease Biology

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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 ~13000 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.

Bone marrow myeloid cell differentiation during dengue virus infection

Dengue virus (DV) infections are amongst the most prevailing mosquito-borne diseases globally, and therefore efforts are being made to understand the disease pathogenesis. Neutrophils have a crucial role in pathogenesis of DV infection and disease severity. However, it is not clear what molecular events trigger uncontrolled neutrophil activation leading to dengue severity. There is a possibility that DV can also impact neutrophil differentiation process and circulating neutrophils may have role in disease manifestation.

We demonstrated that DV serotype 2 (DV2) infection induced the expansion of CD11b+Ly6CintLy6Glow myeloid cells in the bone marrow of AG129 mice as well as in ex vivo expansion of progenitor cells. We show that DV could induce differentiation of promyelocyte cell line HL-60 into neutrophil-like cells as evidenced by the increased expression of CD66b, CD16, CD11b, and CD62L. These cells irreversibly lose their ability to proliferate and undergo arrest in the G0-G1 phase of cell cycle. The functional analysis suggested that DV-triggered neutrophils exhibited less phagocytosis activity and enhanced NETosis as evidenced by the increased production of myeloperoxidase (MPO), citrulated-Histones, DNA/NETs, and superoxide. The mechanism of DV-triggered neutrophil differentiation is being studied further.

Insights into the human gut virome by sampling a population from the Indian subcontinent

Gut virome plays an important role in human physiology but remains poorly understood. An investigation was made of the human gut DNA-virome of a previously unexplored ethnic population through metagenomics of faecal samples collected from individuals residing in Northern India. Analysis showed that, similar to the populations investigated earlier, majority of the identified virome belonged to bacteriophages and a smaller fraction (<20 %) consisted of viruses that infected animals, archaea, protists, multiple domains or plants. However, crAss-like phages, in this population, were dominated by the genera VI, VII and VIII. Interestingly, it also revealed the presence of a virus family, Sphaerolipoviridae, which has not been detected in the human gut earlier. Viral families, Siphoviridae, Myoviridae, Podoviridae, Microviridae, Herelleviridae and Phycodnaviridae were detected in all of the analysed individuals, which supports the existence of a core virome. Lysogeny-associated genes were found in less than 10% of the assembled genomes and a negative correlation was observed in the richness of bacterial and free-viral species, suggesting that the dominant lifestyle of gut phage was not lysogenic. This is in contrast to some of the earlier studies. Further,

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several hundred high-quality viral genomes were recovered. Detailed characterization of these genomes would be useful for understanding the biology of these viruses and their significance in human physiology.

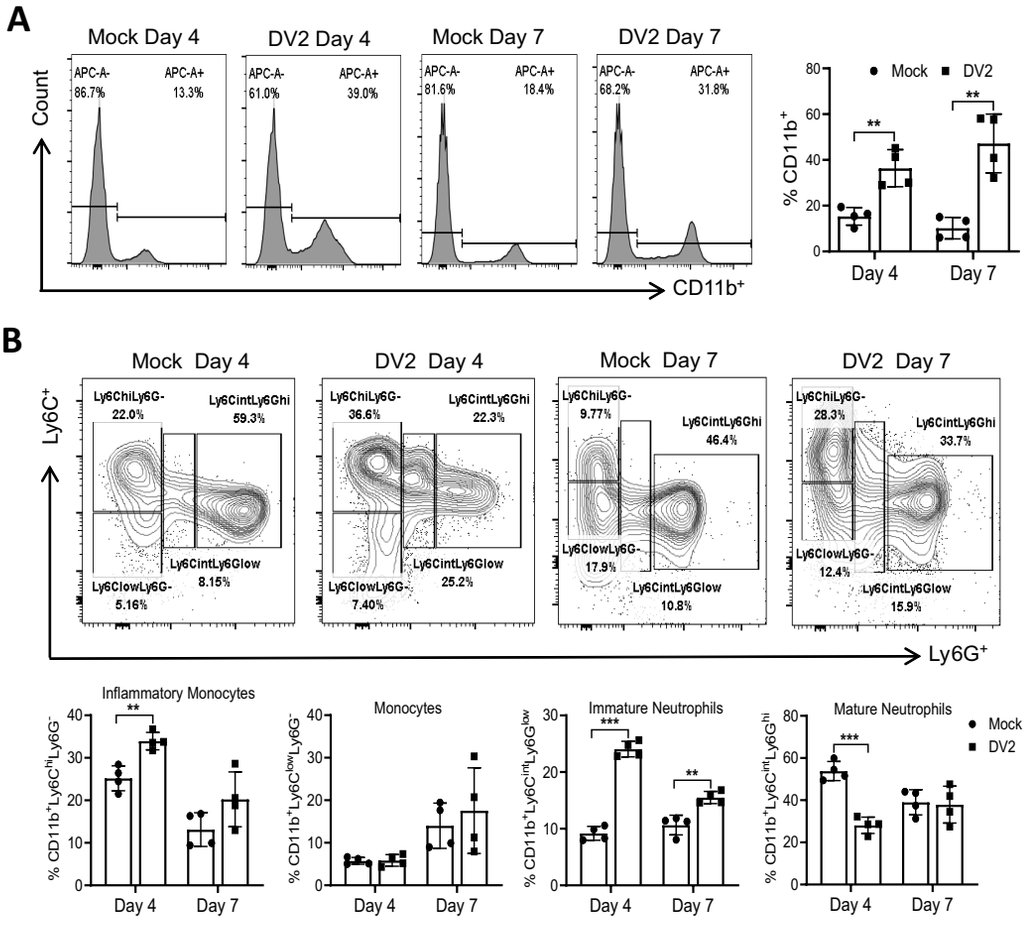

Figure 19: DV2 infection of AG129 mice induces the expansion of CD11b+Ly6CintLy6Glow cell population in bone marrow.

*Six-weeks old AG129 mice (n=4) were mock-infected or infected with 10e5 PFU of DV2 given sub-cutaneous. BM cells were harvested from the femur and tibia bones of the animals on days 4 and 7 pi. For the detection of different myeloid cells, the BM cells were stained with CD11b, Ly6C and Ly6G antibodies, fixed with 1% PFA, and analyzed by FACS Verse. (A) The left panel has the representative data for CD11+ cells from one animal. The right panel has the cumulative data. (B) The upper panel has the representative figure showing the gating strategy to identify myeloid population in the BM showing CD11b+Ly6ChiLy6G- (inflammatory monocytes), CD11b+Ly6ClowLy6G- (monocytes), CD11b+Ly6CintLy6Glow (immature neutrophils), and CD11b+Ly6CintLy6Ghi (mature neutrophils) in the animals. The lower panel shows quantification of these cells. Statistical analysis was performed using Holm-Sidak t-test (**p<0.01; ***p<0.001).*

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Molecular biology of infectious and idiopathic inflammation of the gut

Uncontrolled inflammation is a major culprit in a number of gut illnesses including inflammatory bowel disease (IBD). IBD is a group of autoimmune diseases of the gut. Ulcerative colitis (UC) and Crohn's disease (CD) are the two major forms of IBD. Both CD and UC are accompanied by chronic inflammation in the gut leading to a severely compromised life. Notably, gastroenteritis caused by gastric pathogens such as *Salmonella* and *Campylobacter* predispose individuals for IBD. Efforts of our group is directed towards understanding novel molecular mechanisms that shape acute and chronic forms of intestinal inflammation. Using a multi-pronged methodology involving a range of different model systems we study post-translational modification pathways and epigenetic mechanisms that may be crucial in both IBD and *Salmonella* infections. The results of our studies are expected to provide novel insights into intestinal inflammations and facilitate possibilities of development of strategies for fighting such autoimmune diseases.

Identification of histone demethylase Kdm6B activation during Salmonella infection

Salmonella is a Gram negative enteric pathogen with more than 2500 serovars capable of infecting broad range of host. *Salmonella enterica* var Typhimurium (Hereafter *STm*) is one such serovar and the causative agent of gastroenteritis in humans. *STm* infection is mediated through a battery of pathogen encoded effector proteins which are paramount in the effective mediation of pathogenesis. Evasion of host defence mechanisms involves a coordinated program orchestrated by these effectors. *STm* infections are self-resolving, usually taking not more than 5-7 days, in healthy individuals. However, in immune compromised individuals the disease may prolong, manifest as chronic infections, and lead to fatal outcomes. During chronic infections *STm* thrives intracellularly in host macrophages. *STm* reprograms these macrophages into non-bactericidal macrophages belonging to M2 type spectrum of phenotype (hereafter M2 type). The molecular basis of *STm* mediated macrophage polarization is not fully understood. We hypothesised that reprograming of macrophages by *STm* may require comprehensive alterations in gene expression and host epigenetic modifications.

To probe the involvement of any host epigenetic modifiers during STm infection, we carried out a gene expression analysis based screen using control and STm infected intestinal epithelial cells. Histone demethylase, Kdm6B was observed to be differentially regulated in response to Salmonella infection (Fig. 20). Kdm6B belongs to JMJC domain containing family of demethylases, known to specifically demethylate histone3 lysine 27 trimethylation (H3K27me3) mark triggering target gene activation. In line with this, STm mediated Kdm6B upregulation was accompanied with a concomitant reduction in the overall H3K27me3 mark.

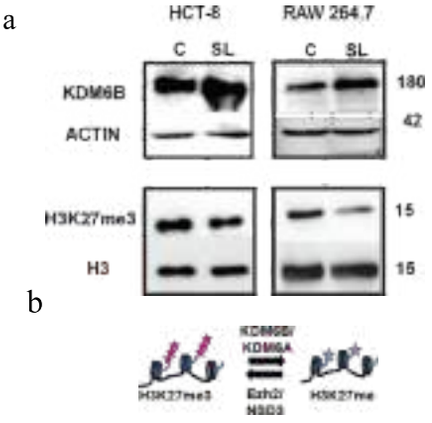

Figure 20: Kdm6B upregulation upon STm infection and alteration of H3K27me3 mark. *(a) Immunoblots showcasing KDM6B and respective Histone H3 lysine 27 trimethylation (H3K27me3 status at 4h post STm infection in HCT-8 and RAW 264.7 cells. Actin and H2 bands represent the loading control. (b) Pictorial representation of epigenetic modifiers (enzymes) involved in maintenance of H3K27me3 mark in cells.*

Kdm6B is recruited to WNT pathway gene promoters to enable M2 Macrophage polarization

To understand mechanistic details of Kdm6B mediated host epigenetic reprograming by STm Chromatin immunoprecipitation coupled RT-PCR array (ChIP-qPCR array) was carried out. The purified input DNA, Kdm6B immuno-precipitated sample and negative control

sample (IgG immuno-precipitated) were subjected to quantitative real-time PCR analysis for a range of regulatory gene promoters. The data obtained was analyzed and avolcano plots were generated. The data revealed that Kdm6B was bound to promoters of several WNT pathway genes, specifically PPAR. After identification of gene promoters bound by Kdm6B, it was important to examine if the expression was actually modulated by this binding. Expression analysis was done which revealed that each of these genes were upregulated during STm infection. Treatment of GSKJ4, an inhibitor of Kdm6B, to these cells prevented the upregulation, thus indicating their dependence on Kdm6B function. It is known that PPAR has a crucial role in fatty acid metabolism pathways required by M2 macrophage. Hence, we hypothesised that Kdm6B depended PPAR activation may govern macrophage polarization.

Possible Kdm6B activation in vivo was examined using Salmonella colitis mice model. Post STm infection of C57BL6 mice for two days, the relevant organs were dissected out and expression of Kdm6B was examined. While, colonic lysates did not show any discernible change in Kdm6B expression, the intestinal crypts, Peyer's patches and MLNs of STm infected animals displayed a dramatic increase in the levels of Kdm6B.

Inhibition of Kdm6B by intraperitoneal administration of its inhibitor drug GSKJ4, followed by infection with STm was carried out in the mice model. Analysis of bacterial burden in infected animals and those inhibited for Kdm6B prior to infection was done. This experiment revealed that > 4 fold higher STm colony forming units in mesenteric lymph nodes and spleen of STm infected mice compared those treated with GSKJ4 drug, indicating a requirement of Kdm6B function for Stm survival in the host.
The basis of Kdm6B function in *STm* survival was investigated by studying macrophage polarization. We isolated mesenteric lymph nodes from *STm* infected and GSKJ4 drug treated mice. Single cell suspensions were prepared and analyzed by FACS using immune cell specific surface markers. Both total macrophage population and M2 subtype population was elevated in MLNs ~~post~~ 48 hours post infection. However, upon GSKJ4 treatment, a significant decrease in M2 subtype was observed (Fig. 20). While no change was observed in the frequency of other cell types. In order to assess the importance of KDM6B in *STm* persistence, a 15 days long infection (using SL3262 strain) was carried out. Results indicated that upon drug (GSKJ4) treatment STm survival and growth gets was adversely affected. Taken together these data led us identify a novel mechanism engaged by STm to induce epigenetic reprograming in host macrophages required for chronic infections.

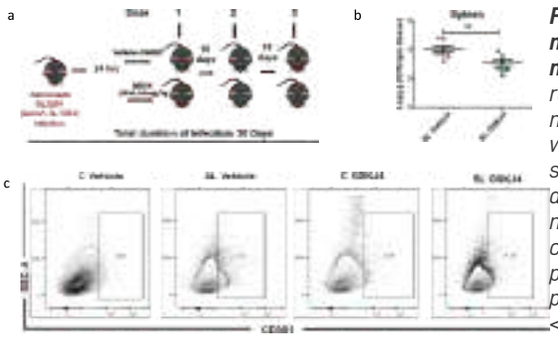

Figure 21: KDM6B demethylase activity is necessary for chronic Salmonella infection and M2 macrophage polarization. *(a) Schematic representation of Salmonella chronic infection model (using attenuated aroA mutant SL3261) along with GSKJ4 treatment. (b) SL CFU obtained from spleen 30 days post chronic STm infection in vehicle and GSKJ4 treated animals. (c) Representative of M2 macrophage population estimated using flow cytometry analysis of CD206+CD301+ double positive cell population on CD45.2+CD11b+Ly6G- cell population in spleen following 30 dpi. ('***'- p-value <.001; '**'- p-value <.01, '*' p-value <.05).*

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Host-Pathogen Interactions of Flaviviruses

Japanese encephalitis virus (JEV) is a major public health concern for India and every year several cases are reported. The virus is spread by mosquito bites and several children succumb to the disease every year. 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.

Characterization of the innate-immune signalling axis during JEV infection

In the periphery, JEV is known to infect and replicate in the keratinocytes, fibroblasts, endothelial cells and various immune cells such as macrophages and dermal dendritic cells. During this incubation period, the virus can either be cleared through an effective peripheral immune response or can infiltrate the CNS. Hence, studying the fibroblast response to virus infection is important. A quantitative proteomics study was performed to understand the JEV-infection driven changes in fibroblasts. Biological processes annotation revealed upregulation of proteins implicated in the innate immune system and host response to virus (Fig. 22A). These were majorly the PRR (Pathogen recognition receptor) pathways involving RIG-I, TLR, NLR, cytosolic DNA sensing and JAK-STAT signaling (Fig. 22B), host response to IFN$\alpha/\beta/\gamma$, antigen processing and presentation, inflammatory responses and regulation of necroptotic and apoptotic death pathways (Fig. 22A, B). JEV stimulated proteins had diverse molecular functions such as binding to various proteins, nucleic acids, peptide antigens and ubiquitin signatures; and enzymatic activities of nucleases, protein ADP-ribosylases, oligoadenylate synthetases, ubiquitin-protein transferases and cytokine-receptor activity etc. Cellular component annotation showed a wide array of sub-cellular localizations, ranging from various cellular organelles, MHC class-I peptide loading complex to proteasome complex. Numerous ISGs belonging to different families (IFI-200, GBPs, TRIMs, IFITs, IFITMs, OASs, ISGylation proteins and MHC presentation proteins) were also seen to be enhanced (Fig. 23). JEV infection enhanced the level of various apoptotic, necroptotic and NLR-mediated cell death proteins. The transcripts of lytic/inflammatory cell death related genes such as *Nlrp3, Caspase-1, Gsdmd, Il1-beta* and *Mlkl* were also seen to be higher. The levels of MLKL (necroptosis marker) and GSDMD (NLR mediated cell death/ pyroptosis marker) proteins were also elevated in virus infected fibroblasts and mouse brain.

We also observed upregulation of other cellular processes such as proteolysis, protein ubiquitination, proteasome degradation and poly ADP-ribosylation (Fig. 22A). Upregulation of the immunoproteasome components, the 20S core proteasome subunits PSMB8, PSMB9, PSMB10, required for protein degradation, and the 11S regulatory complex subunits PSME1, PSME2, required for ubiquitinated protein recognition was seen (Fig. 22C). The immunoproteasome plays a critical role in presenting viral antigenic peptide on MHC-class I molecules to facilitate robust CD8+ T cell activation.

Gene Ontology -enrichment analysis of downregulated proteins majorly revealed biological processes like cell adhesion, lipid metabolic processes, extracellular matrix (ECM) organization, cell migration and canonical Wnt signaling (Fig. 22E). JEV infection resulted in reduced levels of several metabolic enzymes related to sterol synthesis and lysosomal degradation, and various transporters involved in shuttling basic metabolites and ions across membrane (Fig. 22F). The downregulated proteins had molecular functions related to protein/proteoglycan binding, ECM organization, lipid transporter activity etc. and

showed localization to the plasma membrane, extracellular region, collagen trimers and other cell organelles. KEGG analysis of downregulated membrane proteins showed these proteins to be majorly associated with sterol/cholesterol biosynthetic process, transmembrane transport and cell adhesion.

JEV infection resulted in significant decrease in the levels of several collagens, laminin and other proteins engaged in cell-adhesion and ECM organization process. We also observed reduced mRNA levels of various collagens in JEV infected MEFs and mouse brain. A broad range of collagen downregulation during JEV infection, could be a host strategy to enhance the immune cell activation against intracellular pathogens.

Figure 22: Gene ontology (GO) analysis of proteins dysregulated upon JEV infection.

We observed the down regulation of various proteins engaged in lysosomal function, cellular metabolic transport and lipid/sterol metabolism in JEV infected cells. The levels of functional vacuolar-ATPase (V-ATPase) proteins, such as Atp6ap1 and Atp6v0a1, which mediate the acidification of intracellular organelles, were reduced upon infection. Similarly, various members of Solute carrier (SLC) and the ATP-binding cassette (ABC) transporters family were reduced. Our data indicate that JEV infection is likely to hinder metabolite shuttling across cellular compartments and cell surface.

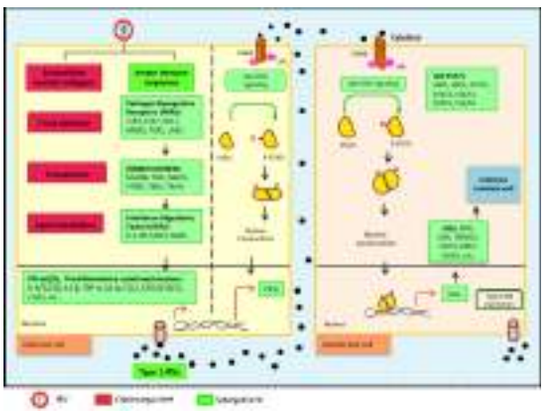

Figure 23. Innate immune response during JEV infection.

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Understanding Pathobiology of Flaviviruses prevalent in India

Our research group investigates the immunopathogenic mechanisms of two important viruses (Dengue virus (DV) and Japanese Encephalitis Virus (JEV)) prevalent in India. We are trying to understand how these virus infections impact the host immune response and develop pathogenesis. Virus infection modulates the microenvironment leading to phenotypic and functional changes in the immune cells and alters disease outcomes. However, the modulation of immune cell functions could be possible in a contact-dependent or contact-independent fashion. Infected cells may secrete bioactive molecules by releasing extracellular vesicles (EVs). These cell-free EVs may significantly impact modulating immune response and disease outcomes. This year, we have made some progress on isolating and characterizing EVs from Dengue infected patients' plasma samples and investigated their role in immune modulation. In parallel, we also assessed the role of long non-coding RNAs in modulating dengue viral replication and antiviral response.

