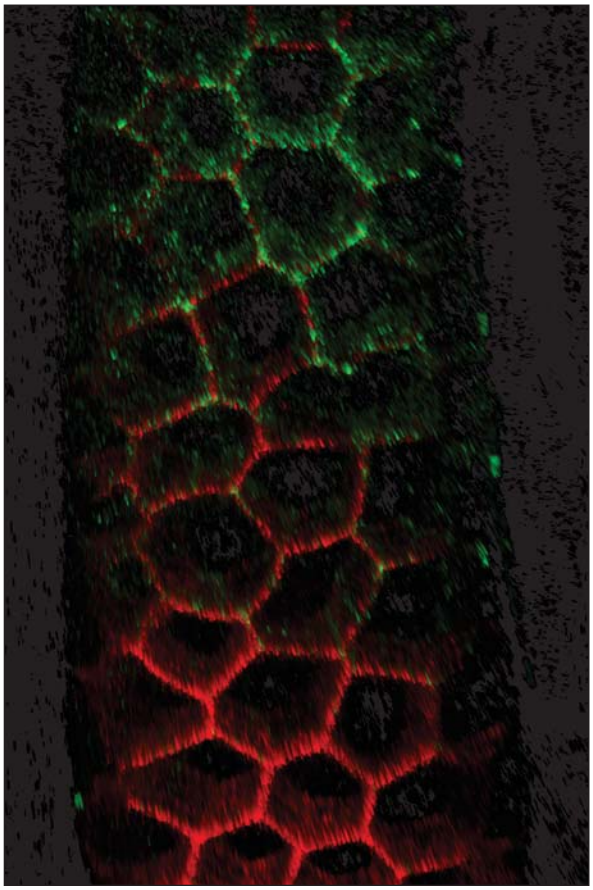
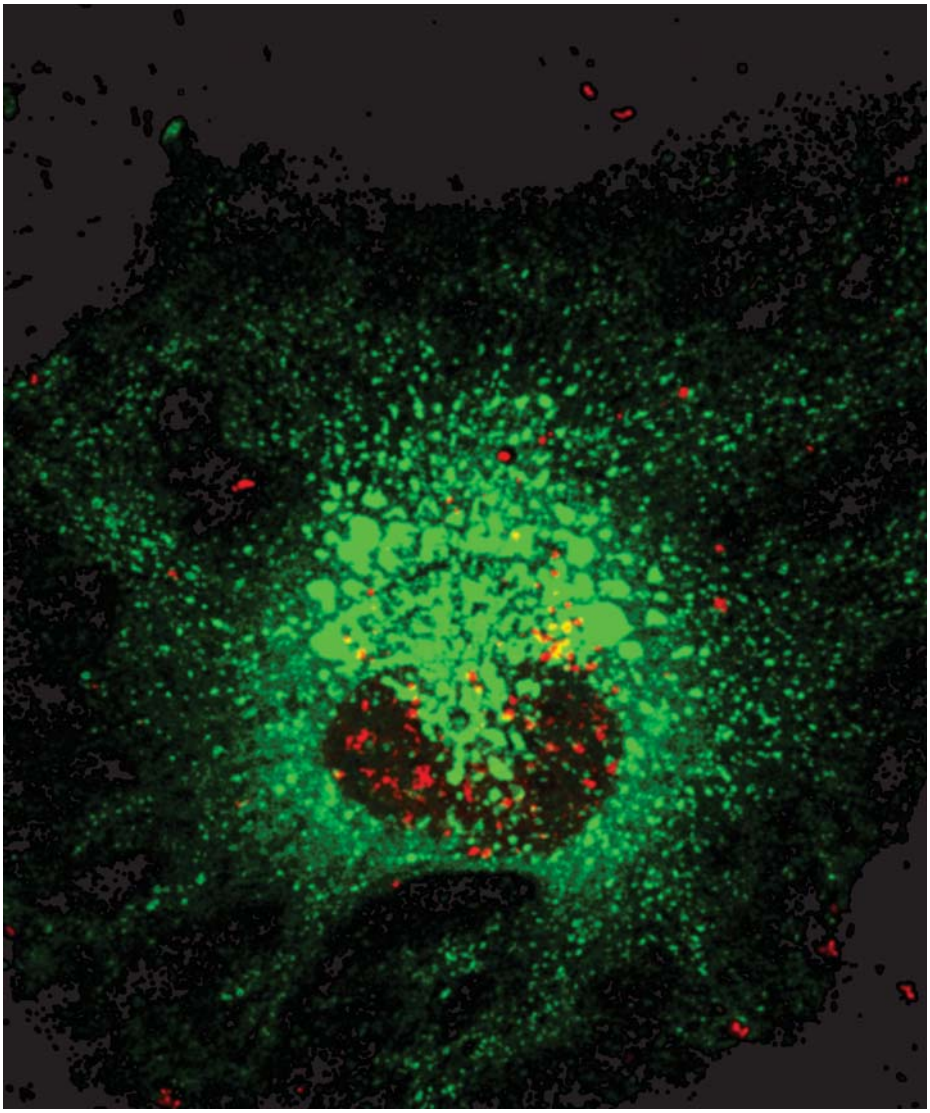
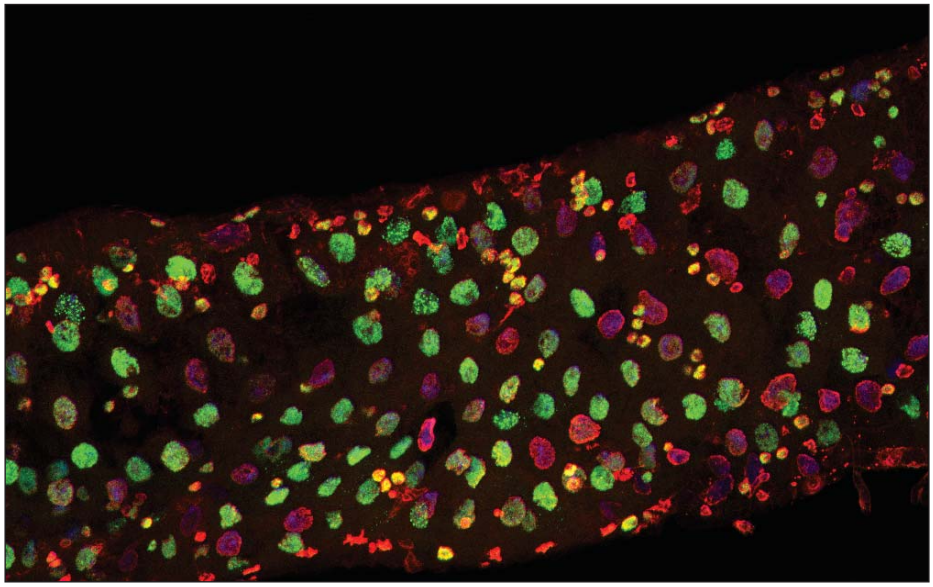
ANNUAL REPORT

2020-2021







United Nations
Educational, Scientific and
Cultural Organization

क्षेत्रीय जैव प्रौद्योगिकी केन्द्र
Regional Centre
for Biotechnology

Photo Credit: Shivam Agarwal

CONTENTS

Mandate of the 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 verticals defining the mandate of the Regional Centre for Biotechnology (RCB). We have continued to strive hard towards achieving these objectives and have made significant progress in each of these areas. RCB continues to be a category-2 institution of UNESCO, the linkage providing an international reach to our academic and training programs. A detailed account of each of the RCB activities is provided in the various sections of this annual report with a summary in the following paragraphs.

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 Ph.D. degree during the reporting period. In the academic year 2018-19, RCB initiated the integrated MSc-PhD degree program that has now matured. In the reporting period, five students graduated with the Master's degree and four 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 Ph.D. programs at Christian Medical College (CMC), Vellore, and National Centre for Cell Science (NCCS), Pune, thus bringing the total number of such recognized centers as ten. A total of 291 students from these recognized centers are registered for their degrees with RCB.

Towards human resource development in the advanced areas of life sciences and biotech sciences, RCB offers short-term innovative training programs for young scientists. In this direction, training workshops were conducted in areas of proteomics and structural biology, 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. The instructors and speakers included experts from prestigious academic research institutions and universities. Besides, RCB continues to provide Indian researchers access to the ESRF synchrotron radiation facility. This program has provided tremendous support to the Indian structural biologists and has benefited a large number of young research students.

The year 2020-21 experienced a devastating pandemic of coronavirus. To aid the Indian efforts towards Covid-19 drug development, RCB scientists established a cell culture-based SARS-CoV-2 antiviral testing platform in the BSL-3 environment and offered it to academia and industry. Over 1000 potential druggable molecules and medicinal plant extracts were tested for anti-SARS-COV-2 activity from more than 100 companies and academic users. RCB scientists also initiated some research on this virus. A summary of their work is presented at the end of the research reports.

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.

Docetaxel is one of the first-line chemotherapeutic drugs used for the treatment of breast cancer patients. The existing clinically used formulation of Docetaxel is less effective and is highly toxic due to its accumulation in other organs of the body. Researchers in Dr. Avinash Bajaj's group designed a nanomicellar formulation of docetaxel where they conjugated the drug to a bile acid-derived phospholipid. The nanomicellar formulation was highly tolerable in mice, rats, rabbits, and monkeys, and was more effective than clinically used formulation in its anticancer activity in the animal model.

Circulating miRNA profiles in the plasma of dengue patients may prove to be valuable for developing early prognostic markers for the disease severity. Researchers led by Drs. Arup Banerjee and Sudhanshu Vrati identified that the expression pattern of hsa-miR-122-5p in plasma from dengue patients could distinguish different stages of dengue infection and may have the biomarker potential.

The nsp14/10 complex of SARS-CoV-2 is responsible for proofreading the newly synthesized RNA during replication of the viral genome. The proofreading activity may also be responsible for compromising the action of drugs such as remdesivir and favipiravir. The homology model of the SARS-CoV-2-nsp14/nsp10 complex was used to carry out *in silico* screening to identify molecules that can potentially inhibit the activity of nsp12. This exercise showed that the HIV-1 protease inhibitor ritonavir may bind to the exoribonuclease active site of the nsp14 protein. Ritonavir binding may, therefore, prevent the association of nsp14 with RNA and thus inhibit the exoribonuclease activity. Overall, these computational studies led by Dr. Deepak Nair suggest that ritonavir may serve as an effective inhibitor of the nsp14 protein and thus potentiate the activity of drugs such as remdesivir and favipiravir.

Post-translational modifications (PTMs) via SUMOylation regulate stress responses and developmental transitions across all eukaryotes. The group led by Dr. Saikat Bhattacharjee demonstrated the biological relevance of SUMO isoform diversification in modulating the timing and amplitude of anti-bacterial immunity in plants. The abundantly expressed SUM1/2-paralogs suppressed mis-primed immune activations and their unregulated perturbations incurred developmental consequences to the host. The basally low SUM3 isoform expressions were stress-induced, and via controlling the dynamics/efficiencies of SUMO1/2-conjugation on substrates modulated intensity of immune responses. Together, these cross-talks reveal an intricate self-regulatory mode orchestrated by the antagonistically functioning SUMO paralogs in host SUMOylome adaptations to pathogen stress.

Plants deploy STP sugar transporters to restrict carbon flux towards pathogens as a defense mechanism. Researchers from Dr. Divya Chandran's group investigated the role of the *Medicago truncatula* STP13 in powdery mildew (PM) resistance and showed that it is an H+-hexose symporter whose expression is regulated by (a)biotic factors. The introduction of the G144R mutation previously identified in the wheat STP13 abolished its transport function. Knockdown and overexpression studies suggested that MtSTP13 conferred basal resistance against PM and that modifications in its function through STP13 or STP13G144R overexpression promoted resistance via sugar-mediated defense signaling. This is the first report demonstrating the role of a sugar transporter in PM resistance in legumes.

Additionally, RCB continues to participate in a multi-institutional research program aimed to understand the biology of preterm birth to identify possible biomarkers to predict the outcomes. A large cohort of pregnant women has been established by THSTI at the Gurgaon Civil Hospital 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. A couple of drug-like molecules have shown antiviral activity against the Chikungunya virus in the cell culture and the animal model of virus infection.

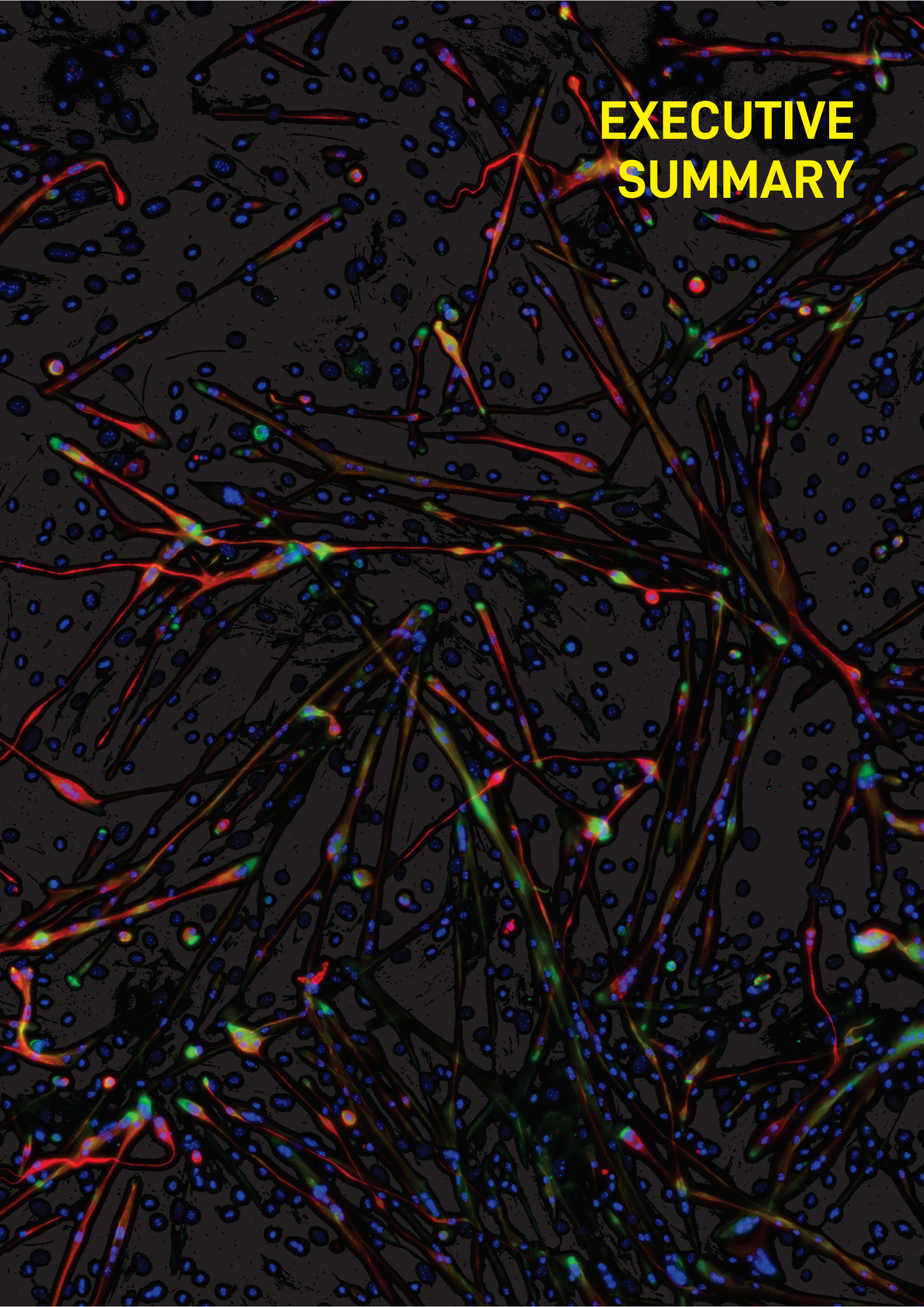
RCB has established a Bio-Incubator with financial support from the BIRAC under the BioNEST (Bio-Incubators Nurturing Entrepreneurship for Scaling Technologies) scheme. The Bio-Incubator has been established to foster innovation, research, and entrepreneurial activities in biotechnology-related areas. During the reporting period,>30 start-up companies were incubating at the Bio-Incubator. Through this mission, we contribute to spurring economic growth in the region in the biotechnology sector.

Finally, I would like to thank my colleagues in the RCB faculty and administration for their excellent cooperation. I must place on record the continued support from 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

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

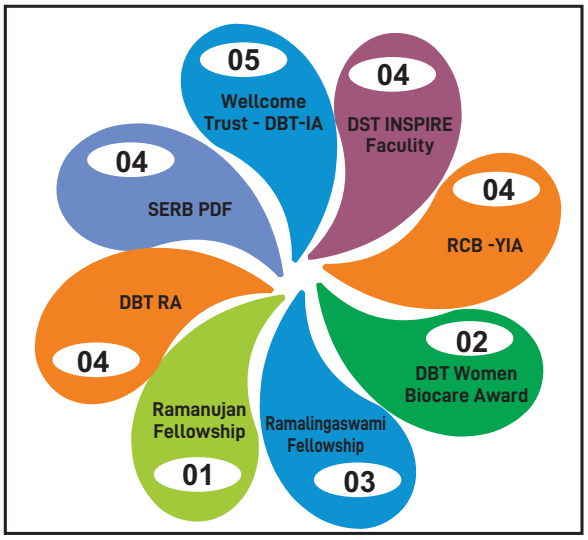
Academic and Training Activities

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

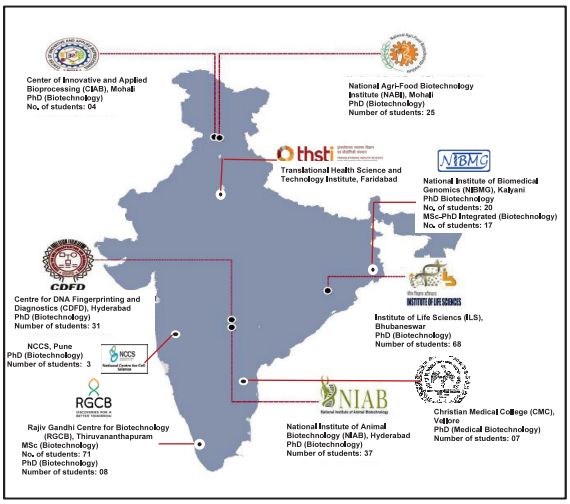
No. of Students studying at RCB

104	PhD (Biotechnology)	MSc-PhD (Biotechnology)	23
07	PhD (Bioinformatics)	PhD (Biostatistics)	04
29	Research Interns	PhD awarded	15

Awards and Fellowships



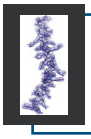
RCB Recognized Centres



Total number of students registered at RCB: 291

Date	Event Organized
29 January 2021	Webinar: Celebrating the Glory of Indian Science: Showcasing the Life and Works of Dr. V. Ramalingaswami
4 & 18 February 2021	Online workshop on Mass Spectrometry Based Proteomics
12 February 2021	Webinar: Celebrating the Glory of Indian Science: Showcasing the Life and Works of Dr. Asima Chatterjee
19 February 2021	Webinar: Celebrating the Glory of Indian Science: Showcasing the Life and Works of Dr. Janaki Ammal
1 March 2021	RCB Foundation Day 2021
3 March 2021	Virtual Workshop on Basics of Electron Microscopy
15-21 March, 2021	Brain Awareness Week

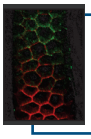
Research Areas



Structural Biology

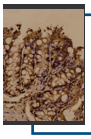
Molecular Medicine

Infectious Disease Biology



Cancer & Cell Biology

Agricultural Biotechnology

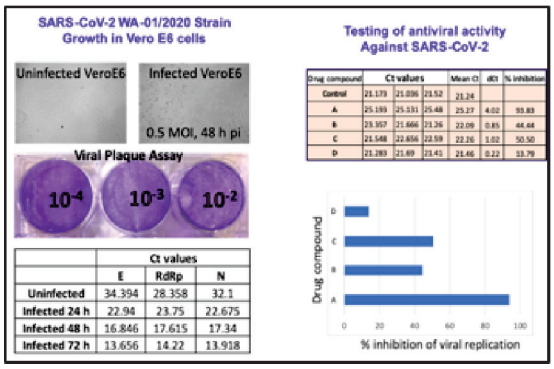


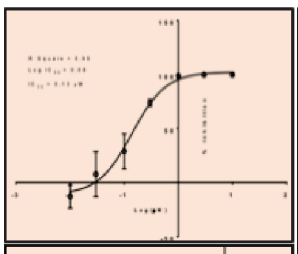
Systems & Synthetic Biology

Publications : 86
Patent Granted : 01

Research Highlights

- The interaction of MN1 (a transcriptional co-regulator) with IGFBP5 and IGF1 implicated in brain tumors (gliomas) was found to be associated with overall patient survival. The findings suggest that MN1 may serve as a prognostic biomarker in clinical settings to categorize patients with better survival outcomes.
- Upregulation of SUMO-conjugations and differential SUMO1-modification was observed during innate immune responses or in an auto-active defensive mutant of Arabidopsis thaliana.
- The structure of basal pilin SpaB from Lactobacillus rhamnosus GG was determine with a view to understand the overall architecture of SpaCBA pilus. A structural model for the whole SpaCBA pilus was proposed which also reveals the mucus binding sites on the pilus.
- The structure of pilus adhesin SpaC from Lactobacillus rhamnosus GG, captured in both open and closed conformations, revealed the mechanism of collagen binding. A novel lectin responsible for mucus binding was identified.
- The role of Orai3 Ca2+ channel in cancer progression was illuminated and the potential therapeutic targeting of Orai3 for better cancer management and treatment was further elaborated.
- A comprehensive analysis of microRNAs (miRNAs) circulating in plasma of dengue virus-infected patients was described and miRNA signatures with biomarker potential for dengue infection and disease progression were identified.
- Delineated an interaction of Dengue virus envelope protein with a host protein TAL-1 that impedes platelets production process in megakaryocytes cells.
- A novel protocol for transient gene expression in rice was developed. This protocol, although developed in rice, represents a model system for monocots and may facilitate the rapid deciphering of the functions of genes.
- Identified a plant sugar transporter that confers resistance against the pea powdery mildew pathogen through host defense activation, indicating its applicability in powdery disease management in legumes.
- Structure-activity studies showed that cholic acid amphiphile can disrupt the fungal membranes, and are effective fungicidal in nature.
- An RNA interference based study targeting the membrane trafficking network in neuronal cells showed an essential role of the dynamic actin network and actin filament associated proteins for the infection of Japanese encephalitis virus.
- The non-lipidated from of the autophagy protein MAP1LC3 was shown to be associated with the Japanese encephalitis virus capsid protein on replication complexes and lipid droplets. Computational modelling identified a putative LC3-interacting region in the capsid.



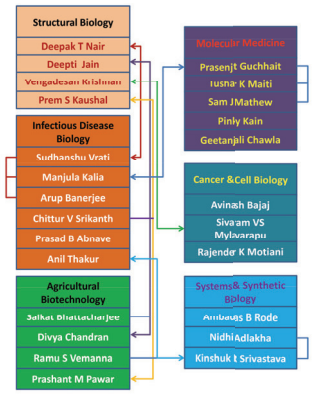


Cytotoxicity testing	1335
Antiviral testing	545
IC50 determination	25

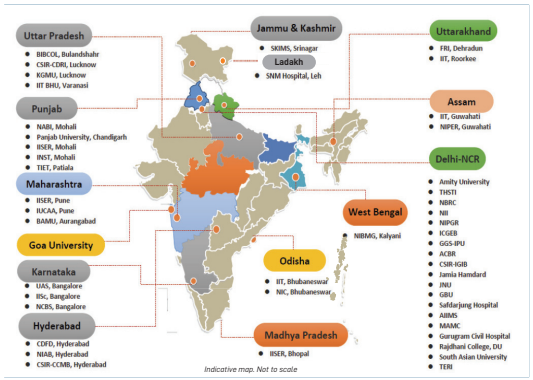
Testing of antiviral activity against SARS-CoV-2

The antiviral activity of a large number of synthetic drug-like molecules / herbal extracts / natural compounds was tested in the cell culture model under the BSL-3 environment. The service was offered to industry and academia across the country. The adjoining table shows the number of antiviral tests conducted during the reporting period.

Intra-institutional collaborations

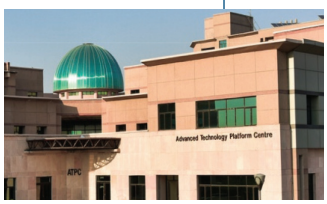


National Collaborations



International Collaborations

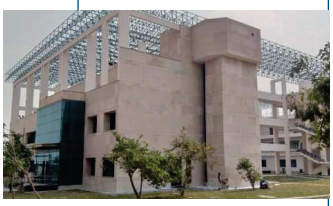
Infrastructure and Support Services



Advanced Technology Platform Centre

Biosafety Support Unit

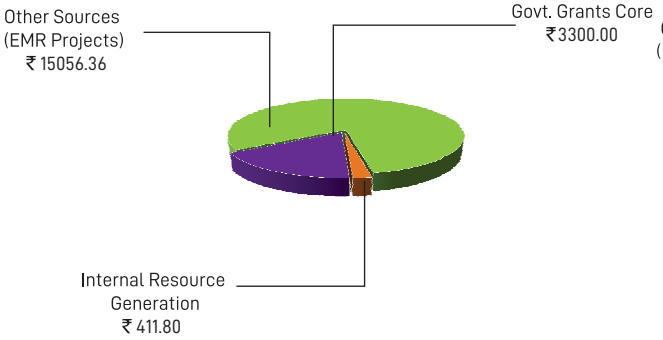
BSC BioNEST BioIncubator



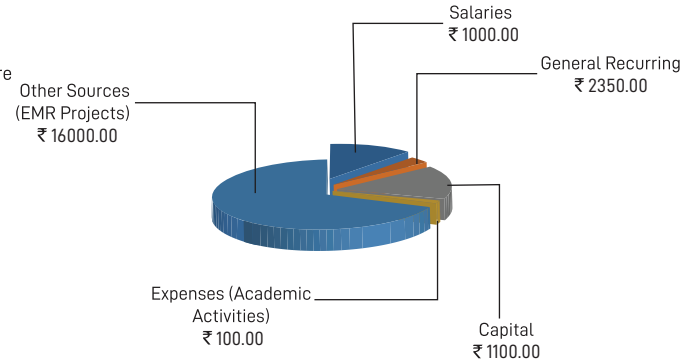
IBDC & DBT HRD-PMU

Financial Figures

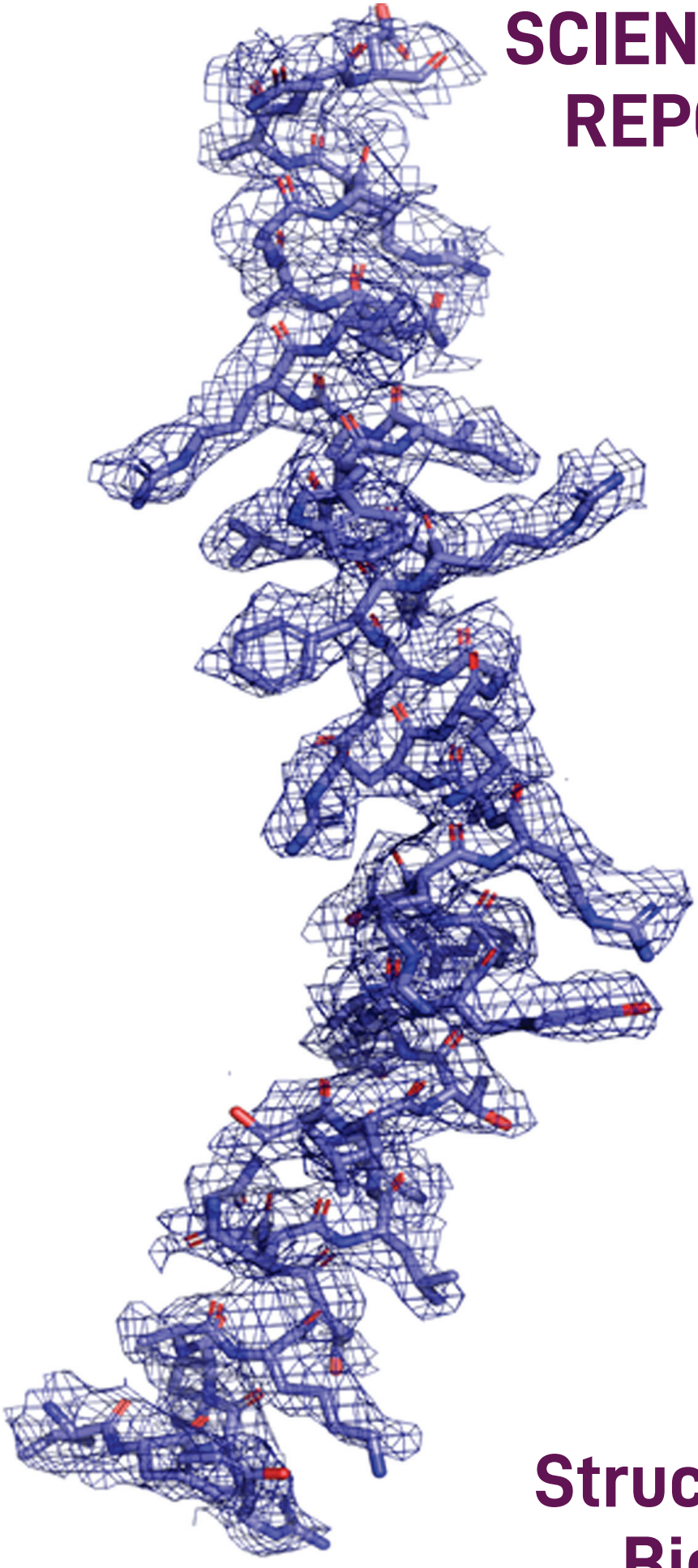
Total Income (Rs. In lakhs) 2020-2021



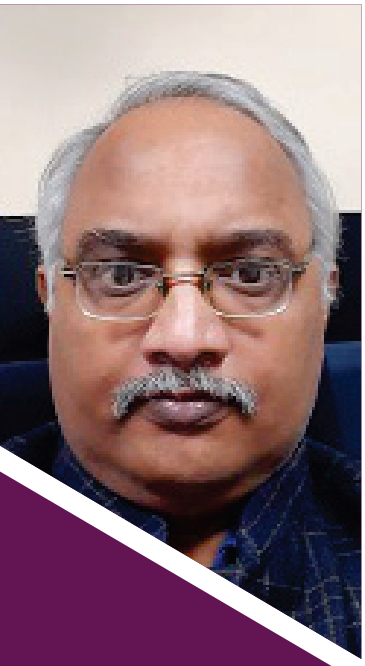
Total Expenses (Rs. In lakhs) 2020-2021



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 mechanism utilized by different molecular determinants of genomic integrity and plasticity to achieve function. The insight gained from these studies will shed light on how organisms evolve and also provide a robust platform for the development of novel therapeutic strategies against pathogenic bacteria and viruses. Within this broad aim, some of the biological processes under scrutiny in our laboratory are DNA replication and viral genome replication.

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 mechanism utilized 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. We show that PfpPol can misincorporate oxidized nucleotides such as 8oxodGTP opposite dA. This event gives rise to transversion mutations that are known to lead to adverse physiological outcomes. The apicoplast genome is particularly vulnerable to the harmful effects of 8oxodGTP due to very high AT content (~87%). We observe that the proofreading activity of PfpPol has the unique ability to remove the oxidized nucleotide from the primer terminus**.** Due to this property, the proofreading domain of PfpPol is able to prevent mutagenesis of the AT-rich apicoplast genome and neutralize the deleterious genotoxic effects of ROS generated in the apicoplast due to normal metabolic processes*(Sharma et al, Scientific Reports 2020)*. The proofreading activity of the Pfprex enzyme may, therefore, represent an attractive target for therapeutic intervention. Also, a survey of DNA repair pathways shows that the observed property of Pfprex constitutes a novel form of dynamic error correction wherein the repair of promutagenic damaged nucleotides is concomitant with DNA replication.

The X family is one of the eight families of DNA polymerases (dPols) and members of this family are known to participate in the later stages of Base Excision Repair. Many prokaryotic members of this family possess a Polymerase and Histidinol Phosphatase (PHP) domain towards the C-terminus. The PHP domain has been shown to possess 3'-5' exonuclease activity and may represent the proofreading function in these dPols. PolX from *Staphylococcus aureus* also possesses the PHP domain at the C-terminus, and we have shown that this domain has an intrinsic Mn^{2+} dependent 3'-5' exonuclease capable of removing misincorporated dNMPs from the primer strand during replication. The misincorporation of rNTPs and oxidized nucleotides such as 8oxodGTP are known to be pro-mutagenic and can lead to genomic instability. We have shown that the PHP domain aids DNA replication by the removal of misincorporated oxidized nucleotides and rNMPs *(Nagpal et al, Scientific Reports 2021)*. Overall, our study shows that the proofreading activity of the PHP domain plays a critical role in maintaining genomic integrity and stability (Fig. 1). The exonuclease activity of this enzyme can, therefore, be the target of therapeutic intervention to combat infection by methicillin-resistant-*Staphylococcus-aureus*.

Viral Genome Replication

The SARS-CoV-2 virus is responsible for the ongoing COVID19 pandemic. The genome of this virus encodes for the nsp14 protein, which houses the exoribonuclease (ExoN) activity responsible for proofreading newly synthesized RNA during replication of the viral genome. The nsp14 protein forms a complex with nsp10 and this complex is functionally active. The nsp14/10 complex activity may responsible for neutralizing the deleterious effect on viral genome replication of prodrugs such as remdesivir and favipiravir.

The homology model of the SARS-CoV-2-nsp14/nsp10 complexavailable at the SWISS-MOD

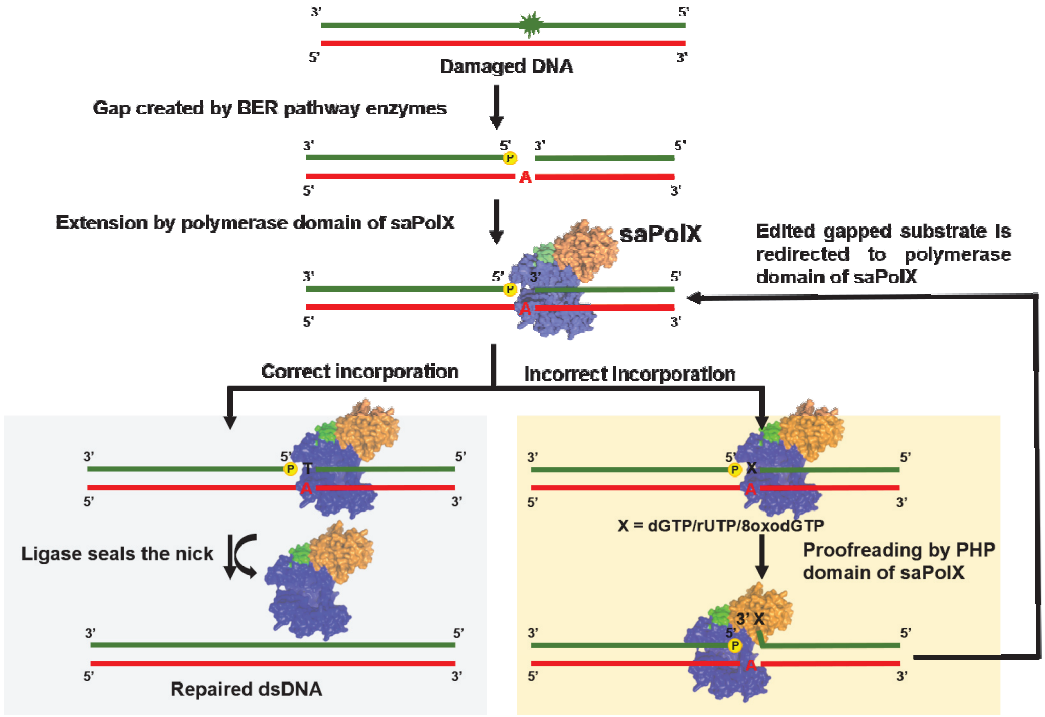
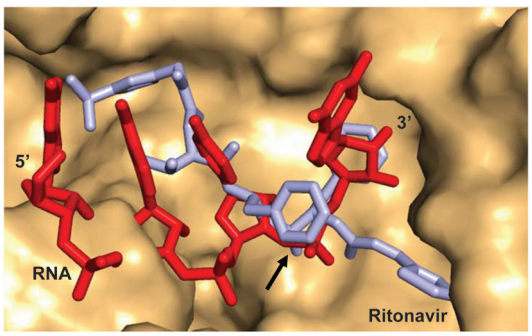
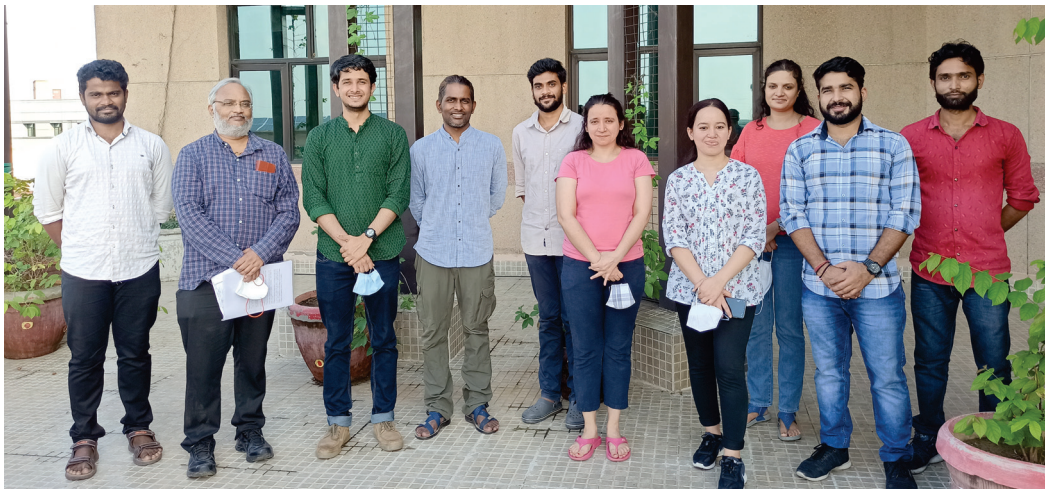


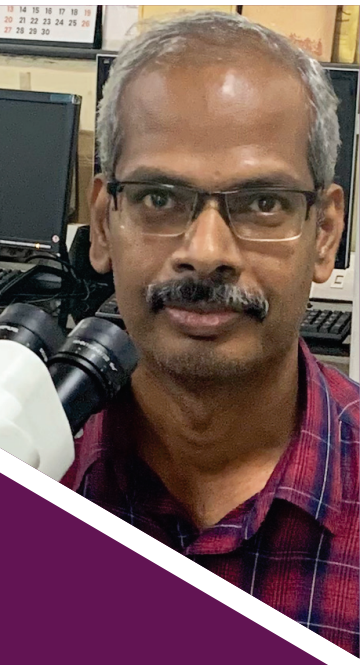
Figure 1: Schematic for the high-fidelity DNA synthesis by saPolX. *The core polymerase domain, PHP domain and linker connecting these two domains are displayed in blue, orange and green colors, respectively.*

website was used to carry out *in silico* screening to identify molecules among natural products, or FDA approved drugs that can potentially inhibit the activity of nsp12. This exercise showed that the HIV-1 protease inhibitor ritonavir may bind to the exoribonuclease active site of the nsp14 protein. A model of the nsp14/10 in complex with substrate RNA showed that ritonavir binding site overlaps with that of the substrate RNA (Fig. 2). A comparison of the calculated energies of binding suggested that ritonavir may bind to the active site of nsp14 with affinity comparable to that of the natural substrate. Overall, our computational studies suggest that ritonavir may serve as an effective inhibitor of the nsp14 protein and thus potentiate the activity of drugs such as remdesivir and favipiravir (*Narayanan & Nair, Int J Biol Macromol 2021*).

Figure 2: Binding site of ritonavir overlaps with that of substrate RNA. *Superimposition of the models of SARS-CoV-2-nsp10-nsp14:RNA (red) and that of SARS-CoV-2-nsp10-nsp14:ritonavir (cyan) are displayed. The surface of protein molecule is displayed in light orange. The site of cleavage on RNA is marked by an arrow.*







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Structural Biology of Host-Microbial Interactions in Health and Diseases

Microbial attachment to the host surfaces is the initial step in colonization. The subsequent events in the pathogenesis or symbiosis are highly dependent on the initial interaction. Interfering with the host-microbial interface is an attractive approach in improving health and combating infections. Since this approach does not directly kill bacteria, it is also a promising alternative to antibiotics which often results in the development of resistance. Such an approach requires detailed knowledge of how microbes attach to the host and how the adhesive strategies differ among microbes. Towards providing the essential foundations for this approach and understanding 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 both the beneficial and pathogenic strains for getting insights into tissue tropism and microbial interaction strategies in health and diseases.

Beneficial strains from gut microbiota

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 catalyzes the pilus polymerization, a housekeeping A-type sortase (SrtA) attaches the assembled pilus to the cell-wall. The LGG pili play a key role in adherence, persistence and beneficial health effects. Our earlier work on backbone pilins has revealed new insights about pilus shaft formation and led us to propose a three-stage pilus assembly mechanism called '*expose-ligate-seal*'.

Our recent work on pilus adhesin SpaC has revealed five-domains architecture with a novel lectin domain. Its N-terminal region contains a receptor-binding domain responsible for attachment with mucin and collagen, while the C-terminal region consists of immunoglobulin (Ig)-like domains that act as stalk to facilitate the attachment. Our imaging analysis confirmed the presence of SpaC at the pilus tip. The open and closed conformations observed in the receptor-binding domain suggested that the SpaC interacts with collagen, like the integrin I-domains. Surprisingly, an inserted arm in the receptor-binding domain showed an acidic pocket for mucus binding through lectin type interaction. The large-size acidic binding pocket indicates the possibility of accommodating longer intestinal mucin oligosaccharides such as GM1 ganglioside, a receptor for diarrhea-associated pathogens eg. *Vibrio cholerae* and human rotavirus). This suggests the LGG likely reduces diarrhoea by inhibiting pathogens through the competitive attachment in the gut.

Obtaining SpaB crystal remained particularly challenging until we implement a three-pronged approach. Ultimately, we determinedthe SpaB structure, which shows the Ig-like CnaB domain with many exciting features (Fig. 1). Imaging studies previously showed the presence of SpaB along the pilus shaft and base. Surprisingly, recombinant SpaB adheres to mucus with a sevenfold higher affinity than other pilins. Remarkably, the C-terminal tail contains positively charged residues that likely account for the atypical mucoadhesiveness,as confirmed by our interaction studies. Our mass spectral analysis confirmed the presence of the isopeptide bond in SpaB. Similar structural features between the SpaB and N-terminal domain of SpaA and the docking analysis suggest that the SpaB can be incorporated into the SpaA pilus shaft only at the base via previously proposed expose-ligate-seal mechanism (Fig. 2). We have also recently solved crystal structures of sortases.

Lactobacillus ruminis (LRU) is a member of indigenous microbiota present in the gut of humans and other 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 and one sortase. In contrast to LGG pili, the LrpCBA lacks mucus-binding but shows affinity to collagen and fibronectin. Since LrpCBA pilus structure and interaction mechanism seems different from that

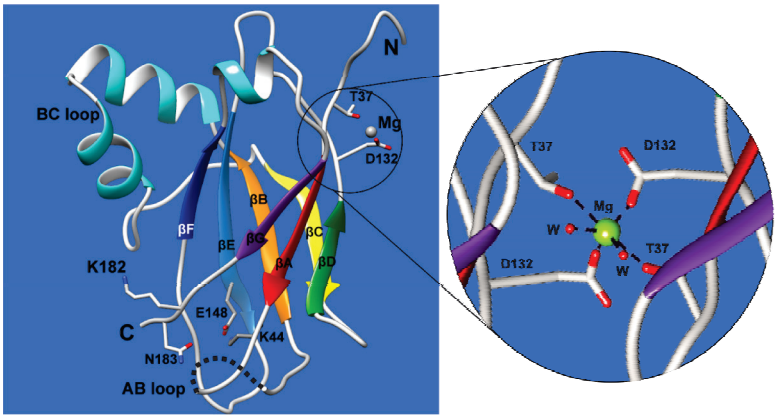
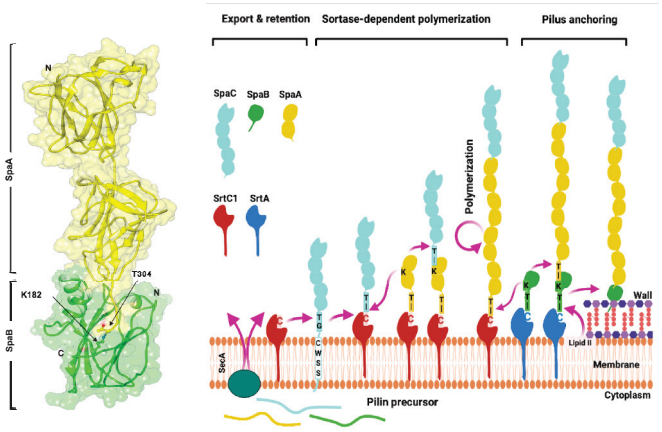


Figure 1: Crystal structure of basal pilin SpaB. *Core β-strands are indicated in rainbow colors. The lengthy BC (turquoise) and disordered AB loop (dotted lines) are labelled. The autocatalytic triad residues (K44, N183, and E148) and the linking lysine (K182) involved in internal and intermolecular isopeptide bond formation, respectively, are shown (sticks). The circle marks identical residues (T37 and D132) from the adjacent molecule and water involved in the octahedral coordination of an Mg^{2+} ion.*

Figure 2: Incorporation of SpaB at the pilus base during SpaCBA pilus assembly. *Ribbon and surface representationof the interaction between SpaB and SpaA (left). Sidechains T304 from the LPHTG pentapeptide motif of SpaA (yellow) and the linking K182 from the FPKN pilin motif of SpaB (green) are within covalent bonding distance (arrows). Schematic representation of the structural model depicting the incorporation of SpaB during the sortase-mediated assembly of the SpaCBA pilus (right).*



of LGG pili, it likely represents a third sortase-mediated pilus type in Lactobacillus species. We have recombinantly produced LRU pilus constituents and crystallized pilin LrpA. Its structure determination is in progress.

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 pilus adhesins and provides sites for other bacteria (secondary colonizers) to develop oral biofilms (plaque). We recently obtaineda structure solution for pilus adhesin PitA from a primary colonizer (*Streptococcus oralis),* an opportunistic pathogen commonly associated with infective endocarditis and other infections.

Collaborative projects

We began structural collaborative projects to study the critical molecules from Mycobacterium and to explore the therapeutic value (anticancer and antiInflammatory) of potential compounds (*piperine,* apigenin and myo-inositol) from pepper and wheatgrass extract.

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Transcription Regulation: Structure and Mechanism

Resistance to antibiotics represents an escalating challenge in the treatment of bacterial infections. Pathogenic bacteria 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. Following model systems are being employed in the lab

Regulation of biofilm and virulence genes in Pseudomonas aeruginosa

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 the AAA+ (ATPase associated with various cellular activities) family of proteins. The representative of this class of proteins which also is a part of

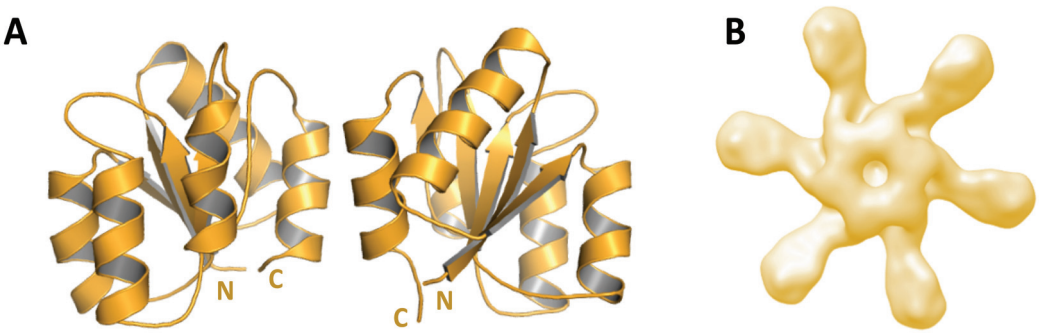

Figure 1: Structure of FleR *(A) Crystal structure of dimer of the sensor domain of FleR (B) SAXS envelop of full length oligomeric, activated protein*

two component system in *Pseudomonas*is FleR which regulates the expression of genes involved in motility, virulence, drug resistance and biofilm formation. The two-component system comprises of the histidine kinase FleS and the transcription regulator, FleR. Recent studies from our laboratory have delineated the mechanism of the regulated assembly of FleR upon phosphorylation. We have determined the X-ray solution scattering structure of the activated, oligomeric, full-length FleR (Fig.1). Docking of the crystal structures or the homology models of individual domains into the SAXS (Small Angle X-ray Scattering) envelope reveals their organization within the activated ring. We show that the activated FleR forms a hexameric assembly stabilized by the interactions between the N-terminus REC and the central ATPase domain. We have also determined the crystal structure of the inactive form of the receiver domain. The analysis uncovers the mechanism utilized by the two-component signal transduction to regulate the assembly of AAA+ domains. Further, through the *in vivo* complementation experiments we have demonstrated that the phosphorylated REC or the receiver domain is required for the transcription activation of FleR presumably due to its role in stabilizing the oligomeric, active state of the protein. We show that deletion of the REC domain, renders the bacterium aflagellate and nonmotile. Our lab is also exploiting thestructuraldata for *in silico* screening of the databases 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.

Regulation of Antibiotic Resistance in Staphyloccocus aureus

Staphyloccocus aureus is an opportunistic human gram-positive pathogen. Antibiotic resistance in *S. aureus* is one of the leading causes of mortality and healthcare expenditure. Thus, understanding the regulatory networks mediating such resistance is of immense importance. The GraXSR (Glycopeptide Resistance Associated) regulonregulates the resistance of *S. aureus* to cationic antimicrobial peptides (CAMP). The CAMPs arevital component of the host innate immune response. The transcription factorGraR, a component of this regulatory network, responds to cell wall stress and is essential for antimicrobial resistance. It is involved in regulating enzymes encoded by the *dltABCD* and *mprF* and *vraFG* operons that lead to an increase in the positive charge on the bacterial cell surface which renders the CAMPs ineffective. We have determined the crystal structure of the adaptor protein present in the same regulatory network and is cotranscribed with GraR. The knockout of the adaptor results in slow growth and causes downregulation of the genes activated by GraR (Fig. 2). Additionally, it was observed that the knockout of the adaptor protein results in increased susceptibility to vancomycin, indicating that this protein could becrucialforthe development of antibiotic resistance in *S. aureus*. The adaptor protein shows sequence similarity with short-chain dehydrogenases and the structure reveals a Rossman fold. Furthermore, the protein harbours an NADP binding motif. The structural analysis and *in vitro* validation are in progress. This work will aid in deciphering the putative network responsible for the increase in glycopeptide tolerance in *Staphyloccocus*. The insights obtained from this study are being used to screen and design small molecule inhibitors of the adaptor protein that can enhance the sensitivity of the bacterium towards available antibiotics.

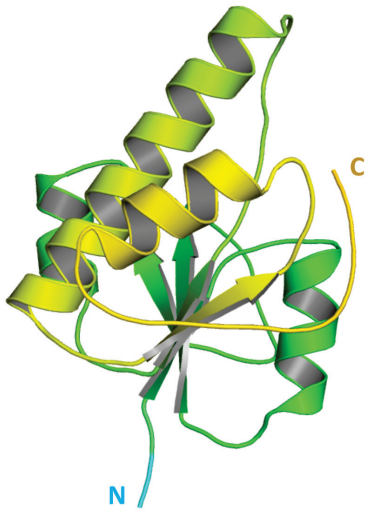

Figure 2: Crystal structure of the adaptor protein from Staphyloccocus aureus. *The structure reveals a Rossman fold.*

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Structural Aspects of Translation Regulation and Ribosome Assembly

Our research goal is to unravel the structural basis of the functioning of the macromolecular complexes involved in translation regulation and ribosome assembly, thereby to identify the potential drug targets. Translation, the process of protein synthesis, in which genetic information present in mRNA is decoded into a polypeptide is a critical step in the central dogma of molecular biology and occurs on the ribosome in all cells. Protein synthesis is one of the most energy-consuming cellular processes which consumes nearly 50% of the cell's energy. The ribosomes are a target of nearly 40% of known antibiotics. Currently, we are focusing 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 cells by applying 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 deadliest 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), the dormancy. Nearly one third of the world population possesses LTBI, from which ~10% of LTBI infected develops acute Tb infection. During latent TB infection, the nonreplicating persistent mycobacteria 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.

To study the host macrophage stress environment, models had 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 oxygen content, low nutrient conditions and different stresses conditions, respectively. To mimic hostmacrophage stress environment in laboratory conditions, we grew *M. smegmatis* under different stresses: hypoxia, nutrition starvation, H_2O_2 stress, acidic pH 5.5 and heat shock stress 45°C. The ribosome was isolated by differential centrifugation and sucrose gradient (Fig 1). The normal cell growth shows the presence of ribosome (that is the 70S in prokaryote), its large subunit (LSU) and small subunit (SSU) and translating ribosome, polysome (Fig 1). In hypoxia, 70S and 50S are present and 30S and polysome are significantly less, suggesting translation may be very slow (Fig 1). Similarly, in nutrition starvation, the polysomes significantly less suggest a slow translation rate (Fig 1). In H_2O_2, pH, and heat shock stresses the pattern looks very similar to the normal growth conditions (Fig 1). We have performed gel electrophoresis and mass spectrometry (MS) analysis to check the presence of any factor that binds to the ribosome or its subunits under different stress conditions. Further, data analysis is in progress. We aim to find out the factors that bind to the ribosome in different stresses and elucidate is the binding mechanism by solving cryo- EM structure of the ribosome with the stress factor.

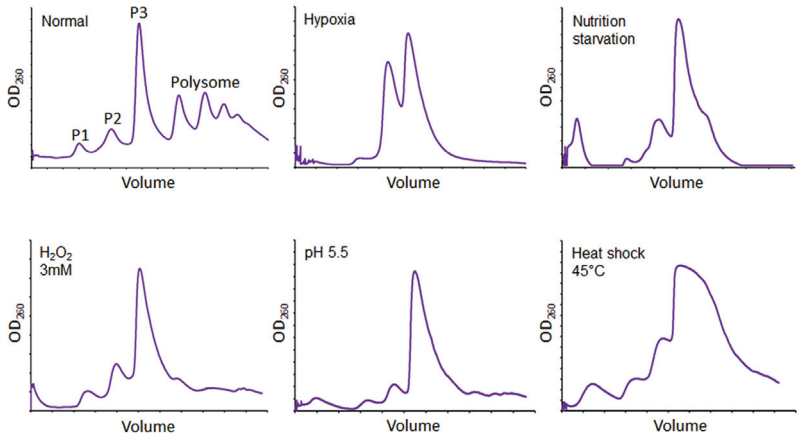

Figure 1: Ribosome isolation and purification under different stresses. *Ribosomes from the M. smegmatis grown under different stress were isolated using differential centrifugation and purified by layering 10% - 50% sucrose gradient and centrifuged. Sucrose gradients were fractionated in the BioComp fractionator. The peaks P1, P2 and P3, correspond to 30S, 50S and 70S subunits, respectively.*

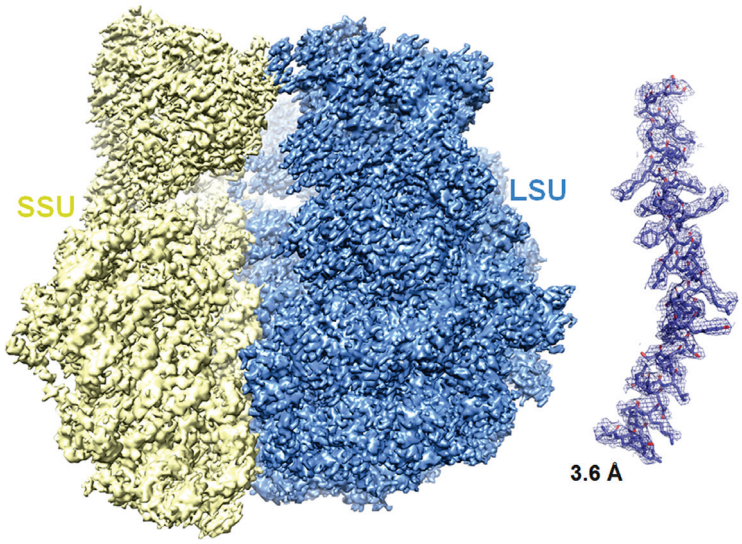

Figure 2: Cryo- EM structure of M. smegmatis 70S ribosome. *Final 3.6 Å resolution map, the small subunit (yellow) and large subunit (blue) are shown. The quality of the refined map is shown in the left panel in blue. The initial optimization of cryo- EM data collections were carried out in JEOL 2200FS 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 Cryo-EM at InStem, NCBS, Bangalore.*

Role of ribosome-associated-factor under-hypoxia (RafH) in translation inhibition during dormancy

During dormancy mycobacteria slow down cellular processes, including translation. The dormancy survival regulon (DosR regulon) upregulates 48 genesthat appear to play crucial roles in dormancy. Our long-term goal is to understand better the life cycle of the Mtb pathogen in its dormancy state. Initially, we are focusing on the RafH protein, regulated by DosR regulon. The translation inhibition by RafH is a unique feature associated with Mtb ribosomes and dramatically different from that occurs in enteric bacteria. In bacteria hibernating protein factor (HPF) binds to the ribosomes (70S)and forms ribosome dimmers (100S). Whereas RafH binds to 70S ribosome and 100S ribosome dimer is not reported in mycobacterial ribosome yet.

The RafH protein was purified by Ni-NTA, His-tag and gel filtration purification techniques. The ribosome was purified using differential centrifugation and sucrose gradient. The ribosome RafH complex was prepared and confirmed by western blotting using anti His antibody. The ribosome-RafH complex quality was checked using negative staining and cryo- electron microscopy. A total of 3750 movies collected in Titan Krios with Falcon 3 camera were processed for 3D reconstruction using Relion 3.1 program. Initially, 2,32,531 particles were picked using Auto-picking in Relion 3.1, out of which 1,75,097 particles were selected after 2D classification, and 1,41,866 particles were selected after 3D classification. Finally, 1,28,721 particles were chosen for consensus 3D refinement that yields overall 3.6Å resolution, cryo- EM map (Fig 2). Our map clearly shows electron density for bulky side-chain amino acid residues that reflect the high quality of cryo-EM reconstruction. Further, cryo-EM map analysis is in progress.

Molecular Medicine

Inflammation and Thrombosis in Human Diseases

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This research program is designed to understand the molecular mechanism of **1)** inflammation and thrombosis in the lung of COVID-19 infected animal and human. Specifically, how these clinical events lead to hypoxemia. **2)** Host inflammatory response to Dengue and Japanese encephalitis virus (JEV) infections in 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)** How hyperglycemia mediated thrombosis and inflammation contributes to lung fibrosis in mice model of type-2 diabetes (T2D)? How platelet - immune cells interaction contributes to thrombo-inflammatory complications in T2D patients? **5)** Metabolome profiles of glucose and fatty acid oxidation pathways in native highlanders with T2D. Are these profiles different from native sea-level counterparts? Does crosstalk between hypoxia-responsive factors and metabolic enzymes alter these pathways in highlanders with T2D? Finally, to find biomarkers and molecular targets to develop potential therapeutics for the above diseases.

COVID-19: To understand the mechanism of lung inflammation and thrombosis in SARS-CoV-2 infection, we established animal model. Our data show significant intravascular clot formation and leukocytes accumulation in the alveolar spaces of hamsters infected with the virus (Fig. 1A-D). We are investigating the detailed molecular mechanism of above clinical events in COVID-19 infections in hamsters, mice and patients.

Dengue and JEV: In previous report, we mentioned the involvement of autophagy-lysosomal pathways in platelet factor 4 (PF4) mediated replication of both Dengue and JEV. PF4 is secreted by activated platelets in viral infections specifically in Dengue. We also mentioned that we found a small-molecule antagonist that abrogates PF4-induced replication of both viruses. We screened more small molecules and found another drug that also inhibits PF4-mediated replication of both flaviviruses. We are investigating the mechanisms. More interestingly, as the

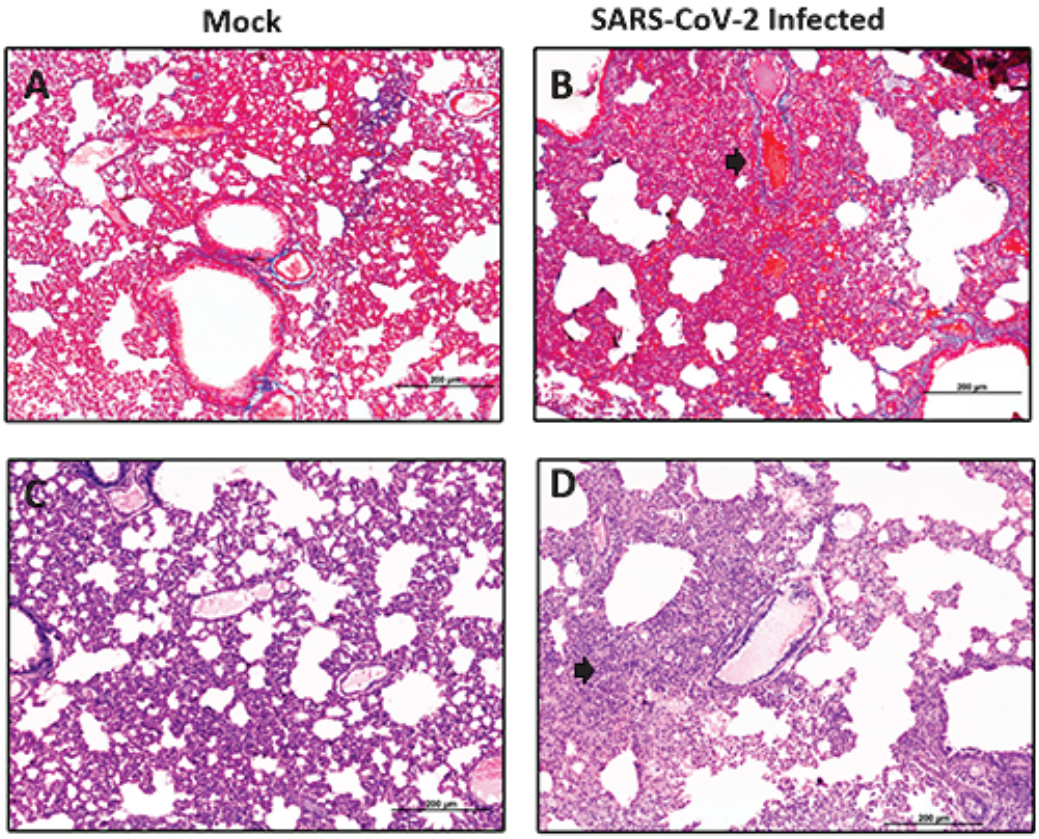

Figure 1: Lung section of hamsters. *(A-B) MT staining and (C-D) H&E staining. (A and C) mock, and (B and D) with SARS-CoV-2 infection at day 6. Arrows indicate intravascular clots and leukocytes accumulation.*

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 (Fig. 2A-B).

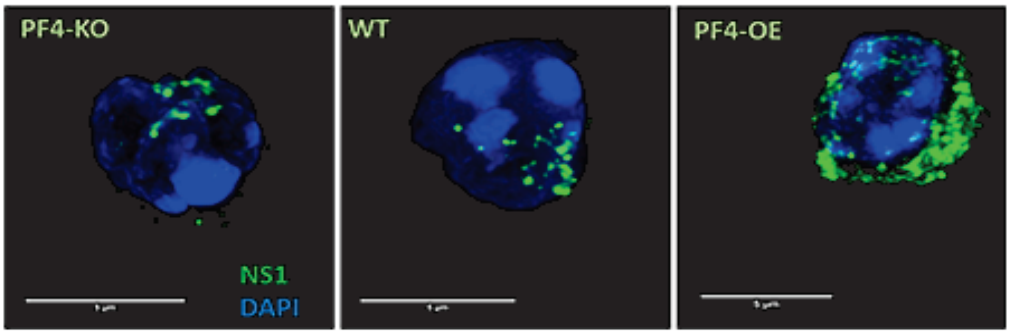

Figure 2: Monocytes isolated from PF4-ko, wild type and PF4-overexpressed mice, and infected with JEV for 24 hrs and stained for viral NS1 protein.

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, EBioMedicine). Thus, suggesting the use of αKGin the prophylaxis of systemic as well as lungs inflammation, commonly observed in AMS and HAPE.

T2D metabolic disorder: In order to investigate, how hyperglycemia triggers thrombosis and inflammation, and in turn promotes lung fibrosis, we developed a LPS-inducedlung fibrosis model using db/db type-2 diabetes (T2D) mice. We also have observed a direct correlation between hyperglycemia and systemic inflammation and platelet activation in T2D mice.

Current focuses: 1) We are investigating the anti-inflammatory and anti-thrombotic effects of the metabolite -ketoglutarate (KG). Recently we have shown the anti-inflammatory effect of the metabolite in hypoxia-induced inflammation in mice (Bhattacharya S et al. 2021, EBioMedicine). **2)** We are working on the insights into molecular mechanism of pro-viral role of PF4 in promoting viral replication. Also, we are testing the anti-viral effects of small molecule antagonists against PF4. **3)** We are testing a detailed prophylactic and therapeutic effects of KGin mice before proposing a clinical trial against inflammatory complications in travellers to high-altitudes. **4)** We are investigating the role of platelets and leukocytes in the progression of lung fibrosis in T2D mice.

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Proteostasis Mechanism in Neurodegenerative Diseases

Neurodegenerative diseases are characterized by progressive loss of structure and function of neurons in specific brain regions. The hallmark of neurodegenerative diseases is often associated with abnormal accumulation of intracellular or extracellular protein aggregates in different parts of the brain. The impairment of protein quality control leads to abnormal accumulation of disease-specific proteins. The cellular system is devised with various protective mechanisms to counteract the misfolded protein load. The ubiquitin-proteasome system, lysosomal degradation pathways, and autophagy are the molecular machineries that evacuate the misfolded protein load. Chaperones also play a critical role in protein refolding to attain proper conformation. However, a breach in any of these protective mechanisms leads to disease manifestation. Our research program aims to understand the mechanism of protein aggregation and protein quality control system in neurodegenerative diseases.

Mechanistic insight of α-synuclein mediated neurodegeneration and neuroinflammation in Parkinson's disease.