Impact of circulating extracellular vesicles on immune cell functions

Extracellular vesicles (EVs) are small membrane vesicles secreted into biological fluids, including plasma from living cells, holding insights into pathological processes. Studying EVs under pathological conditions is extremely important as they play a selective role in intercellular communication and modulation of immune response under diverse pathological conditions. 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 severe dengue (DV) patients. We have developed an ultracentrifugation-based protocol for isolating EVs from plasma and characterized them through biophysical and molecular biology methods. EVs derived from DV+ plasma fall within the size range of exosomes, i.e., 30-200 nm. These EVs carried increased levels of specific sets of proinflammatory cytokines and anti-inflammatory cytokines compared to HD-EVs and OFI-EVs. We also studied the effects of these EVs on immune cell proliferation, activation, and functions by incubating EVs with purified PBMC and naïve T cells. We observed an immunosuppressive activity of DV-EVs by attenuating CD4+ proliferation and inducing apoptosis in CD8+ T cells. In the CD4+ T cells, when we co-cultured with EVs, we noticed increased expression of different subsets of cell surface markers along with the augmented secretion of IFNα in the supernatant (Fig. 24). Further study is in progress to understand the mechanisms.

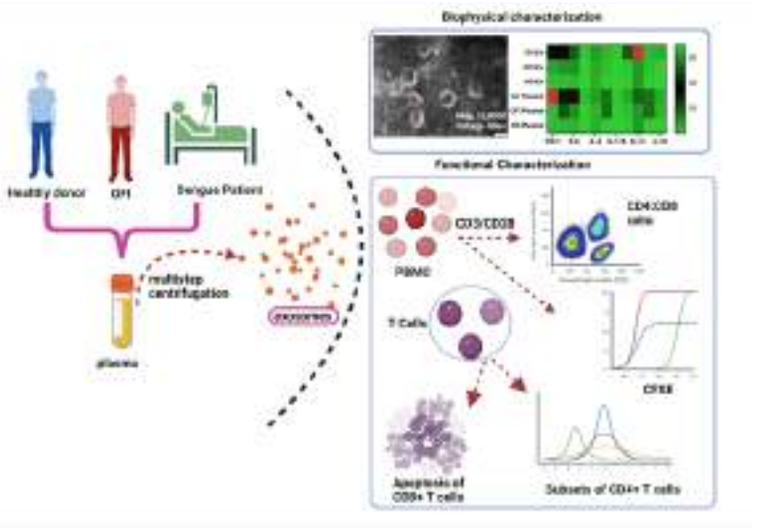

Figure 24. Schematic diagram summarizing characterization of extracellular vesicles from plasma of dengue infected patients and their effect on T cell proliferation

Understanding the involvement of long non-coding RNAs in Dengue pathogenesis

The Long non-coding RNAs (lncRNAs) are transcribed from the mammalian genome, have a length greater than 200 nucleotides, and lack protein-coding potential. LncRNAs are crucial regulators of virus infections and antiviral immune responses. Our previous study described several known long non-coding RNA induced during infection (Pandye et al., 2017). NEAT1 (nuclear paraspeckle assembly transcript 1) was one of them. We reported that lncRNA NEAT1 expression was inversely correlated with IFN-α inducible protein 27 (IFI27/ISG12a) expression and associated with dengue disease progression. IFI27/ISG12a belongs to a family of the ISG12 gene and is localized in the mitochondria.

On the other hand, Human *NEAT1* is transcribed from chromosome 11q13 into two overlapping mono exonic transcripts: *NEAT1_1* of 3.7 kb and *NEAT1_2* of 22.7 kb. *NEAT1* is an essential component for the formation of paraspeckles. Paraspeckles are dynamic nuclear RNP bodies that increase in number and size. Paraspeckles are organized in the form of a core-shell spheroidal structure. The function of the paraspeckles is not well understood. However, they may be involved in retaining specific RNAs and proteins, thus crucial in regulating gene expression. However, the current knowledge regarding their roles in dengue viral infections is still limited. Using two different cell lines (HuH7, THP1) infected with dengue virus serotype 2 (DV2), we assessed the functional consequences of NEAT1 and IFI27 modulation on antiviral response and dengue viral replication. We observed tissue-specific and time-dependent expression of NEAT1_1 isoform and IFI27 in DV2-infected cells.
Further, we knocked down NEAT1 or IFI27 in DV2-infected cells to understand their relative contribution to generating the antiviral response. We observed that knocked down of NEAT1 or IFI27 attenuated viral replication and modulated antiviral response via the RIG-I pathway. Interestingly, the Activating Transcription Factor 3 (ATF3) expression, a regulator of antiviral response, was inversely correlated with IFI27 expression. We also studied the effect of NEAT1 modulation on mitochondrial function. We observed that NEAT1 knockdown induces mitochondrial elongation in DV2 infected cells (Fig. 25) and augments mitochondrial ROS production and cell death via activation of caspase 3. Thus, our study points toward the critical role of lncRNAs in dengue infection.

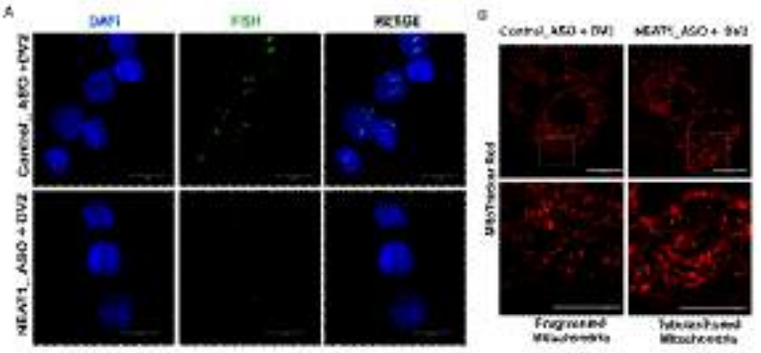

Figure 25. Effect of NEAT1 knockdown on the paraspeckles formation and mitochondrial morphology in dengue infected cells. *(A) The confocal images represent fluorescence in situ hybridization (FISH) data to visualize NEAT1 expression in DV2 infected THP1 cells either transfected with control_ASO or NEAT1_ASO. The green puncta within the nucleus (stained with DAPI, blue) containing the lncRNA NEAT1 within paraspeckles. ASO= Antisense oligo. (B) The confocal images represent the mitochondrial morphology of Huh7 cells either transfected with control_ASO or NEAT1_ASO (Top panels). Mitochondria were stained with MitoTracker Red dye. The zoomed image of the marked white area was shown in the bottom panels.*

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Investigating Adult Stem Cells Dynamics in the Infection Scenario

Adult stem cells (ASCs) with self-renewal and differentiation abilities are present in various organs in the body. They are the fundamental players in tissue maintenance as they serve to restore damaged tissue during homeostasis, injury or disease. However, during severe bacterial/ viral/ fungal infections, tissue regeneration is often hugely inhibited. Recent research suggests that the ASCs function/ behavior is adversely affected by several infectious agents. Indeed, the failure in the maintenance of healthy tissue is the cause of several deadly diseases. Therefore, our research topic is focused on investigating molecular mechanisms in ASCs that are affected during bacterial infections. We would like to know how pathogens impact the ASCs behavior and hence determine the regeneration outcome. The knowledge gained from this study would eventually help to improve the ASCs tolerance to infection burden and thus has profound biomedical importance.

Regeneration of infected tissue

Several organs/ tissues (such as liver, lung, skin, bone, etc.) in our body possess the regenerative potential and are equipped with stem/ progenitor cells. However, they fail to repair the tissue efficiently under several infectious conditions. Recent studies infer that mammalian ASCs may exhaust and terminally differentiate under the circumstances requiring rapid proliferation/ differentiation to replace severely infected tissue. These observations raise an obvious question why ASCs often fail to regenerate tissue efficiently during severe infections? Our research program aims to answer this question. We are investigating how bacterial pathogens affect the ASCs dynamics (i.e. proliferation, differentiation, survival), which could potentially alter the regeneration capacity of infected tissue. There could be multifaceted effects of pathogens on ASCs which may result in diverse outcomes affecting one or more functions of ASCs. To study this complex interplay, we need an *in vivo* system where we can monitor the ASC dynamics in their natural microenvironment. We are using planarian flatworms as a model system for the *in vivo* investigations. Planarian *Schmidtea mediterranea* has an extraordinary regeneration ability. They possess a pool of pluripotent adult stem cells which allows them to grow an entire body from a tiny tissue fragment (Fig. 26A). Various lineage-committed stem cells and their progenies can be easily studied *in vivo* in planarians. The genetic machinery essential for the stemness in mammalian stem cells is conserved considerably within planarian ASCs. Moreover, planarian ASCs can be easily isolated by flow cytometry in ample amounts for next-generation sequencing applications such as RNA-Seq, ChIP-Seq etc. Hence, planarian has emerged as a convenient model system to study *in vivo* adult stem cell dynamics.

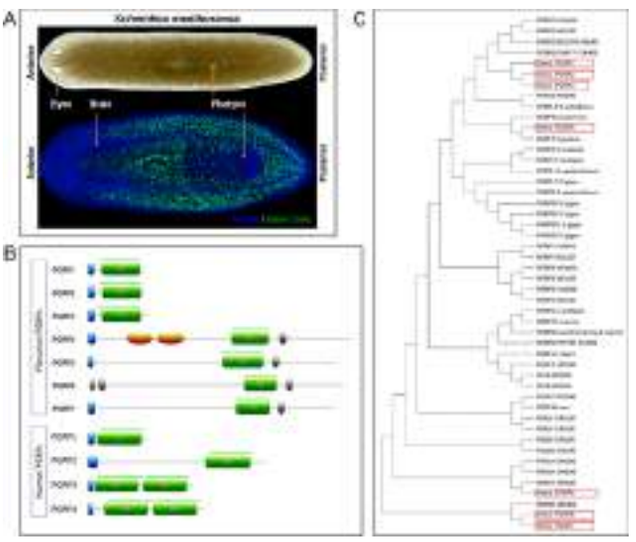

Figure 26: Planarian PGRP domain-containing proteins. *(A) Bright-field image of planarian Schmidtea mediterranea and fluorescence in situ hybridization image showing stem cell distribution in the worm. (B) Domain architecture of seven planarian PGRPs and four human PGRPs. (C) Phylogenetic tree of 48 PGRP sequences from 15 different animals.*

Understanding the Planarian – Bacteria interplay

We know very little about planarian-bacterial interaction and there is a lot to explore. To better understand the interplay between planarian and bacterial pathogens we are currently seeking the answers to the fundamental questions like how do planarians recognize bacteria, and what is the effect of bacterial infection on planarian regeneration? Several potential pattern recognition receptors (PRRs) have been identified in planarians but are not validated for their role in bacterial recognition or immune response. Therefore, we decided to decipher the role of one of the very well conserved PRRs, i.e. Peptidoglycan Recognition Proteins (PGRPs). PGRPs are a group of highly conserved innate immune molecules that specifically bind to the peptidoglycan in the bacterial cell wall. These proteins contain at least one PGRP domain (~165 amino acids long). With an extensive homology search, we have identified seven planarian proteins with a PGRP domain (Fig. 26B). Unlike human PGRPs, all planarian PGRPs contain only a single PGRP domain (Fig. 26B). Out of seven, four planarian PGRPs had the transmembrane domain, so probably they act as membrane-bound sensor PGRPs (Fig. 26B). Whereas, the remaining three planarian PGRPs didn't have any transmembrane region, so these may be functioning as secretory effector PGRPs like the human PGRPs (Fig. 26B). The phylogenetic analysis revealed that 3 planarian PGRPs cluster together and are the closest orthologs of the human PGRP2 (Fig. 26C).

We then wanted to know whether these PGRPs could recognize the bacteria and exhibit infection-induced overexpression. To test this, we used two different modes of infection – through water and the intestinal tract. Interestingly, we observed the infection-induced overexpression of two PGRPs when animals are infected through water (Fig. 27A).

Planarians infected via intestinal route showed overexpression of all 5 PGRPs tested at 1h post-infection, implying that planarians could launch broad-spectrum and heightened antimicrobial response within few minutes after infection through the intestine (Fig. 26B). Most of the PGRPs were overexpressed even at the later time points at 3h and 6h post-infection (Fig. 27B). This data suggests that planarian PGRPs may have a conserved role in bacterial recognition. We are further validating the role of these PGRPs in bacterial recognition and antibacterial response during the regeneration of infected tissue.

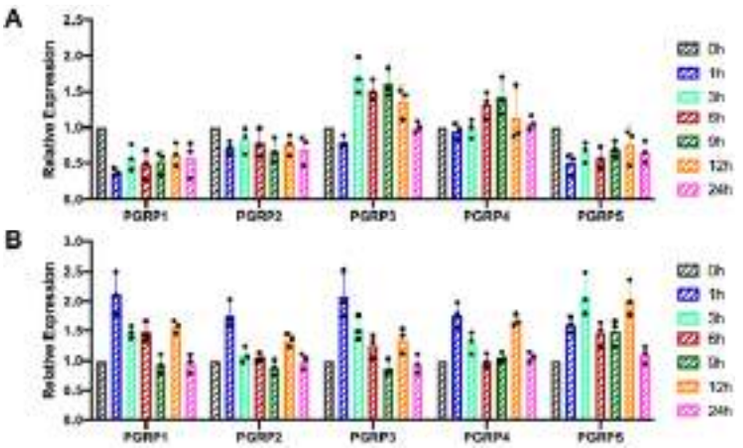

Figure 27. The expression of planarian PGRPs is modulated after bacterial infection via different routes. *(A) PGRP expression after bacterial infection through the water. (B) PGRP expression after bacterial infection via intestinal route*

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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 event 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 mechanism of pathogenicity of *C. glabrata* is 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 *C. 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-tRNAi), 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. This process acts as a buffer for the expression of stress-responsive genes. The Interplay between these two pathways takes place in *C. glabrata* during stress thereby providing the pathogen selective advantage for survival in a highly oxidative and nutrient deficient environment (Fig. 28). We are systematically analyzing the translation initiation and mRNA decay machinery of *Candida glabrata* and *Candida albicans* for understanding stress adaptation. The study endeavors to unravel novel translation regulatory mechanisms harnessed by fungal pathogens to survive in the hostile environments of the host.

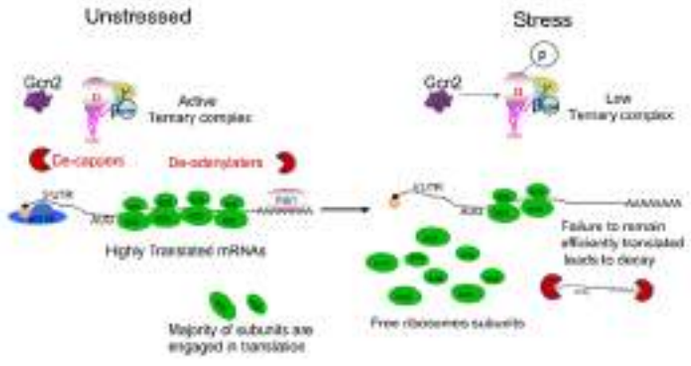

Figure 28: Predicted model of eIF2 phosphorylation mediated translation adaptation of fungal pathogens during stress. *The most of ribosomes are engaged with translation in unstressed condition. Stress activate the kinase Gcn2 which phosphorylate eIF2 to reduce ternary complex. This prevents the binding of ribosomes with mRNA that accelerate the mRNA decay. Newly transcribed stress transcript now translated, which usually not favored under homeostatic conditions.*

Analysis of ribosomal proteins to promote the high-fidelity selection of initiation codon for translation

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. 29A).

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. 29B). 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.

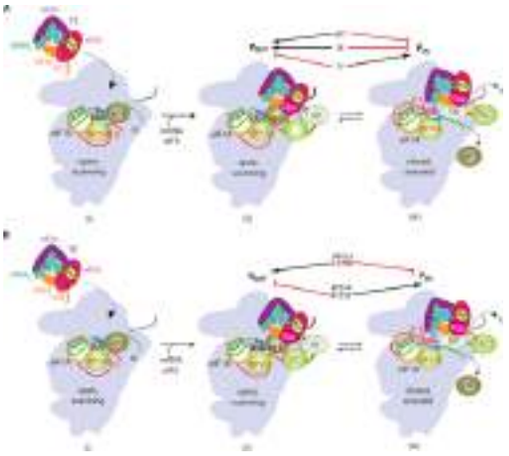

Figure 29: Model describing conformational rearrangements of the PIC and roles of RPS14 residues in start codon recognition (A) Assembly of the PIC and start codon selection in WT cells. *(i) eIF1 and eIF1A elements stabilize an open conformation. (ii) Scans mRNA. (iii) On AUG recognition, the Met-tRNA$_i$ moves from the P_{OUT} to P_{IN} state. (B) Interaction of RPS14-L137 with mRNA enhances scanning (i,ii). Interactions of RPS14-E135 with rRNA stabilize the closed conformation (iii).*

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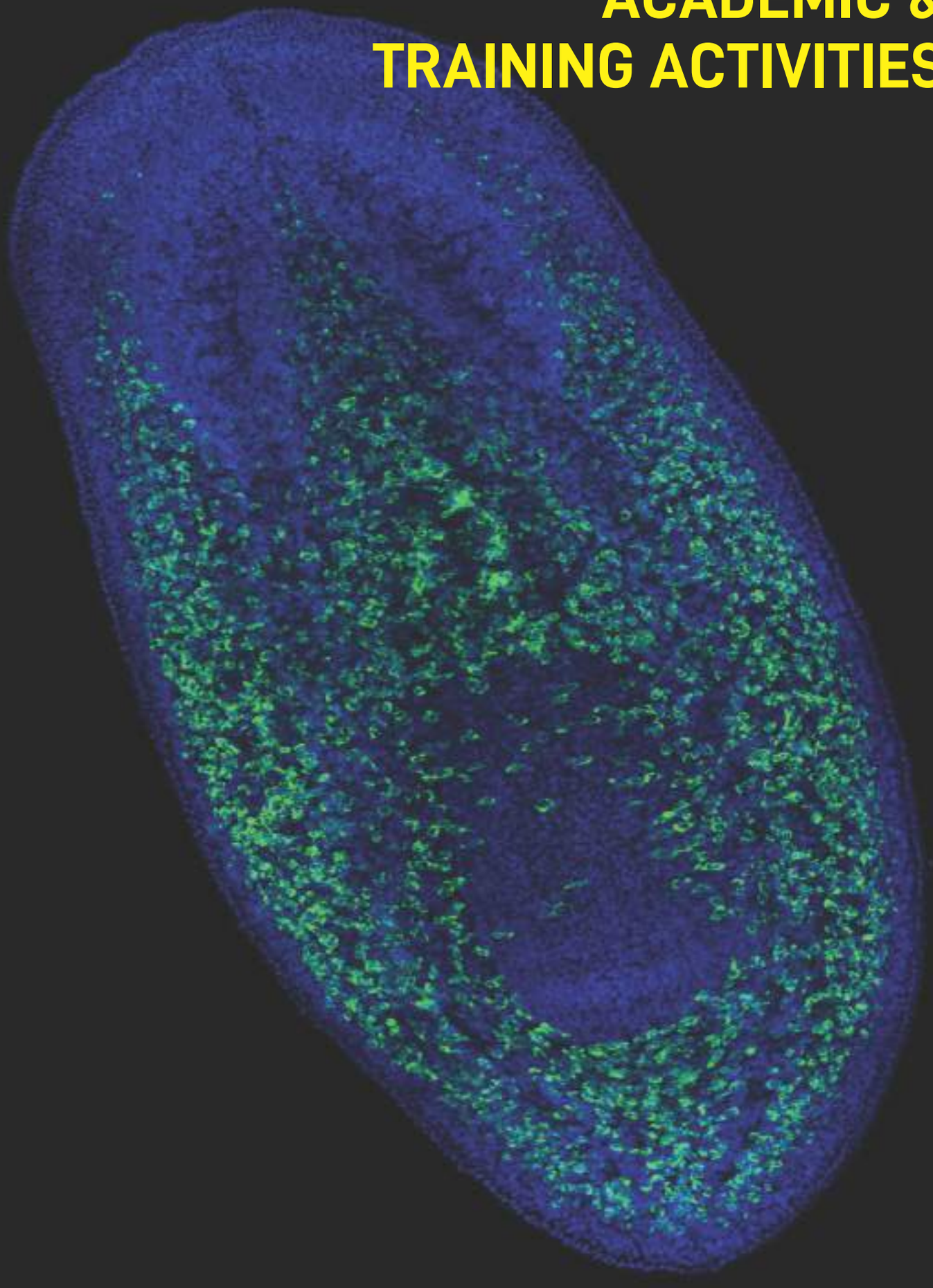
ACADEMIC & TRAINING ACTIVITIES



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 having interest to work 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, 99 students are working at RCB for the PhD degree in Biotechnology. During the period of the report, 10 students were awarded PhD degree.