Parkinson's disease (PD) is a multifactorial malady and the second most common neurodegenerative disorder. It is characterized by loss of dopaminergic neurons in the substantia nigraof midbrain. The pathological hallmark of PD is the formation of intracellular protein inclusions, termed Lewy bodies (LBs). More than 500 proteins have been identified in the Lewy body and α-synuclein is one of the major components. Physiologically, α-synuclein plays a critical role in synaptic vesiclesformation and neurotransmitter release mechanisms. However, genetic mutations as well as aberrant post-translational modifications promote α-synuclein to form amyloid aggregation intermediates and amyloid fibers. It has been documented that the oligomeric species generated during the course of aggregation are the major culprit for PD progression. The oligomeric intermediates are not only neurotoxic but they also possess prion-like property. Neuroinflammation is another pathological feature of PD. α-Synuclein species induce neuroinflammatory cascade, through hyperactivation of glia cells and release inflammatory cytokines in the circulation. Despite many years of research, α-synuclein's precise role in neurotoxicity, neuroinflammation mechanism and potential therapeutic strategy remain as an active research problem. Oligomeric and fibrillar structural diversities make this problem more complex. Keeping these informations in mind, we aim to understand if helix rich and beta rich intermediate species display differential neuronal toxicity and neuroinflammation. We have prepared locked helix rich and beta rich intermediates using chemical cross-linking strategy and studied their physicochemical properties like nucleation dependent aggregation, membrane interaction, cellular internalization followed by cell death, TLR2 binding and induction of IL6 and IL-1beta. Our findings confirm that the helix rich intermediate exposes more hydrophobic surface than the beta rich intermediate species and contributes to the greater roughness of the cellular membrane. Efficient membrane interaction contributes cellular membrane disruption. However, α-sheet intermediate facilitates self-assembly formation of monomeric α-synuclein due to its stronger interaction with monomeric species than the helix rich species. Interestingly, our data also suggested that the beta rich intermediate exhibits stronger TLR2 binding than the helix rich species as well as induction of neuroinflammatory cascade (Fig. 1).

In summary, our data demonstrated that secondary structures play a decisive role during

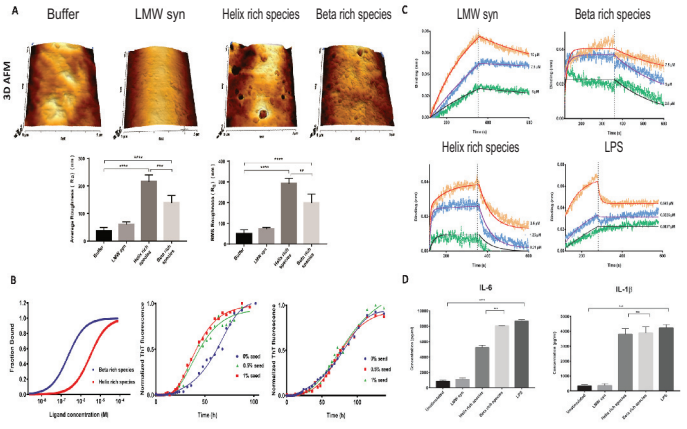


Figure 1: *(A) Membrane perforation and roughness induced by intermediate species of α-synuclein. SH-SY5Y cells were treated with different intermediate species and imaged using atomic force microscopy. Lower panel represents the average roughness and calculated root-mean-square (RMS) roughness of the cell surface induced by the treatment of the intermediate species. (B) Recruitment of monomeric α-synuclein to induce amyloid formation. (C) Interaction of intermediate species with TLR2 in Bio-Layer interferometry (D) The induction of proinflammatory cytokines by α-synuclein species-treated BV2 microglia cells.*

amyloid formation, and targeting them can be a novel intervention strategy for PD progression. This study is published in *ACS Chemical Neuroscience*.

Protein glycation is an age dependent post-translational modification that induces many neurodegenerative disorders including Alzheimer's and Parkinson's diseases. There are a growing evidences supporting that patient with type 2 diabetes has an increased risk of developing PD. Dysregulated glycolysis in cells produces methylglyoxal (MGO) that modifies protein in lysine, arginine and cysteine residues spontaneously. It has been demonstrated that α-synuclein undergoes MGO modification and potentiates PD pathology. MGO-modification restricts α-synuclein in oligomeric conformation and prevent fibrilization. Currently, we are trying to understand the molecular basis of oligomeric restriction and its impact on neuroinflammation.

Ellagic Acid as potential therapeutics for Synucleinopathies

Parkinson's disease cannot be cured and the treatments available are only for symptomatic conditions. L-3,4-dihydroxyphenylalanine (L-DOPA) along with dopamine agonists such as pramipexole and ropinirole are the typical treatment strategy for motor symptoms of PD. However, L-DOPA develops the complication of involuntary movement which is known as L-DOPA induced dyskinesia. Thus, there is a need for new thearputic stratagy and drug development for PD. Till date, many strategies have been designed to prevent α-synuclein aggregation and related cytotoxicity. Polyphenols, small molecules, synthetic peptides, and peptide-derived molecules have been considered as potential candidates that inhibit α-synuclein oligomerization and its fibrillation and a few of them are in clinical trials. We have identified a polyphenolic compound ellagic acid (EA) that inhibits α-synuclein aggregation.

Our results demonstrated that EA inhibits primary nucleation, seeded aggregation, and membrane-induced aggregation. The cytotoxicity of α-synuclein oligomers and fibers treated with EA has been investigated and we found that EA treated oligomers and fibrils showed reduced cytotoxicity. Additionally, we also observed inhibition of membrane binding of α-synuclein by EA in SH-SY5Y cells (Fig. 2). In conclusion, the present study suggests that small molecules such as ellagic acid have anti-amyloidogenic properties and may have therapeutic potential for Parkinson's disease and other proteinopathies. We have published this work in *ACS Chemical Neuroscience.*

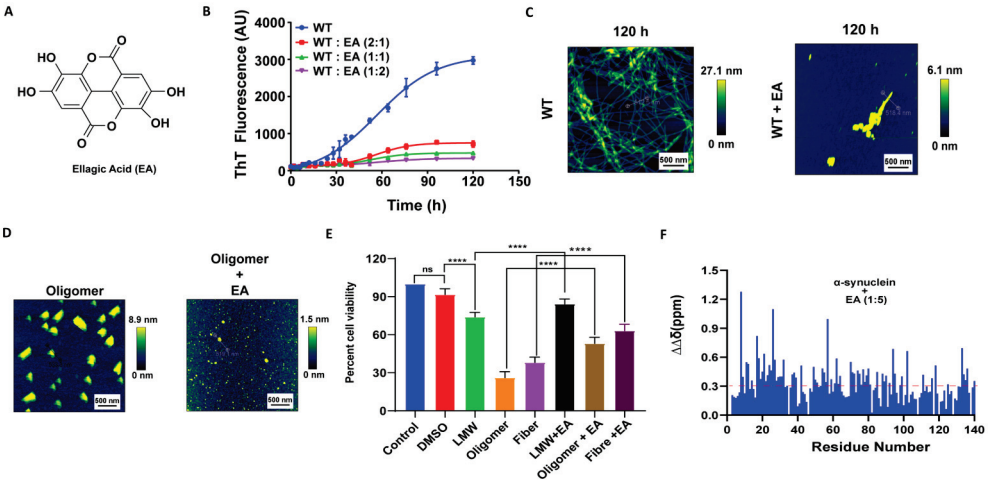
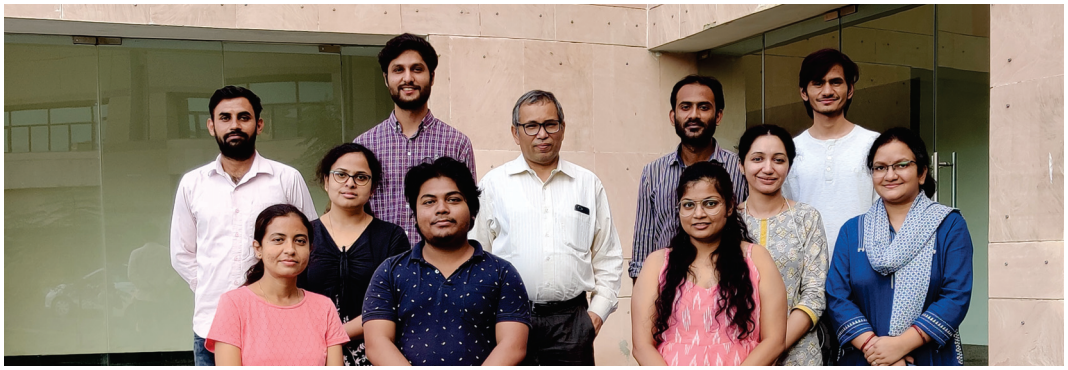


Figure 2: *(A) Chemical structures of Ellagic acid (EA), (B) Kinetics of aggregation inhibition, (C) Representative atomic force microscopy image of aggregation inhibition by EA, (D) Atomic force microscopy image of disaggregation of oligomeric intermediates by EA, (E) Cytotoxic behavior of α-synuclein species (F) Chemical shift perturbation between α-synuclein and EA studied by NMR spectroscopy.*



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Tanushri Dargar

Signals that Regulate Skeletal Muscle Structure and Function

We are investigating the mechanisms that regulate skeletal muscle formation and control its function. The skeletal muscle is one of the largest tissues in our body, essential for vital functions such as locomotion, support, posture maintenance and regulation of whole-body metabolism. The mammalian adult skeletal muscle can get injured due to a variety of reasons, such as accidents, physical activities such as sports, or due to congenital diseases such as Duchenne muscular dystrophy where the skeletal muscle goes through repeated cycles of injury due to mutations in the DMD gene. The skeletal muscle has a tissue resident pool of stem cells known as satellite cells, which help in repair and regeneration of injured skeletal muscle. 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 is a regulator of muscle stem cell differentiation

Satellite cells or 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, and 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. 1). During muscle injury and regeneration, TLE4 protein levels increase immediately after injury, similar to that of the satellite cell marker Pax7, and return to steady state levels once regeneration is complete (Fig. 1). Using co-immunoprecipitation, we found that Pax7 and TLE4 proteins interact with each other (Fig. 1). We also observed that TLE4 expression is transiently downregulated in satellite cells during early stages of muscle regeneration.

To identify whether TLE4 is important for muscle differentiation, we depleted TLE4 by siRNA transfection in the mouse myogenic C2C12 cells, which were allowed to differentiate. Interestingly, Myf5 exhibited ~6-fold upregulation whereas MyHC-emb, a terminal differentiation marker, exhibited significant downregulation at the protein level, following TLE4 depletion (Fig. 2). This suggests that TLE4 is crucial for repressing Myf5 during muscle differentiation. In a fusion index experiment, we found that depletion of TLE4 led to fewer differentiated myofibers and a significantly reduced fusion index, indicating that TLE4 is a crucial regulator of myogenic differentiation (Fig. 2).

We have further characterized the role of TLE4 in myogenic differentiation and find that it occupies a Myf5 enhancer which is bound by Pax7, which regulates Myf5 transcriptional activation during muscle regeneration. Thus, our study identifies TLE4 as a novel regulator of skeletal muscle differentiation. TLE4 binds Pax7, occupies an enhancer of Myf5, ensuring Myf5 transcriptional repression during quiescence. During muscle injury and consequent regeneration, TLE4 is downregulated, which permits Pax7 to activate Myf5 and facilitate differentiation. Therefore, TLE4 is a novel regulator of Myf5 expression and myogenic differentiation.

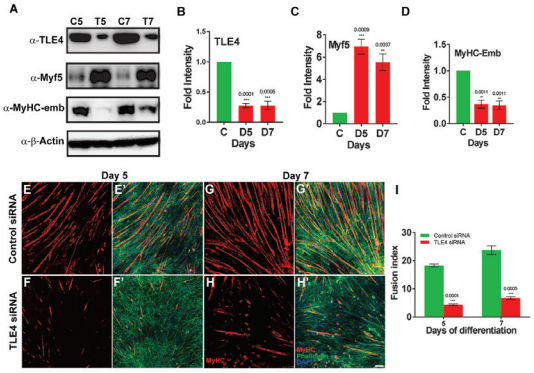

Figure 1: TLE4 is expressed in muscle stem cells and interacts with Pax7. *(A-B''') Immunofluorescence for TLE4 (red), Pax7 (green) (A-A'''), or TLE4 (red), laminin (green) (B-B''') in TA muscle; arrowheads indicate non-satellite cell nuclei. (C-E) TLE4 and Pax7 western blots on uninjured (U) and injured (I) TA at 3-28 dpi (C), and their densitometry relative to uninjured controls (D-E). (F) Co-immunoprecipitation of Myc-Pax7 and FLAG-TLE4 in NIH-3T3 cells.Scale bar: 25 µm (A'''); 25 µm (B''').*

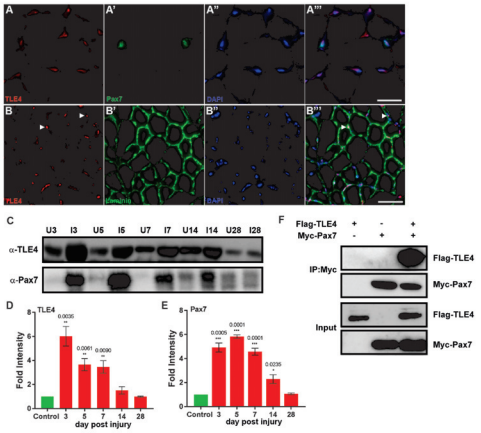

Figure 2: TLE4 represses Myf5 and regulates myogenic differentiation. *(A-D) Western blots for TLE4, Myf5, MyHC-emb and beta-actin on control (C) and Tle4 siRNA (T) treated C2C12 cells at days 5 and 7 of differentiation (A) and densitometry (B-D). (E-H) Control or Tle4 siRNA treated C2C12 cells labeled for MyHC (red), phalloidin (green) and DAPI (blue) at days 5 and 7 of differentiation (E-H'), and their fusion index (I). Scale bar: 100 µm.*

Modulation of MET signaling and its role in myogenesis

Receptor tyrosine kinases such as MET mediate cell-signaling cascades vital to physiological processes. Deranged MET signaling underlies several cancers including Rhabdomyosarcoma (a pediatric cancer), where tumor cells resemble muscle precursors but fail to differentiate. MET signaling is crucial to migration of muscle precursors during muscle formation, in the developing embryo and in post-injury muscle regeneration. Therefore, MET signaling is a shared feature between development, regeneration and disease. In research undertaken by India Alliance Early Career Fellow Dr. Masum Saini to understand its role in myogenesis, mouse genetics tools were employed to ablate MET in muscle precursors during development. Notably, such conditional MET knockout mice do not survive to birth, but are alive until embryonic day (E)14.5. Ongoing efforts focus on identifying the developmental stage of *in utero* lethality, and the significance of MET signaling in it. Additionally, data on brain tumors/gliomas showed that levels of MN1, a transcriptional regulator, can predict glioma patient survival and may serve as a promising prognostic marker.

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Understanding Taste and its Modulation using *Drosophila Melanogaster*

Taste information present at the periphery must be processed by the central circuits for the final behavioral output. Identification and understanding of the neural circuitry regulating taste behavior is required to understand the neural basis of taste preference. In humans, abnormal nutrient consumption causes metabolic conditions like obesity and diabetes. Despite this burden on society, neuronal circuits that regulate appetite and influence feeding behaviors are undetermined. We are using the genetic model system *Drosophila melanogaster that* can sense the same taste stimuli as mammals (sugars, sour, water, salt, umami and bitter) to study the molecular and cellular mechanisms by which specific neural circuits underlie modulation of taste function and orchestrate observable taste driven behaviors (acceptance or rejection).In particular, we are trying to understand (1) novel taste circuits in the brain(2) physiological state and factors that act on the taste cells and circuits and (3) modulation of taste behavior.

Role of pharyngeal LSO neurons in regulating high salt intake

Apart from peripheral taste cells, there are distinct internal taste organs present in adult flies' pharynx namely LSO (labral sense organs), VCSO (ventral cibarial sense organ) and DCSO (dorsal cibarial sense organ). After food intake is initiated, the pharynx controls ingestion of food, and encourages only intake of appetitive food in flies. A recent receptor–to-neuron map of pharyngeal taste organs describes distinctive functional groupings of pharyngeal neurons. In recent years,attention has been paid only on the salt coding at the periphery in flies, but what remains unclear is the role of areas like pharyngeal taste organs that are proposed to act as gate keepers before food ingestion.

Mechanisms that regulate high salt consumption are largely undetermined in any animal. To understand how pre-exposure to high sodium chloride (NaCl) diet modulates subsequent taste behavior, we looked into the molecular mechanisms of high NaCl feeding and its impact on the feeding behavior in adult *Drosophila* not explored so far. We found that wildtype flies are attracted to low levels of NaCl and show reduced feeding preferences towards higher concentrations. We observed that wildtype flies on high NaCl diet for three days maintain their preference for high NaCl even later. Our results demonstrate that wildtype mated females show an appetite for high NaCl diet and increase in mean body weight after feeding on different concentrations of NaCl. Under starvation, silencing neuronal activity of the peripheral labellum sweet and bitter neurons only in flies pre-exposed to high NaCl leads to higher NaCl feeding, suggesting a role of intact pharyngeal neurons in regulating high salt intake. On the other hand, upon silencing LSO (labral sense organ) pharyngeal neurons specifically, NaCl sensitized flies show normal feeding under starved conditions. Our data suggest that pre-exposure to high NaCl enhances taste sensitivity of flies for sugars, as well as for low and high NaCl concentrations via activity dependent mechanisms in LSO neurons irrespective of which taste receptor they express. Altogether, our results propose a role of internal state and activity in LSO pharyngeal neurons in regulating high salt intake.

Neurons like LSO in the pharynx present a regulatory system that has evolved to fine tune our calorie intake with energy metabolism. These microcircuits are even conserved in humans to regulate food intake. Our studies emphasize how non-caloric substances can influence the risk for obesity and diabetes, thereby emphasizing that factors other than altering the protein, fat and carbohydrate content of food, or the counting of calories should be considered in promoting weight loss and preventing metabolic consequences. Our results also suggest that pharyngeal taste organs like LSO play an important role in sodium homeostasis. Furthermore, the linkage between salty and sweet taste modulations may optimize sodium and calorie intakes.

Understandingcentral taste circuits

Recent progress is remarkable to understand the neurobiology of taste and behavior in both vertebrate's and invertebrate's. How different central neural circuits for taste are organized, orchestrate and encode the peripheral information about the stimulus quality that leads to simple behavioral output like acceptance or rejection of food is a central topic of study in the lab. However, the role of various regions in the central nervous system (CNS) in integrating feeding behavior with sensory signals on the availability and quality of nutrients is currently

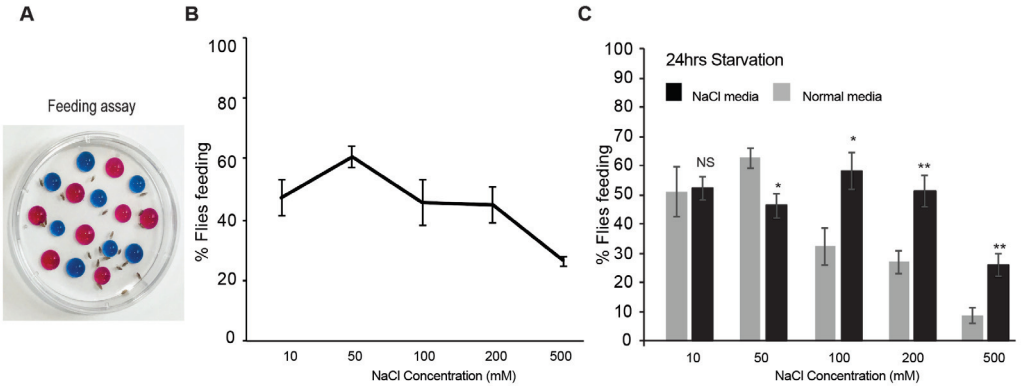

Figure 1: Drosophila salt feeding responses. *(A) Binary choice feeding assay plate (Red-salt + agar/blue-water agar). (B) Mean NaCl feeding responses of wild type flies. (C) WT flies pre-fed on a high NaCl diet show increased preference to high salt even later. Black bars (flies pre- exposed to a high salt diet (200mM NaCl mixed with the normal fly food) for 3 days. Grey bars- flies fed on normal fly media for 3 days.*

insufficiently understood. To understand how the central nervous system is wired to process information about taste we have identified various microcircuits that integrate taste information and send it to higher brain areas. We are mapping of various taste circuits beyond the level of primary taste neurons specifically in insect using *Drosophila melanogaster* as a model system.

To understand the central taste circuits in the fly brain that are involved in feeding decisions and different aspects of feeding behavior we have identified a second order sweet taste projection neurons. Suppression of these sweet gustatory projection neurons (sGPNs) marked by *Np1562* activity by active form of tetanus toxin results in decrease food intake and inhibition of PER responses. The sGPNs activation by applying sucrose and other sugars to the labellum suggested a functional link with Gr5a+ sweet taste neurons. These neurons relay sweet information from the SEZ to the antennal and mechanosensory motor center (AMMC) in the deutocerebrum of fly brain. Starvation and dopamine signaling increases the sucrose sensitivity of the sGPNs providing direct confirmation for state dependent alterations in sweet taste circuit activity. The AMMC is known to receive input from sensory axons of the basal antennal segments involved in sensing gravity, sound and mechanosensation. Our results suggest its role in taste processing as well. It remains to determine if AMMC as a secondary center for sweet taste also receive inputs from other categories of taste neurons, such as water, bitter, salt, sour and fatand, if so, whether the representation of different tastes remains distinct in AMMC.

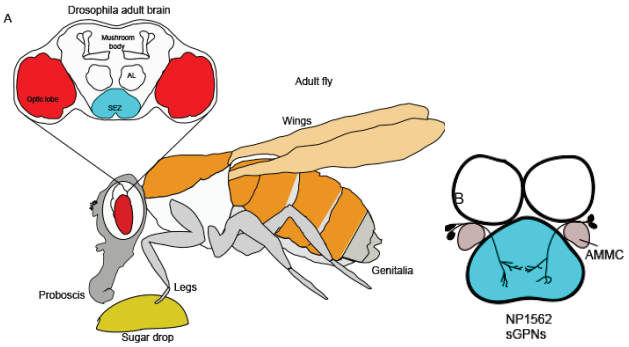

Figure 2: Drosophila taste system. *(A) Adult fly accessing sugar with tarsi. Proboscis, legs, wing margins, and genitalia are peripheral taste organs housing taste neurons in taste hairs. The taste information from the periphery goes to SEZ in the brain. Antennal lobes (AL) receive olfactory information and mushroom bodies are learning-memory centers. (B) NP1562+ Sweet gustatory projection neurons (sGPNs) synapse with peripheral sweet taste neurons and relay taste information from SEZ to AMMC.*

RNA Biology of Aging and Dietary Restriction

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Aging is characterized by organismal and cellular dysfunction and is associated with an increased risk of chronic diseases such as neurodegeneration, cardiovascular diseases and cancer. Dietary restriction (DR) extends lifespan across species and is associated with improved metabolic fitness. We employ genetic, molecular and proteomic approaches to test whether DR-regulated noncoding RNAs can promote a healthy lifespan and delay/prevent age-related diseases.

Post-transcriptional regulators of aging and dietary restriction

Aging is characterized by a progressive accumulation of cellular damage and an increased risk of diseases. Dietary restriction (DR)-reduced nutrient intake without incurring malnutrition is a non-genetic intervention that extends lifespan and is associated with improved metabolic fitness and increased resistance to stress. The beneficial effects of this nutritional intervention are conserved across species, indicating that the molecular mechanisms that underlie DR are evolutionarily conserved. Though, this anti-aging manipulation has been shown to direct profound changes in protein coding RNAs, its effect on non-coding RNA levels has not been explored extensively. Noncoding Ribonucleic acids (ncRNAs) are emerging as key regulators of gene expression and are being recognized as key modulators of aging and late-onset diseases. In contrast to the protein machinery that represents only ~2% of the transcribed genome, the expansion of the noncoding transcriptome in higher eukaryotes reflects greater regulation of cellular processes through control of protein function. Despite growing evidence that ncRNAs are altered during aging, there is little evidence on DR-dependent positive effects on ncRNAs and their targets or the pathophysiological consequences of these alterations. MicroRNAs are one class of non-coding RNAs that play several important physiological roles. Our research program combines the genetically amenable fruit fly model with high throughput technologies such as RNAseq, proteomics and metabolomics to identify and characterize the role of conserved miRNA-mediated networks that operate during aging and dietary restriction (Fig. 1). This research program is of direct relevance to the study of human age-associated diseases, as the inappropriate expression of miRNAs has been linked to several pathogenic states and molecules that alter the function or abundance of miRNAs are emerging as potential therapeutic agents to treat diseases. In addition, identification and characterization of conserved miRNAs that function during dietary restriction will likely lead to the discovery of circulating diagnostic biomarkers of age-related disorders in humans.

MicroRNA-mediated mechanisms in aging and dietary restriction

MicroRNAs (miRNAs) are a class of small non-coding RNAs that negatively regulate gene expression by base-pairing to their target mRNAs. We are using the fruit fly, *Drosophila* melanogaster as a model to study miRNA mediated post-transcriptional networks that operate during aging and late-onset diseases (Fig. 1). This model organism has yielded valuable insights into the molecular mechanisms underlying human aging owing to its' short lifespan (60- 90 days), genetic feasibility, low cost, and ease of handling. To identify miRNAs that are modulated in an age- or diet-dependent manner, we performed high throughput RNA sequencing with total RNA extracted from fruit flies that were exposed to dietary restricted and nutrient-rich diets (Fig.2). Since mutations in miRNA genes that do not respond to dietary restriction will serve as critical tools for understanding mechanisms underlying lifespan extension, we are analyzing the lifespan of DR and age-modulated miRNA mutants or overexpression lines to identify miRNAs that contribute towards DR mediated lifespan extension.These studies, together with analysis of the relevant DR-dependent targets of the identified miRNAs, will aid in defining miRNA-mediated mechanisms that operate during aging and determine how targeted disruption, competitive inhibition, or overexpression of miRNA network components modulate aging.

Illuminating microRNA mediated mechanisms that operate during the pathogenesis of late-onset neurodegenerative disorders

Aging is a major risk factor for the onset of a number of neurodegenerative diseases. Recent studies have found that miRNAs are misregulated in neurodegenerative diseases (NDDs) such as Alzheimer's disease (AD). We are utilizing *Drosophila* AD models to provide mechanistic insights into the roles of miRNAs in aging disease pathogenesis. Since conserved miRNAs have been linked to AD, our system provides a tractable venue both to understand the molecular

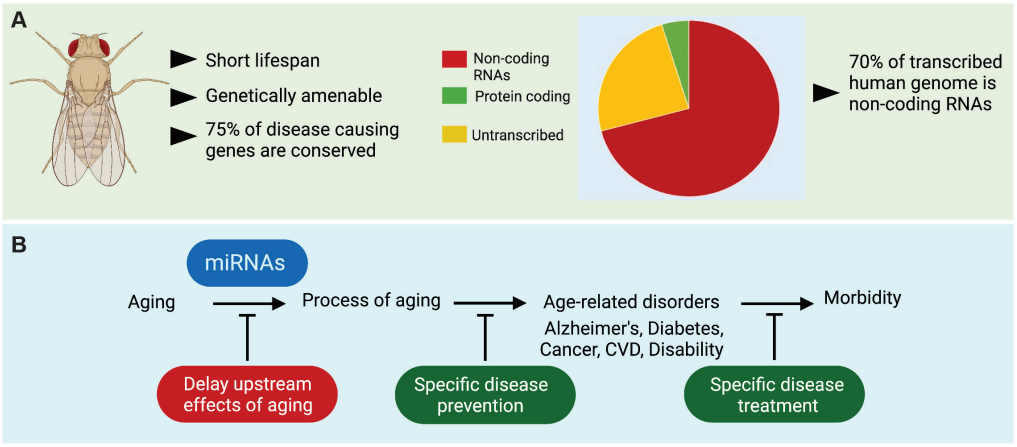


Figure 1: Towards developing RNA-based preventative therapies for late-onset diseases. *(A) Fruit fly model to study aging and late onset diseases. (B) Slowing the rate of aging as a strategy to delay onset of multiple diseases.Schematic representing the various stages at which therapeutic strategies can be designed fortreatment of age-related degenerative diseases. We are testing the efficacy of miRNAs to slow down the rate of aging and prevent multiple diseases simultaneously.*

mechanisms underlying miRNA-mediated neurodegeneration and to explore miRNA-mediated therapies designed to alleviate neurodegenerative symptoms. We have identified a few conserved miRNAs that are altered in a diet-dependent manner in AD models (fig. 2) and are currently examining the effects of modulating these miRNAs on disease progression. Together these studies aim to develop RNA-based therapeutic strategies to fine-tune conserved pathways that can provide broad spectrum health improvement and aid in the development of treatments for late onset diseases simultaneously.

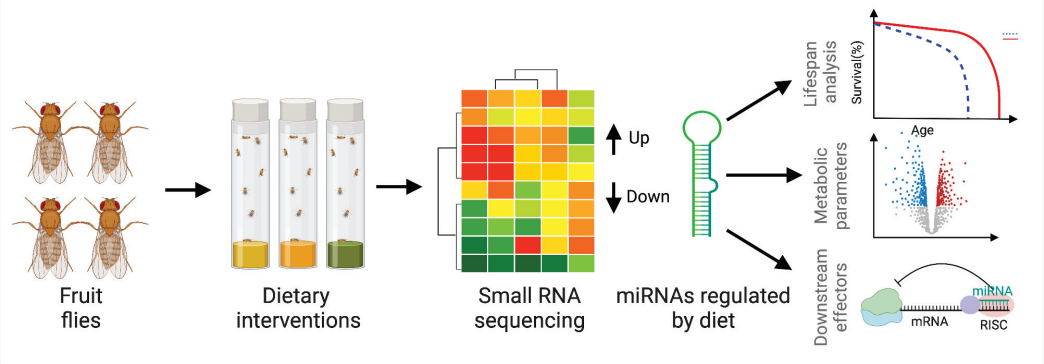
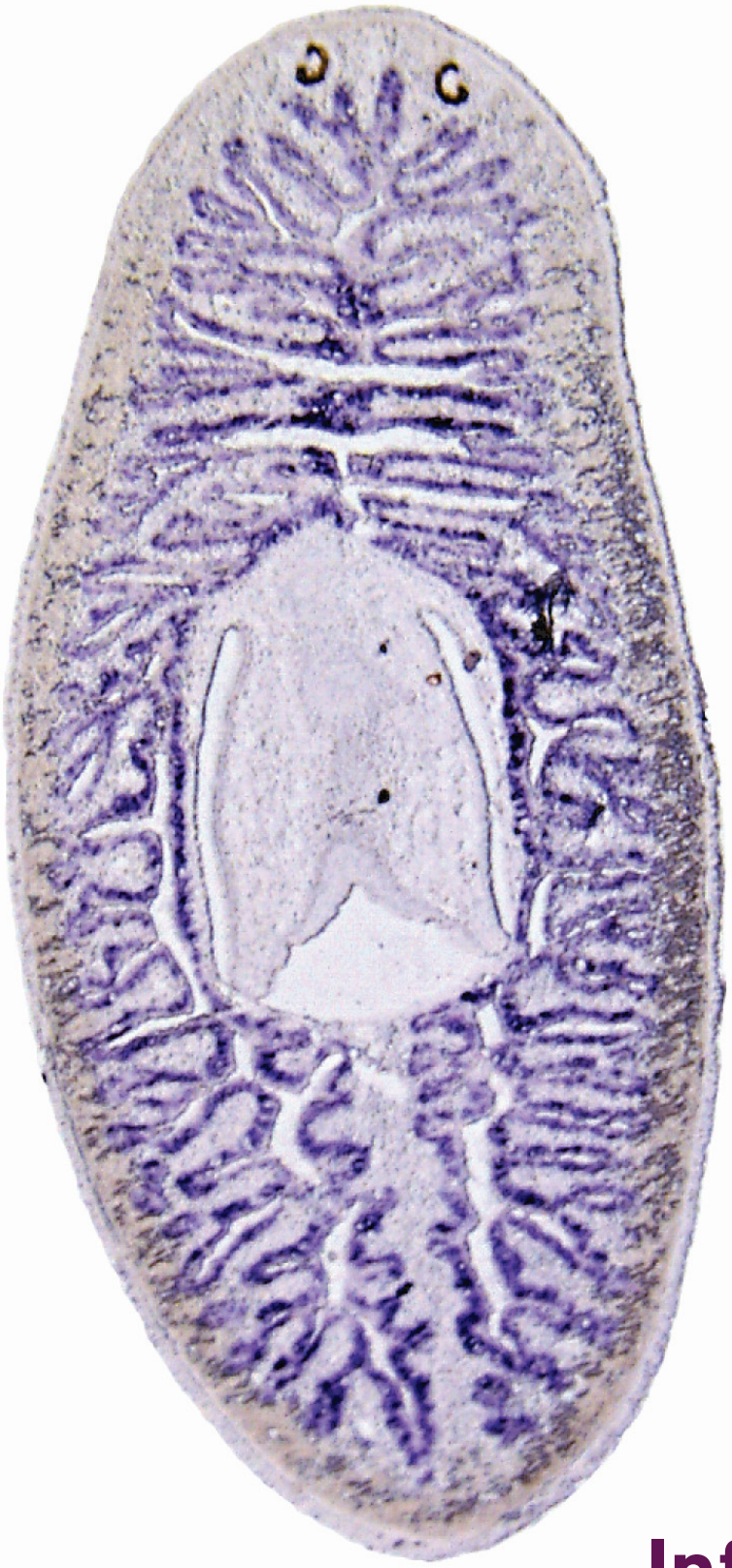


Figure 2: Working model for identification and characterization of age- and diet-modulated miRNAs miRNA networks. *Fruit flies were fed Ad libitum (AL) or nutrient restricted (DR) diet and total RNA extracted from young and aged flies was used to perform small RNAseq. Heat map showing miRNA abundances in adult fruit flies exposed to different diets. The identified age- and diet-modulated miRNAs and their downstream targets are characterized for their ability to extend lifespan and reduce risk factors associated with diseases.*



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 and replication can help in designing novel antivirals for effective therapeutic and prophylactic interventions. We are studying the biology of Chikungunya (CHIK), Dengue (DEN) and Japanese encephalitis (JE) viruses to understand their replication and pathogenesis with a view to design novel antiviral strategies.