2. PhD Programmes in Biostatistics & Bioinformatics

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

In addition to RCB faculty members, a virtual faculty pool has been created with faculty from partner institutions like IIT Delhi, NII New Delhi, ICGEB New Delhi, NIBMG Kalyani, holding an adjunct faculty position with RCB, 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, 12 students are registered with RCB for PhD in these programmes.

3. Ms-PhD Programme in Biotechnology

RCB introduced a PhD (Integrated) 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 may 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, 36 students are registered in the programme. During the reporting period 05 students quitted the program 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 related

research projects in collaboration with other group members in lab. 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 2021-22, 68 research trainees joined for six months' duration at RCB.

5. Academic Programmes at the Recognized Centers of RCB

RCB has given 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 respective programmes. At present, following institutions and their academic programmes are recognized by RCB. The number of students registered under the various programmes are as follows:

Name of Recognized Centre	Courses Recognized	Students Registered	Adjunct faculty
Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad	PhD (Biotechnology)	31	21
Center of Innovative and Applied Bioprocessing (CIAB), Mohali	PhD (Biotechnology)	4	8
National Institute of Animal Biotechnology (NIAB), Hyderabad	PhD (Biotechnology)	56	18
National Agri-Food Biotechnology Institute (NABI), Mohali	PhD (Biotechnology)	27	11
Institute of Life Sciences (ILS), Bhubaneswar	PhD (Biotechnology)	103	26
Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram	Msc (Biotechnology) PhD (Biotechnology)	50 24	33
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) PhD (Biotechnology; Specialization: Biomedical Genomics)	22 25	18
Christian Medical College (CMC), Vellore	PhD (Medical Biotechnology; Specialization: Haematology) PhD (Medical Biotechnology; Specialization: Biomedical Genetics)	08 03	08
National Centre for Cell Science (NCCS), Pune	PhD (Biotechnology)	5	22
ESIC Medical College & Hospital, Faridabad	PhD (Biomedical Sciences)	0	26
Institute of Bioresources and Sustainable Development (IBSD), Imphal	PhD (Biotechnology)	0	13
Total		**358**	**219**

Our Alumni

S. No.	Name of Student	Year of Award	Current Designation	Current Affiliation
	Ph.D.			
1.	Priyajit Banerjee	2021	-	-
2.	Abhin Kumar Megta	2021	Post-doctoral fellow	Washington University
3.	Sunayana Dagar	2021	Post-doctoral fellow	Yale School of Medicine
4.	Sarika Rana	2021	Post-doctoral fellow	Université Libre De Bruxelles
5.	Sulagna Bhattacharya	2021	Analyst	Smartanalyst
6.	Mary K. Johnson	2021	Post-doctoral fellow	National Institute of Health, Maryland, USA
7.	Shilpi Nagpal	2021	Project Associate-II	Regional Centre for Biotechnology
8.	Megha Gupta	2021	Post-doctoral fellow	University of Maryland
9.	Mritunjay Kasera	2021	Post-doctoral fellow	University of Kentucky
	M.Sc.			
10.	Tanushri Dargar	2021	Doctoral Fellow	University of Lyon
11.	Gagan Gupta	2021	Doctoral Fellow	ICGEB, New Delhi
12.	Vanshika Rastogi	2021	Doctoral Fellow	University of Basel
13.	Dikshalee Bassi	2021	-	-
14.	Shadrack Danquah Owusu	2021	Doctoral Fellow	University of Strasbourg

Webinars/ Seminars

Date	Speaker	Title
25 March 2022	**Prof. Ganesh Nagaraju** *Indian Institute of Science, Bangalore*	Unraveling the New Roles of RAD51 Paralogs and FANCJ Helicase in Genome Maintenance and Tumor Supperssion
21 March 2022	**Dr. Kunal Rai,** *Department of Genomic Medicine UT MD Anderson Cancer Center*	Exploiting cancer epigenome for precision medicine
8 March 2022	**Dr. Deepti Jain** *Regional Centre for Biotechnology*	Women in Science & Technology
1 March 2022	**Prof. Usha Vijayraghvan** *Dean, Indian Institute of Science, Bangalore*	Codes for the making of a rice flowering stem: roles for evolutionarily conserved transcription factors
28 February 2022	**Dr. Pramod Garg** Executive Director, THSTI	Biology enetrs the clinic: Are we ready?
25 February 2022	**Prof. Balaji K.N** *IISC Bengaluru*	Elevated Host Lipid Pools Contribute to Mycobacterial Pathogenesis: The Pathogen's Gambit towards Survival
14 February 2022	**Prof. Luigi Fontana, MD PhD FRACP** *The University of Sydney*	Promoting healthy longevity through diet: metabolic and molecular mechanisms.
11 February 2022	**Dr. Dhiraj Kumar** *ICGEB, NewDelhi*	Tracing the trajectory of mycobacterium tuberculosis in the host cells
04 February 22	**Dr. Varadharajan Sundaramurthy** *NCBS, Bangalore*	Endo-lysosomal system in the control of intracellular MTB pathogenesis
4 February 2022	**Prof. Uma Ramakrishnan, Senior Fellow, IA** *National Centre for Biological Science, Bangalore*	Evolution in Small and Isolated Tiger Populations
21 January 2022	**Dr. Ashwani Kumar** *Institute of Microbial Technology, Chanigarh*	Mycobacterium tuberculosis biofilms: relevance during infection
7 January 2022	**Dr. Amit Singh** *Indian Institute of Science, Bangalore*	Decoding Redox Language underlying HIV Latency: From Molecular Mechanism to Therapeutic Implication.
5 January 2022	**Dr. Anand Kumar** *SANOFI, France*	Cryo-EM: Recent developments and impact on drug development!
8 October 2021	**Dr. Jagpreet Singh Nanda** *NICHD, NIH, USA*	Interdisciplinary approaches to understand mechanism of eukaryotic protien synthesis
1 October 2021	**Dr. Mohit Kumar Jolly** *Indian Institute of Science, Bengalore.*	Accepting identity crisis as an identity itself: lessons from interdisciplinary investigations of cancer metastasis.

Date	Speaker	Title
24 September 2021	**Dr Santosh Mishra** *NC State Veterinary Medicine-USA*	Itch and Ouch: Multidirectional approach to uncover mechanisms
17 September 2021	**Mr. Vikram Goel** *Incredible Devices Pvt. Ltd.)*	The success stories of Indian Biotech Start-ups being incubated at BBB Faridabad
17 September 2021	**Dr. Ashish A. Kulkarni** *University of Massachusetts Amherst, USA.*	Nanoscale Approaches for Therapeutic Immune Modulation
3 September 2021	**Dr. Rohit Srivastava** *IIT, Bombay*	Affordable Healthcare Technologies.
27 August 2021	**Dr. Shanta Dhar** *University of Miami Miller School of Medicine, Miami, USA.*	Accessing Mitochondrial Tragets for Therapeutic Gain in Major Diseases
25 August 2021	**Dr. Bushra Ateeq** *IIT, Kanpur*	Mechanistic insights into etiology of prostate cancer: a search for better therapeutic interventions
18 August 2021	**Mr. Arpit Dhupar** *Founder, Dharaksha Ecosolutions Pvt Ltd.*	The success stories of Indian Biotech Start-ups being incubated at BBB Faridabad
13 August 2021	**Dr. Siddhesh Kamat** *IISER*, Pune	Fatty acid chain length drives lysophosphatidylserine dependent immunological outputs
5 August 2021	**Dr. Amit Dutt** *Tata Memorial Centre, ACTREC, Navi Mumbai*	Biological and Therapeutic Insights from Oral and Lung Cancer Genome Analysis
30 July 2021	**Dr. Sagar Sengupta** *NII, New Delhi*	Trying to reach the bed from the bench: the gap remains
23 July 2021	**Prof. Kumar Somasundaram** *Indian Institute of Science, Bengaluru*	Cancer stem-like cells: understanding tumor cellular hierarchy and plasticity
16 July 2021	Prof. Saikrishnan Kayarat IISER, Pune	DNA Cutting and Shredding-how bacteria defeat their viruses
9 July 2021	**Prof. Tapas Kumar Kundu** *CSIR, Lucknow*	Epigenetics: Life Beyond your Genes
2 July 2021	Dr. Soumen Basak NII, New Delhi	Intentinal inflammation gone awry

ID-75 Seminars

Date & Time	Title/ Speaker
25 March 22	Targetting cellular stress responses as an anti-viral strategy for
11 February 22	Science Setu Lecture SeriInterplay between Salmonella and host epigenetics machinery in chronic infections (Dr. CV Srikanth)
10 December 21	RCB Vigyan Pradarshini
13 August 21	The scientific journey of *Dr. Obaid Siddiqi*
23 July 2021	The scientific journey of *Dr. G.N. Ramachandran*
9 July 2021	The scientific journey of *Dr. K S Krishnan*
25 June 2021	The scientific journey of *Dr Bhibha Chowdhuri*
11 June 2021	The scientific journey of *Dr. Darshan Ranganathan*
28 May 2021	The scientific journey of *Dr. Arun Kumar Sharma*
14 May 2021	The scientific journey of *Dr. Shambhu Nath De*
30 April 2021	The scientific journey of *Dr. Kamal Ranadive*
16 April 2021	The scientific journey of *Dr. Shanti Swarup Bhatnagar*

RCB WORKSHOPS

22 October 2021	UNESCO-sponsored Online Workshop on 'Confocal Microscope-based drug screening (High content imaging)'
20 October 2021	UNESCO-sponsored Online Workshop on 'Basics of Electron Microscopy'
12-13 October, 2021	UNESCO-sponsored Online Workshop on 'Mass Spectroscopy Based Proteomics'
5-6 October, 2021	Cloud-based Hands-on Workshop: Computational Structure-based Screening and Explicit Molecular Dynamics

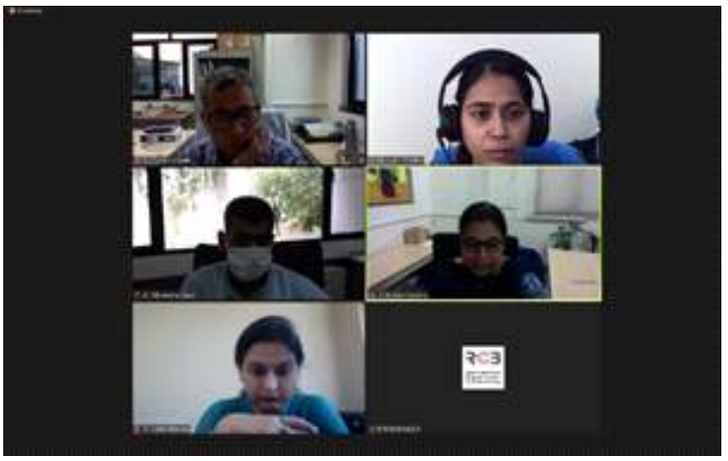
Events organized

Cloud-based Hands-on Workshop: Computational Structure-based Screening and Explicity Molecular Dynamics

Two-day cloud-based hands-on workshop targeting structure-based drug designing and MD simulations was organized by RCB during 5-6th October, 2021. Participants were given a practical experience and in-person guidance on the Maestro GUI, organic molecule sketching, protein selection preparation, and screening for hit identification of molecules against therapeutic targets. The workshop also included a brief recap of background theory for Molecular mechanics, CADD, Structure-based drug design approaches via case studies on the real-time industrial projects. It was attended by 80 people (students and scientists).

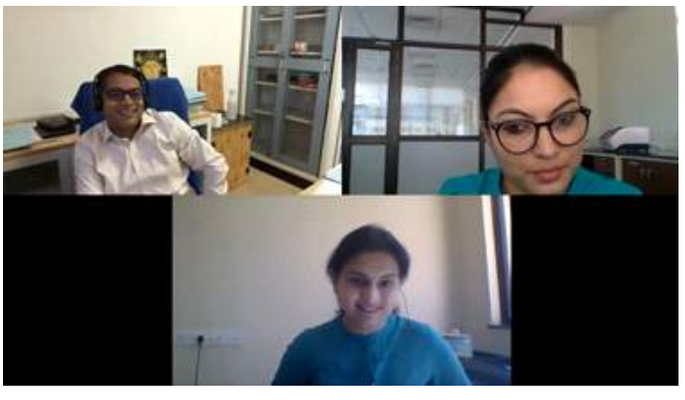
UNESCO sponsored Online Workshop on 'Mass Spectroscopy Based Proteomics'

It was organized during 12-13 October, 2021. The main aim of the workshop was to introduce, demonstrate and provide theoretical underpinnings of high-resolution mass spectrometry-based proteomics technologies and their application to clinical and biological research, through online lectures and virtual demonstrations. The workshop focused on introducing to the participants both basic and newly emerging techniques in proteomics and mass spectrometry. About 50 partcipants from India, China, UAE, Srilanka, Ghana, Nigeria, Nepal attended this workshop.



UNESCO sponsored Online Workshop on 'Basics of Electron Microscopy'

It was organized on October 20th, 2021. The main aim of the workshop was to introduce and demonstrate the fundamental concepts in transmission electron microscopy (TEM) including, cryo-electron microscopy (cryo-EM) and scanning electron microscopy (SEM); their application to get high resolution images through online lectures and virtual demonstrations. The workshop has covered from basic theory of TEM and SEM and practical demonstration on sample preparations for TEM, cryo- TEM, and SEM imaging. The participant got an overview of different EM techniques, their application, and the sample preparation methods. About 40 partcipants from India, Srilanka, Ghana, Nigeria, Nepal, Mauritius attended this workshop.



UNESCO sponsored Online Workshop on 'Confocal microscope-based drug screening (High Content Imaging)'

It was organized on October 22nd, 2021. The main aim of the workshop was to introduce and demonstrate the basics of high content imaging and their application to antiviral drug screening in a high throughput manner. This workshop helped in training the participants who are relatively new to this field and also made them learn about the basics of drug screening in addition to high content imaging so that they can develop the assay for drug screening from scratch. More than 50 partcipants from India, UAE, Srilanka, Nepal attended this workshop.

Vigyan Pradarshini

To commemorate India's 75th year of independence, RCB successfully organized the (Virtual) **Vigyan Pradarshini** as a part of the 'Science Setu' program on the 10th December, 2021.The program featured a brief introduction of RCB followed by 10-minute presentations on various research verticals of RCB. The faculty presented PowerPoint presentations that highlighted the key questions being addressed by different laboratories and the approaches being utilized. The sole objective of the Vigyan Pradarshini was to encourage young minds to the sphere of science and technology.

Indian International Science Festival (IISF) 2021

IISF was held at Panaji, Goa during 10-13 December, 2021 to showcase the advancement of science in India after 75 years of independence. From RCB, Dr. Anil Thakur (Assistant Professor) and students from different laboratories attended the event. The motto of RCB to participate in this festival was to stimulate the young brains of the country for science. RCB being a biotechnology institute, presented the research going on in agriculture biology, structural biology, synthetic biology, Cancer & Cell Biology, Molecular medicine and infectious disease biology. Many school and college students gathered to learn and understand the research going on in RCB in various fields of science in this festival. These students got influenced by knowing the diverse fields of research which RCB is performing. The top-notch instrumentation facility at ATPC and its training programs influenced many people to show interest in using these facilities. This festival also helped people to come across different research groups that they might be interested in doing collaborating work. RCB team, which attended the festival also came across such groups, which might help in future collaborative works.

National Science Day

India celebrates February 28 every year as the 'National Science Day' to pay tribute to the Raman Effect of the Nobel Laureate Sir C.V. Raman. Prof. Sudhanshu Vrati, Executive Director-RCB opened the day with his welcome address and highlighted the importance of Science and Biotechnology in their daily lives. On this Day, RCB invited Dr. Pramod Kumar Garg, Executive Director, THSTI to deliver the science day lecture. on the Science Day lecture was given by "Biology enters the clinic: Are we ready"?

RCB Foundation Day

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. This year, Foundation day was celebrated on 2nd March, 2022 due to 1st March being Gazetted Holiday. The day began with the mini-symposium presentations by final year PhD students before a panel of judges.

Post lunch session began with a welcome address by Prof. Sudhanshu Vrati, Executive Director, RCB. Prof. Usha Vijayraghavan, Dean, IISc Bengaluru, Guest of Honour for the day, delivered the RCB Day Oration. The awards for the best scientific presentation was distributed to the winners.

Hindi Pakhwada-2021

Hindi Pakhwada (Fortnight) is celebrated every year during the month of September and Hindi Diwas on 14 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 1st to 15th September, 2021 at the RCB. The closing ceremony of the fortnight was held on September 15, 2021 under the chairmanship of the Executive Director, RCB at M.K. Bhan Auditorium. On this occasion Executive Director-Prof. Sudhanshu Vrati, Dean-Dr. R.P. Roy and Hindi Nodal Officer Dr. Nidhi Sharma apprised the personnel about the importance of Hindi and its history. A total of four competitions were organized during the fortnight in which the personnel and research students participated enthusiastically. In the function, the Executive Director and the Dean jointly presented cash prizes and certificates to the winning personnel.

Swachhata Pakhwada

Regional Centre for Biotechnology (RCB) observed Swachchata Pakhwada 2021 during 1-15 May 2021. During this fortnight, in addition to various measures to improve workplace hygiene and cleanliness, on the occasion of the "World Technology Day", on 11th May, the following events were organized. The NCR Biotech Science Cluster houses the BIRAC BioNest Bioincubator (BBB) being managed by the RCB. The incubatees (InnoDx Solutions Pvt. Ltd., NextGen InVitro Diagnostics Pvt. Ltd. and Organic 121 Scientific Pvt. Ltd.) of the BBB delivered a talk on various Covid related products. Overall the sessions were informative. Students, scientists, faculty and staff of RCB participated in the events and they took online Swachh Shapath (Mass Pledge) to fulfill our mission of "Clean India" and to make this massive movement a great success.

Scientific Events Conducted

Prof. Deepak T Nair

1. Organizing member of the Cloud-based Hands-on Workshop: Computational Structure-based Screening and Explicit Molecular Dynamics, October 5-6, 2021
2. NCR-Structural Biology Group Virtual Meeting on September 11, 2021
3. NCR-Structural Biology Group Virtual Meeting on July 17, 2021

Dr. Deepti Jain

1. Organizer of Women's Day celebrations at RCB on March 8, 2022
2. Organizer of RCB Day on March 2, 2022
3. Organizer of Science Day celebrations at RCB on February 28, 2022
4. Organizing member of the Cloud-based Hands-on Workshop: Computational Structure-based Screening and Explicit Molecular Dynamics, October 5-6, 2021

Dr. Vengadesan Krishnan

1. Organized a cloud-based hands-on workshop on 'Computational Structure-based Screening and Explicit Molecular Dynamics' during October 5-6, 2021.
2. Conducted virtual training and awareness session on 'How to effectively use Science Direct- Read Quality... Publish Quality' with Elsevier at NCR Biotech Science Cluster on July 7, 2021.

Dr. Prem S Kaushal

1. Organized "Online workshop on Basic of Electron Microscopy" held on October 20, 2021
2. Organizing member of "Cloud-based Hands-on Workshop: Computational Structure-based Screening and Explicit Molecular Dynamic", held on October 5-6, 2021.

Dr. C V Srikanth

1. Coordinated RCB's Contemporary Webinar Series

Dr. Prasad Abnave

1. Guided students for preparing a video documentary on the life and scientific journey of Dr. Kamal Ranadive to commemorate 75th Year of Independence at RCB on 30.04.2021.

Dr. Anil Thakur

1. Represented Regional Centre for Biotechnology at "India International Science Festival (IISF) - Panaji, Goa, India" from 10-13 December, 2021.

Dr. Nidhi Adlakha

1. Co-organised ID75/ Science Setu program (2020-2021)
2. Co-organised Science Setu Lecture Series (2021-2022)
3. Co-organised International Women's Day (08 Mar 2022)
4. Co-organised RCB Day (02 Mar 2022)

Dr. Pinky Kain

1. Conducted one-day workshop on Fly Neuro-genetics at Jolly Grant Hospital, Dehradun, Uttarakhand on 18th December, 2021.
2. Co-organized online Indian Drosophila Research meeting (InDRC) from 13-17th December, 2021.
3. Moderated online Workshop on mass spectrometry based proteomics at RCB, Faridabad from 12-13th October, 2021.

Membership of Professional/Academic bodies/Editorial boards

Prof. Deepak T Nair

1. Member, Academic Management Committee, Regional Centre for Biotechnology
2. Member, IT Committee, Regional Centre for Biotechnology
3. Head, Advanced Technology Platform Centre of the Regional Centre for Biotechnology
4. Co-opted Member, Interdisciplinary Science PAC, SERB
5. Member, Expert Committee to review proposals submitted under the Niche Creating High Science and Focused Basic Research schemes for Healthcare theme of CSIR.