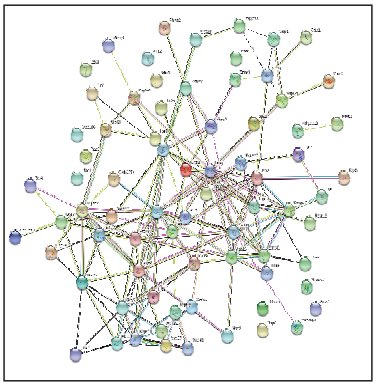
Several projects relating to the goals of the research program are being pursued. Provided below is a summary of some of the key projects under the program.

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 ~9000 compounds that includes small druggable molecules, we have identified lead compounds that show inhibition of CHIK virus infection in 3 different cell types at 5 micromolar concentration. A mouse model of CHIK virus infection in mice has been established where some pf the compounds reported previously as showing antiviral activity in cell culture have shown antiviral potential. Attempts are underway to understand the mechanism of antiviral action of these compounds.

Novel druggable compounds from the CDRI and other commercial libraries will be screened for potential antiviral activities using the high throughput assays developed in the lab.

Japanese encephalitis virus protein NS4A interacts with PTEN-induced kinase 1 (PINK1) and promotes mitophagy in infected cells: Japanese encephalitis virus (JEV), a mosquito-borne neurotropic flavivirus, is responsible for ~70,000 encephalitis cases resulting in up to 20,000 deaths annually, mostly in the Asian continent. To develop novel therapeutics for the disease, it is important to understand the biology of virus replication, and pathogenesis which could be affected by the interaction of the viral and cellular proteins. To understand the biological role of JEV non-structural protein NS4A, we identified its protein interactome (Fig. 1).

A



Cellular Component (GO)

pathway ID	pathway description	count in gene set	false discovery rate
GO:0005739	mitochondrion	22	3.79E-06
GO:0044429	mitochondrial part	15	1.06E-05
GO:0005743	mitochondrial inner membrane	10	0.000131
GO:0031966	mitochondrial membrane	11	0.000289
GO:0005740	mitochondrial envelope	11	0.000435
GO:0031967	organelle envelope	13	0.000702
GO:0043209	myelin sheath	7	0.000702
GO:0044444	cytoplasmic part	37	0.00146
GO:0031090	organelle membrane	21	0.00418
GO:0005737	cytoplasm	46	0.00453
GO:0005840	ribosome	6	0.00577
GO:0005761	mitochondrial ribosome	4	0.00763
GO:0044391	ribosomal subunit	5	0.00887
GO:0044455	mitochondrial membrane part	5	0.00887
GO:0098800	inner mitochondrial membrane protein complex	4	0.0121
GO:0014069	postsynaptic density	5	0.0258
GO:0016020	membrane	38	0.0258
GO:0044422	organelle part	35	0.0279
GO:0044464	cell part	54	0.0279
GO:0005623	cell	54	0.0293
GO:0043231	intracellular membrane-bounded organelle	43	0.0316
GO:0044446	intracellular organelle part	34	0.0316
GO:0005622	intracellular	50	0.0347
GO:0032991	macromolecular complex	25	0.0364
GO:0097386	glial cell projection	2	0.038
GO:0030529	ribonucleoprotein complex	8	0.0459
GO:0044425	membrane part	30	0.0459
GO:0045202	synapse	8	0.0459

Network Stats

number of nodes:	75	avg. local clustering coefficient:	0.387
number of edges:	150	expected number of edges:	96
average node degree:	4	PPI enrichment p-value:	2.13E-07

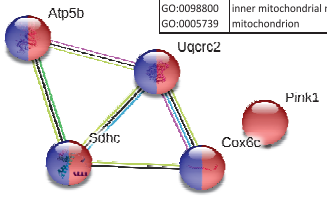
KEGG Pathways

pathway ID	pathway description	count in gene set	false discovery rate
5012	Parkinson s disease	5	0.028
5010	Alzheimer s disease	5	0.0295

B

Cellular Component (GO)

pathway ID	pathway description	count in gene set	false discovery rate
GO:0005743	mitochondrial inner membrane	5	1.15E-06
GO:0005740	mitochondrial envelope	5	2.45E-06
GO:0044455	mitochondrial membrane part	4	2.45E-06
GO:0098800	inner mitochondrial membrane protein complex	3	7.12E-05
GO:0005739	mitochondrion	5	0.000199



Network Stats

number of nodes:	5	avg. local clustering coefficient:	0.667
number of edges:	5	expected number of edges:	0
average node degree:	2	PPI enrichment p-value:	8.06E-07

KEGG Pathways

pathway ID	pathway description	count in gene set	false discovery rate
5012	Parkinson's disease	5	2.29E-09
190	Oxidative phosphorylation	4	7.08E-07
5010	Alzheimer's disease	4	1.21E-06
5016	Huntington's disease	4	1.21E-06
4932	Non-alcoholic fatty liver disease (NAFLD)	3	0.000153

Figure 1: The mouse JEV-NS4A interactome. *(A) The Y2H screen of the mouse brain cDNA library with JEV-NS4A identified 75 interacting protein partners. Each node in the left panel represents an identified protein, edges represent protein-protein associations not necessarily representing physical interactions. The pathway enrichment analysis (right panel) was conducted with the help of STRING (version 10.5) bioinformatics tool at the confidence level of 0.15. The p-value <.05 was used as the cut-off criterion. The red nodes in the interaction map (left panel) represent proteins from the mitochondrion cellular component and the purple nodes denote the proteins enriched in Parkinson's disease.*

(B) The sub-interactome of the genes enriched for Parkinson's Disease (PD) pathway (left panel). The pathway enrichment analysis (right panel) was conducted with the help of STRING (version 10.5) bioinformatics tool at the confidence level of 0.15. The p-value <.05 was used as the cut-off criterion. The red nodes (left panel) depict the proteins enriched in PD while the purple nodes in Alzheimer's disease.

The non-structural protein 4A (NS4A) of flaviviruses has been implicated as a 'central organizer' of the membrane-bound replication complex during the virus replication. However, its role, if any, in the host responses to virus infection, is not understood. Using the yeast-two-hybrid library screen, we identified a multitude of host proteins interacting with the Japanese encephalitis virus (JEV) NS4A protein. Several of these interacting proteins are known to localize to the mitochondria. One of these proteins was the PTEN-induced kinase 1 (PINK1), a serine/threonine-protein kinase known for its role in mitophagy. Here, we demonstrate JEV-NS4A localization to mitochondria and its interaction with PINK1 in Huh7 cells during JEV infection (Fig. 2). The virus infection led to a reduced PINK1 expression and enhanced the mitophagy flux with a concomitant decline in mitochondrial mass. Furthermore, we demonstrated that JEV-NS4A alone was sufficient to induce mitophagy. Our study provides the first evidence of mitochondrial quality control dysregulation during JEV infection, largely mediated by its NS4A protein. Role of PINK1 in JEV replication will be studied further.

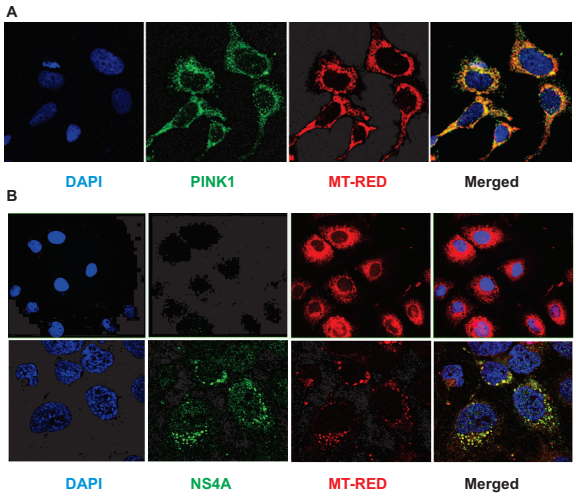
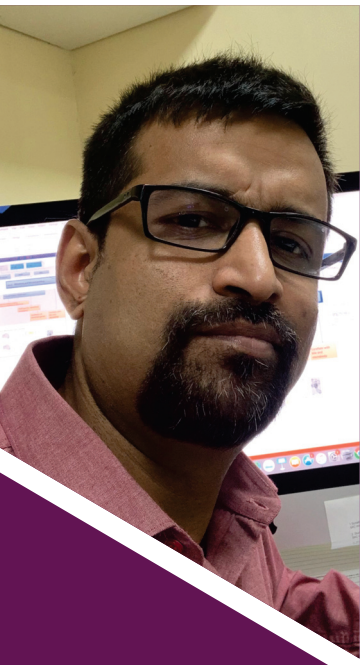


Figure 2: Localization of PINK1 and NS4A to mitochondria. *(A) Mock-infected Huh7 cells grown on coverslips for 24 h, were given a pulse of MitoTracker Red, fixed, and stained with DAPI and PINK1 antibodies. These cells were then stained with anti-rabbit Alexa-Fluor 488 antibody and visualized under a confocal microscope. PINK1 was seen to colocalize with MitoTracker Red (Pearson's coefficient 0.6). (B) Huh7 cells were infected with JEV (MOI 1) and 48 h later were given a pulse of MitoTracker Red, fixed, and stained with DAPI and JEV-NS4A antibodies. These cells were then stained with anti-rabbit Alexa-Fluor 488 antibody and visualized under a confocal microscope. JEV-NS4A was seen to colocalize with MitoTracker Red (Pearson's coefficient 0.6).*

Characterization of distal gut virome through metagenome sequence analysis: It is of interest to gain a comprehensive understanding of human gut microbiome in order to harness its potential. By sampling viruses from the distal gut of a defined "healthy" cohort of individuals, we have established a pipeline for viral metagenomics to characterize gut virome in a previously unexplored Indian population. Towards this, we sequenced DNA from purified virus-like particles (VLPs) as well as total microbial DNA from fecal samples. We have identified the most abundant and prevalent viral families present in the analyzed samples. Concurrent analysis of the microbial DNA has allowed us to determine relationship between viral and co-residing bacterial diversity. In addition, we have predicted the dominant lifestyle of bacteriophages and their potential hosts. Metagenome assembly has resulted in the recovery of several hundred complete genomes. Further analysis will be done to characterize the novel uncultivated viral genomes (UViGs).

Dr. Kanchan Bhardwaj
DBT Biocare Awardee



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Molecular Mechanisms of Infectious and Idiopathic Inflammation of the Gut

In the current program, we aim to utilise a range of different model systems including- cell culture model, mouse model and human patient samples to understand novel molecular mechanisms, particularly those linked to post-translational modification pathways (PTM) and epigenetic modifiers, that possibly govern inflammation in various forms of gut illnesses. As a part of this program we have been pursuing studies on inflammatory diseases of the gut that arise due to- (a) gastric infections caused by Salmonella Typhimurium, and (b) autoimmune disorders such as Crohn's disease and Ulcerative colitis. In these illnesses, we aim to dissect out the molecular details of epithelial-immunocyte crosstalk. The ultimate goal is to target such mechanisms and to use them as a potential for therapeutic interventions against gut inflammation.

Crohn's disease (CD) and ulcerative colitis (UC) are autoimmune diseases of the GI tract which are grouped under the umbrella term- Inflammatory bowel disease (IBD). Earlier, our group had demonstrated the importance of cellular SUMOylation, a post-translational modification (PTM) mechanism, in modulation of gut inflammation in CD and UC. Specificillay, it was shown that during IBD, the overall sumo-conjugated proteome (SUMOylome) of the intestinal epithelium is altered. An elivated expression of SUMO-deconjugase enzyme SENP7 triggers a proinflammatory mechanisms in gut. Together these changes are responsible for an expansion of proinflammatory T cell population leading to colitis. In uninflammed epithelial cells, the copynumbers of SENP7 are normally kept in check by the action of ubiuquitin ligase Siah2. Siah2 engages in a direct physical interaction with SENP7 leading to its ubiquityation followed by degradtion. During inflammation somehow the SIAH2 mediates regulation of SENP7 is lost. In our quest to fully understand these processes we set forth to investigate details of SIAH2 function in IBD, the results are being described below.

The interacting partners of SIAH2 (SIAH2-interactome) was investigated in healthy and inflamed murine intestine using proteomics approach as described in our earlier reports. We used a dextran sulphate sodium (DSS), a chemical irritant known to induce colitis in mice. The animals post DSS treatment (DSS-mice) displayed distinct markers of intestinal inflammation akin to human IBD including features like weight loss, shortening of colon length, epithelial erosion, neutrophil infiltration etc. Colonic tissue lysates were prepared from mock treated and DSS treated mice and immunoprecipitated using specific antibodies and subjected to tandem mass-spectrometry. Multiple search engines were used for analysing the obtained data which led to the identification of a total of 1443 proteins interactors of SIAH2 in healthy colon, and 2000 in those from DSS mice. Several of the identified proteins were regulatory in nature belonging to transcriptional machinery, adapter proteins, enzymes, pathogen recognition receptors, endocytic pathway etc. To infer the regulatory function of SIAH2 interactome, mathematical graph theory based Boolean network modelling was used to create protein-protein interaction network and interacting hubs of SIAH2 (Fig. 1).

To decipher its role in intesinal homeostasis, SIAH2 expression was perturbed in vivo. 6-8-week-oldmale mice were treated with 17 β-estradiol, a compound known to induce SIAH2. The inducer treated mice displayed a 3-fold upregulation of SIAH2 in the gut and therefore were called as $SIAH2^{INDUCED}$ mice. Notably, the ceca and colon of DSS treated $SIAH2^{INDUCED}$ mice were devoid of inflammatory markers as revealed from gross morphology and histopathology (Fig. 2).

Next, immune phenotyping was performed using cells from Spleen, payer's patches and mesenteric lymph nodes from these animals by flow cytometry. In line with our earlier data, induction of SIAH2 prevented the expansion of T cell population which was responsible for low inflammation despite DSS treatment. These changes at the cellular level were accompanied with a significant decrease in pro-inflammatory cytokines -IFNγ, IL17A and IL-9in gut mucosa of $SIAH2^{INDUCED}$ mice. Based on these data we concluded that $SIAH2^{INDUCED}$ mice are resistant to DSS induced colitis.

Since our data thus far pointed toward the involvement of γδ T cells in the progression of colitis, we investigated the effect of γδ T cell depletion on inflammation. An antibody against γδ TCR for neutralization was given intraperitoneally to mock treated and DSS mice. In these animals, the relative γδ T cell population was found to be lesser by a factor of 5-fold in spleen, LPs and MLNs in

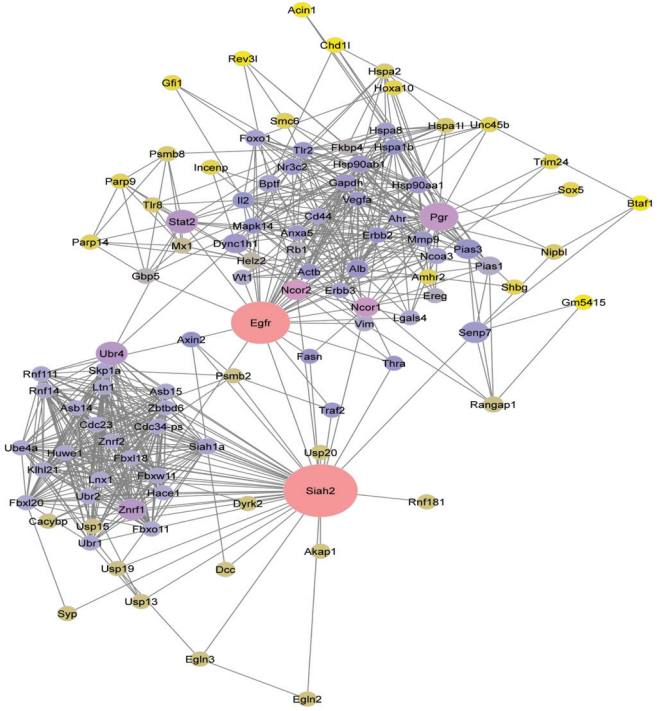
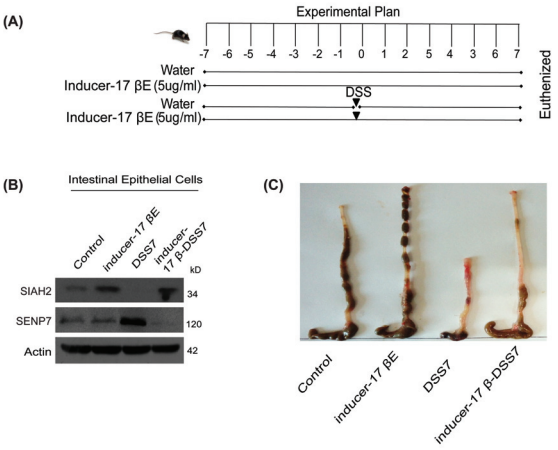


Figure 1: Protein-protein interaction (PPI) network showing SIAH2 and its regulators in *DSS induced colitis. Using a mathematical theory of Boolean network model PPI network was generated. The betweenness centrality theory used in this creating PPI network defines the measure of centrality in a graph based on shortest paths and the route for this path is via network hub proteins in case of biological networks.*

comparison to control animals. Moreover, akin to our previous results IFN-γ - and IL-17A-secreting γδ T cells was higher DSS7 colitis mice, but not in γδ-T-cell-depleted animals. The histopathology of colonic sections revealed massive neutrophil infiltration in DSS7 mice that was absent in animals treated with γδ T cell neutralizing antibody. Thus, γδ-T-cell-depleted mice appeared to be resistant to DSS-induced colitis. Together, our data revealed that in vivo depletion of γδ T cells, experimental induction of SIAH2 is sufficient for preventing the development of colitis.

Figure 2: Induction of SIAD2 expression by treatment of 17 β-estradiol *rescue mice from DSS colitis. (A) Schematic representation of SIAH2 overexpressed mice using 17 Beta Estradiol (SIAH2 Inducer) (n=3). Immunoblot showing induction of SIAH2 by 17-βE treatment. (C) Morphology of mice colon in different categories as indicated in the image.*



Host-Pathogen Interactions of Flaviviruses

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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. 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 also study how the body mounts an immune response and what parameters are essential for blocking/killing the virus. 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.

Analysis of JEV infection in human monocyte-derived dendritic cells

The lack of effective antiviral therapies reinforces the need to understand how the human immune response to JEV infection is regulated. Dendritic cells (DCs) are among the first cells to encounter the virus and are also key antigen-presenting cells that link the innate and adaptive immune system. Apart from a few studies, the primary human innate immune response to JEV remains largely unexplored and incompletely characterized. Here, we have analysed the gene regulatory circuit of JEV infection in human monocyte-derived DCs (moDCs) along with its functional validation. To gain insights into the transcriptional programing of JEV-infected moDCs, we performed an RNA-seq analysis of JEV-infected moDCs. Pathway enrichment analysis of the differentially expressed genes (DEGs) was performed on the basis of biological processes, molecular functions and cellular compartments. The key functional networks observed to be upregulated were those related to activation of the innate immune pathway; cytokine secretion and signaling; inflammation; and cell death. The genes involved in monocarboxylic acid, fatty acid and lipid metabolic processes were found to be downregulated.

We first tested DC maturation signatures, and observed upregulation of CD80, CD86, CD83 and CD40 expression (Fig. 1A). In concordance with our RNA-seq data, we observed a modest but significant upregulation of CD80, CD83, and Cd86 in JEV-infected moDCs (Fig. 1B). Significant upregulation of CD274 (PD-L1) was also observed (Fig. 1A-B). This indicates that JEV-infected moDCs undergo maturation.

Pathway enrichment analysis highlighted the following signaling pathways: NOD-like receptor, cytokine receptor, TNF, RIG-I & Toll-like receptor, Jak-STAT and NF-κB, showing a robust activation of innate immune signaling (Fig. 2A-B). Most of the critical pathogen recognition receptors were upregulated (Fig. 2C), and their activation was validated in independent samples by qRT-PCR (Fig. 2D). Upregulation of several of the crucial transcription factors (TF) and related genes involved in innate immune and inflammatory signaling were also validated (Fig. 2E). JEV infection also led to robust activation of interferons, cytokines and chemokines, and a diverse panel of interferon-stimulated genes (ISGs) (Fig. 2A-C). Activation of a select group of cytokines, chemokines and ISGs was also verified independently by qRT-PCR (Fig. 2D-E). We observed that JEV-infected moDCs secreted significantly high amounts of TNF , MCP-1, RANTES and the cytokines IL-12, IL-6 and IL-8 (Fig. 2F). Collectively our data indicate that JEV

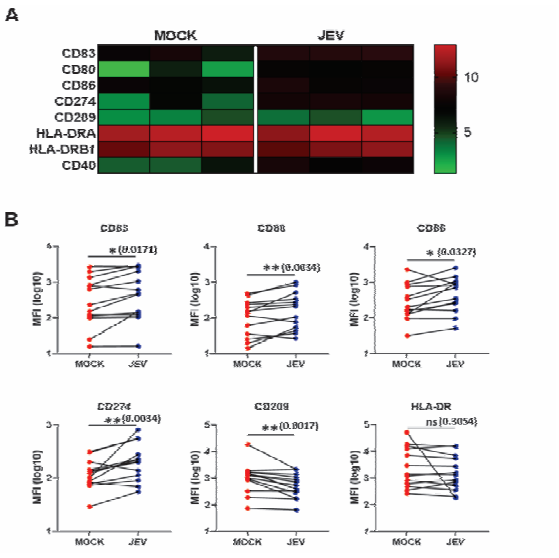


Figure 1: Upregulation of maturation markers in JEV infected moDCs *(A) Heatmap showing transcriptional upregulation of DC maturation and other co-stimulatory markers in mock vs JEV-infected condition in the three donors. (B) The cell surface expression of DC maturation and co-stimulatory markers was quantified by flow cytometry in mock/(5 MOI) JEV-infected moDCs at 24 hpi. Data for each donor is shown as median fluorescence intensity (MFI) with the mean (n = 13 donors). *, p<0.05; **, p<0.01 (Wilcoxon test).*

infection of moDCs leads to their maturation and robust activation of innate and inflammatory response, along with the secretion of an array of inflammatory cytokines.

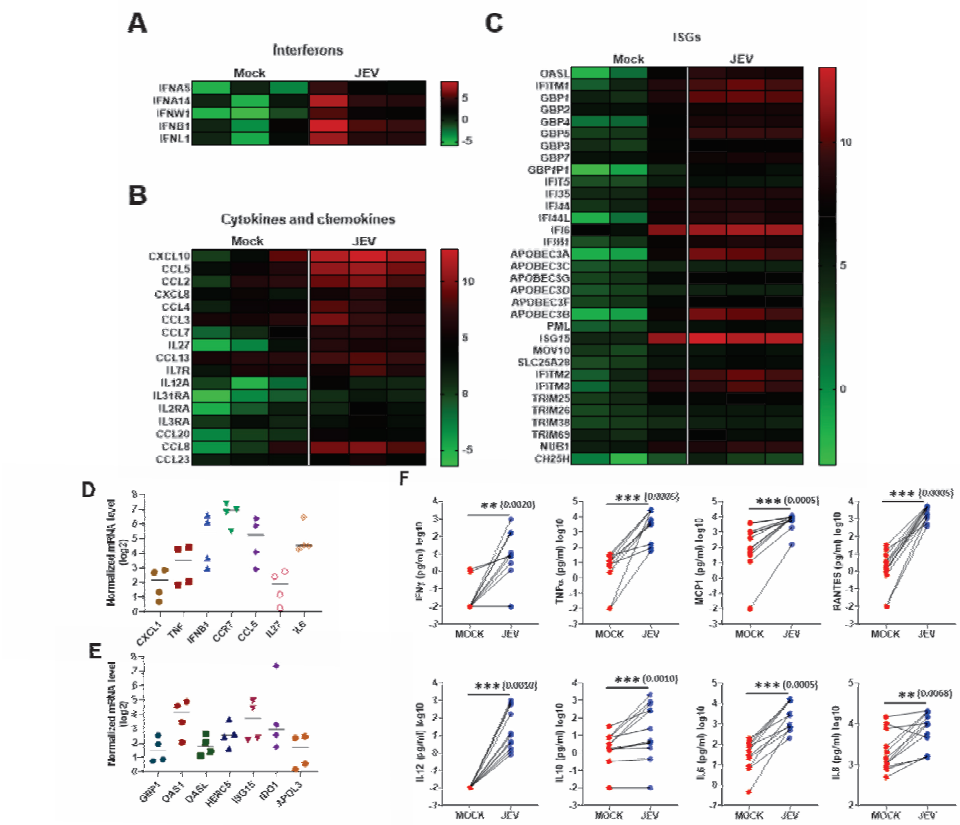
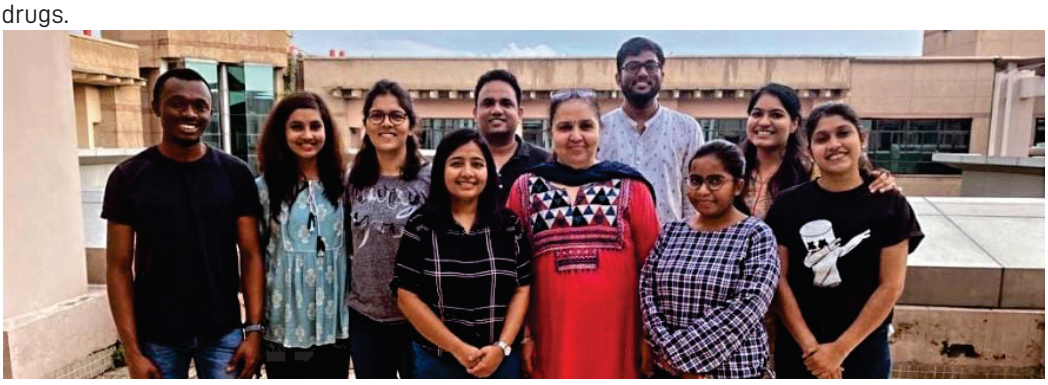


Figure 2: Activation of interferons, cytokines, chemokines and Interferon stimulated *genes (ISGs) in JEV-infected moDCs. (A-C) Heatmap showing DEGs coding for interferons (A), cytokines and chemokines (B), and ISGs (C), between mock and JEV infected condition from three donors. (D-E) Relative mRNA levels of selected cytokines/chemokines (D) and ISGs (E) was analysed in JEV-infected (5 MOI, 24 h) moDCs from four donors. Value from each donor along with the mean shown as log_2 expression normalized to mock infection. (F) Secretion of various cytokines and chemokines was analysed by multiplex bead array following JEV infection of moDCs (5 MOI, 24 h). Data for 12 donors is shown along with the mean. **, p<0.01; ***, p<0.001 (Wilcoxon test).*

Drug repurposing for JE

Several FDA approved drugs have the potential to be repurposed for treatment of infectious diseases. Previously, a high-throughput screening platform for measuring autophagy flux was successfully established, and a panel of FDA-drugs was tested for its effect on autophagy flux, JEV induced neuronal cell death and JEV replication. A total of 10 drugs showed moderate reduction in virus induced cell death and some of these showed inhibition of virus replication. Of these five drugs showed significant reduction of JEV induced inflammatory cytokine production and ROS levels and were shortlisted for studies on innate and adaptive immune responses in JEV infected human monocyte derived dendritic cells (moDCs), and survival studies in the mouse model. These five drugs are Fluoxetine, Flubendazole, Memantine, Methotrimperazine and Rilmenidine.

Four drugs were tested in the JE survival model. Two of the drugs flubendazole and fluoxetine did not show any protective effect. The other two drugs Rilmenidine and Methotrimperazine showed delay in onset of JE symptoms and enhanced survival, suggesting a protective effect of these drugs.



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Understanding Pathobiology of Flaviviruses prevalent in India

Our research group investigates the immunopathogenic mechanisms of two important viruses prevalent in India 1) Dengue virus (DENV) and 2) Japanese Encephalitis Virus (JEV). 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 peripheral and tissue infiltrating immune cells. However, there is a lack of in-depth knowledge of the phenotypic heterogeneity of immune cells due to viral infection. How virus-induced phenotypic changes are related to cell-fate decisions in the immune response andimpart adverse disease outcomes is still unclear. Thus, we have undertaken multiple projects to decipher the mechanisms of immune modulation at the cellular and molecular levels. To understand complex interactions between viruses and hosts, we have taken an integrated 'omics' approach extracting molecular information from clinical samples, followed by validation and mechanism study using cellular or animal models. Our work encompasses studying the impact of viral infection on immune cell phenotypes and functions.

This year, we have made some progress on understanding neutrophils and dengue virus interaction and their effect at the phenotype and functional level. In parallel, we assessed the level of infiltrating immune cells in the brain during JEV infection and studying their impact on viral replication and immune response in the brain.

Impact of Dengue virus on Neutrophil phenotypes and functions

Neutrophils are the most abundant circulating white blood cell and constitute the first line of defense against pathogens. While neutrophil activation has been recently shown to be associated with DENV infection, there is a gap in understanding the mechanism that warrants detailed investigation. Here, we studied the impact of dengue virus serotype 2 (DENV-2) on neutrophil phenotypes.

The mature and suppressive phenotypes can be defined based on the expression level of the cell surface markers, e.g., CD16, CD62L expressed uniquely on the neutrophils. We observed that Neutrophils incubated with DENV-2 lead to an increased population in the suppressive phenotype ($CD16^{high}$, $CD62L^{low}$) of neutrophils.Further, a spontaneous decondensation of nuclei along with the relocation of granular proteins (MPO) into the nucleus was observed in neutrophils incubated with DV-2 (Fig.1A). Increase released of extracellular DNA in DENV treated neutrophils was observed, indicating that the interaction of DENV-2 with neutrophils probably prime neutrophils towards releasing neutrophil extracellular traps (NETs) (Fig.1B). We also observed that Neutrophil and DENV-2 interactions also enhanced neutrophil life span and delayed apoptosis. Further studies are in progress to understand the role of DENV induced suppressive phenotypes on endothelial dysfunction and immune response.

We also studied the effect of the dengue virus on neutrophil biogenesis using the human promyelocytic HL-60 cell line as an in vitro model. Neutrophils originate from bone marrow (BM), and differentiation of promyelocytes ultimately leads to neutrophil generation. Differences in neutrophils phenotype can arise during the biogenesis process. To understand the influence of DENV on neutrophil generation, we chose a human promyelocytic HL-60 cell line. The HL-60 cells can undergo differentiation when stimulating with a suitable inducer (e.g., Retinoic Acid). Incubation of HL-60 with DENV-2 itself triggered HL-60 cells to differentiate into neutrophils

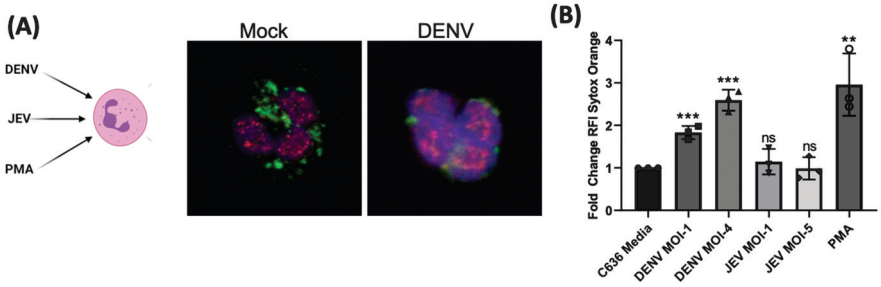

Figure 1: Effect of Dengue virus on neutrophil morphology. *(A) Neutrophils were isolated from healthy donors and incubated with DENV, JEV or PMA. After 3h of incubation, neutrophils were stained with Cit-His (red) and MPO (green). Nucleus was stained with DAPI. (B) Extracellular DNA release was measured using SYTOX assay. Data from three individual donors are shown as dot in the bar graph.*

terminally. Proteomics study revealed that DENV-2 triggered unique proteome changes into neutrophils associated with the Unfolded Protein Response (UPR), cell cycle regulation, RNA metabolism, and neutrophil-mediated immunity. Further study is in progress to understand the molecular signals triggered by DENV-2 in HL-60 cells that help to initiate differentiation into neutrophils.

Molecular modulator for JEV induced microglial activation and neuroinflammation

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 crucial to understand the regulators that drive microglia's phenotype changes and induce inflammation in the brain. Interferon regulatory factor 8 (IRF8) is a myeloid lineage transcription factor involved in microglial activation and interferon regulation. Our previous study observed an augmented expression of IRF8 in microglia and mice brain during JEV infection. However, the impact of IRF8 modulation on JEV replication and antiviral response remains elusive. Using *Irf8*$^{-/-}$ mice as a model system, we observed an impaired microglia/macrophages activation and reduced immune cell infiltration in the brain, leading to reduced proinflammatory (Fig. 2A-C) and antiviral response, which in turn enhances viral replication in *Irf8*$^{-/-}$ infected mice. From our RNA-Seq data of WT and *Irf8*$^{-/-}$ infected mice brain, it was evident that IFNγ appeared to be associated with IRF8 expression and was severely compromised in *Irf8*$^{-/-}$ mice. The gain of function of *Irf8* by overexpressing functional IRF8 in an IRF8 deficient cell line attenuates viral replication and enhances IFNγ production. Together, our data suggest a possible association between IRF8 and IFNγ that drives immune cell infiltration and modulate JEV replication in the brain. Further study is in progress to understand the cross-talk between IRF8 and IFNγ pathwayduring JEV infection.

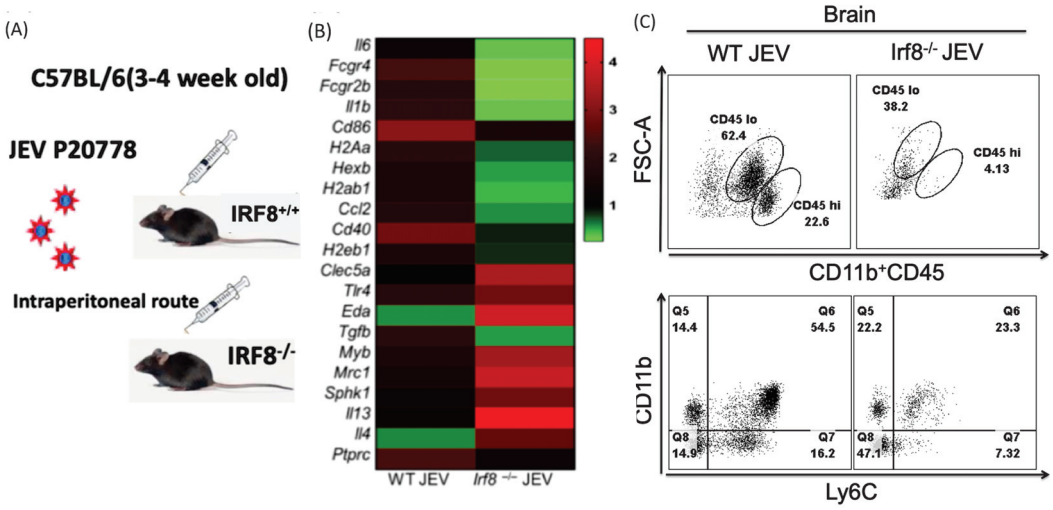

Figure 2: Effect of Interferon regulatory factor on microglial gene activation and infiltration of immune cells into JEV infected mice brain. *(A) Schematic diagram representing JEV (P20778) JEV-S3 infection through intraperitoneal route in IRF8 wild type (IRF8*$^{+/+}$*) and knock out (IRF8*$^{-/-}$*) mice. (B) PCR array heatmap showing microglial activation marker expression in JEV infected IRF8*$^{+/+}$ *and IRF8*$^{-/-}$ *mice brain. (C) Flowcytometry data showing difference in infiltrating macrophages (CD45*^{hi}*CD11b*^{hi}*) and lymphocytes (Ly6C) in JEV infected IRF8*$^{+/+}$ *and IRF8*$^{-/-}$ *mice brain.*

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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 fundamental players in tissue maintenance as they serve to restore damaged tissue during injury or disease. However, during severe bacterial/ viral infections, tissue regeneration in mammals is hugely inhibited. Recent research suggests that the mammalian ASCs function is affected during infections. Sometimes these ASCs over-proliferate and develop cancer, or they exhaust by terminal differentiation. Both scenarios lead to regeneration failure. 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 and viral infections. We would like to know whether pathogens influence the ASCs behavior and hence determine the regeneration outcome. The knowledge gained from this study would eventually help to improvethe ASCs tolerance to infection burden and thus has profound biomedical importance. Following are our strategic objectives and broad plan of action.

To study adult stem cells dynamics during bacterial infections

In mammals, the number of organs/tissues such as liver, lung, blood are equipped with stem/progenitor cells and possess regenerative potential. However, they fail to repair the tissue efficiently under several infectious conditions. For example, chronic hepatitis viral infections cause inappropriate regeneration/scar formation and often lead to hepatic cirrhosis and liver failure. Lung infection with influenza virus causing pneumonia or bacterial cystic fibrosis severely damages the lung epithelium. The improper repair of the injured epithelium often leads to respiratory failure. A recent study infers that mammalian ASCs have limited tolerance to proliferation/ differentiation burden. The ASCs exhaust and terminally differentiate under the circumstances requiring rapid proliferation/differentiation to replace severely infected tissue. These observations raise an obvious question of whether ASCs function is adversely affected during infections? Our research will attempt to satisfy this question. We will study the ASCs dynamics (i.e. proliferation, differentiation, survival) in response to the bacterial infection in both *in vivo* and *in vitro* systems. We will investigate whether pathogens affect the ASCs function/ behavior, which could ultimately determine/ alter the regeneration capacity during infections (Fig. 1).

We are using planarian flatworms for in vivo investigations. Planarian *Schmidtea* mediterraneahasan 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. Various lineage-committed stem cells, and their progenies can be studied in *vivo* in planarians (Fig.2). 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

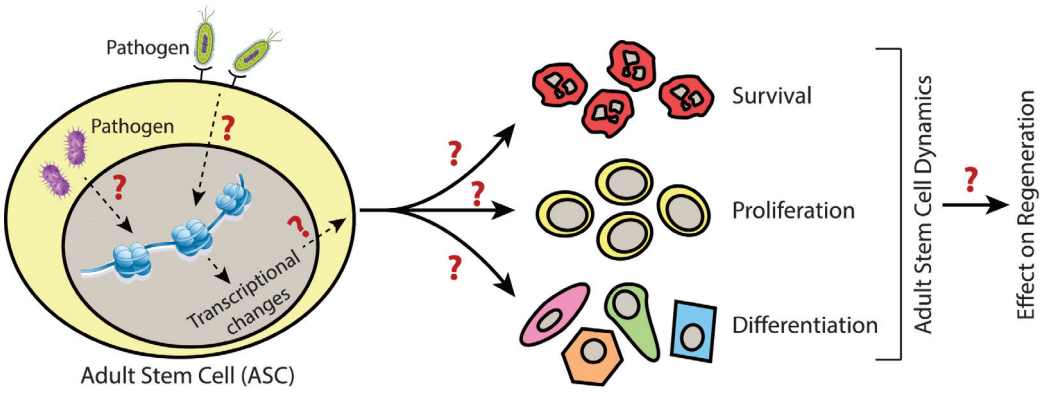

Figure 1: *The schematic of research questions we are trying to address*

cytometry in ample amount for next-generation sequencing applications such as RNA-Seq, ChIP-Seq etc. Hence, planarian has emerged as a convenient model system to study adult stem cell dynamics in vivo. We have previously observed that the regeneration ability in planarian *Dugesia japonica* remains unaffected after infection with several different types of bacterial species. We want to perform thorough investigations by using technically amiable planarian species *Schmidtea mediterranea to* get further detailed insights. We will be infecting planarians with different bacterial species and check the effect on regeneration. Further, we will investigate the survival, proliferation, differentiation dynamics of different types of adult stem cells and their progenies present in these animals. We would like to know whether bacterial infections module the stem cell behaviors and hence regulate the outcome of regeneration. We will use both Gram-positive and Gram-negative bacterial species for the infection. Several genetic factorsand signaling pathways (e.g. Wnt, Notch, JAK/STAT, Hippo, TGF-β, Hedgehog, MAPK/ERK) have been identified that precisely regulate the behavior/ activities of the various types of ASCs. Our research will further investigate the involvement of these signaling pathways in regulating stem cell dynamics in the infection scenario. It will be the first comprehensive study providingmeticulous insights into ASCs behaviors during infections.

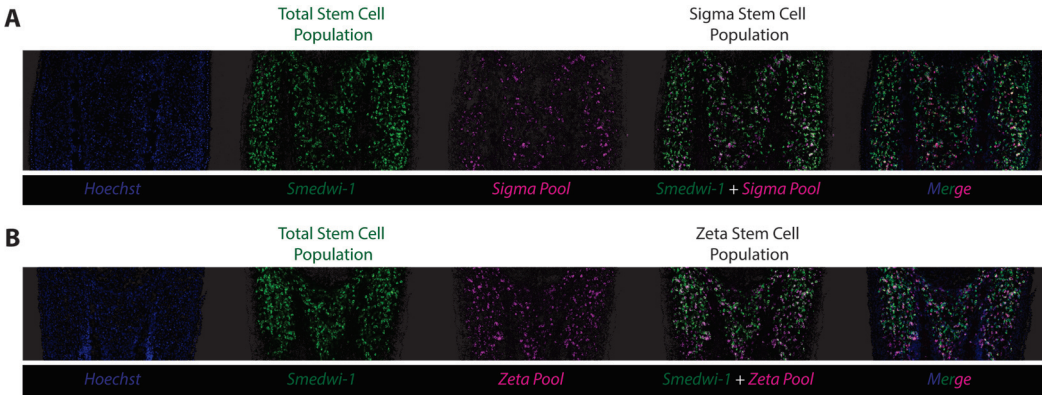

Figure 2: In vivo localization of stem cells in planarian Schmidtea mediterranea. *A) In-situ hybridization image of Schmidtea mediterranea showing the in vivo localization of pluripotent stem cell population known as Sigma stem cells. The Smedwi-1 and Sigma Pool double positive cells represent Sigma stem cells. Sigma pool contains the mixture of probes for genes such as SoxP1, and SoxP2. B) In-situ hybridization image of Schmidtea mediterranea showing the in vivo localization of epidermal lineage committed stem cell population known as Zeta stem cells. The Smedwi-1 and Zeta Pool double positive cells represent Zeta stem cells. Zeta pool contains the mixture of probes for genes such as zfp1 and SoxP3.*

To identify the molecular mechanisms governing the ASCs dynamics during infections.

By utilizingthe next-generation sequencing (RNA-Seq) technique, we will identify the transcriptional response of planarian ASCs to bacterial infections. With the help of RNA interference (RNAi) screening, we will uncover the molecular mechanisms used by planarian ASCs to maintain stem cell function during chronic bacterialinfections. The genes emerged from the RNAi screening in planarians will be further tested *in vitro* in mammalian primary ASCs culture. We will investigate the role of those genes in maintaining mammalian ASCs function during infections. We will also select a few genes for *in vivo* functional validation. We envision increasing the mammalian ASCs potency and wish to observe better tissue regeneration by the manipulated ASCs in the infection scenario.In the long term, our research would allow us to develop strategies to increase the tolerance of existing/ transplanted ASCs so that they perform more efficiently during infection-induced tissue injury.

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Translational Control of Gene Expression in Yeast and Fungal Pathogens

Our research group studies the 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, controlling cell proliferation, growth, and development. Initiation of translation at correct start codon in the mRNA is one of the first 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 mRNA subgroups for host adaptation needs to be thoroughly investigated. Our quest is to probe the translation process of yeast and pathogenic fungi to identify the novel therapeutic targets to treat the fungal diseases in humans.

Analysis of translation initiation factors to promote the high-fidelity selection of Initiation codon

Identification of the correct translation initiation codon is essential to ensure the synthesis of the functional cellular proteins in the proper amounts. 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 the scanning PIC, eIF1 and eIF1A promote an open, scanning-conducive conformation of the 40S subunit with TC bound in a 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.1A).

Recent Cryo-EM structures have revealed interactions unique to the closed complex between arginines R55/R57 of eIF2α with mRNA, including the -3 nucleotide of the "Kozak" context(usually an A) enhancing AUG selection. We found that R55/R57 substitutions reduced recognition of a UUG start codon at *HIS4* and *in vitro*, R55G-R57E accelerated dissociation of the eIF2·GTP·Met-tRNA$_i$ ternary complex (TC) with a UUG start codon, indicating destabilization of the closed complex. R55/R57 substitutions also decreased usage of poor-context AUGs in *SUI1* and GCN4 mRNAs *in vivo*. In contrast, eIF2α-R53 interacts with the rRNA backbone only in the open complex, and the R53E substitution enhanced initiation at a UUG codon and poor-context AUGs, while reducing the rate of TC loading *in vivo* and decreasing TC dissociation at UUG codons *in vitro*, indicating destabilization of the open complex. Thus, distinct interactions of eIF2α with rRNA or mRNA stabilize first the open, and then closed, conformation of the PIC to influence the accuracy of initiation *in vivo* (Fig. 1B).Currently we are also identifying the roles of ribosomal proteins of small 40S subunit to determine the high-fidelity selection of AUG initiation codons.

Delineate the protein translation regulation mechanisms that play important roles in virulence of human fungal pathogens

The host-pathogen interactions at the molecular levels are the key to the fungal pathogenesis. Fungal pathogens utilize several mechanisms like adhesion, invasion, phenotype switching and metabolic adaptation to survive in the host environments & drug responses. Post transcriptional and translational mechanisms have emerged key regulations adapted to ensure survival and virulence in the fungal pathogens. The protein translation initiation or degradation of the mRNA play pivotal roles in these regulation by influencing protein synthesis. At the time of pathogenesis, the human fungal pathogens exposed to stressful conditions in host that reduce global protein translation. The reduction in global protein translation influence expression of stress responsive genes that allow pathogen survival by modulating protein translation. Here we hypothesized infungal pathogens, altered gene expression at the time of stress can be regulated through translation initiation by modulating the key players like eIF2α kinases and other

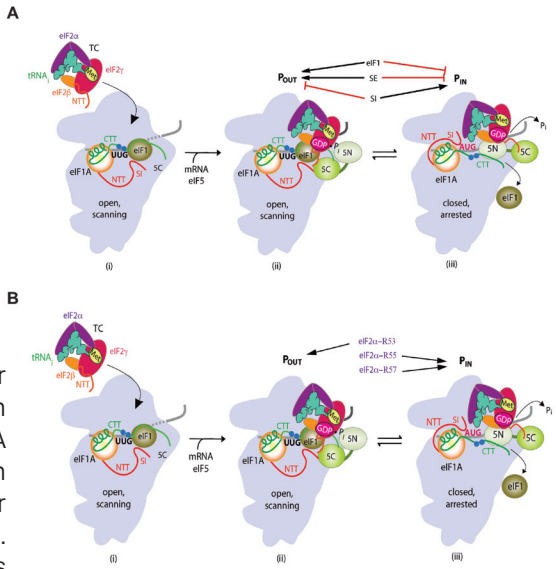


Figure 1: Model describing conformational rearrangements of the PIC and roles of arginine residues of eIF2 in start codon recognition *(A) Assembly of the PIC and start codon selection in WT cells.(i) eIF1 and (SE) elements stabilize an open conformation. (ii) Scans mRNA. (iii) On AUG recognition, the Met-tRNA$_i$ moves from the P$_{OUT}$ to P$_{IN}$ state. (B) Interaction of eIF2α-R53 with rRNA enhances TC loading (i) scanning (ii). Interactions of eIF2α-R55 and -R57 with mRNA stabilize the closed conformation (iii).*

translation initiations factors in a manner distinct from higher order eukaryotes. In addition to translation initiation mRNA decay pathway during stress assist in degrading costly mRNAs acting as a buffer for expression of stress responsive genes. Interplay between these two pathways might take place in fungal pathogens thereby providing the pathogen selective advantage for survival in host environments (Fig. 2). We are systematically analysing the translation initiation and mRNA decay machinery of *Candida albicans* and *Candida glabrata* for stress adaptation. The endeavor of study is to unravel a novel translation regulatory mechanisms harnessed by fungal pathogens to survive in the hostile environments of the host.

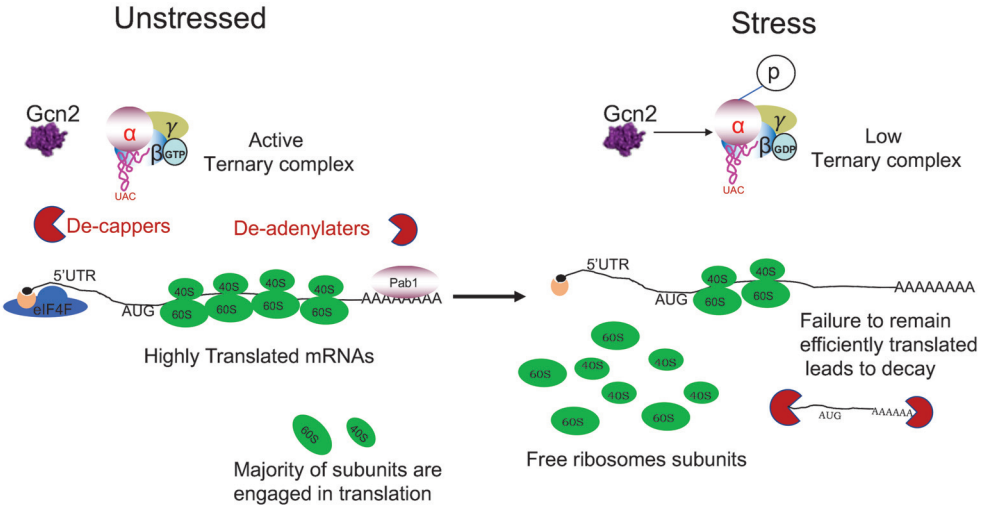
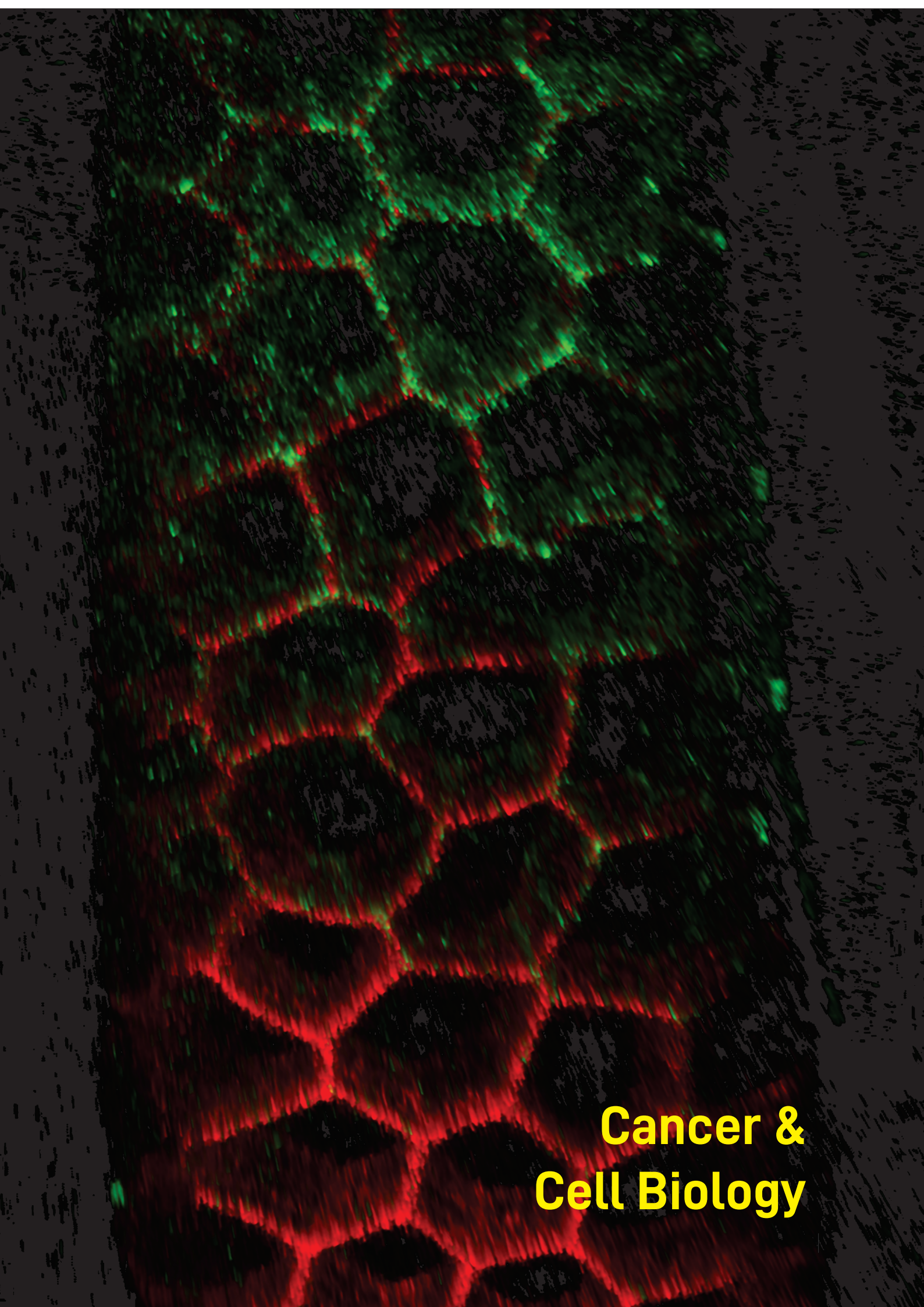


Figure 2: Predicted model of eIF2 phosphorylation mediated translation adaption of fungal pathogens during stress. *The most of ribosomes are engaged with translation in unstressed condition. Stress activate the kinase Gcn2 which phosphorylate eIF2α to reduce ternary complex. This prevents the binding of ribosomes with mRNA that accelerate the mRNA decay. Newly transcribed stress transcript now translated, which usually not favored under homeostatic conditions.*


Cancer &
Cell Biology

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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 biomaterials for effective therapeutics.

We designed a DTX-conjugated amphiphile (LCA-DTX-PC, 1) where a phosphocholine moiety was tethered to 3 -hydroxyl group of lithocholic acid (LCA), and DTX was appended at C24 carboxyl-terminal of LCA using an ester linkage (Fig. 1A). We used a highly aggressive syngeneic murine breast (4T1) tumor model in BALB/c mice, and observed a significant decrease in tumor growth kinetics on treatment with DTX-PC NMs compared to untreated and DTX-TS-treated mice (DTX-TS is a polysorbate suspended DTX) (Fig. 1B). DTX-PC NMs induced a ~3.2-fold reduction in mean tumor volume compared to untreated mice, and >2-fold reduction over DTX-TS-treated mice after 21 days (Fig. 1C). DTX-TS treatment recorded a>15% decrease in mice body weight compared to untreated and DTX-PC NMs treated mice (Fig. 1D). There was a ~13 days increase in median survival in DTX-PC NMs-treated mice compared to untreated and DTX-TS-treated mice (Fig. 1E). H&E analysis demonstrated an increase in cell death on DTX-PC NMs treatment (Fig. 1F), that was confirmed by an increased number of TUNEL positive (red) apoptotic cells (Fig. 1G).

Biodistribution studies showed a 2.0-3.5-fold increase in the accumulation of DTX-PC NMs in tumor tissue with a decrease in lungs and spleen over DTX-TS treated mice. We also observed a 2-3-fold increase in drug accumulation in the form of the free drug after 1, 6 and 24 h in tumor tissues over normal tissues (except liver), thereby confirming the esterase-mediated release of DTX in the tumor tissues. Pharmacokinetic studies in BALB/c showed a ~3.5-fold increase in initial mean plasma drug concentration (C0), and ~4-fold increase in mean area under the curve (AUC) on DTX-PC NMs treatment compared to DTX-TS treatment. Interestingly, unlike DTX-TS, we did not observe any free drug (DTX cleaved from LCA-DTX-PC) released in blood plasma upon administration of DTX-PC NMs that may be instrumental for reduced toxicity of these NMs. Similarly, DTX-PC NMs treatment evidenced a >3-fold increase in mean C0 and mean AUC in SD rats compared to DTX-TS.

RNA-sequencing (RNA-Seq) of tumor tissues showed differential expression in 205 genes on DTX-PC NMs treatment including genes responsible for cellular proliferation, inflammation, angiogenesis, immune, and defense responses that were validated by qRT-PCR. DNA methylation of CpG islands due to increased activity of DNA methyltransferases (Dnmt/s) is known to repress the expression of tumor suppressor genes and confer DTX resistance. qRT-PCR showed a 1.2-1.5-fold decrease in the expression of Dnmt1, Dnmt3a, and Dnmt3b in DTX-PC NMs-treated tumors compared to untreated tumors,which was further confirmed by activity assays (Fig. 2A). We hypothesized that this decrease in Dnmt's activity might be responsible for differential gene expression through DNA demethylation in DTX-PC NMs-treated tumors. Literature mining and in silico analysis showed 36 differentially expressed genes with 1, 2, or 3 CpG islands in their promoter regions that were validated by qRT-PCR.

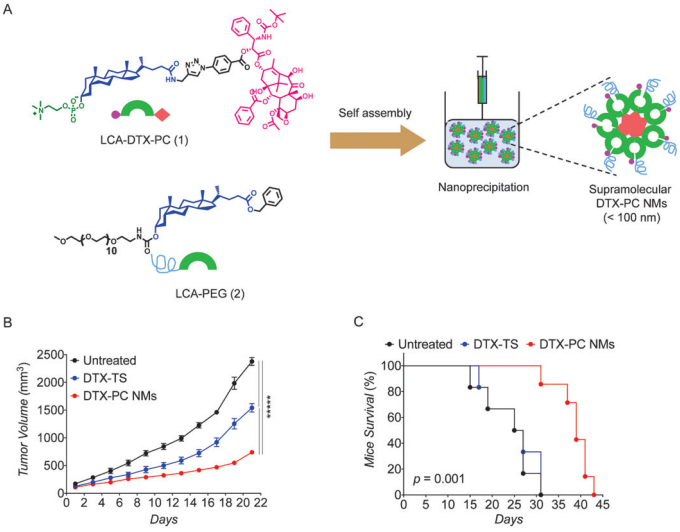

Figure 1: *A) Molecular structure of LCA-DTX-PC (1) and of LCA-PEG (2), and schema showing the preparation of DTX-PC NMs. B) Change in tumor volume (mean ± SEM, n ≥ 6/group) of 4T1 tumor-bearing mice on different treatments. C) Kaplan-Meier curve showing the effect of different treatments on survival (n ≥ 6/group).*

One of the significantly upregulated genes by DTX-PC NMs treatment is Sparcl1 (Secreted protein acidic and rich in cysteine-like 1). qRT-PCR revealed a >5-fold increase in Sparcl1 expression after DTX-PC NMs treatment over untreated tumors (Fig. 2B), that was further confirmed by immunoblot analysis (Fig. 2C, D). We proposed that if upregulation of Sparcl1 expression in DTX-PC NMs-treated tumors is correlated to a decrease in Dnmt expression and activity, then it should be mimicked by 5-aza-2'-deoxycytidine (DAC) treatment that inhibits the activity of Dnmt/s and induces demethylation of CpG islands. Indeed, the treatment of 4T1 cells with DAC led to a >2-fold increase in Sparcl1 expression (Fig. 2E). In silico analysis of 10 kb promoter sequence of the mouse Sparcl1 sequence identified three potential CpG islands upstream of the translational start site. Targeted methylation (bisulfite sequencing) analysis showed decreased methylation of Sparcl1 CpG islands in DTX-PC NMs-treated tumors. We also observed a significant rise in tumour growth kinetics (Fig. 2F), and a ~2-fold increase in tumor volume on day 21 (Fig. 2G) on using a combination of Sparcl1 siRNA and DTX-PC NMs compared to only DTX-PC NMs treatment. Therefore, these results confirm that DTX-PC NMs suppress Dnmt/s activity and reduce DNA methylation, leading to an increased expression of tumor suppressor genes like Sparcl1 which contribute to tumor regression. We confirmed that DTX-TS causes a similar increase in Sparcl1 gene expression, thereby validating the DTX-mediated action of DTX-PC NMs. Differential gene expression analysis for triple-negative breast cancer (TNBC) subtype from TCGA-BRCA data sets showed that SPARCL1 expression is significantly downregulated in TNBC patients, thereby making it one of the potential targets of DTX-PC NMs therapy.

In summary, we demonstrated that DTX-PC NMs target demethylation of CpG islands of Sparcl1 by suppressing DNA methyltransferase activity, and increase the expression of Sparcl1 that leads to tumor regression. Therefore, this unique system has the potential to improve the quality of life in cancer patients, and can be translated as a next-generation chemotherapeutic.

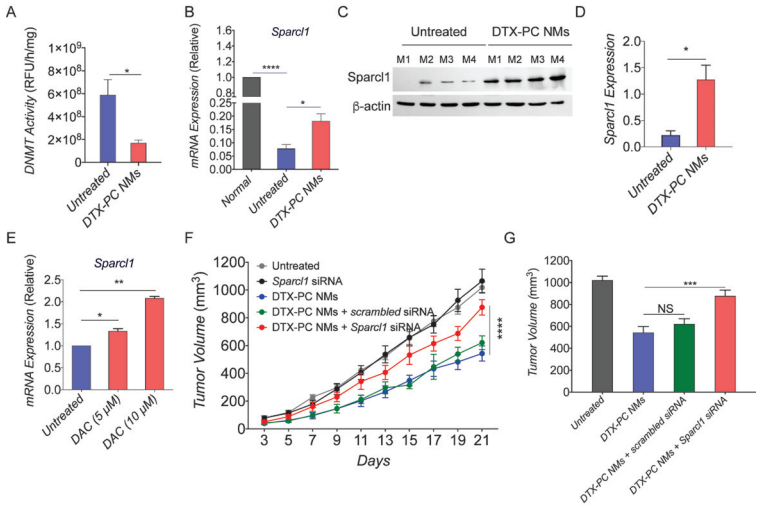

Figure 2: A) *Change in Dnmt activity. B) Normalized gene expression of Sparcl1. C, D) Immunoblot (C) and quantification. (D) of Sparcl1 protein expression. E) Change in expression of Sparcl1 in 4T1 cells after treatment with 5-aza-2'-deoxycytidine (DAC). F) Change in tumor volume on different treatments showing the effect of DTX-PC NMs upon knockdown of Sparcl1 expression. G) Final tumor volume on day 21.*

Molecular Mechanisms of Cell Division, Intercellular Communication and Cellular Dynamics

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

Nucleolin interacts with MSec and is required for TNT formation

Tunneling nanotubes (TNTs) are thin, long, hollow, tubular cytoplasmic connections between cells that serve as communication conduits for the homotypic and heterotypic transport of a variety of cellular cargo across multiple animal cell types. However, there is a glaring dearth of molecular mechanistic knowledge regarding the formation and function of TNTs, a niche we work in. A key protein required for TNT formation in multiple cell types is MSec. We had identified nucleolin (NCL), an RNA binding protein (RBP), as a high-confidence protein interactor from our MSec interactome screen. Following biochemical validation of this interaction (Fig. 1A), we found that NCL is required for TNT formation (Fig. 1B-D). We observed clear localization of NCL in a punctate pattern inside TNTs (fig. 1E), closely apposed with the helical F-actin TNT core (fig. 1F), similar to MSec (fig. 1G, H). These results suggested that NCL interacts with MSec and is essential for TNT formation, but that both proteins while individually essential, are not sufficient for TNT formation.

Nucleolin binds to and regulates 14-3-3ζ mRNA levels in the cytosol, and modulates cortical actin dynamics by regulating cofilin phosphorylation

NCL contains four RNA-binding domains (RBDs) in its C-terminal domain (CTD, fig. 2B), through which it is known to bind to a variety of RNAs. Through a series of assays, we demonstrated that the RBDs of NCL are required for TNT formation. We identified potential NCL mRNA targets that might function in TNT formation, by performing RNA immunoprecipitation (RNA-IP) using our stable cell lines expressing EGFP-NCL and empty EGFP (negative control), processed the immunoprecipitates to extract bound mRNAs in the presence of RNase inhibitors and analyzed the eluted RNA fractions by RT-qPCR using sequence-specific primers against a few mRNAs, revealing significant enrichment of 14-3-3ζ mRNA, which was corroborated by agarose gel analysis. Using luciferase reporter experiments and RNA-IPs, we determined that the NCL RBD region is important for binding to the 14-3-3ζ mRNA. Overall, these

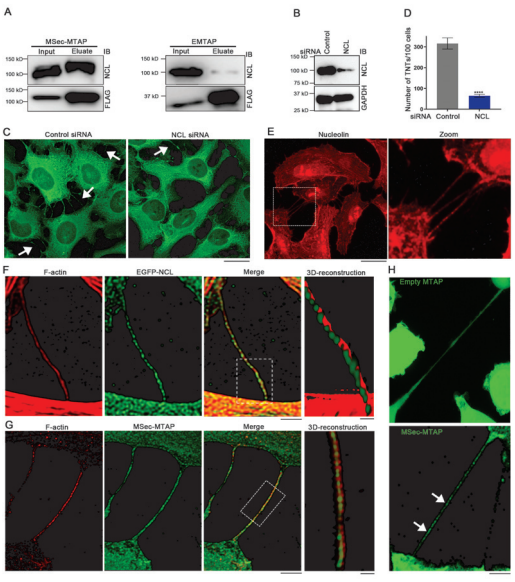

Figure 1: Nucleolin interacts with MSec and is required for TNT formation. *A) Msec interacts with NCL in U2OS cells. B) Knockdown of MSec. C) Confocal micrographs showing TNTs. D) Quantification of TNT counts. E) Endogenous NCL confocal images. Right: Zoomed view. F, G) Deconvolved confocal images of F-actin (red) with NCL (green – F) or tagged MSec (green - G). Right: zoomed 3D reconstructions. H) Live cell snapshots of TNTs. Arrows = punctate organization of MSec in TNTs.*

results confirmed that the 14-3-3ζ transcript is a new mRNA that binds specifically to and is regulated by NCL in U2OS cells. Confocal image analysis following in situ hybridization (ISH) experiments for 14-3-3ζ mRNA revealed preferential reduction in the total cellular levels and cytosolic mRNA levels but not in the nuclear levels. Our further results suggested that NCL indirectly modulates phosphorylated-cofilin levels by regulating 14-3-3ζ mRNA levels, thus possibly controlling F-actin polymerization and TNT formation. Furthermore, MSec on the one hand, and NCL-14-3-3ζ on the other, make unique functional contributions essential for TNT formation (Fig. 2).