6. Member Secretary, Data Management Group for implementation of Biotech PRIDE Guidelines
7. Member, DBT Apex BTIC management committee
8. Member, DBT Committee constituted for drafting SOPs for SAHAJ
9. Member, Screening Committee for assessment of proposals received under DBT-BUILDER Programme.
10. Member, Technical Committee to review proposals submitted to the European Synchrotron Radiation Facility Access Program of the Regional Centre for Biotechnology
11. Member, Technical Evaluation Committee of IBDC
12. Life Member, Indian Crystallographic Association
13. Life Member, Indian Biophysical Society
14. Life Member, Society of Biological Chemists
15. Elected Member, Guha Research Conference

Dr. Deepti Jain

1. Member, Travel Grant & Symposia Management Committee, CSIR
2. Member, National Committee of International Union of Crystallography, INSA
3. Review Editor of Frontiers in Bioengineering and Biotechnology
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)
8. Member, Biofilm Society of India

Dr. 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, Board of Studies, Regional Centre for Biotechnology

Dr. Prem S Kaushal

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

Prof. Prasenjit Guchhait

1. Member, Editorial Board for the journals, *Frontiers in Hematology*; *Annals of Clinical and Experimental Immunology*; *Austin Hematology; Cardiology: Open Access; Journal of Hypertension and Cardiology*; *World Journal of Hypertension*
2. Member, Board of Study of the Apeejay Stya University, Gurugram
3. Steering committee member, Good Clinical Practice Professional Certification Scheme (GCPPCS), CDSA, THSTI, Faridabad
4. Member, Academic committee of ESIC Hospital and Medical College, Faridabad
5. Registrar in-charge, Regional Centre for Biotechnology (RCB), Faridabad
6. Chairperson, Academic Committee of RCB
7. Member, Academic Committee of RCB
8. Member, Board of Study of RCB, 2017-present.
9. Member Secretary, Institutional Ethics Committee (Human Research), RCB
10. Chairperson, Institutional Biosafety Committee
11. Chairperson, Institutional Animal Ethics Committee, RCB
12. Member Secretary, Institutional Committee for Stem Cell Research, RCB
13. Co-Chairperson of Infectious disease research facility of NCR Biotech Science Cluster
14. Member of the core committee of NCR Biotech cluster scientific committee
15. DBT nominee for Institutional Biosafety Committee, THSTI, Faridabad

Dr. Tushar K Maiti

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

Dr. Sam J Mathew

1. Member, Institutional Stem Cell Research Committee, THSTI, Faridabad
2. Member, Indian Society for Developmental Biology (InSDB)
3. Member, Institutional Review Board (IRB), of Indraprastha Institute of Information Technology (IIIT), New Delhi
4. Member Secretary, RCB Institutional Animal Ethics Committee (IAEC)
5. Member, RCB Institutional Biosafety Committee (IBSC)

Dr. Pinky Kain

1. Associate Editor, Science Progress
2. Editor, Acta Scientific Neurology
3. Associate Editor, Neuroscience Insights

Dr. Geetanjali Chawla

1. Member, American Medical Writers Association (AMWA)
2. Associate Editor, Journal of Experimental research on human growth and Aging (JERHA)
3. Guest editor for a special issue on "Multifaceted and Diversified Roles of MicroRNAs in *Drosophila melanogaster*" for Frontiers in Cell and Developmental Biology
4. Review editor on the editorial board of Metabolic Physiology (specialty section of Frontiers in Physiology).

Dr. Sivaram Mylavarapu

1. Reviewer for SERB SUPRA grant proposals
2. Reviewer for DBT Ramalingaswami fellows' annual progress
3. Member, Institutional Ethics Committee, RCB
4. Invited external member, PhD interview committee of CSIR-IGIB
5. Life Member, Indian Society for Cell Biology (ISCB)
6. Member, Institutional Stem Cell Research Committee, THSTI Faridabad

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

Prof. Sudhanshu Vrati

1. Life Member, Indian Society for Cell Biology
2. Life Member, Society of Biological Chemists, India
3. Life Member, Association of Microbiologist of India
4. Life Member, Indian Immunology Society
5. Life Member, Indian Virology Society
6. Member, Scientific Advisory Committee, ILS, Bhubaneswar
7. Member, Scientific Advisory Committee, NIBMG, Kalyani
8. Member, Academic Council, South Asian University, New Delhi
9. Editorial Board Member, Therapeutic Advances in Vaccines (SAGE, UK)
10. Independent Director, BIBCOL, Bulandshahar
11. Member, Covid-19 Solidarity vaccine Trial - WHO Candidate Vaccine Prioritization Working Group
12. Coordinator, INSACOG

Dr. C V 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

Dr. Manjula Kalia

1. Member, American Society for Microbiology
2. Member, American Society for Virology
3. Editor, Microbiology Spectrum
4. Review Editor, Frontiers in Cellular & Infection Microbiology
5. Review Editor, Frontiers in Neurology

Dr. Arup Banerjee

1. Contributing member of the F1000 Faculty Infectious Diseases of the Nervous System Section in F1000Prime
2. Editorial Board member (Infectious Diseases), Scientific Reports

Dr. Prasad Abnave

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

Dr. Saikat Bhattacharjee

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

Dr. Divya Chandran

1. Member, Plant Biology Review Committee, Ramalingaswami re-entry fellowship annual progress, March 03, 2022
2. Council Member, Haryana Science & Technology Council, Women's Indian Chamber of Commerce and Industry, 2021
3. Member, International Society for Molecular Plant-Microbe Interactions
4. Member, British Society for Plant Pathology
5. Associate Editor, Plant Molecular Biology Reporter

Dr. Rajendra P Roy

1. Member, Governing Body, NCCS, Pune
2. Member, Research Area Panel - Scientific Advisory Committee, NCCS, Pune
3. Member, Program Advisory Committee – Interdisciplinary Biological Science, DST-SERB.
4. Member, American Peptide Society
5. Member, Guha Research Conference
6. Member, Association of Microbiologists of India

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. Book Editor, "Biomass for Bioenergy and Biomaterials" published by Taylor & Francis Co.
2. Review Editor, Frontiers in Bioengineering and Biotechnology
3. Member, American Society of Microbiology

Distinctions, Honours and Awards

Prof. Deepak T Nair

1. Best Poster Award for Dr. Minakshi Sharma in the RCB Foundation Day Symposium for her poster titled "Translesion and proofreading ability of PfPrex aid in the replication of the apicoplast genome in *P. falciparum*."

Dr. Prasad Abnave

1. INSPIRE Faculty Fellowship, DST

Dr. Anil Thakur

1. Ramalingaswami Fellowship from DBT, India

Dr. Sam Mathew

1. Cover image for the article published in Journal of Cell Science: Agarwal M*, Bharadwaj A* and Mathew SJ (2022) TLE4 regulates muscle stem cell quiescence and skeletal muscle differentiation.*Journal of Cell Science* 135(4). jcs.256008.

Dr. Pinky Kain

1. Received Funding to attend Neural Circuits CSHL meetings from 16-19th March, 2022.
   Received Best second oral presentation award for a research talk at Agriculture, Biological and life Sciences (ICABLS) conference by Vidya Kutir Foundation, Delhi (25-26th September, 2021)

2. India Alliance DBT/Wellcome Intermediate Fellowship

Dr. Geetanjali Chawla

1. India Alliance DBT/Wellcome Intermediate Fellowship
2. Ben Barres Spotlight Award (2021)
3. Highlighted in the coffee table book titled '75 under 50 (aged) scientists shaping today's India', released by the Ministry of Science and Technology, Govt. of India, on the National Science Day, February 2022.

Prof. Sudhanshu Vrati

1. Elected Fellow, National Academy of Sciences, India
2. Elected Fellow, Indian Academy of Science, Bangalore
3. Elected Fellow, Indian National Science Academiy, New Delhi
4. Elected Member, Guha Research Conference
5. JC Bose National Fellowship

Dr. Rajender K. Motiani

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

Dr. Karthigeyan Dhanasekaran

1. Ramalingaswami Re-entry Fellowship

Dr. Ramu S Vemanna

1. Ramanujan Fellowship
2. Innovative Young Biotechnologist Award, DBT

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

Dr. Nidhi Adlakha

1. INSPIRE Faculty Fellowship, DST

Dr. Ambadas Rode

1. Functional nucleic acids: Recent landscapes and therapeutic applications" (ielc22/05): EMBO lecture course grant. 32850 Euros (November 2021).
2. Ramalingaswami Fellowship

Lectures Delivered, conferences attended, visits abroad and outreach

Prof. Deepak T Nair

1. Attended the Virtual ESRF User Meeting 2022 held from February 7-9, 2022.
2. Attended the Virtual user meeting for discussion of a new synchrotron facility in India organized by TIFR on January 16, 2022.
3. Session Chair at the Online 2nd Annual Symposium on Single particle CryoEM and Cellular Tomography organized by the Cryo-Electron Microscopy & 3-Dimensional Image Processing Society of India on December 18, 2021.
4. Delivered an invited talk titled "A polar filter in DNA polymerases prevents ribonucleotide incorporation." at the 48th National Seminars in Crystallography (NSC-48) held at IIT, Roorkee from November 25-27, 2021.
5. Attended IUCr CCP4/CCP-EM virtual workshop held from August 9-10, 2021.
6. Represented RCB in the Networking Session of the PDF Meeting 2021 organized by IndiaBioscience on May 19, 2021.

Dr. Deepti Jain

1. Delivered a talk on "Women in Science" on the occasion of Women's Day at Regional Centre for Biotechnology, March 8, 2022.
2. Delivered an Invited talk titled "Women in Science and Technology and Science and technology for women" held online on March 7, 2022 organized by Haryana State Council for Science and Technology and DST for celebration of Vigyan Utsav.
3. Nominated to showcase research, training and academic activities at RCB at the India International Science Festival at Goa, between December 10-13, 2021.
4. Organized online Vigyan Pradarshini on December 10, 2021, to commemorate 75 years of India's independence and showcase achievements of RCB in various research fields.
5. Delivered an Invited talk titled "The antiactivator employs an allosteric mechanism to inhibit the ATPase activity of transcription regulator FleQ in *Pseudomonas aeruginosa*" at the National Seminar in Crystallography-48 held at IIT-Roorkee on November 25-27, 2021
6. Invited webinar titled "Allies and Adversaries in the Microbial World" held online for student and faculty of Bhaskaracharya College of Applied Sciences, (Delhi University) on the occasion of international microorganism day on September 18, 2021
7. Organizer of outreach event each month (ID75 series of webinars) as a part of DBT Science Setu program to commemorate India's 75 years of independence from Jan 2021-August 2021
8. Hosted a short-term M.Sc. student trainee in my laboratory as part of the SERB Scientific Social Responsibility (SSR) program between December, 2021-January, 2022.

Dr. Vengadesan Krishnan

1. Participated in an online national workshop on 'Innovations in KOHA - LMS for Library Automation: Practical Approach' organized by Central Library, Poornima Institute of Engineering & Technology, Jaipur during February 22-26, 2022.
2. Delivered an invited talk on 'Structural insights into pili-mediated probiotic-host interaction and pathogen exclusion' at the one day online National Seminar cum workshop on 'Crystallography and Biomolecules' organized at Pondicherry University, Pondicherry on December 8, 2021.
3. Attended and delivered an invited talk on 'Structural insights into PI-2 pili from *Streptococcus oralis*, an early colonizer in dental plaque' at the 48th National Seminar on Crystallography (NSC48) organized at Indian Institute of Technology, Roorkee during November 25-27, 2021.
4. Participated and presented work on 'Structural analysis of pilus components in *Lactobacilus ruminis*' at the online EMBO Practical Course, 'Solution Scattering from Biological Macromolecules' held at Hamburg, Germany, during October 25 to November 03, 2021.
5. Attended 'DeLCON committee virtual meeting' on September 22, 2021.
6. Attended and participated in the following webinar series and sessions organized by DeLCON and publishers.

i. Attended a webinar on 'Effective writing skills for promoting research - what do we need to know' organized by Elsevier onDecember 13, 2021.
ii. Attended a training session on '360-degree view on research management & academic journal publishing' organized by Elsevier on November 12, 2021.
iii. Attended a webinar on 'UNIDAY: Virtual Publishing Workshop for Researchers' organized by Wiley on October 28, 2021.
iv. Attended a webinar on 'UNIDAY: Virtual Publishing Workshop for Researchers' organized by Wiley on July 28, 2021.
v. Attended a session on 'How to effectively use ScienceDirect- Read Quality... Publish Quality' organized by Elsevier on June 25, 2021.
vi. Attended a session on 'Accessing Wiley Journals & Publication Tips for Authors' organized by Wiley on June 17, 2021.
vii. Attended a session on 'Elsevier Knowledge Hub - Publication Ethics and Research Integrity in Science' organized by Elsevier on May 11, 2021.

Dr. Prem S Kaushal

1. Delivered a talk on "Career options in Science" on International Women's Day on March 8, 2022, organized by Regional Centre for Biotechnology, Faridabad.
2. Showcased the structural biology research activity at RCB, through a virtual mode, in Vigyan Pradarshini, organized to commemorate India's 75th year of independence on December 10, 2021.

3. Delivered a Lecture (virtual mode) on "Recent advances in single-particle cryo-electron microscopy (cryo-EM) to determine the structure of biological macromolecules" at Virtual Workshop on 'Basics of Electron Microscopy' on October 20, 2021, by ATPC, RCB Faridabad.
4. Delivered a webinar on "Life and work of the great Indian Scientist Professor G.N. Ramachandran" on July 23, 2021, organized by RCB, as a part of Science Setu to commemorate the 75th Year of Indian Independence.
5. Mentored the students to showcase the "Life and work of the great Indian Scientist Dr. K.S. Krishnan" on July 10, 2021, organized by RCB, as a part of Science Setu to commemorate the 75th Year of Indian Independence.
6. Attended 2 days "Webinar on Transparency Audit with Respect of Compliance under Section 4 of RTI Act, 2005" organized by the Indian Rubber Manufacturers Research Association (IRMRA), Thane, on May 20-21, 2021.

Prof. Sudhanshu Vrati

1. Chaired the second Round Table on Industry-Acadmia Collaboration in Life Sciences in Indian Biopharma Industry, organized by CII on 8th October, 2021.
2. Delivered an invited talk on "Making of a rotavirus Vaccine" on 30 September, 2021 in Merck India.
3. Executive Director, RCB delivered an invited talk in a Webinar on 'Global Research Perspectives of Pandemic COVID-19' organized by, Alumni Association of JNU on 14th June 2020.
4. Delivered an inaugural lecture on 'Development of the Indian Rotavirus Vaccine' on 29 April, 2022 at SRM University, Sonepat.

Dr. C V Srikanth

1. Delivered an invited talk titled 'Unwrapping the *Salmonella* Typhimurium mediated host epigenetic modifications and their long-term consequences' at the 'Advances in Basic and Translational Research in Biology (ABTRiB)' organised by Tezpur University, Assam on March 11, 2022.
2. Delivered an invited talk titled 'Determinants of peaceful coexistence and long term side effects of non-Typhoidal *Salmonella* infections' at the 'SBS Webinar series' organised by IIT Mandi, on March 3, 2022.
3. Delivered an invited talk titled 'Learning to tame the gut inflammation the 'SUMO Way' at the 'Alumni Webinar Series' organised by Department of Genetics, University of Delhi, South Campus on February 28, 2022.
4. Delivered an invited talk titled 'Interplay between Salmonella and host epigenetics machinery in chronic infections' at RCB as a part of RCB's Science Setu Lecture Series, on February 11, 2022.

Dr. Manjula Kalia

1. 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 15-17 February 2022.
2. Delivered an invited talk titled 'Pharmacological modulation of autophagy as a potential therapeutic for Japanese Encephalitis Virus' at the 6th Annual International Conference of INSCR Microbes in Sustainable Development organized in association with the Department of Zoology, University of Delhi, (and its various colleges), held online from 15-18 November 2021.

Dr. Prasad Abnave

1. Contributed an invited video interview for the special programme series 'Science for a Self-Reliant India- Vaccine: India Fights back' for Vigyan Prasar (India Science), Department of Science and Technology (DST), Government of India.
2. Participated in the "Proteomics Advanced Winter School (PAWS)-2021" faculty training workshop at the IIT Bombay during November 8-19, 2021.
3. Hosted a student (during) for virtual e-internship under Knowledge Augmentation through Research in Young Aspirants (KARYA) Programme of DST Rajasthan.

Dr. Sam J Mathew

1. Invited speaker at the 90th Annual Meeting of the Society of the Biological Chemists (SBCI), India, delivering the talk titled "The Wnt signaling pathway as a therapeutic target to treat Rhabdomyosarcoma tumors" in the online conference on December 19, 2021.

Dr. Pinky Kain

1. Delivered an invited talk titled "Understanding gustatory processing using *Drosophila* as a model system" at a Virtual Launch event organized by Sci-ROI@India on 18th February, 2022.
2. Delivered a research talk title "Understanding novel foraging- feeding circuits in *Drosophila*" at Indian Drosophila Research meeting organized by IISER Pune, India (InDRC, 13-17th December, 2021)
3. Delivered an invited talk titled "Role of Drosophila taste system in understating mechanisms mediating health and obesity" at International conference on psychology and mental health, Dubai (22-23 November, 2021).
4. Delivered an invited talk titled "Metabolic aging and Covid-19" at Agriculture, Biological and life Sciences (ICABLS) conference by Vidya Kutir Foundation, Delhi (25-26th September, 2021)
5. Delivered an invited talk titled "Activity and state dependent modulation of salt taste behaviour in Drosophila" at Insect Olfaction and taste in 24hrs around the globe, CA, USA (11-12th August, 2021).
6. Delivered an invited talk titled "Understanding taste and its modulation using Drosophila as a model system" at NeuroFemIndia-Celebrating women in Neuroscience (9-13 April, 2021).

Dr. Geetanjali Chawla

1. Presented a talk titled "Enhancing healthy lifespan with diet and non-coding RNA networks", at the Sci-ROI@India virtual launch event, organized by Winstep Forward, February 18-19, 2022.
2. Attended and presented a talk titled "Sequential co-targeting by clustered microRNAs regulates both developmental and adult function", at the Indian Drosophila Research Conference (InDRC 2021), organized by Indian Institute of Science and Education Research, Kolkata, December 13-17, 2021 (Virtual).
3. Attended and showcased the Molecular Medicine Research theme of RCB at the Vigyan Pradarshini program organized by the RCB on December 10, 2021 (Virtual).
4. Attended and presented poster titled highlighting research program at the India Alliance annual conclave organized by DBT-Wellcome India Alliance during October 25-28, 2021 (Virtual).
5. Serving as a volunteer in the Evidence synthesis team of the Lancet Commission for Reimaging healthcare in India (since February, 2021).
6. Served as a mentor in the Freedom Employability academy since 2018.

Dr. Avinash Bajaj

1. Delivered an invited talk titled Unlocking the Chemistry of Bile Acids for Biomedical Needs held online at Central University of Karnataka on March 22, 2022.
2. Delivered an invited talk titled Microbial Membranes as Potential Therapeutic and Diagnostic Targets at INYAS National Frontiers of Science meeting (NatFoS 2022) held at Timber Trail, Parwanoo, HP during March 13-15, 2022.
3. Delivered an invited talk titled Nanoparticle-mediated gene therapy strategies for mitigating inflammatory bowel disease at 1st Annual Meeting of School of Chemical Biology held at INST Mohali during September 24-25, 2021.
4. Delivered an invited talk titled Nanoparticle-mediated Gene Therapy Strategies for Mitigating Gut Inflammation at 6th Annual Cell and Gene Therapy Symposium (Virtual Meeting) held at Centre for Stem Cell Research, Vellore from September 1-3, 2021.

Dr. Rajender K Motiani

1. Delivered an invited talk titled "Dysregulation of Calcium Homeostasis in Human Pathophysiology" at the Department of Life Sciences, Shiv Nadar University, Delhi-NCR, September 2, 2021.
2. Supervised students to prepare a documentary on Dr. Darshan Ranganathan as part of RCB Science Setu ID75 program.
3. Attended DBT/Wellcome Trust India Alliance Annual Conclave from October 25-28, 2021.

Dr. Karthigeyan Dhanasekaran

1. Delivered a General talk highlighting the achievements of Cancer and Cell Biology related research at RCB as a part of the Science Exhibition conducted in ID75 event series (held online on December 18, 2021).

Dr. Saikat Bhattacharjee

1. Delivered a virtual Seminar titled '*Inositol polyphosphates: choreographing signaling rhythms in diverse plant stress responses*' at the 'Molecular Intricacies of Plant Associated Microorganisms (MIPAM) organized by Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad on February 17, 2022.
2. Attended the virtual Newton Bhabha Fund Researcher Link Workshop on Sustaining Food Production Under Environmental Stress organized by National Agri-Food Biotechnology Institute (NABI), Mohali January 18-20, 2022.

Dr. Divya Chandran

1. Co-organized an outreach event to celebrate International Women's day at RCB on March 08, 2022.
2. Delivered an invited lecture entitled 'New insights on the molecular mechanisms of powdery mildew resistance in legumes' as part of the Molecular Intricacies of Plant Associated Microorganisms (MIPAM) virtual meeting organized by the Centre for DNA Fingerprinting and Diagnostics, Hyderabad on February 17, 2022.
3. Hosted a short-term M.Sc. student trainee in my laboratory as part of the SERB Scientific Social Responsibility (SSR) program between January-February, 2022.
4. 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, January-March 2022.
5. Assisted in showcasing RCB's research, training and education-related activities at the Mega Science, Technology & Industry Expo, India International Science Festival, Goa, between December 10-13, 2021.
6. Delivered an invited lecture entitled 'Unravelling legume-powdery mildew interactions through functional genomics' as part of the Webinar Series on 'Emerging Topics in Plant Biology' organized by the Department of Plant Science, Central University of Kerala on October 08, 2021.
7. Hosted two high school (Grade XI) students from Shiv Nadar School, Faridabad for a two-week training program in plant-microbe interactions from October 27-November 09, 2021.
8. Co-organized a monthly webinar series to showcase the life and works of Indian Scientists as part of the DBT 75th year of Indian independence celebratory event and Science Setu, April-August 2021.

Dr. Ramu S Vemanna

1. Delivered an invited talk on 'Biotechnological Applications to Improve Plant Traits and Productivity' as part of the Webinar Series on 'Emerging Topics in Plant Biology' organized by the Department of Plant Science, Central University of Kerala on August 21, 2021.
2. Attended ACS Science Talk (virtual lecture series) entitled "Decoding chemosensory systems for Flavor Innovations" by Prof. Prof. Thomas F. Hofmann on July 30, 2021.
3. Delivered an invited talk during a virtual tour for College of Agriculture, Hassan, B. Tech (Biotech) students as a part of Plant Biotechnology Applications and Opportunities on July 14, 2021.
4. Delivered an invited talk on "Genome editing and agro-chemicals - improve plant traits and productivity"- Two Day International Webinar on *Applications of Plant Biotechnology* organised by Department of Botany, & Department of Biotechnology, Sri Venkateswara University, Tirupati, INDIA jointly with Faculty Agro-Based Industry, Universiti Malaysia Kelantan, Malaysia in collaboration of Universitas Bengkulu, Indonesia during June 27-28 2021.

Dr. Prashant Pawar

1. Attended virtual 7th International Conference on Plant Cell Wall Biology (PCWB2021) organised by Saitama University, Japan, from June 27 to July 1, 2021.
2. Attended Leibniz Institute of Plant Biochemistry Symposium (virtual) on Plant Cell Walls 2021 organised by Leibniz Institute Halle, on May 7, 2021.

Dr. R P Roy

1. Delivered an invited talk titled 'Enzymatic transformations at the chemistry-biology interface' at the 'International hybrid meeting on physics and chemistry of advanced materials (PECAM)' organized by IIT, Delhi, Oct 24-28, 2021.

Dr. Ambadas B Rode

1. Attended a virtual 'National Conference on Nucleic Acid Science & Technology' organized by CSIR-Institute of Minerals & Materials Technology, Bhubaneswar during August 10-13, 2021.
2. Delivered an invited talk titled 'Molecular engineering of functional nucleic acids for biomedical applications' in online National e-conference on 'Role of chemistry for sustainable future' organized by Shiv Chhatrapati College Aurangabad, Maharashtra on July 13, 2021.

Dr. Nidhi Adlakha

1. Delivered an invited talk titled 'Understanding metabolic engineering as a tool to improve product yield in the industrial biotechnology sector' held on August 18, 2021 organised by Microbiology Society, India.

Reviewer of proposals/thesis/research articles

Prof. Deepak T Nair

1. Reviewer of research proposals submitted to the SERB Program Advisory Committee for Interdisciplinary Biological Sciences
2. Reviewer of proposals submitted to the DBT Task Force on Research Resource Service Facility and Platforms
3. Reviewer for *Nucleic Acids Research, Structure, Nature Communications, & Biochemistry.*
4. Reviewer of proposals submitted for synchrotron beamtime to the European Synchrotron Radiation Facility Access Program of the Regional Centre for Biotechnology
5. Examiner for PhD theses from JNU and AcSIR

Dr. Vengadesan Krishnan

1. Reviewer for thesis from All India Institute of Medical Sciences (AIIMS) and Jawaharlal Nehru University (JNU), New Delhi.
2. Reviewer for *Current Research in Structural Biology*, *Protein & Peptide Letters*, and *Frontiers in Microbiology*

Dr. Prem S Kaushal

1. Reviewer for research grants of DST-SERB

Prof. Prasenjit Guchaait

1. Reviewer for research proposals for BIRAC, DBT, Govt. of India, 2019-present.
2. Reviewer for Scientific Journals: *Blood*, *eLife*, *Bioengineered*, 2021-2022
3. PhD thesis reviewer for 3 students of other University in India

Dr. Tushar K Maiti

1. Reviewers for Biochemical J, Biomacromolecules, J Proteomics, Bioscience Report, Int J Biol. Macromol
2. Reviewer, DST-CRG grant proposal

Dr. Sam J Mathew

1. Reviewer for research proposals for DBT, CSIR, Israel Science Foundation, Medical Research Council (UK), and INSERM-CNRS (France).
2. Member of the Joint Review Committee for review of ongoing and completed research projects under the International Cooperation Division, DBT, on January 4-5, 2022.
3. Reviewer for PhD thesis from Manipal University, Sastra University and AcSIR.
4. Reviewer for *Cell Death and Disease*, *Developmental Biology*, *FASEB J*, *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, Neural Regeneration Research, Science Progress, Neuroscience insights, Annals of the Entomological Society of America, Journal of Biosciences, International journal of Gastronomy and Food Science, International journal of Autism* and *related disabilities.*

Dr. Geetanjali Chawla

1. Reviewer for PhD thesis from Shiv Nadar University
2. Reviewer for *Applied Biochemistry and Biotechnology, Journal of Bioscience, MicroRNA*

Dr. Sivaram Mylavarapu

1. PhD thesis and viva voce examiner for Ms. Ahana Addhya, National Institute of Immunology, Jawaharlal Nehru University, New Delhi.
2. PhD thesis and viva voce examiner for Mr. Shaunak Anilkumar Burse, CSIR-Institute of Genomics and Integrative Biology (CSIR-IGIB), AcSIR, New Delhi.

Dr. Manjula Kalia

1. Reviewer for *Autophagy, Journal of Virology, Advanced Science, Emerging Microbes & Infection*
2. Reviewer for PhD thesis from ICGEB, NII, AIIMS, Mewar University.
3. Reviewer for research grants from SERB.

Dr. Prasad Abnave

1. Reviewer for *Nature Communications, Pathogens*
2. Review Editor for *Frontiers in Cellular & Infection Microbiology, Frontiers in Cell and Developmental Biology*

Dr. Anil Thakur

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

Dr. Avinash Bajaj

1. Invited Member, Biomedical and Health Science, Program Advisory Committee, SERB
2. Reviewer for *American Chemical Society, Royal Chemical Society*

Dr. Rajender K Motiani

1. Reviewer of research proposals submitted to SERB: Core Research Grants and Power Grants.
2. Reviewer for *Journal of Biological Chemistry, Mitochondrion, Pigment Cell & Melanoma Research, Cells, International Journal of Molecular Sciences, Cell Communication & Signaling, Communication Biology, Journal of Bioscience* and *Cell Calcium*.
3. Ph.D. Thesis Examiner of Ms. Surbhi Sharma, Institute of Genomics and Integrative Biology (IGIB), New Delhi; Mr. Narendra Tirpude, Institute of Himalayan Bioresource Technology (IHBT), Palampur and Ms. Rutambhara Purohit, Indian Institute of Technology (IIT)-Madras, Chennai.
4. Ph.D. Viva Examiner of Ms. Akansha Rai, CSIR-Institute of Genomics and Integrative Biology (IGIB), New Delhi.

Dr. Karthigeyan Dhanasekaran

1. Reviewer for IEEE Access

Dr. Saikat Bhattacharjee

1. Expert for Plant and Molecular Biology, Question Paper Settling, JNU Entrance Examination, National Testing Agency (NTA)
2. Reviewer for *Planta* and *Phytopathology*

Dr. Divya Chandran

1. Reviewer for SERB and DBT research proposals
2. Reviewer for *Plant Physiology and Biochemistry*, *3 Biotech*, *Microbial Genomics*, *Frontiers in Plant Science*

Dr. Ramu S Vemanna

1. Reviewer for SERB and DBT research proposals
2. Reviewer for *Plant Physiology*, *Plant Biotechnology, Canadian Journal of Plant Pathology, Journal of Frontiers in plant sciences, Plant Physiology and Biochemistry, Journal of Soil Science and Plant Nutrition, Plant Molecular Biology Reporter, Plant Cell,*

Tissue and Organ Culture, Applications in plant sciences, Plant Physiology reports, Crop Science.

Dr. Prashant Pawar

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

Ambadas B Rode

1. Reviewer for research grants of DST
2. Reviewer for *Applied Biochemistry and Biotechnology*

Dr. Nidhi Adlakha

1. Reviewer for research grants of DBT and CSIR
2. Reviewer of PhD thesis from ICT Mumbai
3. Reviewer for *Applied and Microbial Technology, Frontiers in Bioengineering and Biotechnology, Frontiers in Microbiology* and *Biotechnology for Biofuel*

EXTRAMURAL ACTIVITIES & NETWORKING

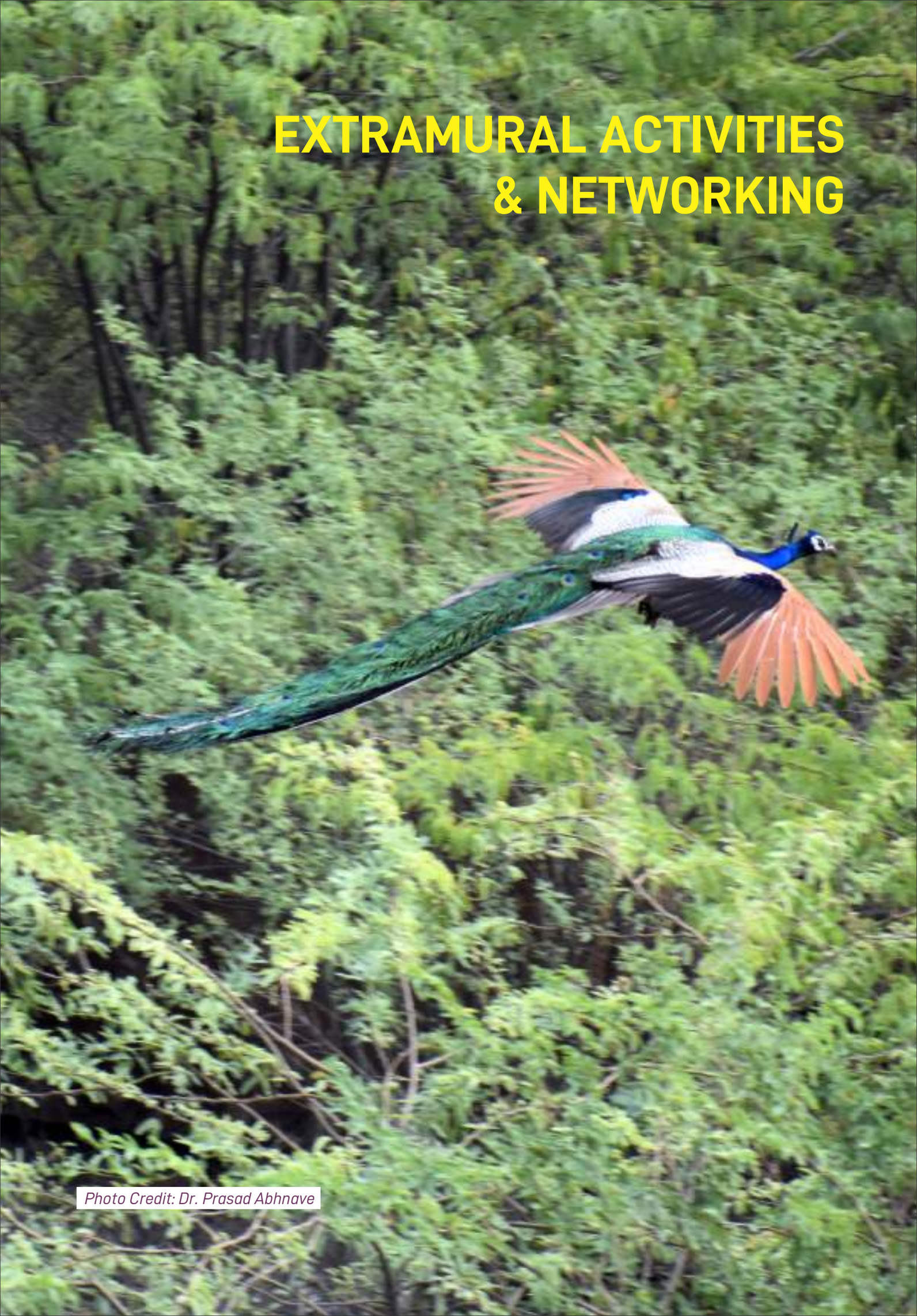


Photo Credit: Dr. Prasad Abhnave

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.

In the last five years, researchers from 28 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: - Institute of Microbial Technology (Chandigarh), Jawaharlal Nehru University (New Delhi), Institute of Life Sciences (Bhubhaneswar), Institute of Stem Cell & Regenerative Medicine (Bangalore), All India Institute of Medical Sciences (New Delhi), Indian Institute of Science (Bangalore), Poornaprajna Institute of Scientific Research (Bangalore), Regional Centre for Biotechnology (Faridabad), Indian Institute of Science Education & Research-Pune, Indian Institute of Technology-Delhi, Indian Institute of Technology-Roorkee, Indian Institute of Technology-Kharagpur, National Centre for Cell Sciences (Pune), Indian Institute of Science Education & Research-Thiruvananthapuram, Central Drug Research Institute (Lucknow), Saha Institute of Nuclear Physics (Kolkata), St. Xaviers College (Kolkata), National Institute of Mental Health & Neurosciences (Bangalore), National Institute of Science Education & Research (Bhubhaneswar), CSIR-Institute of Genomics & Integrative Biology (New Delhi), CSIR-Central Leather Research Institute (Chennai), University of Madras (Chennai), International Centre for Genetic Engineering and Biotechnology (New Delhi), Indian Institute of Technology-Bombay (Mumbai), Translational Health Science and Technology Institute (Faridabad), National Chemical Laboratories (Pune), National Centre for Biological Sciences (Bangalore), National Centre for Cell Sciences (Pune) and National Institute of Plant Genome Research (New Delhi).

The ESRF access program has enabled Indian researchers to publish more than 170 research papers involving basic and applied research in the last five years, in international peer-reviewed journals. Due to this program, a number of researchers, especially 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

The 'Indian Biological Data Centre (IBDC)' is the first national repository for life science data in India (ibdc.rcb.res.in.). As per the Biotech-PRIDE (Promotion of Research and Innovation through Data Exchange) guidelines, IBDC is mandated to archive all life science data generated from publicly funded research in India. The data center is supported by the Government of India (GOI) through the Department of Biotechnology (DBT). It is being established at the Regional Centre of Biotechnology (RCB), Faridabad in the national capital region in collaboration with the National Informatics Centre (NIC), India.

The data center has started its operation by providing nucleotide data submission and analysis services. For this purpose, two data portals were developed within IBDC. The first one is the 'Indian Nucleotide Data Archive' (INDA) which is accepting all type of Nucleotide data submission as per international data formats. INDA actively collaborates with all major international nucleotide data archives such as GenBank, ENA and DDBJ. Any data set submitted to INDA automatically gets IBDC as well as INSDC accessions (GenBank, ENA and DDBJ). So far, over 48 billion bases of nucleotide data has been submitted to INDA. The other is the 'Indian Nucleotide Data Archive-Controlled Access' (INDA-CA), which does not share data with any other repository and provides only controlled access to the submitted datasets. Over 1.5 lakh covid genome sequences have been submitted at INDA-CA. Further, a dedicated 'COVID data portal' has also been developed that archives and analyses the COVID 19 genome sequences being generated by the INSACOG in

India. Other sections of IBDC are also under development that will handle various kinds of life science data sets. Currently, the IBDC team consists of 11 personnel including data curators, programmers and system administrators.

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 (Indian Institute of Science, Bangalore), Dr. S. Batra, (CSIR-Central Drug Research Institute), Dr. Debasisa Mohanty, (National Institute of Immunology),Dr. Dinakar M Salunke, Dr. Dinesh Gupta, (International Centre for Genetic Engineering and Biotechnology-New Delhi), Mr. Sudhir Chandra (National Informatics Institute), Dr. Rajesh Kumar (Institute of Advanced Virology, Thiruvanathapuram), Prof Sudhanshu Vrati, Dr. Deepti Jain (RCB)
Dr. Deepti Jain	Prof. Sudhanshu Vrati, Prof. Deepak T Nair, Dr. Divya Chandran, Ambadas Rode (RCB), Dr. Gopaljee Jha, (NIPGR, New Delhi), Prof. Sunil Kumar Khare (IIT Delhi)
Dr. Vengadesan Krishnan	Dr. Priti Saxena (SAU, New Delhi), Dr. Amit Kumar Pandey (THSTI, Faridabad), Dr. Airi Palva (University of Helsinki, Finland), Dr. Partha Roy (IIT, Roorkee), Dr. R P Roy (RCB, Faridabad)
Dr. Prem S Kaushal	Dr. Rajesh Ringe (IMTECH), Dr. Anil Thakur (RCB) Prof. Nisheeth Agarwal, THSTI, and Prof. N Gourinath (JNU).
Prof. Prasenjit Guchhait	Prof. Josef T Prchal (Univs of Utah, Salt lake city, USA), Prof. Perumal Thiagarajan (Baylor College of Medicine, Houston, USA), Prof. Jorge Di Paola (Washington Univs, St Louis, USA), Prof. Tulika Seth, Prof. Rajesh Khatgawat, Prof. Naval Vikram, (AIIMS, New Delhi), Prof. Parvaiz Kaul (SKIMS, Srinagar), Prof. Ramandeep Singh, Dr. Shailendra Asthana, Dr. Milan Surjit, Dr. Tripti Srivastava, Dr, Sweety Shamal, (THSTI, Faridabad), Prof. Anirban Basu (NBRC, Manesar), Dr. Surajit Karmakar (INST, Mohali), Dr. Garima Agarwal (IIT, Mandi), Dr. Soumen Basak (NII, New Delhi), Prof. Sudhanshu Vrati, Dr. Manjula Kalia, Dr. Tushar K Maiti (RCB, Faridabad)
Dr. 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, West Bengal), Dr. Neel Sarovar Bhavesh (ICGEB, New Delhi)
Dr. Sam J Mathew	Dr. Gabrielle Kardon (University of Utah, USA), Dr. Manoj Menon (IIT, New Delhi), Dr. Ramandeep Singh (THSTI, Faridabad), Dr. Janvie Manhas (AIIMS, 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	Dr. Elezebeth Mathews (Central University of Kerala), Dr. Alagu Maneckavelu (Central University of Kerala), Prof. Pankaj Kapahi (The Buck Institute for Research on Aging, CA, USA), Dr. Nick Sokol (Indiana University).
Prof. Sudhanshu Vrati	Dr. Sweety Samal (THSTI), Dr. Renu Wadhwa (AIST, Japan), Dr. Anirban Basu (NBRC, Manesar), Dr. Arup Banerjee (RCB), Dr. Gulam Seyed (ILS, Bhabaneshwar)
Dr. C V Srikanth	Dr. Vineet Ahuja, Gastroenterology, AIIMS, Delhi Dr. Girish Ratnaparkhi, IISER, Pune Dr. Pramod Garg, Gastroenterology, AIIMS, Delhi Dr. Sujoy Paul, Gastroenterology, AIIMS, Delhi Dr. Prasenjit Das, Gastroenterology, AIIMS, Delhi