Following these leads, we plan to investigate the mechanistic roles of NCL and other RBPs in regulating TNT formation. It is still unclear whether mRNA stabilization, or its levels of translation, are important for TNT formation. There are other RBPs present in the MSec interactome, suggesting the interesting possibility that mRNA stabilization, or other effects, regulate TNT numbers. We shall use a combination of biochemistry, cell biology and high-resolution optical imaging to address these questions.

The exocyst complex regulates membrane Notch levels to promote stem cell divisions for continued fertility

Mitotic proliferation of germline stem cell (GSCs), the precursors of gametes, is tightly regulated for continued fertility in adulthood through canonical Notch-Delta signaling with the intimately-associated niche cells in the round worm, *Caenorhabditis elegans*. Our work reveals a requirement of the exocyst complex, a conserved intracellular trafficking protein, in regulating GSC divisions cell autonomously. We report a conserved biochemical interaction between the exocyst component Sec6 and Notch. The exocyst complex, in conjunction with the Rab GTPases Rab5 and Rab11, maintains optimal plasma membrane Notch levels in *C. elegans* GSCs and mammalian cells. The engagement of the exocyst to the plasma membrane was dependent on anterior polarity proteins Par3/Par6, most likely through the novel and conserved interaction of Sec6 with 14-3-3ζ (Par5). This work reveals a novel, and possibly conserved functional and biochemical exocyst-Notch crosstalk in stem cells.

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Wellcome-DBT, IA Early Career Fellow

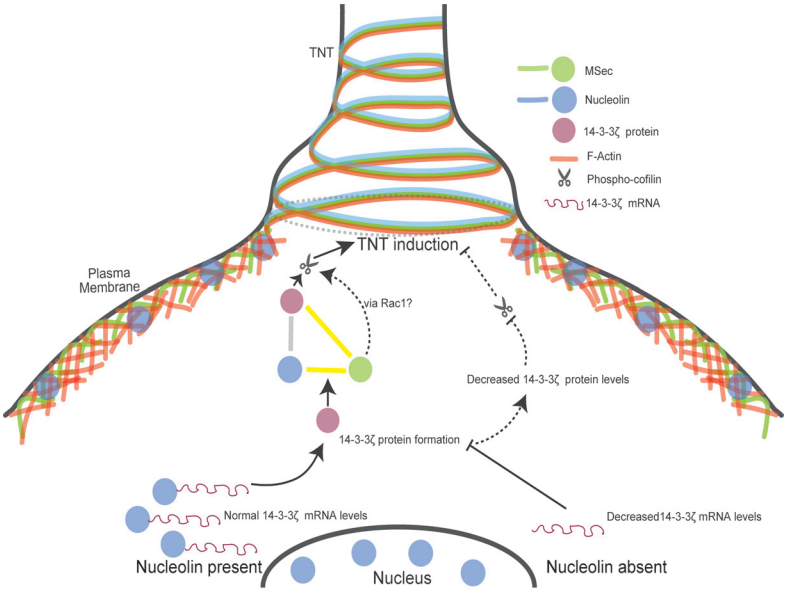

Figure 2: A preliminary model for the RNA-mediated control of tunneling nanotube formation. *Nucleolin binds to and stabilizes the levels of 14-3-3ζ mRNA, leading to optimal 14-3-3ζ protein levels, which ensure cofilin inactivation through phosphorylation to promote F-actin polymerization and TNT formation. MSec interacts with nucleolin and 14-3-3ζ, but independently supports cofilin phosphorylation.*

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Understanding Molecular Mechanisms Regulating Calcium Signaling and their Role in Human Pathophysiology

Calcium (Ca^{2+}) signaling regulates a 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 and 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 stigmas, impart long-term psychological trauma and are a huge economic burden. The current therapeutic regimes are not efficient in alleviating pigmentation defects. Therefore, it is critical to identify 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 Ca^{2+} homeostasis in these cells. Although the role of plasma membrane Ca^{2+}handling proteins is reported in pigmentation, the significance of organellar Ca^{2+} dynamics and the functional relevance of intracellular Ca^{2+} handling proteins remains unappreciated. Our preliminary data suggested that organellar Ca^{2+} signaling indeed plays an important role in regulating pigmentation. We have recently (starting Sep. 2020) received 5 years' funding for this research programme from the India Alliance DBT/Wellcome Trust in the form of an India Alliance Intermediate Fellowship. One of the ongoing projects under the ambit of this program is focused on understanding the role of endoplasmic reticulum (ER) Ca^{2+} dynamics in regulating pigmentation. Our data suggests that decrease in ER Ca^{2+} levels upon silencing of SERCA2 (ATPase responsible for bringing Ca^{2+} into the ER) leads to significant increase in pigmentation (Fig. 1A).

Our preliminary data further implies that SERCA2 knockdown results in induction of ER stress and that in turn may result in hyperpigmentation (Fig. 1B). Going forward, we will perform an array of experiments for validating these observations. Further, we will corroborate this lead in primary human cells and animal models. Finally, we will determine the precise molecular choreography connecting SERCA2 with pigmentation. This knowledge will empower us with the possibility of targeting this signaling cascade for calibrating pigmentation and managing hyperpigmentary disorders.

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 a mean survival time of less than 5 years. For developing effective treatment strategies, it is necessary to understand the molecular mechanisms that drive PC progression. Ca^{2+} signaling plays a critical role in tumorigenesis by regulating the hallmarks of cancer

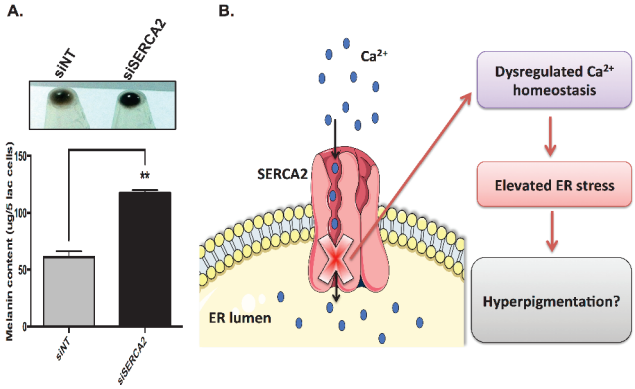


Figure 1: SERCA2 regulates melanogenesis. A) Pellet pictures and melanin content assay demonstrating that SERCA2 silencing results in enhanced melanogenesis in LD pigmentation model. B) SERCA2 knockdown results in decrease in ER Ca^{2+} stores that induces ER stress and most likely that leads to hyperpigmentation.

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 SOCE in most of the non-excitable cells. Interestingly, recent findings implicate that instead of Orai1, Orai3 is the major contributor of SOCE in certain cancers. Further, Orai3 drives tumorigenesis in these cancers by regulating cell proliferation and apoptosis.

For delineating the role of Ca^{2+} signaling in PC progression, we performed bioinformatics/ expression analysis of Ca^{2+} channels using "GEPIA" (Gene Expression Profiling Interactive Analysis). Our extensive bioinformatics analysis found that Orai3 is significantly overexpressed in PC samples in comparison to healthy pancreas. Further, higher Orai3 expression is associated with poor prognosis and less survival time. Moreover, our preliminary data in two independent pancreatic cancer cell lines suggests that Orai3 could be a critical regulator of PC progression (Fig. 2). Going forward, we aim to elucidate the precise role of Orai3 in PC progression using *in vitro* assays and *in vivo* animal models. Further, we will decipher in detail the molecular mechanisms through which Orai3 regulates PC development. Taken together, this project will identify and characterize a novel therapeutically relevant regulator of PC progression.

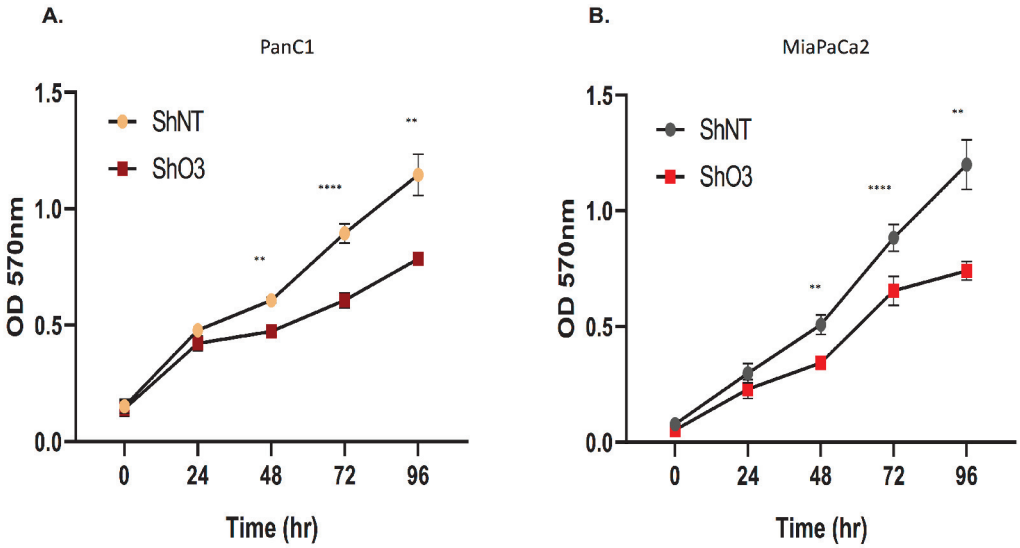


Figure 2: Orai3 regulates pancreatic cancer cell proliferation/survival. *A. MTT based cell proliferation/cell number analysis in shNT control and shOrai3 stable PanC1 cells. B. MTT based cell proliferation/cell number analysis in shNT control and shOrai3 stable MiaPaCa2 cells. These data suggest that Orai3 plays a critical role in pancreatic cancer cell proliferation/survival.*

Karthigeyan Dhanasekaran

Principal Investigator

Understanding the Structure and Function of Centrosome/Cilia Complex

Centrosomes are microtubule-based, membrane less organelles. These subcellular structures are being studied for more than a century but their significance has been limited to cell division and the associated pathogenesis in aneuploidy and cancer until the recent developments in cell biology. Today, we understand the biogenesis of centrosomes and cilia to a large extent and yet fail to connect all possible events from nucleation to faithful segregation. This is partly due to the lack of tools and partly due to the lack of more focused research involving the physiological context-based centrosome biology. Our lab is majorly focused towards the centrosome and ciliary functional aspects regulating the physiological and pathological events revolving around centriole-based structures. We are motivated to study the structural composition as well as the regulatory aspects controlling the genesis and maintenance of centrosomes and cilia. The initial focus of our team is to address the following.

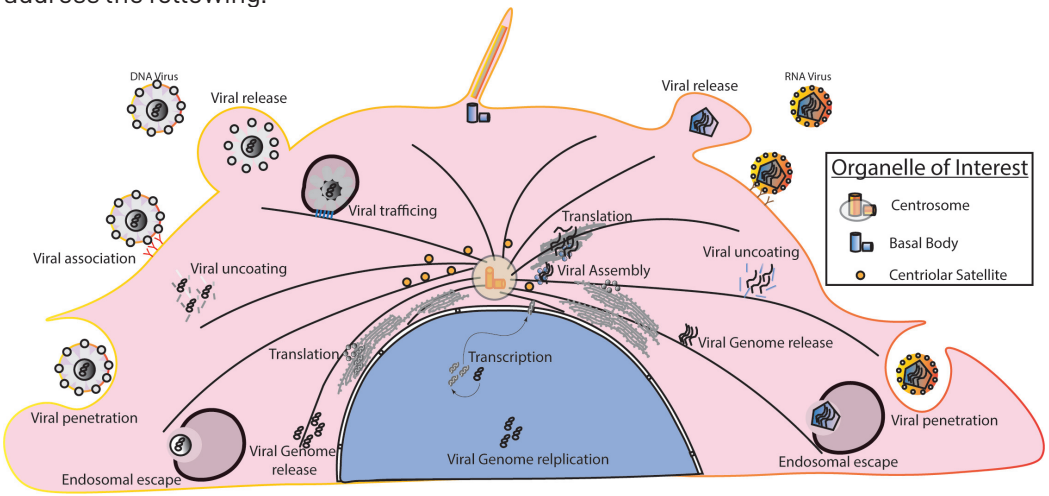


Figure 1: Cartoon representing the events in the viral lifecycle at the single cell level. *The box represents the subcellular structures that our lab is focusing on at present.*

Impact of viral proteins on centrosome and cilia

Not many have attempted to study the significance of viral proteins associating to centriole-based structures during viral pathogenesis or their influence over these structures. Studies till date have documented quite a few viral proteins bound to the centrosome, andinstances where the virus itself is targeted to the cell centre by using the cytoskeleton fibres associated with the centrosome. This coordinated transit often aids in viral replication and assembly events that help in propagating the virus (Fig 1). Although centrosomes have been in the limelight in the context of propagation, the idea of the centrosome as a major platform to integrate and regulate viral infection, replication and assembly remains a hypothesis worth investigating. Despite documenting some of the viral particles and a few viral proteins that specifically bind to the centrosome and centrosome-associated microtubules, the underlying mechanisms mediating such events remain unexplored and incomplete. At present, we would like to understand the host-virus interactions (Fig 2), with emphasis on how viruses are transported from the point of entry to the centre of the cell during the early stages of infection and how they are regulated to further move towards various subcellular organelles in the process of hijacking those structures for viral survival and replication. Also, knowing the targeting requirements of both viral proteins and particles could be useful in designing strategies to combat viral infection by breaking the host-pathogen interface to establish disease pathology. Gaining better insight into the mechanism by which viral proteins are regulated by centrosome-associated signalling

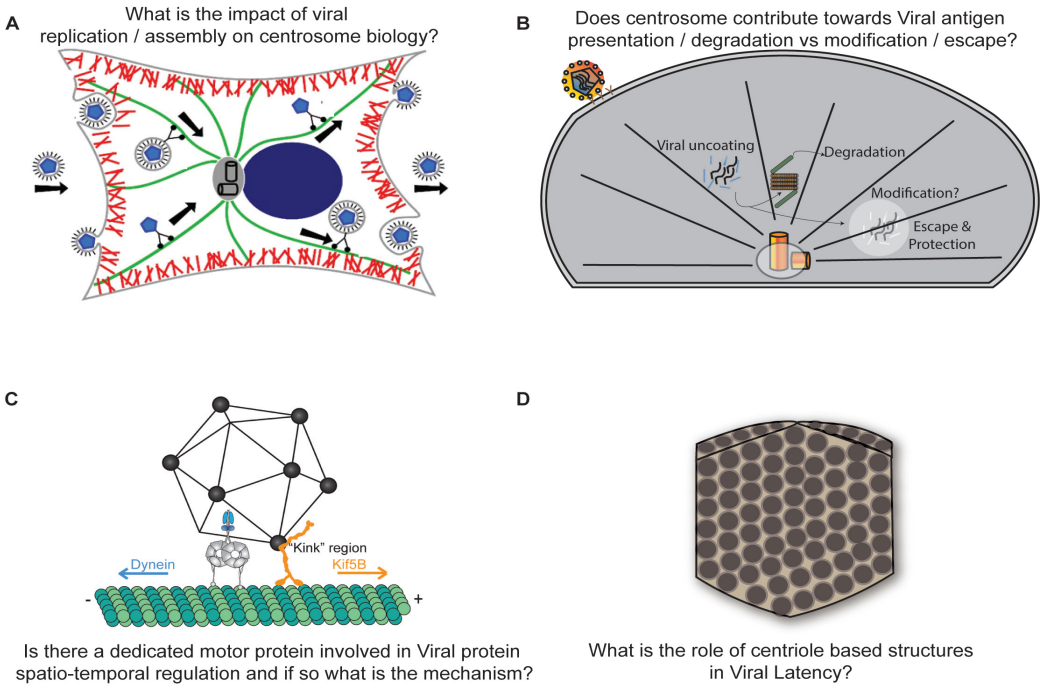
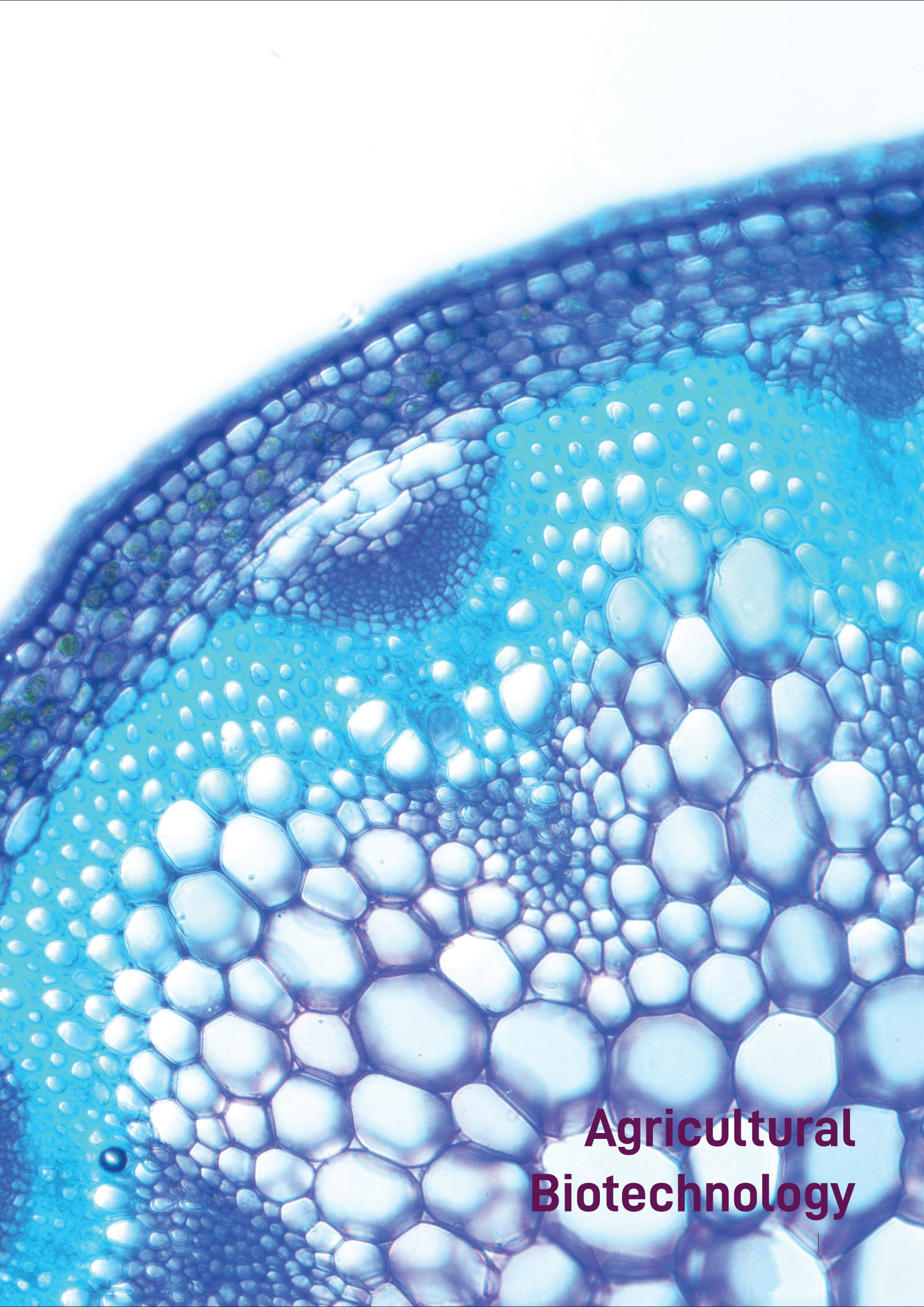


Figure 2: *Highlighting the gaps in the field of Centriolar Biology (A-D) related to viral pathogenesis that we are addressing in depth.*

might improve our understanding of how the centrosome could contribute towards viral pathogenesis. This might potentially usher us towards designing novel therapeutic strategies against such pathogens during the course of our research in the future.

Fate of the centrosome and centriolar satellites components in supernumerary and acentrosomal scenario

Centriolar satellitesare often regarded as components associated to the centrosome/cilium complex, but they are the least studied membrane-less subcellular organelle. In fact, a majority of these satellites perform functions related to centrosomes, cilia and microtubules. This makes the situation even more complex to tease apart the functions exclusive to centriolar satellites from other microtubule-based organelle functions. Recent proteomic profiling data shows that a major chunk of the satellite components neither overlaps with the centrosome or with the ciliary basal body. We are also aware of the fact that centriolar satellites exist in microtubule organizing centres (MTOCs) lacking centrosomes. Furthermore, the distribution pattern of centriolar satellites shows some level of tissue specificity, which remains unexplored and falls under our lab interest currently. Hence, it will be worthwhile to investigate the compositional diversity across varying physiological and pathological scenarios. Along this line, we are now attempting to document the proteomic profile of centriolar satellites in various cell types with and without a normal functional centrosome. Simultaneously, we are also interested in looking at the dynamics of some of the well-established satellite components under these circumstances using microscopy. This approach can help us to connect the tissue specific distribution and explicit functioning of these satellites in such cell types. Also, the understanding of the cell biology related to centrosome defects like acentrosomal and supernumerary centrosomes will have implications in instances like cancer and ciliopathies involving centrosome dysfunction. Crosstalk between centrosomes and centriolar satellites is not just a physical transit, rather it is more dynamic and an active communication that serves functions like retention, degradation, sorting and scaffolding. We will be addressing these functions using cell biology-based assays to study these aspects in our lab.



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Molecular Mechanisms of Signal Transduction in Innate Immune Responses of Plants

Plant deploy diverse intracellular immune sentinels to sense pathogen effectors and mount a rapid defense response. For successful improvement of broad spectrum defenses, it is hence essential to unravel the functional intricacies of plant immune signaling networks. Using a class of rapidly evolving effector from *Pseudomonas syringae (Ps)* pathovars that are differentially sensed in *Arabidopsis thaliana*, we are identifying defense modulators that trigger immunity. Immune responses in plants involve massive adjustments in cellular phosphate balances serving as energy reserves. Inositol phosphates (InsPs) are key signaling messengers that orchestrate such crosstalk. We are deciphering molecular pathways of specific InsPs that facilitate stress-appropriate adaptations in plants. Lastly, post-translational modifications not only regulate immune assemblies in plants but also are targets of pathogen effector-mediated perturbations. We are characterizing the role of a selective post-translational modifications in regulating immune assemblies, functions of defense modulators, and their coupling to downstream signaling pathways.

Interference with nonsense mediated RNA decay (NMD) processes elicits effector-triggered immunity against the HopA1 effector from Pseudomonas syringae pv syringae strain 61

Ps encodes ~57 different Type III effectors (T3Es), most of which remain functionally uncharacterized. Among these, HopA1 effectors are important determinants in host range expansion and overall increased pathogenicity. In *A. thaliana*, RESISTANT TO PSEUDOMONAS SYRINGAE6 (RPS6) gene confers effector-triggered immunity (ETI) against $HopA1_{pss}$ derived from Ps pv. *syringae* strain 61 but not to $HopA1_{pst}$ from the tomato pathovar. These responsive differences between the two HopA1s represents a unique system to study pathogen adaptation skills and host jumps. Previously, we reported the generation of a chemical (Dexamethasone, Dex)-inducible transgenic line that expresses $HopA1_{pss}$. We performed RNAseq on Dex^- and Dex^+ samples and identified 4576 upregulated and 4176 downregulated transcripts. Gene Ontology (GO) annotations classified differentially upregulated genes (DEGs) into defensive routes validating that ETI (termed $ETI^{HopA1pss}$) is elicited in these plants. The DEGs included upregulated expressions of several resistance genes which under steady-state are regulated by alternative splicing (AS) and nonsense mediated decay (NMD) pathway. Proteins such as UP-FRAMESHIFTs (UPFs) are modulators of AS and NMD, and immunity is constitutively activated in the upf mutant *(upf1 upf3)*. We observed 55% DEG and 97% differentially alternatively-spliced (DAS) transcript overlaps in our RNAseq data with similar datasets from *upf1 upf3* mutant suggesting that AS/NMD disturbances are associated with $HopA1_{pss}$ (Fig. 1A,B). Immuno-enrichment of $HopA1_{pss}$ identified 207 unique co-eluting proteins several of which are known interactors of UPF1. These results implied that indeed UPF1-associated processes that cause PTI are suppressed by $HopA1_{pss}$. The several resistance transcripts that were upregulated remained deficient in polysome association in the transgenic plants. In vitro translation assays showed that both HopA1s displayed strong translational inhibition propensities (Fig.1C). Overall, with our results here we deduce virulence role of HopA1s in suppressing PTI elicited defense responses. We are determining how $HopA1_{pss}$ but not $HopA1_{pst}$ elicits ETI in resistant plants.

Selective Inositol phosphate kinases mediate crosstalk between defense and phosphate homeostasis pathways

The propensity for polyphosphorylation on $InsP_6$ generates $InsP_7$ and/or $InsP_8$ with high-energy phosphoanhydride bonds that are harnessed during energy requirements of a cell. With co-factor roles $InsP_7$/$InsP_8$ modulate multiple signaling networks. We previously identified that *A. thaliana* INOSITOL PENTAKISPHOSPHATE 2-KINASE (IPK1), INOSITOL 1,3,4-TRISPHOSPHATE 5/6-KINASE 1 (ITPK1), and DIPHOSPHOINOSITOL PENTAKISPHOSPHATE KINASE 2 (VIH2), but not the other InsP-kinases, suppress salicylic acid (SA)-dependent immunity. Previously, it was identified that *ipk1-1* or *itpk1-2* mutants display constitutive phosphate-starvation response (PSR). Phosphate (Pi) homeostasis is regulated by the transcription factor PHOSPHATE STARVATION RESPONSE 1 (PHR1) and its paralog PHL1. To determine crosstalk between activated defenses and PSR in *ipk1-1* or *itpk1-2* mutants, we generated *ipk1-1 phr1 phl1* or *itpk1-2 phr1 phl1* triple mutants and measured the relative expression levels of defense-associated transcript *PR1*. Introducing *phr1 phl1* mutation in *ipk1-1* or *itpk1-2* substantially reduced the upregulated *PR1* expression suggesting that elevated PSR associated with PHR1/PHL1 activities contributes positively to the enhanced defense-gene expressions in the above InsP-kinase

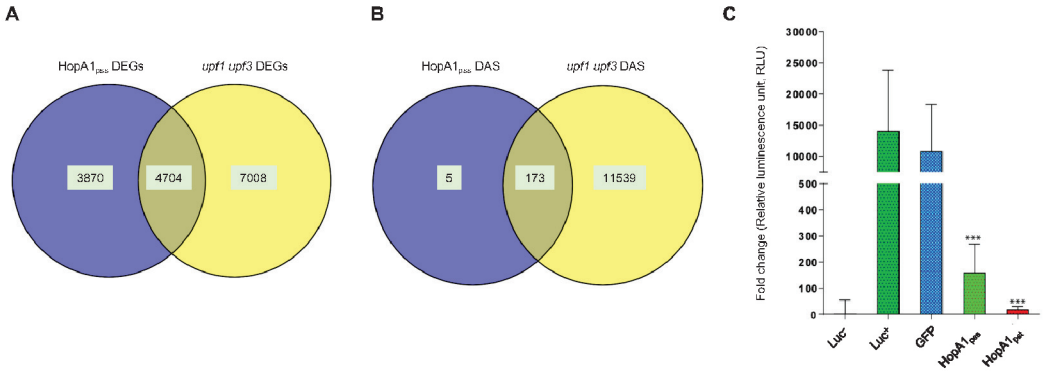


Figure 1: ETI^{HopA1pss} perturbs AS/NMD pathway. *Venn diagram of overlap in (A) DEGs, and (B) DAS transcripts between ETI^{HopA1pss} and upf1 upf3 mutant. (C) HopA1$_{pss}$ or HopA1$_{pst}$ suppress reporter (Luciferase, Luc) gene translations in vitro. Equimolar amounts of HopA1s (or GFP as a negative control) was used in the above reactions. Statistical analysis is according to Student's t-test with pairwise comparison between GFP, HopA1$_{pss}$, or HopA1$_{pst}$ to Luc^{+} (p ***<0.001).*

mutants (Fig. 2A). Several PSI genes have SA-binding elements. We determined that inhibiting SA-signaling routes reduced but not abolished PSI gene upregulations in *ipk1-1* or *itpk1-2* mutants. With these results, it is suggestive that heightened SA-signaling sectors aggravate but are not the direct cause of PSR in *ipk1-1* or *itpk1-2*. Our investigations also demonstrated that PSR is associated with increase in SA (free and total) levels (Fig. 2B), albeit its defensive signaling is re-routed to support phosphate deficiencies and suppress immunity (Fig. 2C). Thus, in immune responses PSR is activated likely to provide for the needed phosphate-derived energy, whereas in Pi-deprived conditions defense signaling networks are suppressed to allow more Pi acquisition through the soil microbiota. Overall, we reveal that selective InsPs function as crosstalk mediators that program stress-appropriate adaptations.

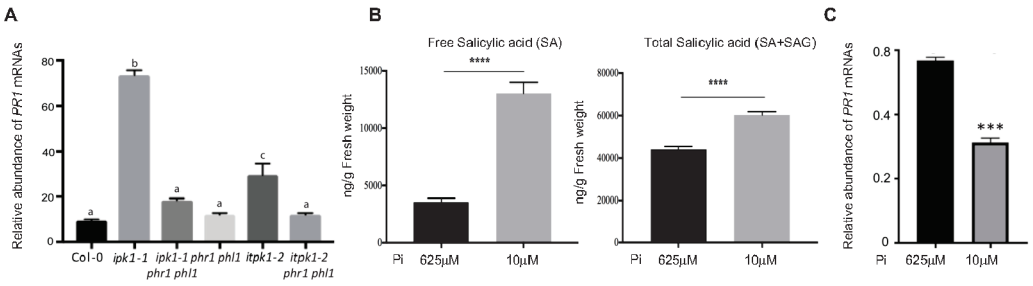
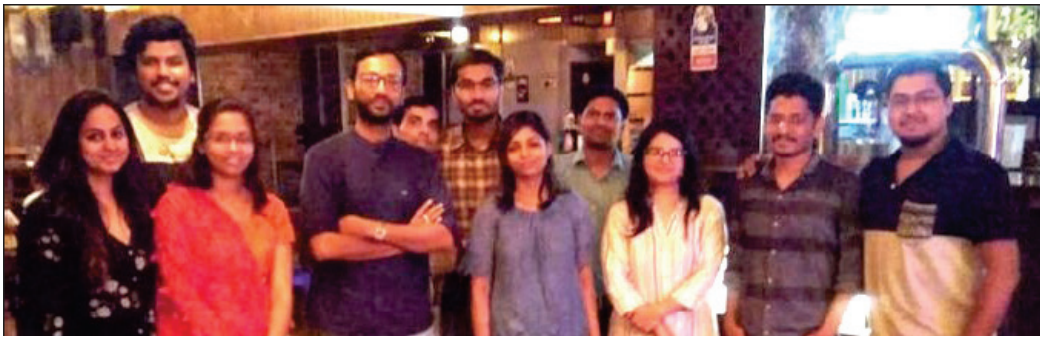


Figure 2: Crosstalk between defense and Pi homeostasis. *(A) PHR1/PHL1 positively regulate enhanced defenses in ipk1-1 or itpk1-2. Different letters are according to post-hoc Tukey's test (p<0.05). (B) Pi-starvationcausesB) increase in SA and SAG levels, and (C) down-regulation of PR1 expression. Plants grown with (625 μM) or without (10 μM) Pi for 3-days were used for the above analysis. Data shown in B and C are mean values ($\pm$SD, n=3) analyzed by Student's t-test (***p<0.0001,****p<0.00001).*



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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 factorsand pathogen virulence determinants that significantly impactdisease development**.**

A sugar transporter confers PM resistance in legumes

Obligate biotrophic fungal pathogens establish a long-term feeding relationship with their host, during which they siphon sugars from host cells through haustoria. Plants in turn deploy sugar transporters to restrict carbon allocation towards pathogens, as a defense mechanism.The Arabidopsis hexose transporter, sugar transport protein 13 (STP13), was previously shown to confer resistance against hemi-biotrophic and necrotrophic pathogens by limiting sugar flux towards these pathogens. By contrast, expression of Lr67res, a transport-deficient STP13 variant carrying two amino acid substitutions (G144R & V387L), conferred resistance against biotrophic fungi in wheat and barley.

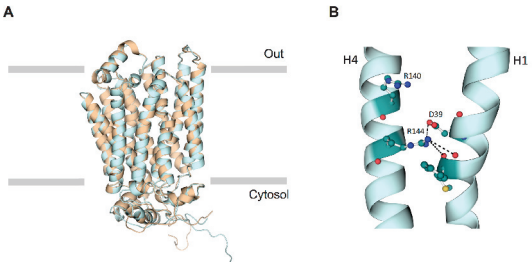

Figure 1: Homology model of MtSTP13.1. *(A) Superimposition of the model of the protonated form of wildtype MtSTP13 (wheat color) on mutated (G144R, V388L) (cyan) in ribbon representation. The grey bars depict the approximate location of the membrane. (B) The possible hydrogen bonding interactions around the proton binding site in the mutant are shown as dotted lines.*

Our study, published in searchable citation, provides novel insights into the role of STP13 and its variant in PM resistance in legumes. We report that the M. truncatula STP13.1 is a proton-hexose symporter involved in basal resistance against the pea PM, and that Lr67res-mediated resistance, so far reported in monocots, is transferable to legumes. Among the 30 MtSTP genes, MtSTP13.1 exhibited the highest fold-induction in PM-challenged leaves, and in leaves treated with the fungal pathogen-associated molecular pattern chitosan. Functional characterization in yeast verified that MtSTP13.1 is a plasma membrane-localized protein and a broad substrate specificity hexose transporter. Introduction of the Lr67res-specific G144R mutation but not V388L abolished MtSTP13.1's hexose uptake ability. Homology modeling studies performed in collaboration with Dr. Deepti Jain (RCB) revealed likely mechanisms for G144R-based inhibition of transporter function (Fig. 1). The protonation state of D39, an important residue involved in proton binding, regulates sugar transport in STPs. Of the two substitutions, the G144R mutation results in an increase in positive charge in the vicinity of the proton donor/acceptor pair. Additionally, R144 lies within hydrogen bonding distance of D39 and may change the microenvironment necessary for protonation/deprotonation of D39. We also speculate that R144 may interact with the main chain peptide present in helix 1 which will compromise the flexibility and local movement hindering the conformational change critical for transport.