RCB Principal Investigator	Collaborators
Dr. Manjula Kalia	Prof. Sudhanshu Vrati (RCB); Dr. Dinesh Mahajan (THSTI); Dr. Shailendra Asthana (THSTI); Dr. Nimesh Gupta (NII)
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. Prasad Abnave	Dr. Eric Ghigo (Institut Hospitalo Universitaire Méditerranée Infection, France)
Dr. Anil Thakur	Dr. Alan G. Hinnebusch (NIH, USA), Dr. Ishaan Gupta (IIT – Delhi), Dr. Rekha Puria (GBU Greater Noida)
Dr. 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).
Dr. Sivaram Mylavarapu	Dr. Sourav Banerjee, NBRC Manesar; Dr. Anjana Saxena, CUNY USA; Dr. Megha Kumar, CSIR-CCMB Hyderabad; Dr. Jayanta Bhattacharya, THSTI-IAVI; Dr. Amitabha Mukhopadhyay, IIT Delhi, New Delhi; Dr. Divya Chandran, RCB Faridabad, Dr. Tushar K Maiti, RCB Faridabad
Dr. Rajender K Motiani	Dr. Rajesh S Gokhale (IISER, Pune), Dr. Sridhar Sivasubbu (CSIR-IGIB, New Delhi), Dr. Shantanu Chowdhury (CSIR-IGIB, New Delhi).
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. Mary Wildermuth (University of California Berkeley, USA), Dr. Shri Ram Yadav (IIT, Roorkee), Dr. Atul Goel (CDRI, Lucknow), Dr. Yashwant Kumar (THSTI, Faridabad), Dr. Bonamali Pal (Thapar Institute of Engineering and Technology, Patiala), Dr. Senjuti Sinharoy, Dr. Senthil Kumar Muthappa (NIPGR, New Delhi), Dr. Deepti Jain, Dr. Saikat Bhattacharjee, Dr. Sivaram Mylavarapu (RCB, Faridabad), Dr. Neha Sharma, Dr. Nirpendra Singh (ATPC, NCR Biotech Science Cluster, Faridabad)
Dr. Ramu S Vemanna	Dr. Sheshshayee MS, Dr. Prasanna Kumar M (University of Agricultural Sciences, Bangalore), Dr. Kiran Mysore, Dr. Patrick Zao (Noble Research Institute, USA), Dr. Gopaljee Jha, (NIPGR), Dr. Maneesh Bhandari (Forest Research institute, Deharadun). Dr. Saikat Bhattacharjee, Dr. Avinash Bajaj (RCB)
Dr. Prashant Pawar	Dr Nidhi Adlakha (RCB), Dr Yashwant Kumar (THSTI), Dr Gyan Misra (IARI, New Delhi), Dr Harsh Kumar Dixit (IARI, New Delhi), Dr Ewa J Mellerowicz (Umea Plant Science Centre, Swedish University of Agricultural Sciences, Sweden), Dr Clint Chapple (Purdue University, USA), Dr Jeongim Kim (University of Florida, USA)
Dr. R P Roy	Dr. Srinivasa-Gopalan Sampathkumar (NII, Delhi), Prof S. Ramakumar (IISc, Bangalore)

RCB Principal Investigator	Collaborators
Dr. Ambadas B Rode	Prof. Naoki Sugimoto (FIBER, Konan University), Prof. Sheshnath Bhosale (Goa University), Dr. Ramandeep Singh (THSTI, Faridabad).
Dr. Nidhi Adlakha	Dr. Syed Shams Yazdani, Dr. Charanpreet (ICGEB, New Delhi), Dr. Tarun Sharma (THSTI, Faridabad), Prof. Rakesh Bhatnagar (JNU, New Delhi)

Extramural Funding

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
1.	Prof. Deepak T Nair	Does variation occur in the dinB gene during stress adaptation?	Department of Biotechnology	58.9 lakh	2018-22
2.	Prof. Deepak T Nair	Renewal of access to Structural Biology Facilities at ESRF, France	Department of Biotechnology	2639.8 lakh	2020-23
3.	Dr Vengadesan Krishnan	Structural studies on pilus proteins from *Lactobacillus ruminis*, Department of Biotechnology	Department of Biotechnology	44.5 lakh	2018-22
4.	Dr Vengadesan Krishnan	Investigating Functional Role of Polyketide Modifying Enzymes in Mycobacterial Biology	Science & Engineering Research Board	46.7 lakh	2019-22
5.	Dr Vengadesan Krishnan	Structural studies on pilus proteins from *Streptococcus sanguinis*, a primary colonizer in oral biofilm development (dental plaque)	Science & Engineering Research Board	45.1 lakh	2020-23
6.	Dr. Deepti Jain	Insights into the signal transduction mechanism of GraXSR regulon required for antibiotic resistance in *Staphyloccocus aureus*	Science & Engineering Research Board	43.8 lakh	2019-22
7.	Dr. Deepti Jain	Structure and mechanism of FleQ, master regulator of transcription of flagellar and biofilm genes in *Pseudomonas aeruginosa*	Department of Biotechnology	68.1 lakh	2018-22
8.	Dr. Deepti Jain	Targeting Bacterial Motility and Adherence for Inhibition of Biofilms from *Pseudomonas aeruginosa*	Department of Biotechnology	84.6 lakh	2022-25

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
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 lakh	2021-22
10.	Dr. Prem S Kaushal	Understanding the translation strategies adopted by *M. tuberculosis* during dormancy	Science and Engineering Research Board	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 host	SERB, DST	57.1 lakh	2019-23
12.	Prof. Prasenjit Guchhait	Role of platelet activation in the development of systemic inflammations in patients with type-2 diabetes.	DBT	71.5 lakh	2019-23
13.	Dr. Tushar K 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
14.	Dr. Tushar K Maiti	Multi-Omics Signatures of Human Placenta: Real time assessment of underlying mechanisms for prediction of birth outcomes and development	DBT	64.8 lakh	2020-23
15.	Dr. Tushar K Maiti	MOMI: Biorepository local analysis- INDIA	BMGF	61.6 lakh	2021-22
16.	Dr. Tushar K Maiti	Inter-Institutional Program for Maternal, Neonatal and Infant Sciences A translational approach –interdisciplinaryGrou p for Advanced Research on BirtH outcomes - DBT INdia Initiative (GARBH-Ini Phase II)	DBT	138 lakh	2021-26

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
17.	Dr. Sam Mathew	Functional characterization of skeletal muscle myosin heavy chain-embryonic in adult muscle regeneration and disease.	Department of Biotechnology	77 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	Indian Council of Medical Research	54 lakh	2021-24
19.	Dr. Sam Mathew	Regulation of mammalian growth, homeostasis and differentiation by Transducin-like Enhancer of Split (TLE) proteins.	Science and Engineering Research Board	53 lakh	2022-25
20.	Dr. Masum Saini (Supervisor: Dr. Sam J Mathew)	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 lakh	2018-22
21.	Dr. Pinky Kain	Understanding taste and its modulation using *Drosophila melanogaster*	Wellcome Trust/DBT India Alliance Intermediate grant	350 lakh	2016-22
22.	Dr. Geetanjali Chawla	Post-transcriptional regulators of aging and dietary restriction	Wellcome Trust/DBT India Alliance Intermediate grant	359 lakh	2018-22
23.	Dr. Geetanjali	MicroRNAs in aging	Elife	4.6 lakh	2021-22
24.	Prof. Sudhanshu Vrati	DBT-AIST international center for translational and environmental research (DAICENTER)	DBT	145 lakh	2018-22
25.	Prof. Sudhanshu Vrati	Sub-Network1: Studies on anti-SARS-CoV2 acitivity of selected medicinal plants and formulations in cell culture model of virus infection	DBT	39.2 lakh	2020-21

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
26.	Prof. Sudhanshu Vrati (PI)	Covid-19 Bioresource at the NCR Biotech	DBT	94.4 lakh	2020-22
27.	Prof. Sudhanshu Vrati	DBT-HRDPMU	DBT	404 Lakh	2022-22
28.	Prof. Sudhanshu Vrati	Award of JC Bose Fellowship to Prof. Sudhanshu Vrati	DST-SERB	66.5 lakh	2021-25
29.	Dr CV Srikanth	From the gut SUMO cycles its way into gastrointestinaldisorders	MHRD	93.3 lakh	2020-23
30.	Dr. Manjula Kalia	Pharmacological Modulation of Autophagy as a Potential Therapeutic for Japanese encephalitis	DBT	81.2 lakh	2019-22
31.	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
32.	Dr. Arup Banerjee	Understanding the therapeutic role of adult stem cell-derived exosome in combating virus-induced neurodegenerative disease	DBT	Total grant: 81.4 Lakh Grant for RCB: Rs. 29 lakh	2018-21
33.	Dr. Arup Banerjee	Investigating the molecular modulators of microglial activation and their effect on JEV pathogenesis	SERB	41.1 lakh	2018-21
34.	Dr. Prasad Abnave	Investigating molecular mechanisms governing the proliferation-differentiation balance in adult stem cells during chronic infections.	DST	35 lakh	2019-24
35.	Dr. Prasad Abnave	Investigating histone methylation changes induced in adult stem cells during bacterial infections.	SERB-SRG	28.3 lakh	2020-22
36.	Dr. Anil Thakur	Translation dynamics govern fungal virulence and drug resistance in Candida species	DBT	42.5 lakh	2020-25

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
37.	Dr. Anil Thakur	Characterization of translation initiation codons dynamics to determine pathogenicity of Candida albicans	SERB	23.5 lakh	2020 -22
38.	Prof. Avinash Bajaj	Elucidating the Role of Post-transcriptional Regulation of Sphingolipid Metabolic Genes in Breast Cancer Progression.	SERB	9 lakh	2021-24
39.	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
40.	Prof. Avinash Bajaj	Engineering of Membrane Targeting Molecular Probes for Diagnosis of Mycobacterial Infections	SERB	50.4 lakh	2019-22
41.	Prof. Avinash Bajaj	Combating Topical and Medical Device Related Multidrug Resistant Fungal Infections Using Molecularly Engineered Anti-Fungal Hydrogel	DBT	92.4 lakh	2019-22
42.	Prof. Avinash Bajaj	Spatiotemporal Targeting of Multiple pathway using engineereed polymer gatekeepers in porous nanomaterials for cancer combination therapy	DST	60.8 lakh	2018-21
43.	Prof. Avinash Bajaj	Development of Biocompatible surfaces for ESKAPE pathogens	DBT	41.3 lakh	2017-21
44.	Prof. Avinash Bajaj	Deciphering the Impact of Time-Restricted Feeding (TRF) as a Neoadjuvant Intervention with Chemotherapy for Cancer Treatment, and its Regulatory Mechanisms	NCR Cluster Grant	20 lakh	2020-22
45.	Prof. Avinash Bajaj	Engineering of Drug-Loaded Smart Vectors (DLSVs) for Targeted Delivery of Chemotherapeutics	RCB-IIT Delhi	10 lakh	2021-23

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
46.	Dr. Sivaram Mylavarapu	Understanding the role of transgelin-2 in cell division	Science & Engineering Research Board (SERB)	57.3 lakh	2022-25
47.	Dr. Sivaram Mylavarapu	Prolyl Isomerization of Dynein Light Intermediate Chain Subunits as a Regulatory Driver in Mitosis	Science & Engineering Research Board (SERB)	22 lakh	2018-21
48.	Dr. Sivaram Mylavarapu	Delineating the role of Rab5 GTPase isoforms in mammalian cell cytokinesis	RCB-IITD Collaborative Project Proposal Scheme (MFIRP)	10 lakh	2021-23
49.	Dr. Rajender K Motiani	Role of ER and Mitochondria in Pigmentation: Organellar Calcium signaling perspective.	DBT/ Wellcome Trust India Alliance	360 lakh	2020-25
50.	Dr. Rajender K Motiani	Demystifying the mystery of STIM1 augmentation: *Understanding molecular mechanisms controlling expression of STIM1, a novel regulator of melanoma progression and skin pigmentation*.	SERB Startup Research Grant	31 lakh	2019-22
51.	Dr. Karthigeyan Dhanasekaran	Impact of Flaviviral proteins on centrosome and cilia.	Science and Engineering Research Board (SERB)	27.8 lakh	2022-24
52.	Dr. Karthigeyan Dhanasekaran	Centrosome as a target for viral pathogenesis intervention	Ramalingaswami Fellowship, Department of Biotechnology	42.5 lakh	2021-26
53.	Dr. Saikat Bhattacharjee (Co-PI)	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	Science and Engineering Board	*Total grant:* 78 lakh *Grant for RCB:* 9.9 lakh	2021-24

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
54.	Dr. Saikat Bhattacharjee	Investigating a key regulatory defense assembly and pathogen effector-induced perturbations during innate immune signaling of plants	Department of Biotechnology	92.0 lakh	2018-21
55.	Dr. Saikat Bhattacharjee	The identification and characterization of defense signaling pathways primed by Sea6 Energy products	Sea6 Energy Pvt. Ltd., Bengaluru	8.1 lakh	2020-21
56.	Dr. Divya Chandran (PI)	Generation of a retrotransposon-based mutant population of chickpea for functional genomics studies	Department of Biotechnology	*Total grant:* 128 lakh *Grant for RCB:* 39.1 lakh	2022-25
57.	Dr. Divya Chandran (PI)	Nanocarriers for topical delivery of pathogen-specific RNAi molecules for sustained protection of pea crop against powdery mildew	Department of Biotechnology	*Total grant:* 63.5 lakh *Grant for RCB:* 38.3 lakh	2021-24
58.	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	Science and Engineering Board	43.9 lakh	2020-23
59.	Dr. Naini Burman (Mentor: Dr. Divya Chandran)	Functional characterization of HY5 homolog in rice	Department of Science and Technology (INSPIRE faculty)	35 lakh	2018-23
60.	Dr. Babitha K.C. (Mentor: Dr. Divya Chandran)	Modulation of stomatal aperture regulating genes to improve carbon gain and crop yield	Department of Biotechnology (BioCARe)	52.9 lakh	2019-22
61.	Dr. Ramu S Vemanna	Identification and functional characterization of genes involved in protein translation, degradation, and develop inhibitors to understand bacterial pathogenicity in rice	Science and Engineering Research Board	89 lakh	2017-22

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
62.	Dr. Ramu S Vemanna	Influence of drought stress on ribosomes and protein synthesis and understanding the functional relevance of Ribosomal Protein L10 in rice.	Science and Engineering Research Board	28 lakh	2020-22
63.	Dr. Prashant Pawar	Understanding plant cell wall biosynthesis to optimise lignocellulosic biomass	Department of Science and Technology (INSPIRE)	35 lakh	2018-23
64.	Dr. Prashant Pawar	Investigating GDSL lipase/esterase family to understand the mechanism and role of polysaccharide O-acetylation in plants for bioenergy applications	Science and Engineering Research Board (SRG)	26.7 lakh	2020-22
65.	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 lakh	2021-24
66.	Dr. Ambadas B Rode	Rationally targeting & tuning riboswitch mediated gene regulation for therapeutic and synthetic biology application	Department of Biotechnology	88 lakh	2018-23
67.	Dr. Ambadas B Rode	Design and synthesis of small molecules to target nucleic acids structures for therapeutic applications: Targeting riboswitches for antibacterial therapy	Science and Engineering Research Board (SRG)	19.3 lakh	2019-21
68.	Dr. Nidhi Adlakha	Understanding mechanism underlying plant invasion and survival by *B. cinerea* using temporal secretome mining approach	Science and Engineering Research Board	27.0 lakh	2019-21
69.	Dr. Nidhi Adlakha	Development of *Paenibacillus polymyxa* as a platform for the production of branched chain alcohols	DBT-Mission Innovation- IC4 grant	*Total grant:* 89.6 lakh *Grant for RCB:* 0 lakh	2019-22

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
70.	Dr. Nidhi Adlakha	Unravelling transcriptional regulation of cellulase gene overexpression in Talaromyces sp. NA01	Intra-cluster grant	20 lakh	2020-22
71.	Dr. Nidhi Adlakha	Identification and characterization of novel inducer system for efficient decomposition of plant biomass	Department of Science and Technology (INSPIRE faculty)	35 lakh	2015-21
72.	Dr. Nidhi Adlakha	Aptamer-nanoparticles conjugate: a next generation theranostic agent for phytopathogenic fungi	Department of Biotechnology	*Total grant:* 57 lakh *Grant for RCB:* 19.35 lakh	2022-25
73.	Dr. Nidhi Adlakha	Development of stable enzyme preparation for generating diet for PKU patients	RCB-IITD grant	*Total grant:* 20 lakh *Grant for RCB:* 10 lakh	2021-23
74.	Dr. Kinshuk Raj Srivastava	Biocatalytic combinatorial synthesis of cyclic dipeptides for diverse biological applications	DBT	42.5 Lakh	2019-24
75.	Dr. Kinshuk Raj Srivastava	Development of imine reductase based biocatalytic technology for the synthesis of chiral amines and amino acids for diverse industrial applications	SERB	25 Lakh	2021-23
76.	Dr. Rajendra P. Roy	Semisynthetic histones with defined chemical marks for interrogation of eraser specificity	SERB	40.7 Lakh	2020-23
77.	Dr. Rajendra P. Roy	Award of JC Bose Fellowship to Dr.R.P. Roy	SERB	34.1 Lakh	2016-21
78.	Prof Sudhanshu Vrati (Co-ordinator) Prof. Deepak T Nair (PI) Dr. Deepti Jain (PI)	Development of small molecule antivirals against Chikungunya and Japanese Encephalitis virus	Department of Biotechnology	480.7 lakh	2020-23
79.	Prof Sudhanshu Vrati (Co-ordinator) Prof. Deepak T Nair (PI)	Setting up of the Indian biological Data Centre-Phase 1	Department of Biotechnology	7578.8 lakh	2020-23

S.No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
80.	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	Department of Biotechnology	197.3 lakh	2021-26

RESEARCH & INNOVATION INFRASTRUCTURE

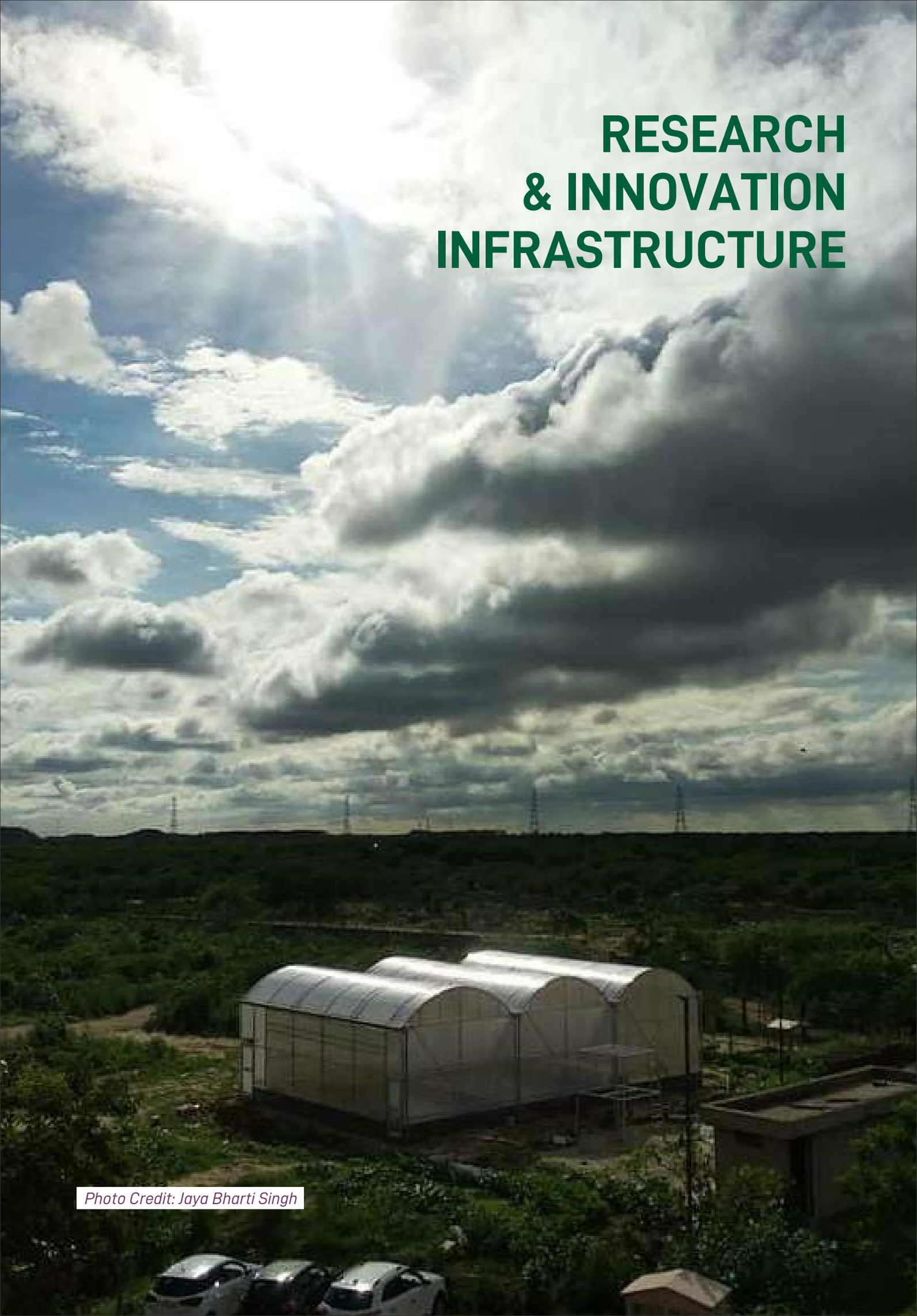


Photo Credit: Jaya Bharti Singh

BSC BioNEST Bio-Incubator (BBB)

BBB, RCB, supported by DBT-BIRAC's Bioincubators Nurturing Entrepreneurship for Scaling Technologies (BioNEST) scheme, has been the go-to Bioincubation facility, for the young bio-entrepreneurs, to realise and translate their dream projects/ideas into products of commercial value as well as medical / environmental relevance. BBB ecosystem with its sprawling 35,000 Sq. ft area in the prime location of NCR Biotech Science Cluster is equipped with central instrumentation facility, lab & culture facility, office suites and has supported hitherto 39 startups, whose thrust areas include diagnostics, health-care, med-tech, industrial biotech, Biopharma (Vaccines & Therapeutics), environmental and agro-food technologies. The incubatees gain from the services offered viz, IP, Business Mentorship & Strategic Support, assistance for funding as well as from access to the pool of Mentors and Advance Technology Platform Centre.

The customized ongoing strategic programmes under Awareness, Entrepreneurship Development, Ideathon Competition, Workshops are yielding their positive impacts over knowledge & awareness of startup culture, cultivation of startup culture, startup boost up challenge for innovative minds, knowledge & awareness about cutting-edge technology, and support to young startups respectively.

The successful recent product launches from our incubatees include 'Mushroom Mistri' (India's first authenticated line of beverages that are blended with bio-active mushrooms) by Meraki Herbzz; COVID-19 IgM/IgG Antibody Detection card Test by Vanguard Diagnostics Pvt. Ltd., Covid-19 Real time PCR kit and Viral RNA purification kits by InnoDx Solutions Pvt. Ltd. BBB incubatees positively took the challenges posed by Covid-19 pandemic and are contributing to solutions through development of indigenous rapid diagnostic kits.

BBB, with its recently gained status of being a 'Associate BIRAC Partner', continues to attract budding Innovators. BBB's programmes have relevance to capacity building, Skill India, Make in India and Atmanirbhar Bharat.

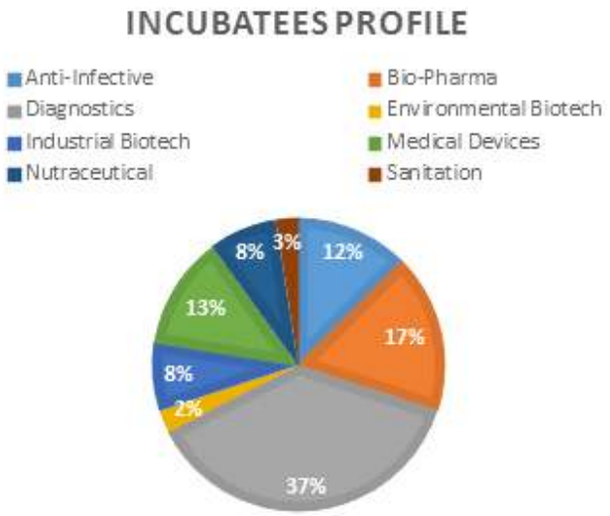
Incubatee companies at BBB

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 Biotechnology	Residential
17	Dharaksha Ecosolutions Pvt. Ltd.	Environmental Biotech	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

S.No.	Company	Area	Type of Incubatee
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
37	Translational Research Innovations Pvt. Ltd	Industrial Biotech	Residential
38	Biolytics Research & Innovation Pvt. Ltd.	Diagnostic	Residential
39	Dr. Suman Das	Diagnostic	Residential

BBB Startups & Domain of work



Awards won by startups till date

S.No.	Name of Incubatee Company	Grant & Awards
1	SHC Shine Biotech Pvt. Ltd	SPARSH, Tie WInER award, BIRAC Covid 19 grant
2	Bioheaven 360 Genotec Pvt. Ltd.	DBT-AI
3	NextGen InVitro Diagnostics Pvt. Ltd.	BIPP
4	VaxFarm Life Sciences LLP	BIG, NBM Fund
5	InnoDx Solutions Pvt . Ltd.	DST-CAWACH, DST NIDHI4 COVID 2.0, Samadhan award
6	Stellar Diagnostics India Pvt. Ltd.	BIPP, Grand challenge for TB grant, India Health Fund grant
7	Incredible Devices Pvt. Ltd.	BIRAC-SEED
8	AptaBharat Innovation Pvt. Ltd.	BIG, SBIRI, GCI
9	Peptomer Therapeutics Pvt. Ltd.	NaaVic ICAR NIVEDI
10	Biotide Solutions LLP	BIG
11	PriDignity Pvt. Ltd.	BIG

S.No.	Name of Incubatee Company	Grant & Awards
12	Advinogen Innovations Pvt. Ltd	BIG
13	Ruhvenile Biomedical OPC Pvt. Ltd	DST NIDHI4 COVID 2.0
14	Vanguard Diagnostics Pvt. Ltd	FICCI Healthcare Excellence Award; Startup of the year award in medical Devices sector
15	TechInvention Lifecare Pvt. Ltd	Time2Leap Award, BIG, India SME excellence awards" in healthcare sector
16	Dharaksha Ecosolutions Pvt. Ltd.	UN Young Champion Award 2018, Forbes 30 under30, Entrepreneur 35 under 35 award, Won National Bioentrepreneurship Competition (NBEC-2021)

Products developed & commercialised by Startups at BBB

S.No.	Name of the Startup	Products Developed	Remarks
1	InnoDx Solutions Pvt. Ltd.	RT-PCR Diagnostic Kit	ICMR approved and commercialized
2	NextGen InVitro Diagnostics Pvt. Ltd.	• RT-qPCR Diagnostic Kit –COVSCAN • Rapid antigen test kit - COVSCAN	• ICMR approved and commercialized • ICMR approved
3	Organic 121 Scientific Pvt. Ltd.	• Surface Coating (COVIDCOAT) • Vegetable washing powder –FRESHSHIELD • Plant based organic fumigation product (TRIYOGANI)	Commercialized
4	Vanguard Diagnostics Pvt. Ltd.	• Viral transport media kit • Viral Lysis transport medium kit • DIPAS-VDx COVID-19 IgG ELISA Test Kit	• ICMR approved and commercialized • ICMR approved and commercialized • ICMR approved
5	Sleepiz India Pvt. Ltd.	• Sleepizone Remote monitoring device	• CE Certified
6	Dharaksha Ecosolutions Pvt. Ltd.	• Bioplastic packaging material	
7	Meraki Herbzz	• Ready to consume Cordyceps	
8	BioCredence	• Edible Cordyceps	
9	Shc Shine Biotech Pvt. Ltd.	• Ready to use petriplate & reagents	

Biosafety Support Unit

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).

Major activities undertaken by BSU during the year 2021-22 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 Review Committee on Genetic Manipulation (RCGM) and assisted RCGM secretariat in organizing scheduled meetings of the RCGM, various sub-committees and monitoring teams, etc.

Major accomplishments

1. **Review of applications:**
   BSU evaluated applications submitted to Review Committee on Genetic Manipulation (RCGM) for consideration in RCGM meetings (203rd to 229th Meetings) during year 2021-22 and extended its support towards conducting 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). The unit has assessed a total of 1550 applications in the field of Biopharma, including 321 COVID-19 related applications, and a total of 615 Agri-Biotechnology related applications during the 2021-22.

2. **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.

Notified:

SOPs for exchange of infectious biosamples/biospecimen from Biorepository, 2021 (drafted by Department of Biotechnology, June 07, 2021) BSU has assisted in drafting the SOPs to ensure biosafety during the collection, processing, storage and transaction of biosamples/biospecimens which require BSL-2 or above containment facility for undertaking research and development activities; and handling of GE organisms and non-GE HMOs.

List of Infective Microorganisms corresponding to different Risk Groups, 2021 (provided by Department of Biotechnology, December 09, 2021) The "List of Infective Microorganisms corresponding to different Risk Groups" was revised, updated and superseded the Annexure I of "The Regulations & Guidelines for Recombinant DNA Research and Biocontainment, 2017" (notified by the Department of Biotechnology vide OM No. BT/BS/17/635/2015-PID, dated 01st April 2018). Based on feedback received from IBSCs registered on the IBKP Portal, Public consultation from stakeholders from industry and academia and deliberations of the Sub Committees and Expert Committee, BSU prepared the draft list of microorganisms.

GOVERNMENT OF INDIA
MINISTRY OF SCIENCE & TECHNOLOGY
DEPARTMENT OF BIOTECHNOLOGY

OFFICE MEMORANDUM

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.)

Apart from scientists at RCB and cluster institutes, researchers from other institutes in Delhi-NCR as well as other states such as IIT Kanpur, IIT Roorkee, Jamia Hamdard, AIIMS Delhi, Translational Health science and Technology Institute (THSTI), NIPGR, ICGEB etc. have availed our services. BioLayer Interferometry instrument runs at 85-90% of its working capacity in terms of usage hours. Protein Production and Molecular interaction facility has processed more than 1000 samples.

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.

The facility has been providing its services to various internal and external investigators, from academia and industry such as NCR Biotech cluster, ICGEB-New Delhi, Premas biotech, PGI-Chandigarh, CDRI-Lucknow, JNU-New Delhi, Delhi University, AIIMS, NCL-Pune, ICT-Mumbai, Zydus Cadila-Ahmedabad, and many more. Around 2000 samples have been processed and analyzed till date.

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.

Genomics facility has processed more than 5000 samples during the reporting period. 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. Genomics facility has processed approximately 7800 samples from more than 1300 users.

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. This facility has processes more than 550 samples during the reporting period.

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).

Apart from RCB, this facility has provided valuable services to CSIR-IGIB, ICAR-NBPGR, Jamia Hamdard, Shiv Nadar University, Ridge IVF Pvt. Ltd. and InnoDx Solutions Pvt. Ltd., BBB. During the reporting period, this facility processed around 250 samples. Besides, this facility also provides regular training to new graduate students, equipping them with skills to address their research questions better. Thus, this facility continues to contribute to scientific advancement.

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, 2021 to March, 2022, more than 250 different users from 55 different user institutions (Research Institutes, Universities, Hospitals and Commercial organizations) have processed about 9000 samples at different facilities of the ATPC. A cumulative revenue of more than Rs. 98 lakhs was generated during the reporting period by different facilities of the ATPC

Manpower trained

During the reporting period, the following UNESCO-sponsored workshops were organized by ATPC to educate participants regarding basic methods in mass spectrometry and microscopy.

S. No.	Facility	Name of Workshop	Duration	No. of Participants
1.	Mass spectrometry	Mass Spectrometry based Proteomics	12-13 October, 2021	49
2.	Optical Microscopy	Basics of Electron Microscopy	20 October, 2021	36
3.	Electron Microscopy	Confocal Microscope-based drug screening (High content imaging)	22 October, 2021	51

High Performance Computing Cluster & IT Infrastructure

High Performance Computing Cluster & IT Infrastructure

In terms of IT Infrastructure & Computing Facilities hosted and managed by RCB, a high performance computing (HPC) cluster with 8 nodes and a total of 128 processors and 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 state of the art Computer facilities. All the computer facilities 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 200+ client machines with windows 10, Linux (CentOS, Red Hat Enterprise Linux) and Mac OS X. There is a common Personal Computer in each lab for students to access various commercial off-the-shelf software such as Adobe Premium & Standard Suite 6, Systat 13, Sigma Plot, PyMol, Graphpad Prism, SPSS, Turnitin, Endnote x6/x8/x9, and Corel Draw Graphics Suite x6 for preparing manuscripts, various reports and presentations. Biometric Attendance System has also been enabled for the staff, to register attendance by simply presenting his/her biometric (fingerprint). 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 inter connection is distributed to users and facilities through RCB's network infrastructure comprising about 1000 metres of fibre, with a 10Gbps backbone, 105+ wireless access points, and 40+ switches that provide on-campus 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), 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 250+ 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 comprising of Polycom HDX 7000 system. 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 800 scientific textbooks and 300 administrative 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 provide access to online resources to users 24 X 7 via Intranet/Internet.

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 for conducting Online Classes
- Micro websites for various research workshops & conferences and facility for online registrations.
- Vendor Registration portal 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), a national facility established at RCB has started functioning in collaboration with NII, ICGEB and NIC with support from the Department of Biotechnology, Govt. of India. The computational infrastructure of IBDC include High Performance Computation (HPC) cluster and High capacity archival data storage. The data is being curated at RCB and 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 has recruited two personnel who are developing a pipeline for structure-based drug discovery. The development of the space allocated to the centre and the procurement of computers is at an advanced stage. The centre will help researchers carry out structure based drug design to identify potential drugs against different pathogens. The RCB IT-department is providing technical support for the development of this centre.

Office of Connectivity

Office of Connectivity has been conceptualized as the cluster office for the NCR Biotech Science Cluster and is responsible to establish a governance structure for the management and utilization of common facilities. It is working towards creating an innovative and efficient management structure, so that the advantage of having different institutions co-located in a cluster, with their respective competencies can be nurtured through systematic sharing of knowledge and resources. Office of Connectivity has the mandate for integrating the partner institutions of the cluster to focus on seamless connectivity for accomplishing best results in accelerated technology absorption by implementing strategic networks and scaling up of the innovative technology initiatives by facilitating coordination, collaboration and sharing of efforts and resources within the Cluster setting for various key projects.

Office of Connectivity is acting as a hub for the whole cluster to focus on seamless connectivity for accomplishing best results by bringing together NCR Biotech Science Cluster stake-holders by facilitating, coordination, collaboration and sharing of efforts within the Cluster setting for various multidisciplinary collaborative research programs across the partner institutions along with the establishment and management of Common Facilities of the NCR Bio-cluster.
During the FY 2021-22, the NCR Biotech Science Cluster has ensured development of the following common facilities:

a) Equipping the OoC building to accommodate Indian Biological Data Centre (IBDC), DBT HRD Project Management Unit (HRD PMU) and a few project offices for THSTI.
b) Completion of Biosafety Level-3 (BSL-3) Facility
c) Completion of Vertical Extension of Hostel Building

The OoC and BSL-3 Facility of the NCR Biotech Science Cluster were inaugurated on 15 July, 2021 by Dr. Jitendra Singh, Hon'ble Minister of State (Independent Charge), Ministry of Science and Technology & Earth Sciences, Government of India.

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

Human resource development in Biotechnology and its allied areas are 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 entrusted RCB as the Nodal Implementation Agency for management of key human resource development programmes through establishment of DBT-HRD Project Management Unit (DBT-HRD PMU).

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

1. Ramalingaswami Re-entry Fellowship Programme
2. Junior Research Fellowship Programme
3. Post-Graduate Teaching Programme

Summary of the activities undertaken in the year 2021-2022 are given below.

1. Ramalingaswami Re-entry Fellowship (RRF) Programme

RRF 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 2021-2022, a total of 57 Indian researchers working abroad joined the Ramalingaswami Re-entry Fellowship programme against the call for applications initiated in 2020-2021 by DBT-HRD PMU.

DBT-HRD PMU has disbursed total grant of Rs. 37.00 crores to 210 Ramalingaswami fellows working in different universities/institutions across the country in the year 2021-2022.

The 12th Ramalingaswami Conclave of mentors and fellows was organized by DBT-HRD PMU on 26th February – 3rd March, 2022. The inaugural session was held on 26th February in the MK Bhan Auditorium, RCB followed by area-specific technical sessions in online mode. The Chief Guest for the Inaugural Session were Hon'ble Dr. Jitendra Singh, Minister of State (IC), Ministry of Science and Technology & Earth Sciences, GoI along with Dr. Rajesh Gokhale, Secretary, Department of Biotechnology, GoI. The Inaugural Session was attended by several DBT officials, ongoing and alumni Ramalingaswami fellows, RCB faculty, staff and students. A total of 12 area-specific technical sessions were organized with the participation of 172 Ramalingaswami fellows and 59 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.

2. Junior Resarch Fellowship Programme

The DBT - Junior Research Fellowship programme supports students to pursue doctoral studies in the discipline of Biotechnology and Life-sciences across any recognized universities/institutions in India.

Biotechnology Eligibility Test (BET) which is the qualifying examination for issuance of fellowship award letters was conducted on 14th August, 2021. A total of 11,956 applications were received out of which 10,588 candidates appeared for the examination which was conducted at 92 centres in 51 cities across the country. A total of 445 Category-I and 216 Category-II qualifying candidates were shortlisted for the fellowship. A total of 382 research scholars joined the programme as DBT-JRF fellows, with the joining/activation processed by DBT-HRD PMU, this being the highest number of scholars joining the programme since its inception in year 2004.

DBT HRD-PMU has disbursed fellowship grant of Rs. 43.90 crores for 972 fellows in the year 2021-2022.

For the benefit of the DBT-JRF fellows, 2 'Crafting Your Career' workshops were organized by DBT-HRD PMU in association with Indiabioscience, Bengaluru to increase awareness of diverse career options available in biotechnology in India as well as building skill-sets for a successful career pathway. There was enthusiastic participation for these workshops by the DBT-JRF fellows.

Guidelines for implementation of the DBT-JRF programme have been revised by DBT-HRD PMU through the duly constituted committee and the revised draft has been placed for approval for implementation from FY: 2022-23.

3. DBT Post-Graduate (DBT-PG) Programme

In FY 2021-22, DBT HRD PMU managed DBT supported Post Graduate (DBT PG) Programme in Biotechnology (M.Sc. and M.Tech. courses) for around 1500 students across India. The programme received an initial grant support of INR 30 Crores for disbursal to host universities. Besides routine programme management activities, DBT HRD PMU organised the annual national entrance examination, Graduate Aptitude Test – Biotechnology (GAT-B) on 14th August, 2021 for around 8000 applicants. HRD PMU also conducted two career development workshops in partnership with NCBS-IndiaBioscience where 430 students had participated.

Inauguration of 12th Ramalingaswami Re-entry Fellowship Conclave, 2021-22

DBT HRD PMU (HRD PMU) Team

FINANCIAL STATEMENTS

REGIONAL CENTRE FOR BIOTECHNOLOGY, FARIDABAD

BALANCE SHEET AS AT 31st MARCH, 2022

Amount (In Rs.)

LIABILITIES	Schedule	31.03.2022	31.03.2021
Corpus / Capital Fund	1	5,76,91,500	5,04,72,628
Reserves and Surplus	2	69,15,63,146	63,13,33,584
Earmarked/Endowment Funds	3	-	-
Secured Loans and Borrowings	4	-	-
Unsecured Loans and Borrowings	5	-	-
Deferred Credit Liabilities	6	-	-
Current Liabilities and Provisions	7	2,58,49,09,735	2,39,19,41,294
TOTAL		**3,33,41,64,381**	**3,07,37,47,506**
ASSETS			
Fixed Assets	8	49,46,47,815	51,41,89,952
Investment From Earmarked/Endowment Funds	9	-	-
Investment-Others	10	94,60,81,097	1,12,94,13,171
Current Assets, Loans, Advances etc.	11	54,12,62,757	24,30,96,130
Biotech Science Cluster (BSC)	8	1,35,21,72,712	1,18,70,48,253
TOTAL		**3,33,41,64,381**	**3,07,37,47,506**
Significant Accounting Policies and Notes on Accounts	24		
Contingent Liabilities		NIL	NIL

Schedules 1 to 24 form an integral parts of Accounts

02 JUN 2022

(SANJEEV KUMAR GOYAL)
FINANCE OFFICER
संजीव कुमार गोयल, वित्त अधिकारी
S. K. Goyal, Finance Officer
क्षेत्रीय बैव्टीयोगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana-121 001

(Dr. SUDEEP BHAR)
CONTROLLER of ADMINISTRATION
डॉ. सुदीप भार, प्रशासन नियंत्रक
क्षेत्रीय बैव्टीयोगिकी केन्द्र
फरीदाबाद, हरियाणा

(Dr. SUDHANSHU VRATI)
EXECUTIVE DIRECTOR
प्रो. सुधांशु व्रती / Prof. Sudhanshu Vrati
कार्यकारी निदेशक / Executive Director
क्षेत्रीय बैव्टीयोगिकी केन्द्र / Regional Centre for Biotechnology
फरीदाबाद - 121 001 (हरियाणा), भारत / Faridabad-121 001 (Haryana), India

02 JUN 2022

REGIONAL CENTRE FOR BIOTECHNOLOGY,FARIDABAD

INCOME & EXPENDITURE ACCOUNT FOR YEAR ENDED 31st MARCH, 2022

Amount (in Rs.)