Transient knockdown and overexpression studies suggest that MtSTP13.1 plays a role in basal defense against PM in legumes, and that modifications in MtSTP13.1 function, through overexpression of *MtSTP13.1* or the *MtSTP13.1*^{G144R} variant, promotes resistance in pea.Virus-induced gene silencing (VIGS) of MtSTP13 repressed expression of defense-associated genes and enhanced PM susceptibility in *M. truncatula* whereas transient overexpression (OE) of *MtSTP13.1* or *MtSTP13.1*^{G144R} enhanceddefense gene expression and PM resistancein pea. Based on our findings, we propose a model in which STP13.1-mediated sugar signaling triggers defense responses against PM in legumes (Fig. 2).

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 light and pass on this signal to masterregulators, which in

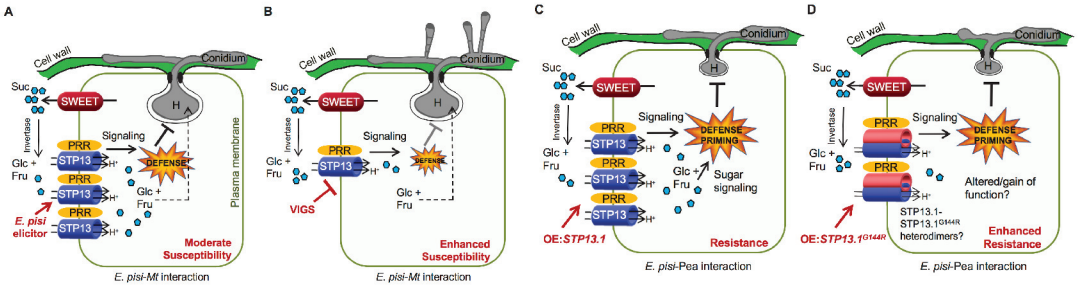

Figure2: MtSTP13-mediated PM resistance in legumes. *(A) Induction of STP13.1 expression/activity upon fungal elicitor (chitosan) recognition triggers defense & increased hexose import into fungal feeding cells, resulting in moderate susceptibility. (B) STP13 knockdown dampens defenses& enhances susceptibility (C) STP13.1 OE enhances defenses & resistance. (D) STP13.1^{G144R}OE activates robust defense through partial impairment of STP13.1 function via heterodimerization or via gain of function.*

turn bring about changes in downstream components, leading to changes in gene expression. One of these master regulators is HY5 transcription factor. We identified three or thologs in rice based on the presence of COP1-binding and bZIP domains. Of these, OsbZIP48 has been functionally characterised by us. We are now looking into how these three genes work in tandem as well as independent of each other. In order to identify the residues responsible for abolishment of OsbZIP48 interaction with OsCOP1, mutational studies are being carried out. Additionally, in a recent publication in Frontiers in Plant Science (2020), we present a rapid and efficient protocol for transient gene expression in rice, a useful toolthat had remained elusive for years.

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 CO_2uptake, 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. One approach is to use CRISPR-CAS9 to modulate genes encoding anion channels that regulate stomatal aperture, such as *ALMT12* (*aluminium-activated malate transporter*) and *SLAC1* (*slow anion channel-associated 1*). Guide RNAs targeting *ALMT12* and *SLAC1* exonic regions are being transformed in rice. Additionally, we identified small molecule interactors of these genes that could overcome the effect of ABA on stomata and keep them partially open in Arabidopsis by blocking anion channels. To identify guard cell-specific E3 ligases upon ABA treatment, analysis of the Arabidopsis guard cell-specific transcriptomeis underway.

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Functional Genomics and Crop Improvement for Stress Adaptation

Crop improvement largely depends on genetic variability that exists in natural germplasm. However, due to domestication the variability is narrow, and there is a need to introgress many traits from wild relatives to improve stress adaptation and productivity. We aim to create genetic variability by using genome editing approach by targeting the genes encoding DNA mismatch repair mechanisms in rice. Plants are exposed to diverse stresses including pathogen infestations. The pathogen *Xanthomonas oryzae pv. oryzae* causes bacterial blight in rice resulting in >25% of crop loss. To control this pathogen, we are using genome editing technologies and chemical genomic approaches. The emphasis is to improve plant health in changing climatic conditions.

Creating genetic variability by editing (using CRISPR-CAS9) the genes associated with DNA mismatch repair and characterization of their relevance in crop improvement

Crop improvement depends on crossing two compatible genotypes having a variable phenotype with relevant traits. The advantages of DNA mismatch repair mechanisms to create genetic variability has been reported (Plant Phys. Rep. 2020). To create genetic variability in rice, DNA mismatch repair genes *MSH1, MSH2 and MLH1* were targeted by gene editing approach. Several rice lines were developed by targeting *MSH1* gene and analyzed for T-DNA insertion and mutations in target gene. Amplification of *MSH1* with gene-specific primers flanking the sgRNA region and sequencing of the PCR product revealed mutations in L12, L14, L15 and L23 lines with altered phenotypes due to INDELs in whole genome. Plants had higher leaf area, leaf width, panicle length and spikelet number (Fig. 1A). We also identified phenotypic variabilities in rice plants targeting the *MSH2* gene involved in nuclear DNA mismatch repair mechanisms. One of the plants edited at the gRNA region showed higher tiller numbers, early flowering, more biomass and yield (Fig. 1B) *(J. Food & Agri. Chem. 2020)*. The MLH1 targeted rice plants showed lethal phenotypes. Many plants showed loss of pollen viability due to microsatellite instability associated with MLH1 depletion. Most of the plants did not set seeds because of complete spikelet sterility (Fig. 1C). The stress adaptation of all these plants will be studied. We also used DNA damage and repair inhibitor drugs to create variability and developed rice lines with phenotypic variability. We have three libraries of seeds with different phenotypic variability. These seeds may be used to test any agronomic trait or they can be used to backcross to stabilize the trait.

Controlling bacterial blight disease in rice by chemical genomic approach

Xanthomonas oryzae pv. oryzae (Xoo) causes bacterial leaf blight which damages rice crops, and if left untreated, causes complete crop loss. To achieve food security, it is important to develop novel control strategies against these bacteria. Since cholic acid molecules act as antimicrobial peptides, we hypothesized that cholic acid (CA) derived small molecules could be effective against *Xoo*. The library, composed of 9 small molecules having CA backbone carboxylic group at 24 position, was modified with different alkyl chains having glycine units (Fig. 2A). These amphiphiles were screened against *Xoo* and CA having hexyl (C6) side chain showed 99% bacterial growth inhibition at low concentrations.

To assess the antibacterial effect of amphiphiles on bacterial membrane, a membrane potential sensitive cationic dye, 3, 3'-diethylthiadicarbocyanine iodide [$DiSC_2(5)$] was used, which accumulates in a lipid rich environment of a hyperpolarized cell membrane, leading to fluorescence quenching. Interestingly, treatment with C6 amphiphile makes bacterial membrane depolarized leading to dequenching of accumulated dye and increase in fluorescence (Fig. 2B). *Xoo* can form biofilms to sustain in a natural environment, so we anticipated that C6 can degrade biofilms. Biofilms were formed on a coverslip and treated with the compound for 6 hours. Biofilms were stained with SYTO9 (stains both live and dead cells) and PI (stains dead cells only). C6 at 32 µg/mL was able to degrade biofilms effectively as more number of PI stained cells were found (Fig. 2C).

To assess the effect of CAAs on rice upon *Xoo* infection, 45-days-old Tn1 rice plants were infected with *Xoo* by leaf clipping method with ~10^6 CFU/mL. After 24 h of *Xoo* infection, 16 µg/mL of C6 amphiphile was sprayed on infected plants. The bacterial multiplication in C6 treated samples was significantly reduced compared to untreated and DMSO control after 96 hours post

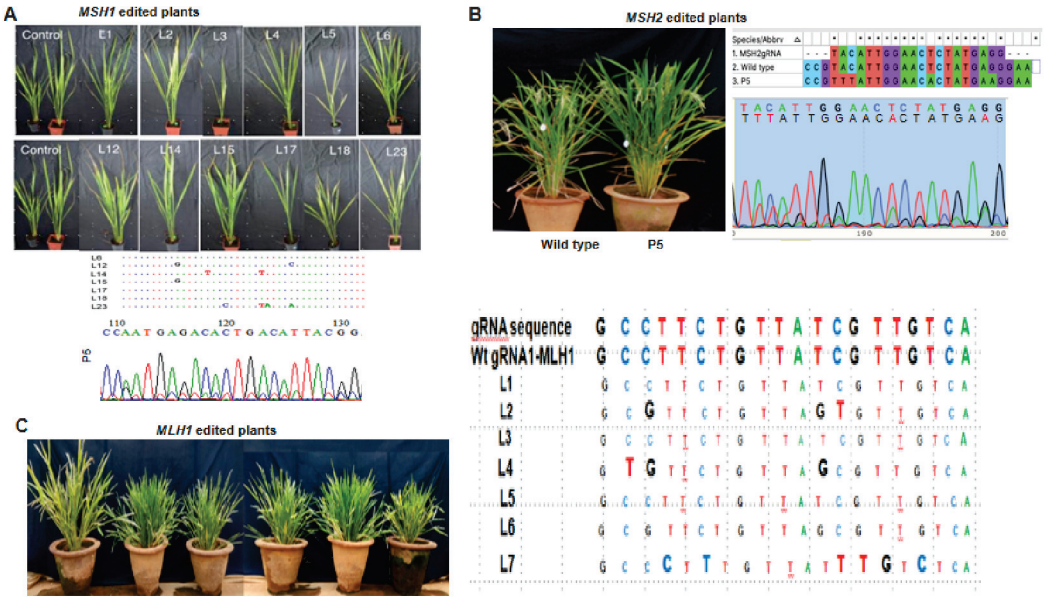

Figure 1: Genetic variability in rice created by targeting the DNA mismatch repair genes using gene editing approach. *(A) MSH1 targeted rice plants showing altered phenotypes and sequences showing mutations. (B) superior phenotype in MSH2 targeted P5 plant and mutations in MSH2 gene, (C) MLH1 targeted plants showing dwarf phenotype and variations in genomic DNA. The CRISPR-Cas9 and sgRNAs targeting MSH1, MSH2 and MLH1 were independently cloned in pRGEB32 vector.*

spray (hps) (Fig. 2D). As a result pathogen-induced lesion length on C6 sprayed plants was also reduced compared to untreated plants (Fig. 2E). These results indicate that C6 amphiphile could effectively inhibit *Xoo* growth on host plant after infection. The expression of plant defense responsive genes involved in salicylic acid biosynthesis, signalling and pathogenesis-related mechanisms were studied and found to be upregulated (Fig. 2F). The molecules were found to activate plant defence and also kill the bacteria. Due to the dual mode of plant protection, these molecules have the potential to be used as agrochemicals.

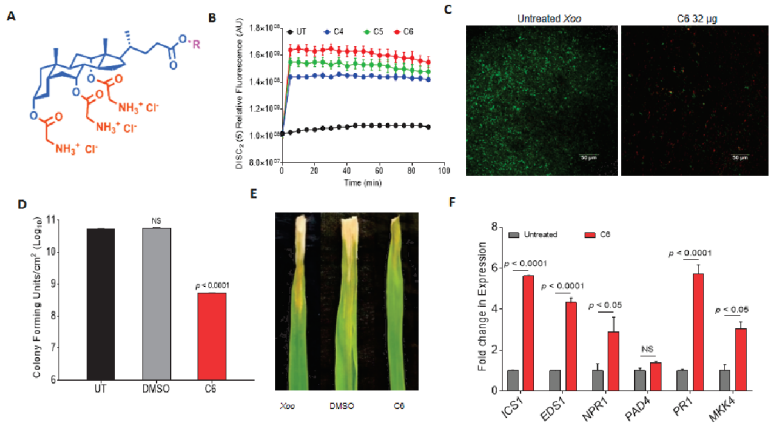

Figure 2: Effectiveness of cholic acid derived amphiphiles against Xanthomonas oryzae pv. oryzae. *(A) Structure of cholic acid derived amphiphiles. (B) Disruption of Xoo inner membrane detected by fluorescence intensity of DiSC2(5) over time after treatment with CAA 4, 5 and 6. (C) Confocal microscopic images of Xoo biofilms. (D) Xoo growth rates in infected leaves at 96 hours of post spray. (E) Lesion length in rice after 8 dpi, (F) Expression of plant immunity associated genes.*

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Unravelling the Plant Cell Wall Biosynthesis and Architecture for Bioenergy Applications

Our research group focuses onunderstanding the molecular mechanism of plant cell wall biosynthesis and assembly, and exploring novel ways of altering wall structure for effective conversion to value-added products. One of the critical factors which plays a vital role in wall assembly and disintegration is acetyl groups substituted on the polysaccharide backbone or side chain. Fine-tuning 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 these to redesign the cell wall for different bioenergy applications.

Overexpression of fungal xylan acetyl esterase (AXE) in plants

All matrix polysaccharides, i.e., pectin, xyloglucan, mannan and xylan, are acetylated. Arabidopsis and poplar stem cell walls are abundant in xylan, and around 50-70% of xylose residues are acetylated. Synthesis occurs in the Golgi and acetylated xylanis transported to the cell wall. To keep the balance of the acetyl pool, the presence and action of xylan acetyl esterases (AXE) are indispensable in the Golgi and cell wall. Therefore, the identification and characterization of AXEs are necessary to understand the mechanism of xylan acetylation in plants. Also, these AXEs can be utilized to alter the level of acetylation in plants.

Many fungal AXEs belonging to the carbohydrate esterase (CE) family have been characterized. To manipulate poplar xylan acetylation, AXE from the CE5 family was expressed in the apoplast using an N-terminal attached plant cell wall signal peptide and a xylem specific promoter (Fig. 1).WP:CE5 fragment was introduced into poplar, and three independent transgenic trees were selected for further analysis. To test the esterase activity in transgenic lines, we used poplar wood as a substrate that is abundant in acetylated xylan. All transgenic lines showed an increase in esterase activity at a similar level whereas esterase activity was undetected in wild type plants. To test the effect of AXE expression on wood acetylation, the cell wall powder was saponified, and the free acetyl groups were analyzed by the K-ACET Megazyme kit. As expected, all the lines showed decreased in cell wall-bound acetylation. To analyze the digestibility of wall polysaccharides in transgenic lines, the cell wall powder was digested with cell wall degrading enzymes without any pretreatment, and the monosugar release was analyzed. All the transgenic lines showed an increase in cellulose and xylan digestibility, i.e., an increase in saccharification efficiency in comparison with wild type trees.

The hydrolysate was also analyzed after 2 h of incubation to determine the glucose production rate, which was also enhanced in the poplar transgenic line 11 by 50%. Overall, these results suggest that expressing acetyl xylan esterase in poplar is a good strategy to process lignocellulosic biomass for biofuel production.

Identification of plant localized AXEs in Arabidopsis

In a previous study published in *Plant Biotechnology Journal (2015)*, we observed a slight increase in esterase activity in wild type Arabidopsis. This led us to hypothesize that AXEs might be present in Arabidopsis and play an important role in maintaining the stability of xylan polysaccharide. There are only two rice AXEs identified in plants, but AXEs are not yet identified in Arabidopsis. In this project, we aim to identify the AXEs and elucidate their role in cell wall synthesis and degradation.

Based on bioinformatics analysis, four putative Arabidopsis AXEs were selected from the cell wall esterase (CWE) family for further analysis. All four CWEs were cloned into an expression vector containing constitutive 35S promoter. These five constructs were transiently expressed in Nicotiana benthamiana leaf tissue and harvested after three days for further analysis. CWE family is known to have both esterase and lipase activity. The soluble and wall protein fractions were isolated, and both activities were tested. The esterase activity was tested using 4-nitrophenyl acetate as a substrate.As expected, both wild type and wall-bound control (AnAXE1) showed a similar level of esterase activity (Fig. 2).

The esterase specific activity in the soluble fraction was increased in AtCWE1 and AtCWE4 expressed leaves as compared to the above controls. In the wall-bound protein fraction, AnAXE1

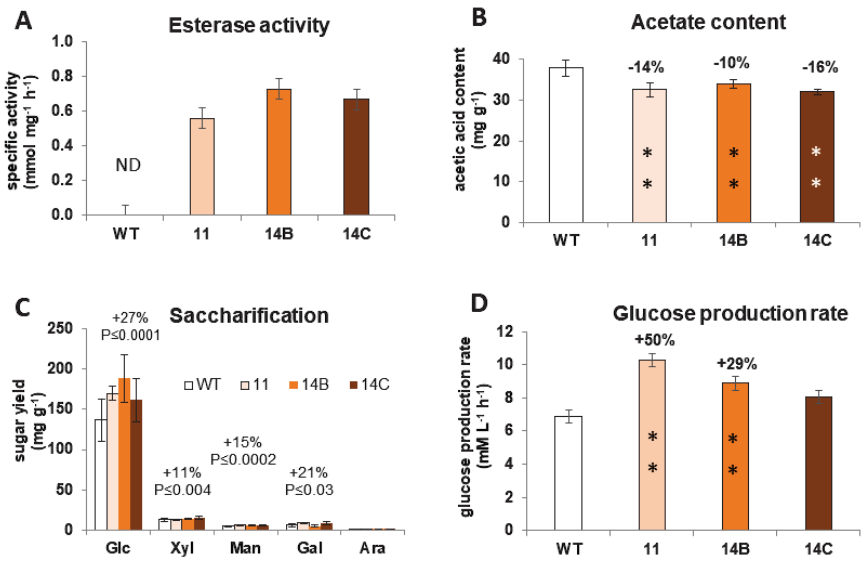


Figure 1: Analysis of transgenic poplar lines expressing WP: *CE5(A) Acetyl xylan esterase activity was calculated using wood powder as substrate. (B) The total cell wall acetyl content was measured in poplar wood by Megazyme K-ACET kit. (C) The untreated wood powder was subjected to enzymatic digestion for 72 h, and sugars were measured. (D) Glucose was measured after 2h of enzymatic hydrolysis. Graph represents mean ± SD. Asterisks represent significant differences at P≤0.01.*

showed an increase in esterase activity as it is localized in the cell wall. All other AtCWEs, except AtCWE1, exhibited an elevated level of esterase activity. However, when lipase activity was tested in the same leaf tissue, it was similar in wild type, AnAXE control, and all AtCWE expressed leaves. These results suggest that all above AtCWE are esterases but not lipases. The next step is to perform the subcellular localization studies of these AtAXEs using confocal imaging. Furthermore, to assess which polysaccharide substrates are preferred by these AtCWEs, we are investigating polysaccharide acetylation level in mutant and overexpressor lines of the above AtCWEs. Chemotypic characterization of these acetylated modified lines will reveal the role of polysaccharide acetylation in plant cell wall organization, growth, and development.

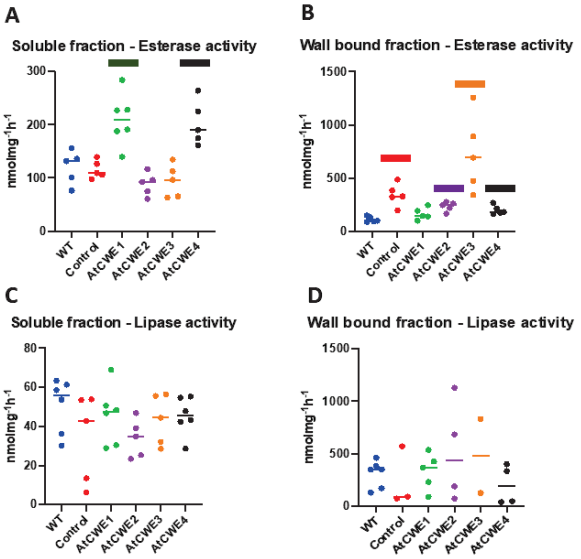
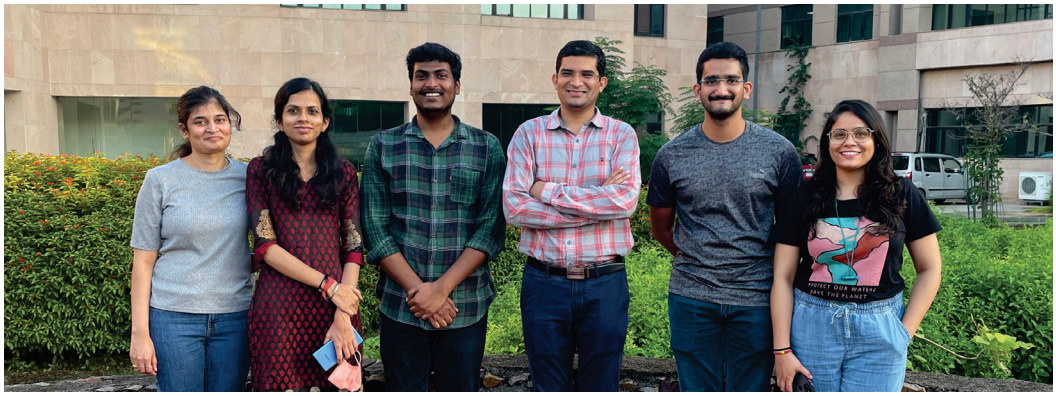
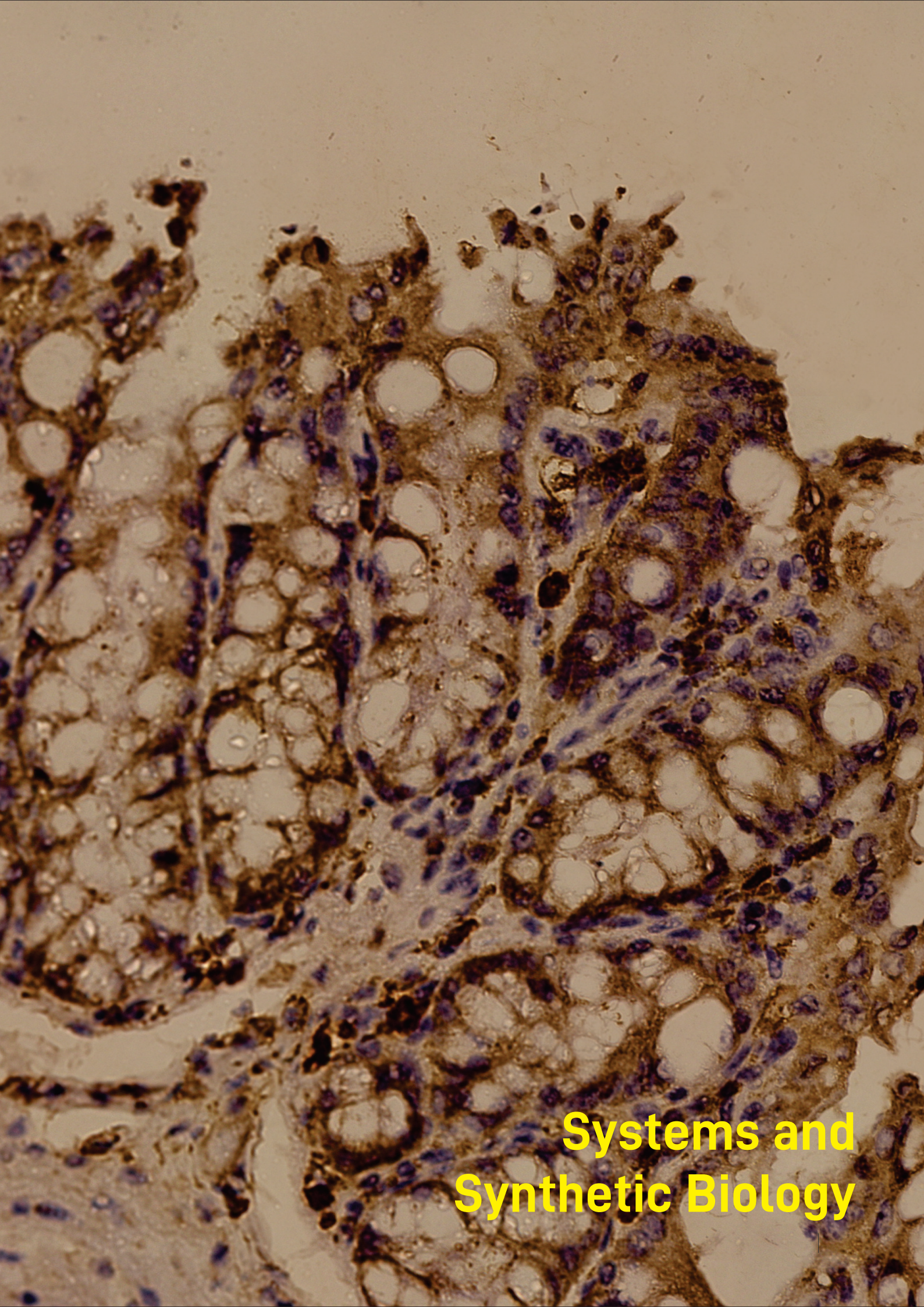


Figure 2: Esterase and Lipase activity in transiently expressed N. benthamiana leaves. *(A) and (B) represent esterase activity using 4-nitrophenyl acetate as a substrate andquantification of released product 4-nitrophenol at 400 nm. (C) and (D) represent lipase activity using 4-nitrophenyl palmitate as a substrate and quantification of released product 4-nitrophenol at 410 nm. Dots represent biological replicates. The horizontal bar at the top of the genotype represents a significant difference at p < 0.05.*





Systems and Synthetic Biology

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Molecular Engineering of Functional Nucleic Acids for Biomedicaland 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 rely on theirbase-pair identitiesbut also on the inherent ability to formtertiary structures such as triplexes, G-quadruplxes and riboswitches etc. These structures are diverse and are involved in remarkably broad spectrum of biological processes, from gene expression to genome maintenance. Thus, these structures gained attention as a therapeutic target. Besides thisthe modular nature of nucleic acid structures makes it a promising synthetic biology tool.Specifically, we are developing synthetic riboswitches for conditional and spatiotemporal gene regulation for diverse applications. We also aim to design and synthesize new synthetic molecules to target riboswitches for antibacterial therapy.

Targeting riboswitches mediated gene expression for antimycobacterial therapy

Riboswitches are typically found in the 5' untranslated regions (5'UTRs) of certain bacterial mRNAs, that recognize fundamental metabolites and undergo conformational changes leading to regulation of expression of genes involved in the synthesis or transport of the bound metabolite. The occurrence of riboswitches in pathogenic bacterial strains including *Mycobacterium tuberculosis* (*M. tuberculosis*), *Staphylococcus aureus* (*S. aureus*) and *Clostridium difficile* (*C. difficile*) and its involvement in the regulation of genes essential for survival and pathogenesis makes it a promising target for the discovery of new leads for antimicrobial and antimycobacterial therapy. Targeting riboswitches for antimicrobial and antimycobacterial therapy is an emerging research area and thus needs to develop new synthetic molecules to target more classes of riboswitches. The Flavin mononucleotide (FMN) riboswitchregulates the biosynthesis and transport of riboflavin which is then converted to essential flavoenzyme cofactors.Thus, we envision that repression of riboflavin synthesis pathways by targeting FMN riboswitches with small molecules could be lethal (Fig 1A).We have synthesized series of riboflavin analogs and were characterized by using Nuclear Magnetic Resonance (NMR) and MALDI-TOF analysis.

The minimum inhibitory concentration (MIC_{99}) were determined for all the synthesized compounds against *M. tuberculosis* H37Rv strain. The MIC_{99} values for riboflavin derivatives are in the rangeof 6-50 μM. We also determined the cytotoxicity of these analogs against THP-1 macrophages and found IC_{50} values 25 M, resulting in selectivity indexes of greater than 1. To rationalize the observed antimycobacterial results as well as to investigate possible interactions of thesynthesized compounds, we performed *in vitro* binding experiments as well as *in silico* molecular docking study with FMN riboswitch aptamer. The active compoundshows binding with the FMN riboswitch aptamer with binding constant of 5.42 0.37 10^5 M^1(Fig. 1B). On the other hand, the active compounddoes not show any interaction with the mutant riboswitch aptamer. Visual inspection of the docked conformations of these riboflavin analogs revealed that these compounds occupy the same co-ordinates of riboswitch binding pocket as observed for FMN (Fig. 1C). The antimycobacterial activity, *in silico* docking and molecular binding experiments results indicate that the synthetic riboflavin analogs might bind to the FMN riboswitch and block the essential riboflavin synthetic genes expression thereby resulted in inhibition of *M. tuberculosis* growth.

Rational reengineering of riboswitches for precise control of gene expression

Artificial control of gene expression is one of the core technologies used in synthetic biology for engineering biological systems for its applications in biotechnology, medicine and bioremediation. To engineer biological system to perform more sophisticated tasks, synthetic biology needs more tools that can precisely regulate gene expression. Synthetic riboswitches have potential to reprogram bacteria and human cellular functions by controlling the gene expression attranscriptional or translational level and have emerged as a promising tool to improve biological system. Like their natural counterparts, the synthetic riboswitches are

triggered in response to a specific inducer molecule. The key features of a synthetic riboswitch-based gene regulation systems are its conditional, spatio-temporal and concentration-dependent thus useful for diverse biomedical applications. The aptamer domain that recognizes the specific ligand is indispensable for function of both natural as well as synthetic riboswitches.

In this project we aim to develop new orthogonal riboswitches by developing more effective synthetic ligands which will allow more precise and dynamic control of gene expression. To validate the function of each riboswitch, the green fluorescent protein (GFP) gene was expressed under the control of constructed riboswitches. Activation ratios greater than 10-fold were achieved in most switches, with lower background expression in the absence of ligands. Among the developed library we have displayedrepresentative six riboswitches which provided a low level of background expression in the absence of the ligand and higher level of GFP gene expression in the presence of ligand (Fig. 2A).Next, we have used developed riboswitches for riboswitch mediated balanced gene expression in multienzyme pathways which is crucial for engineering metabolic pathways to improve the yield of biosynthesis of product(Fig.2B). Further studies are in progress.

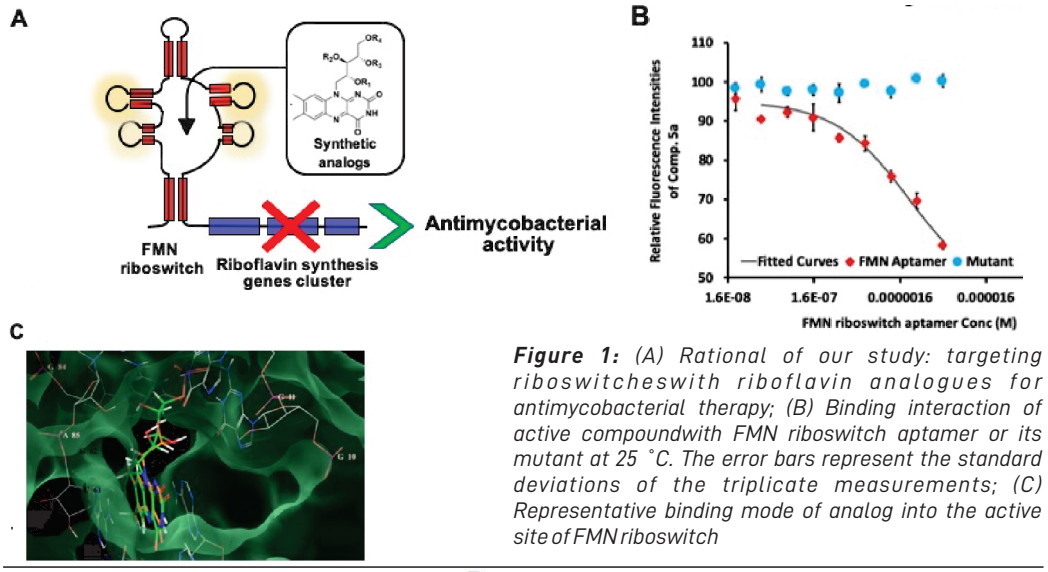

Figure 1: *(A) Rational of our study: targeting riboswitcheswith riboflavin analogues for antimycobacterial therapy; (B) Binding interaction of active compoundwith FMN riboswitch aptamer or its mutant at 25 ˚C. The error bars represent the standard deviations of the triplicate measurements; (C) Representative binding mode of analog into the active site of FMN riboswitch*

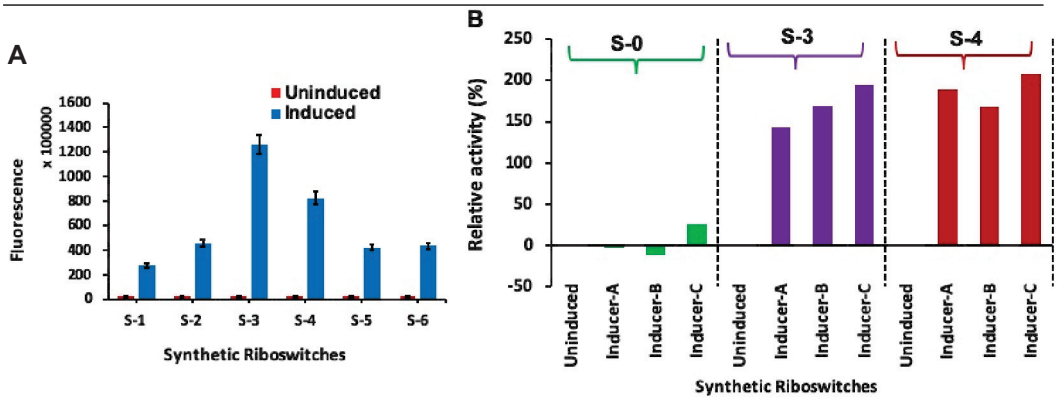

Figure 2: *(A) Characterizations of synthetic riboswitches function by measuring the green fluorescent protein (GFP) fluorescence in presence and absence of inducer ligand; (B) Increase in total relative activity of enzymes expressed under the control of synthetic riboswitches. Error bars indicate standard deviations from biological triplicate measurements.*

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

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Investigation of novel CAZymesfor the development of a cost-effective platform for polysaccharide degradation

The major goal of our research is to develop superior biocatalysts for pharma, chemical, food, flavors, and agro-based industries. We intend to build a technology that is greener, and reduces cost, with improved sustainability. For agro-based industries, the lab aims at the development of superior 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 the Auxiliary Activity (AA) family. So far, characterized LPMOs have very low catalytic activity and are thus not suitable for scale-up. Therefore, our lab mined the genome of LPMO hyperproducer *Botrytis cinerea* strain for the presence of these atypical hydrolytic enzymes that mediate oxidative degradation of the polysaccharide biomass. Interestingly, the genome harbors nine variants of LPMO sequence (Fig.1A) making *B. cinerea* a hyperproducer of oxidative enzymes. Next, we aimed at identifying an LPMO variant which is induced maximally in the presence of polysaccharide at the level of RNA and protein. IBAQ (Intensity based absolute quantification) and RT-PCR based expression analysis clearly suggested upregulation of BcLPMO9C (CCD49290) at 10, 20 and 30 hpi. The identified LPMO is unique as it possesses an additional linker and a carbohydrate binding module. *In-silico* studies predicted that both linker and carbohydrate binding domain play a crucial role in substrate binding. To validate this, we cloned and purified truncated variants from *Pichia pastoris.* Further,the truncated constructs will be characterized biochemically for their role in substrate binding and catalysis (Fig. 1).