INCOME	Schedule	31.03.2022	31.03.2021
Income from Sales/ Services	12	2,64,24,139	2,84,95,778
Grants/Subsides	13	29,36,23,802	26,50,00,000
Fees/Subscriptions	14	77,03,500	40,34,200
Income from Investments	15	-	-
Income from Royalty, Publication etc.	16	-	-
Interest Earned	17	44,370	11,31,305
Other Income	18	25,93,590	13,23,179
Increase/(Decrease) in stock of Finished goods and works in progress	19	-	-
Deferred Income-Fixed Assets		6,56,52,294	6,80,61,947
TOTAL (A)		**39,60,41,695**	**36,80,46,409**
EXPENDITURE			
Establishment Expenses	20	12,43,23,570	10,80,82,773
Other Administrative Expenses etc.	21	19,71,82,181	16,39,82,939
Expenditure on Grants , Subsidies etc.	22	-	-
Interest	23	-	-
Depreciation (Net Total at the year-end-corresponding to Schedule 8)		6,56,52,294	6,80,61,947
Prior period Adjustment A/c (ANN-A)			-
TOTAL(B)		**38,71,58,045**	**34,01,27,659**
Balance being excess of Income Over Expenditure (A-B)		**88,83,650**	**2,79,18,750**
Transfer to special Reserve(Specify each)			-
Transfer to /from General Reserve		88,83,650	2,79,18,750
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 Accounts

(SANJEEV KUMAR GOYAL)
FINANCE OFFICER
S. K. Goyal, Finance Officer
Regional Centre for Biotechnology
Faridabad, Haryana / Faridabad, Haryana-121 001

(Dr. SUDEEP BHAR)
CONTROLLER of ADMINISTRATION

(Dr. SUDHANSHU VRATI)
EXECUTIVE DIRECTOR
Prof. Sudhanshu Vrati / Executive Director
Regional Centre for Biotechnology

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, 2022.

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 acturial 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.6.56 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 by Income Tax Act 1961. During the previous year depreciation has been charged at per rate prescribed.

(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 inward freight, duties and taxes and 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 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

B. K. Goyal, Finance Officer
Regional Centre for Biotechnology

02 JUN 2022

Prof. Sudhanshu Vrati
Executive Director
Regional Centre for Biotechnology

to various factors, the expenditure on approved heads of accounts is incurred within the overall sanction of the project.

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 and expenditure under Phase- II shall be capitalised on receipt of occupancy certificate from MCF.

14. Interest earned on saving bank account and fixed deposits during the financial year 2021-22 of Rs.253.89 Lakhs has allocated to the respective projects on pro-rata basis.

Schedule 25: Contingent Liabilities

NIL

(SANJEEV KUMAR GOYAL)
FINANCE OFFICER

संजीव कुमार गोयल, वित्त अधिकारी
S. K. Goyal, Finance Officer
क्षेत्रीय बैवप्रौद्योगिकी केंद्र
Regional Centre for Biotechnology
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(Dr. SUDEEP BHAR)
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डॉ. सुदीप भार, नियंत्रक नियंत्रक
क्षेत्रीय बैवप्रौद्योगिकी केंद्र
फरीदाबाद, हरियाणा

(Dr. SUDHANSHU VRATI)
EXECUTIVE DIRECTOR

02 JUL 2022

प्रो. सुधांशु वती / Prof. Sudhanshu Vrati
कार्यकारी निदेशक / Executive Director
क्षेत्रीय बैवप्रौद्योगिकी केंद्र / Regional Centre for Biotechnology
फरीदाबाद / Faridabad

Speed post

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(15)/RCB/SAR/2022-23/717-718 दिनांकः 28-09-2022

सेवा में,

डा.सुधांशु व्रती
कार्यपालक निदेशक
क्षेत्रीय जैव प्रौधोगिकी केन्द्र
तृतीय मील पत्थर, फरीदाबाद-गुड़गांव एक्सप्रेसवे,
फरीदाबाद-121001

विषयः क्षेत्रीय जैव प्रौधोगिकी केन्द्र वर्ष 2021-22 के लेखों पर पृथक ऑडिट रिपोर्ट।

महोदय,

मुझे क्षेत्रीय जैव प्रौधोगिकी केन्द्र के वर्ष 2021-22 के लेखों पर पृथक ऑडिट रिपोर्ट अग्रेषित करने का निर्देश हुआ है।

संसद के दोनों सदनों में प्रस्तुत करने से पहले वर्ष 2021-22 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)

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 2022

We have audited the attached Balance Sheet of Regional Centre for Biotechnology (RCB), Faridabad at 31 March 2022 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 Law, 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, Income and Expenditure Account and Receipts and Payments Account dealt with by this report have 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:

We have audited the Balance Sheet of Regional Centre for Biotechnology (RCB), Faridabad at 31 March 2022 and the Income and Expenditure Account/ Receipts and Payments Account for the year ended on that date.

Based on our audit, we observed the followings –

A. ASSETS

A.1 Biotech Science Cluster (Capital work in progress) [Schedule 8 : 13521.72 lakh]

Although works amounting to Rs 12146.73 lakh[1] had been completed long ago in 2015 and 2021 and was also put to use, yet the same was still shown under CWIP As a result, Regional Centre for Biotechnology could not charge depreciation amounting to Rs 4250.54 lakh on such buildings. Hence, RCB understated its expenditure (depreciation) and overstated the Fixed Assets each by Rs 4250.54 lakh.

B. LIABILITIES

B.1 Current Liabilities & Provisions

B.1.1 Project Grant/ Fellowship [Schedule 7 : Rs 12580.11 lakh]

(a) A balance of Rs 12580 lakh reported as 'Project Grant/ Fellowships' was a net figure consisting of credit balance of Rs 12964.77 lakh and debit balance of Rs 384.66 lakh under 89 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 it, 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 384.66 lakh.

(b) Amount of Rs 115.83 lakh pertaining to fellowship receivable from CSIR, DBT and DST Inspire was booked by RCB as its own expenditure in its books of accounts for the year 2021-22. As a result, RCB understated it projects-receivable by Rs 115.83 lakh and overstated expenditure by same extent.

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

RCB did not make any provision for wages (March 2022) payable to contractual staff and different Annual Maintenance Con`tracts. As a result, it understated its current liabilities and expenditure each by Rs 43.64 lakh.

C. INCOME AND EXPENDITURE

C.1 Income

C.1.1 Deferred Income – Fixed Assets [Rs 656.52 lakh]

It was reported in previous year's Audit Report 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.

However, RCB again adopted same practice and an expenditure of Rs 656.52 lakh booked towards depreciation on Fixed Assets was set off by booking as Deferred Income in Income and Expenditure Account for 2021-22.

C.2 Expenditure

C.2.1 Other Administrative expenses etc. [Schedule 21 : Rs 19.72 lakh]

[1] As per completion/ occupancy certificates issued by Municipal Corporation of Faridabad, cconstruction activities relating to Phase-I (costing 7698.35 lakh) completed in July 2015 and Phase-I Extension (costing Rs 4448.38 lakh) completed in May 2021

Accounting policy adopted by RCB for chemicals, glassware, consumables and stationary were 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.

Hence, t the figure of Rs 633.47 lakh[2] reported by RCB, as expenditure incurred on chemicals, consumables and stationary during 2021-22, is not correct.

D. General

D.1 Difference in figures of TDRs reported in financial statements and confirmed by Bankers

RCB under Schedule 10 : Investments (Other Fixed Deposits) appended with it's Balance Sheet as at 31 March 2022 had reported an amount of Rs 9460.81 lakh as Term Deposits Receipts (TDRs) with commercial banks. However, the confirmation of TDRs balance provided by its bankers indicated the same as Rs 9403.26 lakh only, which needs reconciliation.

E. Grants-in-aid

With a view to minimize the cost of Government borrowings and to enhance efficiencies in fund flow to Autonomous Bodies, Government of India implemented the Treasury Single Account (TSA) system. Under this system each Autonomous Body shall open bank accounts with Reserve Bank of India in e-Kuber. All expenditure from Grants-in-aid/ fund received from Government of India by the Autonomous Body was required to be made through these designated accounts only. It was also instructed to Autonomous Bodies to don't open/ operate/ park funds in any other account for any operation pertaining to funds received from Government of India. However, in respect of some transactions like payment of TDS, Income Tax and GST, Opening of Letter of Credit in favour of foreign suppliers, court attachment from salaries of employees etc., Autonomous Bodies may utilize the services of their existing account at commercial banks.

On 01 April 2021 RCB had carry forward grant of Rs 241.14 lakh. Department of Biotechnology during 2021-22 issued a sanction for release of core Grants-in-aid of Rs 4115.06 lakh[3] to RCB through account (No.10676601001) opened with Reserve Bank of India under TSA system. An expenditure of Rs 4343.89 lakh was incurred by RCB during 2021-22, leaving an unspent balance of Rs 12.31 lakh, as on 31 March 2022.

Audit noticed that while citing the reasons to meet committed expenditure, RCB on eight occasions during 2021-22 transferred a total amount of grants-in-aid of Rs 2826.00 lakh from TSA account to it's other commercial bank accounts, which are being operated for keeping income generated from internal resources and grants-in-aid received from departments, other than core-grants received from Department of Bio-technology. As RCB did not provide any details of these committed expenditure for which the funds were frequently transferred to commercial banks, therefore, their utilization for envisaged purpose and also in full could not be verified in Audit. Hence, the possibility of parking of unspent balance of core-grants to these commercial banks cannot be ruled out.

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[2] Consumables/ chemicals (Rs 619.35 lakh) and Printing and Stationary (Rs 14.11 lakh)

[3] Rs 4200.00 lakh minus Rs 84.94 lakh lapsed

(v) Subject to our observations in the preceeding paragrpahs, we report that the Balance Sheet, Income & Expenditure Account and Receipts & 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 Biogtechnology, Faridabad as at 31 March 2022; 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

1. Adequacy of Internal Audit System

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

2. Adequacy of Internal control system

Internal control mechanism in RCB needs strengthening in following areas :

(a) 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, RCB did not maintain the Assets Register in the form GFR-22. The Assets Register maintained by RCB did not reflect the value of Fixed Assets.

3. System of physical verification of fixed assets

(a) Physical verification of fixed assets

Physical verification of fixed Assets for the year 2021-22 was not conducted.

(b) Physical verification of library

Physical verification of library for 2021-22 was not conducted.

4. System of physical verification of inventories

Physical verification of inventories (Chemical/ Glassware) for the year 2021-22 was not conducted.

5. Regularity in payment of statutory dues

RCB did not remit TDS on Goods and Service Tax/ Income Tax on time, as a result penalty of Rs. 1.99 lakh was paid by it to respective Departments during 2021-22.

Dy. Director (Inspection)

INSTITUTIONAL GOVERNANCE

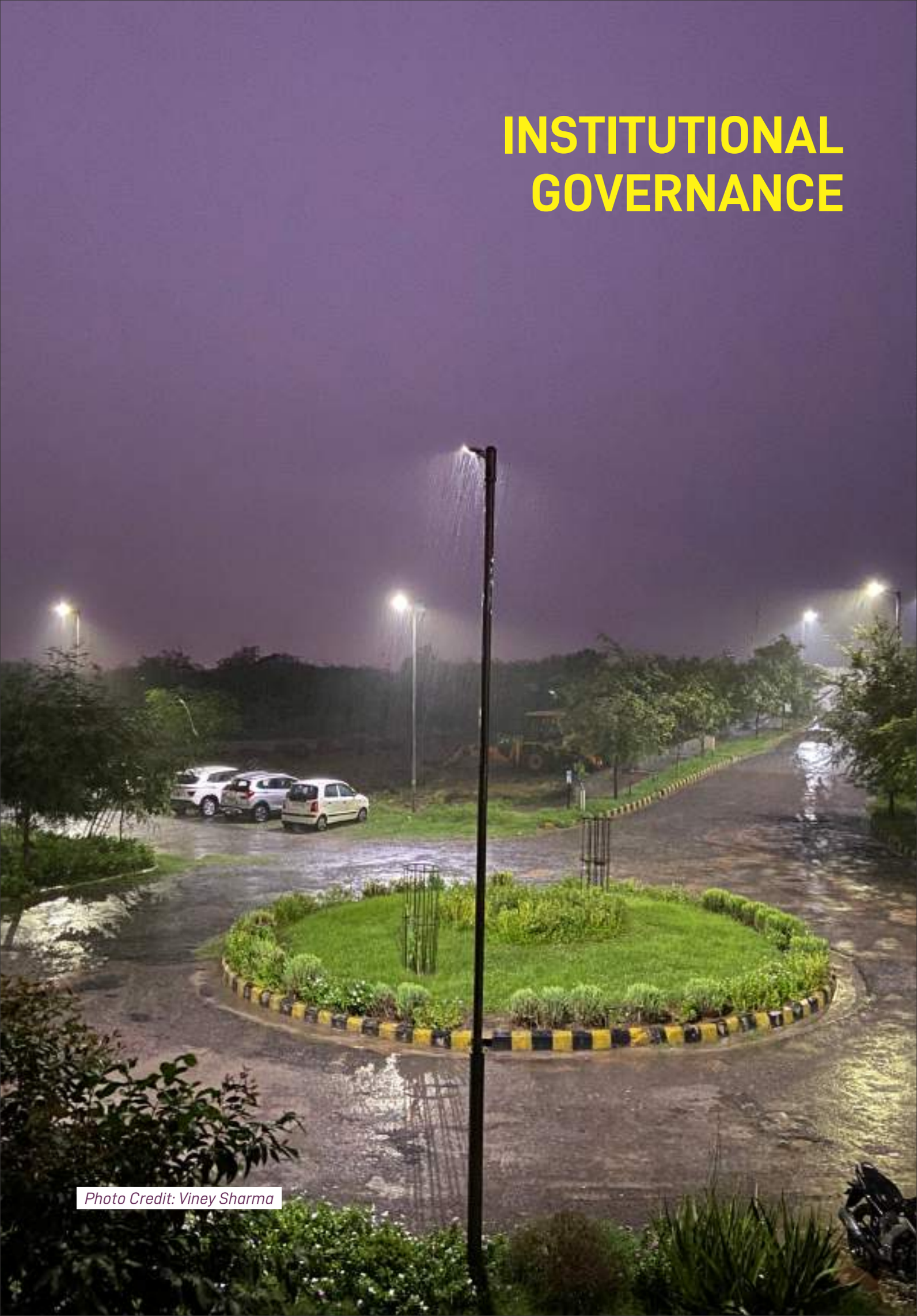

Photo Credit: Viney Sharma

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  New Delhi - 110 003
- **Director (Ex-officio Member)**
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  Thiruvananthapuram - 695 014, Kerala
- **Director (Ex-officio Member)**
  National Institute of Biomedical Genomics
  Kalyani- 741 251
  West Bengal
- **Executive Director (Ex-officio Member)**
  Translational Health Science & Technology Institute
  Faridabad - 121 001
- **Director (Ex-officio Member)**
  UNESCO Delhi Office
  New Delhi - 110 021
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  Former Professor & Head, Department of Pharmacology
  All India Institute of Medical Sciences
  New Delhi - 110 029
- **Dr. Alka Sharma (Special Invitee)**
  RCB Coordinator
  Scientist-G, Department of Biotechnology
  Govt. of India
  New Delhi
- **Dr. Nitin K Jain (Ex-officio Member)**
  RCB Nodal Officer
  Scientist-F, Department of Biotechnology
  Govt. of India
  New Delhi
- **Prof. Sudhanshu Vrati (Convenor)**
  Executive Director
  Regional Centre for Biotechnology
  Faridabad - 121 001

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  All India Institute of Medical Sciences
  New Delhi 110 029
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  Israel
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  Faridabad 121 001

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- **Deans (Members, Ex-officio)**
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  New Delhi

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  Govt. of India
  New Delhi 110 066
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  Ministry Of External Affairs
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  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

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  Regional Centre for Biotechnology
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- **Shri Pitambar Behera (Member)**
  Sr. Finance Officer
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- **Finance Officer (Member Secretary, Ex-officio)**
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  Faridabad 121 001

Scientific Personnel

Faculty

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Dr. Rajendra Prasad Roy

Professor
Dr. Prasenjit Guchhait
Dr. Deepak T. Nair
Dr. Avinash Bajaj

Associate Professor
Dr. Sivaram V. S. Mylavarapu
Dr. C. V. Srikanth
Dr. Vengadesan Krishnan
Dr. Tushar Kanti Maiti
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. Kinshuk Raj Srivastava
Dr. Prashant Pawar
Dr. Prasad Abnave
Dr. Anil Thakur
Dr. Karthigeyan Dhanasekaran

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

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

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

DST INSPIRE Faculty
1. Dr. Naini Burman
2. Dr. Prashant M. Pawar
3. Dr. Nidhi Adlakha
4. Dr. Prasad Abnave

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2. Dr. Babitha Chandrashekhar

Ramalingaswami Fellowship
1. Dr. Kinshuk Srivastava
2. Dr. Ambadas Rode
3. Dr. Anil Thakur
4. Dr. Karthigeyan Dhanasekaran

Ramanujan Fellowship
1. Dr. Ramu S. Vemanna

DST SERB-NPDF
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2. Dr. Bhargab Kalita
3. Dr. Vijay Kumar
4. Dr. Eira Choudhary
5. Dr. Ruchira Chakraborty

DST-WOS-B
1. Dr. Sangeeta Yadav

MK Bhan Fellow
1. Dr. Shouvik Das
2. Dr. Nitu Singh

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

DBT-RA
1. Dr. Chanchal Kumari
2. Dr. Vineet Kumar
3. Dr. Nitu Singh
4. Dr. Sangeeta Yadav
5. Dr. Archana Prasad
6. Dr. Yashika Walia Dhir

Management

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Executive Director
Prof. Sudhanshu Vrati

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Technical Assistant
Mr. Ramesh Chandiramouli

Academics, Administration, Finance and Purchase

Controller of Administration
Dr. Sudeep Bhar

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

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Mr. C.B. Yadav
Mr. Rakesh Yadav

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Mr. Sudhir Kumar
Mr. Chakrawan Singh Chahar

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Mr. Praveen Kumar V.
Mr. Amit Naryal

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Mr. Naveen Kumar

Instrumentation Engineer
Mr. Pankaj

Senior Technical Officer
Mr. Mahfooz Alam

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Mr. Atin Jaiswal
Mr. Suraj Tewari

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Mr. Nagavara Prasad G.
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Mr. Dharmender Gupta
Mr. Manoj Kumar Soni
Dr. Reena Rani

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Mr. Amit Kumar Yadav

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Technical Officers
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Ms. Richa Mehra
Mr. Ghanshyam Sharma
Ms. Meena Kapasiya

Instrument Engineer
Mr. Rajesh Kumar

Software Engineer
Mr. Mohit Kumar Vats

BSC BioNEST Bio-incubator

Chief Operations Officer
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Mr. Sudhanshu Shekhar

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Ms. Malvika Garg

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Ms. Sapna Rani

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Ms. Natasha Thapa

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Ms. Sarita Sharma

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Mr. Akshay Bhardwaj

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Mr. Yashpal
Mr. Naveen Swaroop

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Mr. Syed Asrafuzzaman
Ms. Shreya Malik
Mr. Dilip Joy T

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Mr. Raman Kumar Nimesh

Accounts Assistant
Mr. Nimesh Kumar Singh
Mr. Kuldeep Singh

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

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Mr. Navin Kumar Yadav

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Mr. Puneet Sharma

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Indian Biological Data Center

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Mr. Gautam Kanwal

Technical Assistant-B
Mr. Mayank Mamgain

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Mr. Murari Uthayakumar
Mr. Navajeet Chakravartty
Mr. Pawan Kumar
Mr. Sanjay Deshpande

Database Engineers/ Software Developers
Mr. Kalpanath Paswan
Mr. Ankit Tomar

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Regional Centre
for Biotechnology

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