Development of Paenibacillus polymyxa as a platform for production of branched chain alcohols

The research group has earlier developed a platform for exploiting lignocellulosic biomass for 2,3- butanediol production using a commercial hydrolytic enzyme cocktail. Based on the understanding developed, we aim to exploit the strain for the production of branched chain alcohols, such as isobutanol and isopentanol, as they have an energy density close to gasoline and, unlike ethanol, are not corrosive and do not absorb water and thus can be utilized. In this direction, we have initiated media optimization of *Paenibacillus polymyxa* for enhanced biomass production using the Plackett Burman design. The effect of various variables was evaluated based on the Plackett Burman design and interestingly, it was observed that optimizing the medium with 2g/L ammonium sulfate, pH6.5, 1X mineral concentration, 35Cincubation, and180 rpm agitation yielded maximum biomass. We also found that the age and size of inoculum are very crucial in promoting growth in *Paenibacillus* sp. as 5% inoculation of 16-h-old seed supported maximal growth (Fig. 2).

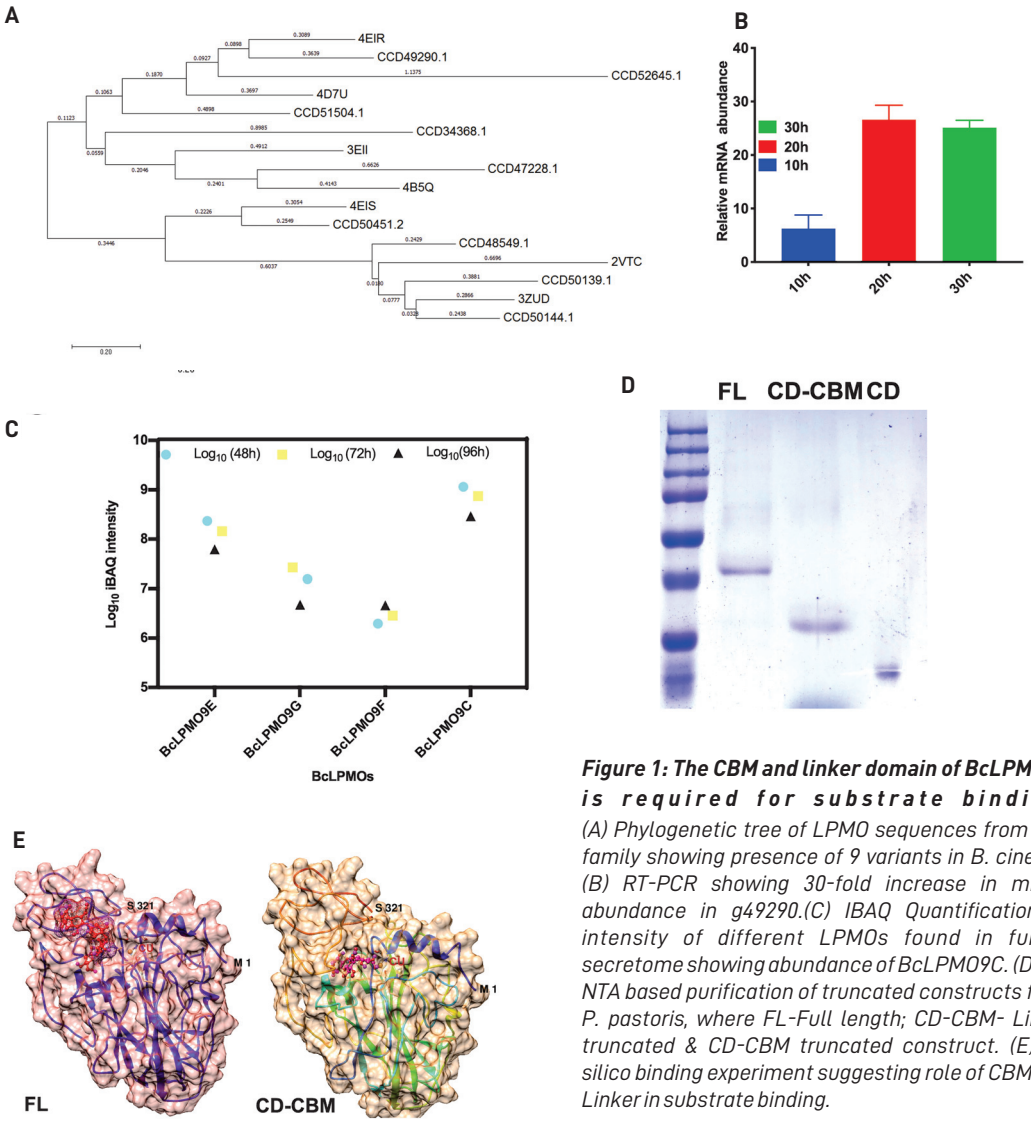

Figure 1: The CBM and linker domain of BcLPMO9C is required for substrate binding. *(A) Phylogenetic tree of LPMO sequences from AA9 family showing presence of 9 variants in B. cinerea. (B) RT-PCR showing 30-fold increase in mRNA abundance in g49290.(C) IBAQ Quantification of intensity of different LPMOs found in fungal secretome showing abundance of BcLPMO9C. (D) Ni-NTA based purification of truncated constructs from P. pastoris, where FL-Full length; CD-CBM- Linker truncated & CD-CBM truncated construct. (E) In-silico binding experiment suggesting role of CBM and Linker in substrate binding.*

S.No.	Glucose	Ammonium sulfate	Agitation	Temperature	pH	Mineral Conc	Inoculum size	Age of seed	Actual biomass (g/L)	Predicted biomass (g/L)
1	-1	+1	+1	-1	+1	-1	+1	-1	3.22	3.585
2	-1	-1	+1	-1	+1	-1	-1	1	3.07	3.862
3	+1	+1	-1	+1	+1	-1	-1	-1	2.65	3.198
4	+1	-1	-1	-1	+1	+1	+1	+1	2.99	2.72
5	+1	+1	-1	-1	-1	-1	-1	+1	4.57	4.321
6	-1	-1	-1	-1	-1	+1	-1	-1	2.37	2.13
7	+1	-1	+1	+1	+1	+1	-1	-1	5.01	5.1
8	+1	-1	+1	+1	-1	-1	+1	+1	4.42	4.877
9	+1	+1	+1	-1	-1	1	+1	-1	5.95	6.11
10	-1	-1	-1	+1	-1	-1	+1	-1	2.13	2.303
11	-1	+1	+1	+1	-1	1	-1	+1	3.19	3.777
12	-1	+1	-1	+1	+1	+1	+1	+1	2.56	2.321

Figure 2: Plackett Burman design for media optimization for increased biomass. *Table indicates effect of different variables on biomass production.*

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Biocatalysis and Synthetic Biology for the Synthesis of High-Value Products

Enzymes are the most frequently used biocatalysts that are used to produce a range of high value compounds including pharmaceuticals and commodity chemicals. Advent of genetic tools and bioinformatics resources enable biological engineers to engineer enzymes and construct synthetic multi-enzyme pathways in proven heterologous production platforms for production of valuable compounds. My research program, as illustrated in Fig. 1, is focused on developing a biocatalytic/synthetic biology platform for the synthesis of natural product derived therapeutics and other value added compounds. We are trying to achieve such a challenging goal by a) first developing the molecular level understanding about factors governing enzyme's substrate scope and activity, as well as their spatio-temporal communications with other enzymes of biosynthetic pathways under consideration, b) further exploiting the gained knowledge to develop biocatalytic *in vitro* and *in vivo* synthetic biology platforms for combinatorial biosynthesis of desired compounds, and c) further assessment of their bioactivity followed by their scale-up.

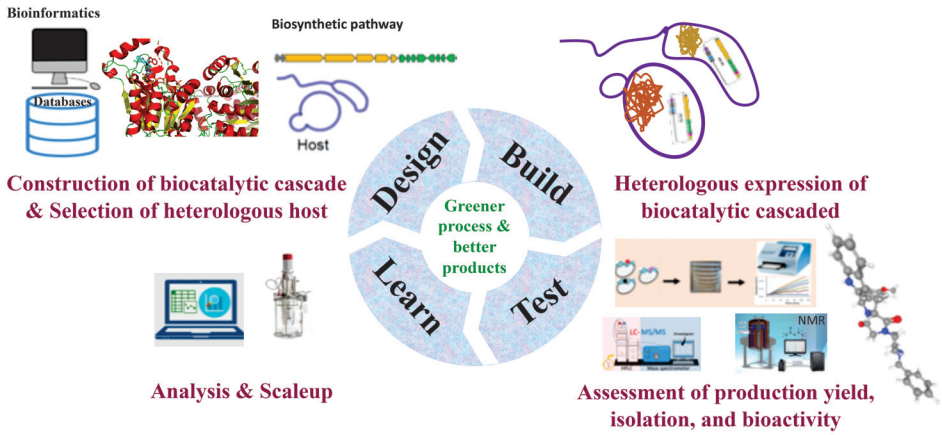


Figure 1: *Schematics of work flow for discovery and development of natural product derived therapeutics.*

Biosynthesis of natural product derived therapeutics using synthetic biology

An organism's genome encodes enzymes and pathways with enormous biosynthetic potential to produce thousands of molecules with diverse chemical structure and biological activities. These natural products are invaluable and continue to play a pivotal role in drug discovery efforts as more than half of the drugs approved so far are derived from natural products. In addition to their use for their biological properties, for instance as antibiotics, anticancer and immunosuppressive agents, antivirals, anthelmintics, enzyme inhibitors, nutraceuticals, and vaccines, they are also used as polymers, surfactants, fragrances, food ingredients, bio-herbicides, etc. Advances in whole genome sequencing, metabolic engineering, and chemical biology provide valuable insights into the biological routes for synthesis of these natural products. Accessing these natural products promises to reinvigorate the drug discovery and development pipeline and provide us with the ability to extend nature's chemistry through combinatorial biosynthesis.Recent advancements in molecular biology, recombinant technologies, and synthetic biology tools are enabling biological engineers to re-engineer the biosynthetic pathways identified from genomic sequences and insert them into heterologous hosts (*E. coli*, *Bacillus subtilis*, *S. cerevisiae*, etc.) in a plug-and-play fashion for the production of a combinatorial library by systematically switching/adding enzymes or using an enzyme with broad substrate scope. We begin our studies with database mining and chemo-informatics analysis of natural product/drug databases which enable us to deduce structure-activity relationships. Mining of genome databases for targeted natural product pathways provides critical information related to the necessary set of required biosynthetic enzymes for the synthesis of core scaffold and late-stage tailoring to produce bioactive compounds. We have been routinely expressing single enzyme or multi-enzyme cascades in *E. coli* and/or yeast for the production of combinatorial libraries followed by isolation and assessment of their bioactivity. We further generate the structural diversity of compounds by engineering enzymes as well as by plug and play of enzymes from diverse pathways.

Development of a biocatalytic platform for synthesis of chiral amines for diverse industrial applications

Enantiomerically pure chiral amines are the most valuable building blocks for the synthesis of active pharmaceutical intermediates, fine chemicals and agrochemicals. In medicine, about 40% of the APIs contain the chiral amine moiety. Chemical synthesis of chiral amines is very inefficient; it involves application of expensive toxic metals, the stereoselectivity in chemical synthesis is difficult to control and the product contains a mixture of enantiomers, requiring purification to achieve chiral amine compounds. The challenges in synthesis of chiral amines are now met by the biocatalyst. Repertoire of biocatalysts, including enzymes such as transaminases, monoamine oxidases, amine dehydrogenases, phenylalanine ammonia lyases, and imine reductases are increasingly attractive for the synthesis of chiral amines. Along this direction, we have begun the development of Phenyl Alanine Ammonia lyase (PAL) and Imine Reductase (IRED)-based biocatalytic technology (Fig. 2) for the sustainable production of a diverse range of chiral amines of industrial interest.

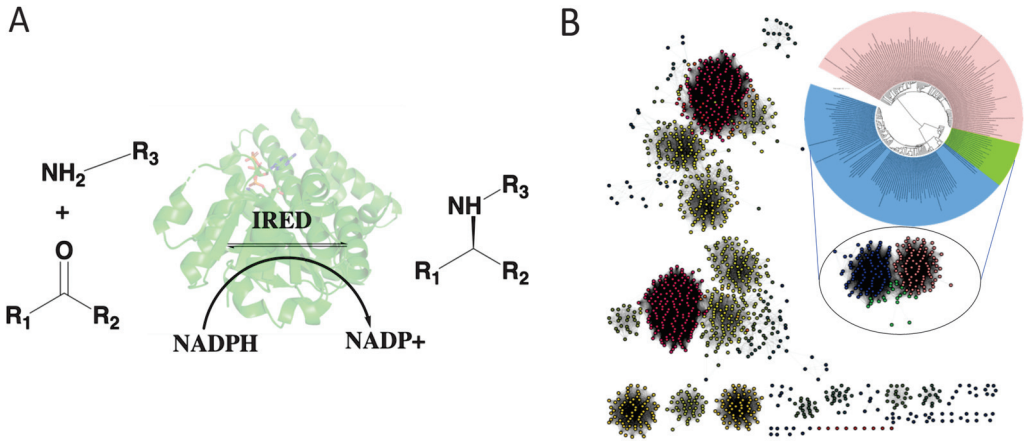


Figure 2: *Schematic representation of imine reductase catalysed reaction (A), and sequence and phylogenetic distribution of imine reductase superfamily (B).*

Investigation of multi-enzyme complex for improved cascade biosynthesis

Transient multi-enzyme assemblies appear to be a cardinal feature of biosynthetic/metabolic pathways; however, their role and their supramolecular organization remains enigmatic. These transient multi-enzyme complexes are very dynamically formed through assembly of sequential enzymes glued by protein-protein interactions. Development of a molecular-level understanding about transient physical interactions of enzymes with myriads of their interacting partners in biosynthetic pathways is critical for the construction of synthetic versions of engineered pathways and to synergize *in vivo, ex vivo* and *in vitro* biosynthesis which will improve metabolic flux and titer of targeted value-added products. Towards this end, we have been probing and characterizing the structure of multi-enzyme complexes (metabolons) from diverse natural product biosynthetic pathways. This effort will provide evidence and an understanding of the spatial and functional orchestration among multiple enzymes in natural metabolic/biosynthetic pathways. The gained understanding will be exploited to develop whole cell or cell free multi-enzymatic cascades for production of desired high value products (e.g. pharmaceutical and fuels).

SARS-CoV-2 related Research and Development at RCB

The ongoing COVID19 pandemic is caused by the SARS-CoV-2 virus. The RNA genome of the virus is replicated by the RNA-dependent-RNA polymerase activity present in the nsp12 protein. The inhibition of this enzyme should adversely affect viral replication and lower the viral titres. Researchers in Dr. Deepak T. Nair's group carried out the *in silico* screening to identify possible inhibitors of this enzyme. It was predicted that the methylcobalamin form of Vitamin B12 could bind to the active site of nsp12 and inhibit the function of the enzyme. Efforts are underway to check the effect of methylcobalamin on the activity of nsp12 *in vitro* and replication of the SARS-CoV-2 in cell culture.

The nsp14 protein is involved in proofreading of newly synthesized progeny RNA and removing any errors that might arise during replication. Due to its ability to excise out misincoporated nucleotides, this enzyme could reduce the ability of drugs like remdesivir, faivpiravir and ribavirin to inhibit virus replication. The HIV-1 drug ritonavir was identified as a potential inhibitor of nsp14 and it is possible that this molecule may potentiate the activity of aforementioned drugs. Currently, efforts are underway to purify the nsp14 enzyme to test the ability of ritonavir to inhibit its proofreading activity. Also, *in silico* screening to identify other possible inhibitors of nsp12 and nsp14 are in progress. The inhibitors identified using computational tools will be first tested for their ability to inhibit the cognate enzyme *in vitro* and then for their ability to reduce viral replication in cell culture.

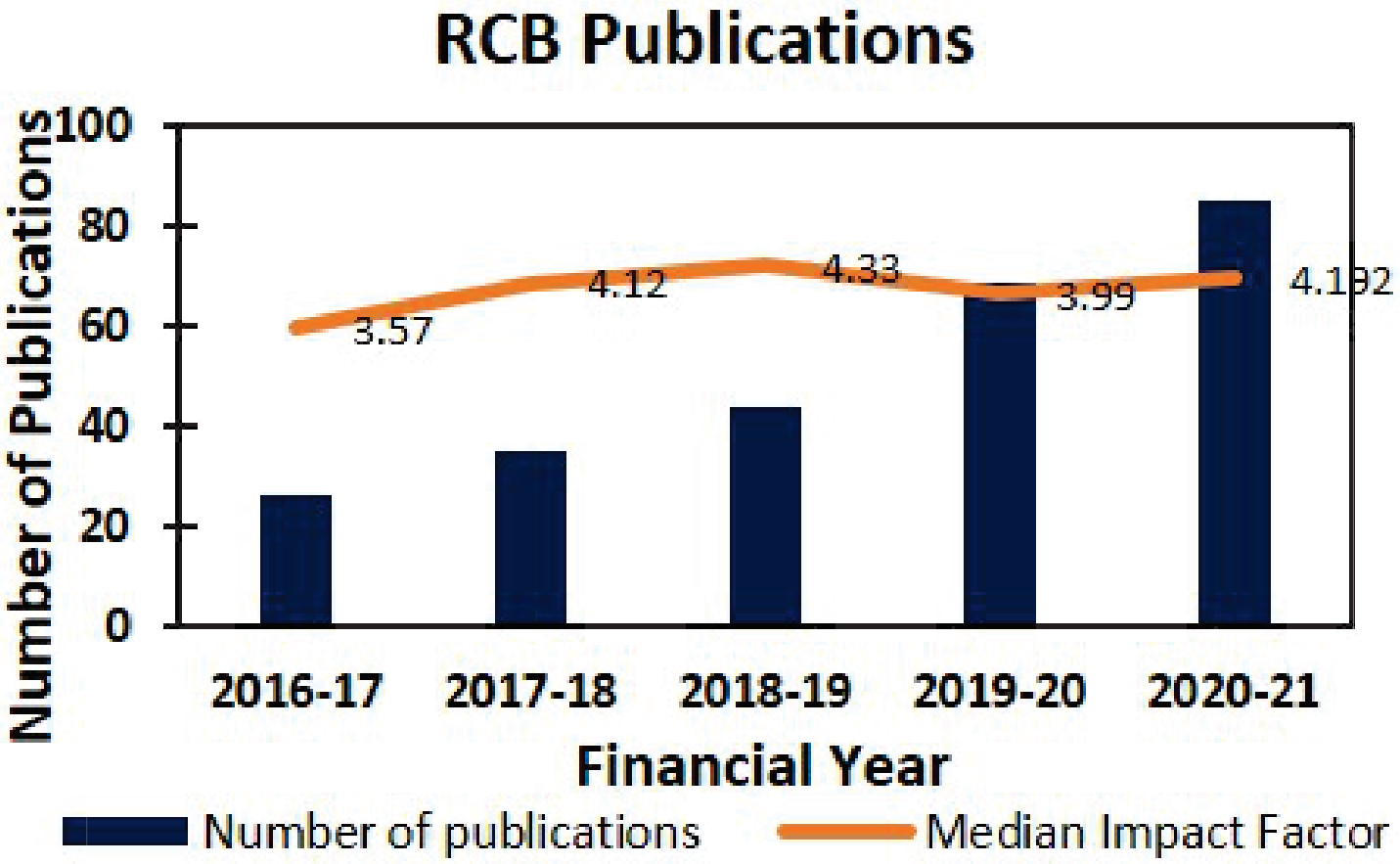
SARS-CoV-2 genome contains structured RNA elements that might be involved in the key processes such as RNA synthesis, transcriptional regulation and protein translation resulting in multiplication of the RNA genome. Despite diverse structures and crucial functions compared to proteins, RNAs are under-exploited therapeutic target for antiviral therapy. Dr. Ambadas Rode's laboratory has virtually screened compounds from in-house database as well as open database libraries against SARS-CoV-2 RNA targets. With the developed virtual screening platform, each ligand was docked against defined active site of SARS-CoV-2 RNA targets to gauze their binding affinities as well as to gain an insight into their binding modes along with various thermodynamic interactions governing the binding affinity. The docking results suggested that certain number of molecules could snugly fit into active site with varying degrees of affinities producing high docking score and significant binding energy. The knowledge derived from this initial screening may be a useful starting point for structure-based lead optimization to generate compounds with high selectivity and potency against SARS-CoV-2.

Dr. Prasenjit Guchhait's laboratory described the molecular mechanism of inflammation and thrombosis in the lung of SARS-CoV-2 infected animal and human. Study showed a significant intravascular clot formation and leukocytes accumulation in the alveolar spaces of hamsters infected with the virus. Study also described the therapeutic use of a metabolite -ketogluterate in abrogating the inflammation and clot formation induced by the SARS-CoV-2 virus.

RCB established a platform to screen the antiviral activity of drug molecules/medicinal plant extracts in the cell culture model of SARs-CoV-2 infection under the BSL-3 environment. These services were utilized by a large number of labs from academia and industry to screen for potential antivirals against SARS-CoV-2.

During the pandemic time, BSC BioNEST Bio-Incubator (BBB) start-ups rose to the challenge and developed affordable products/technologies to combat SARS-CoV-2. These products included the detection kits, Viral transport/lysis media kit, disinfectants, etc. Two of our start-ups won COVID-related awards and grants. InnoDx Solutions Pvt. Ltd. won SAMADHAN Award COVID-19 and ShcShine Biotech Pvt. Ltd. secured COVID-19 research consortium award. NextGen InVitro Diagnostics Pvt. Ltd. obtained ICMR approved and commercialized a RT-qPCR diagnostic kit and a Rapid Antigen Test kit. Organic 121 Scientific Pvt. Ltd. commercialized Surface Coating (COVIDCOAT), vegetable washing powder (FRESHSHIELD) and plant-based organic fumigation product (TRIYOGANI). Vanguard Diagnostics Pvt. Ltd. obtained ICMR approval and commercialized the Viral Transport Media kit, Viral Lysis Transport Medium kit, and DIPAS-VDx COVID-19 IgG ELISA Test Kit. InnoDx Solutions Pvt. Ltd. also commercialized a RT-PCR diagnostic kit.

PUBLICATIONS & PATENTS



Peer-reviewed Publications

1. Nagpal S, Nair DT (2021). The PHP domain of PolX from Staphylococcus aureus aids high fidelity DNA synthesis through the removal of misincorporated deoxyribo-, ribo- and oxidized nucleotides. *Sci Rep* 11:4178.
2. Narayanan N, Nair DT (2021). Ritonavir may exhibit exoribonuclease activity of nsp14 from the SARS-CoV-2 virus and potentiate the activity of chain terminating drugs. *Int J Biol Macromol* 168:272-278.
3. Narayanan N, Nair DT (2020). Vitamin B12 may inhibit RNA-dependent-RNA polymerase activity of nsp12 from the SARS-CoV-2 virus. *IUBMB Life* 72:2112-2120.
4. Sharma M, Narayanan N, Nair DT (2020). The proofreading activity of Pfprex from *Plasmodium falciparum* can prevent mutagenesis of the apicoplast genome by oxidized nucleotides. *Sci Rep* 10:11157.
5. Kumar MA, Pratap S, Kant A, Palva A, von Ossowski I, Krishnan V (2020). Crystal structure of the atypically adhesive SpaB basal pilus subunit: Mechanistic insights about its incorporation in lactobacillar SpaCBA pili. *Curr Res Struct Biol* 2: 229-238.
6. Kant A, Palva A, von Ossowski I, Krishnan V (2020). Crystal structure of lactobacillar SpaC reveals an atypical five-domain pilus tip adhesin: Exposing its substrate-binding and assembly in SpaCBA pili. *J Struct Biol* 211: 107571.
7. Banerjee S, Katiyar P, Kumar V, Waghmode B, Nathani S, Krishnan V, Sircar D, Roy P (2021). Wheatgrass inhibits the lipopolysaccharide-stimulated inflammatory effect in RAW 264.7 macrophages. *Curr Res Toxicol* 2: 116-127.
8. Banerjee S, Katiyar P, Kumar V, Saini SS, Varshney R, Krishnan V, Sircar D, Roy P (2021). Black pepper and piperine induce anticancer effects on leukemia cell line. *Toxicol Res* 10: 169-182.
9. Banerjee S, Katiyar P, Kumar L, Kumar V, Saini SS, Krishnan V, Sircar D, Roy P (2021). Black pepper prevents anemia of inflammation by inhibiting hepcidin over-expression through BMP6-SMAD1/ IL6-STAT3 signaling pathway. Free Radic Biol Med, (doi: 10.1016/j.freeradbiomed.2021.03.019)
10. Koripella RK, Sharma MR, Bhargava K, Datta PP, Kaushal PS, Keshavan P, Spremulli LL, Banavali NK & Agrawal RK (2020). Structures of the human mitochondrial ribosome bound to EF-G1 reveal distinct features of mitochondrial translation elongation. *Nat Commun* 11: 3830.
11. Singh A, Bisht P, Bhattacharya S, Guchhait P (2020). Role of platelet cytokines in Dengue virus infection. *Frontiers in Cellular and Infection Microbiology*, 10:561366
12. Thakur S, Saha S, Guchhait P, Eswaran S (2020). Fullarazirman, nano water-soluble Fullerene C60-Mn (II) Triadduct complex with anti-cancer activity comparable to Doxorubicin. *J Biomedical Nanotechnology*. 16:481-491.
13. Thakur S, Goswami K, Rao P, Kaushik S, Singh B, Sharma PK, Asthana S, Bhattacharjee S, Guchhait P, Eswaran S (2020). A Fluoresceinated Aminohexanol Tethered Inositol Hexakisphosphate: Studies on Arabidopsis thaliana, Drosophila melanogaster and Docking with 2P1M Receptor. *ACS Omega* 5:9585-9597.
14. Sardoiwala NM, Kushwaha A, Dev A, Nishith S, Guchhait P, Karmakar S, Roy Choudhury S (2020). Hypericin loaded transferrin nanoparticles induce PP2A regulated BMI1 degradation in colorectal cancer specific chemo-Photodynamic Therapy. *ACS Biomaterials Science & Engineering*, 6,5, 3139-3153.
15. Kumari R, Maiti TK (2021). Calpain-2 participates in the process of calpain-1 inactivation by Shinkai-Ouchi et al. Bioscience Reports,41:BS20203690.
16. Srikanth S, Rizvi ZA, Pandey RP, Dalal R, Rathore DK, Kumar B, Pandey M, Kumar Y, Goel R, Maiti TK, Tiwari A, Johri AK, Pandey AK, Awasthi A (2021). Gefitinib results in robust host-

directed immunity against Salmonella infection through proteo-metabolomic reprogramming. Front. Immunol 12: 648710.

17. Kumar B, Dey AK, Saha S, Singh AK, Kshetrapal P, Wadhwa N, Thiruvengadam R, Desiraju BK, Bhatnagar S, Salunke DM, Rashid F, Malakar D, Maiti TK, GARBH-Ini Study Group (2021). Dynamic alteration in the vaginal secretory proteome across the early and mid-trimesters of pregnancy. J Proteome Res 20:1190.

18. Basak T, Dey AK, Banerjee R, Paul S, Maiti TK, Ain R (2021). Sequestration of eIF4A by angiomotin: A novel mechanism to restrict global protein synthesis in trophoblast cells. Stem Cells 39:210.

19. Hussain N, Chatterjee SK, Maiti TK, Goswami L, Das S, Deb U, Bhattacharya SS (2021). Metal induced non-metallothionein protein in earthworm: A new pathway for cadmium detoxification in chloragogenous tissue. J Hazard Mater 401:123357.

20. Kumari M, Hanpude P, Maiti TK (2020). -Synuclein exhibits differential Membrane perturbation, nucleation, and TLR2 binding through Its secondary structure. ACS Chem Neurosci. 11:4203.

21. Dey AK, Kumar B, Singh AK, Ranjan P, Thiruvengadam R, Desiraju BK, Kshetrapal P, Wadhwa N, Bhatnagar S, Rashid F, Malakar D, Salunke DM, Maiti TK. GARBH-Ini Study Group (2020). Salivary proteome signatures in the early and middle stages of human pregnancy with term birth outcome. Sci Rep 10:8022

22. Pant A, Bag S, Saha B, Verma J, Kumar P, Banerjee S, Kumar B, Kumar Y, Desigamani A, Maiti S, Maiti TK, Banerjee SK, Bhadra RK, Koley H, Dutta S, Nair GB, Ramamurthy T, Das B (2020). Molecular insights into the genome dynamics and interactions between core and acquired genomes of Vibrio cholerae. Proc Natl Acad Sci USA 117:23762.

23. Masum Saini, Ajaya Nand Jha, Rajiv Tangri, Md.Qudratullah Sher Ali (2020). MN1 overexpression with varying tumor grade is a promising predictor of survival of glioma patients. Human Molecular Genetics 29(21): 3532-3545 [*communicating author].

24. Kain P* (2020). Realigning minds and mental health resilience during Covid-19. Acta Scientific Neurology, 3: 12 (Editorial).

25. Kain P* (2020). The Bitter Truth: Lessons from Pandemic Covid-19. Acta Scientific Neurology, 3:9.

26. Kumar S and Kain P* (2020). Defeating the Devil in the Waste: Remediation of Infectious Covid-19 Waste. Acta Scientific Neurology, 3:8.

27. Kain P (2020). Loss of Smell and Taste: Potential of Using Them as Markers for Early Detection of Covid-19. Adv Neur Neur Sci, 3:2.

28. Sehrawat S, Khasa R, Deb A, Prajapat SK, Mallick S, Basu A, Surjit M, Kalia M, Vrati S (2021). Valosin-containing protein/p97 plays critical roles in the Japanese encephalitis virus life cycle. Journal of Virology 95 (11) : e02336-20.

29. Banerjee A, Tripathi A, Duggal S, Banerjee A, Vrati S (2020). Dengue virus infection impedes megakaryopoiesis in MEG-01 cells where the virus envelope protein interacts with the transcription factor TAL-1. Scientific Reports 10(1):19587.

30. Khasa R, Sharma P, Vaidya A, Vrati S, Kalia M (2020) Proteins involved in actin filament organization are key host factors for Japanese encephalitis virus life-cycle in human neuronal cells. Microbial Pathogenesis 149:104565.

31. Saini J, Bandyopadhyay B, Pandey AD, Ramachandran VG, Das S, Sood V, Banerjee A, Vrati S (2020) High-Throughput RNA Sequencing Analysis of Plasma Samples Reveals Circulating microRNA Signatures with Biomarker Potential in Dengue Disease Progression. mSystems 5(5): e00724-20.

32. Levine MM, Abdullah S, Arabi YM, Darko DM, Durbin AP, Estrada V, Jamrozik E, Kremsner PG, Lagos R, Pitisuttithum P, Plotkin SA, Sauerwein R, Shi SL, Sommerfelt H, Subbarao K, Treanor

JJ, Vrati S, King D, Balasingam S, Weller C, Aguilar AO, Cassetti MC, Krause PR, Restrepo AMH (2020) Viewpoint of a WHO Advisory Group Tasked to Consider Establishing a Closely-Monitored Challenge Model of COVID-19 in Healthy Volunteers. Clinical Infectious Diseases 28: ciaa1290.

33. Verma P, Srivastava A, Srikanth CV, Bajaj A (2021) Nanoparticle-mediated gene therapy strategies for mitigating inflammatory bowel disease. Biomater Sci. Mar 10;9(5):1481-1502.

34. Awasthi A, Nain V, Srikanth CV, Puria R. (2020). A regulatory circuit between lncRNA and TOR directs amino acid uptake in yeast. Biochim Biophys Acta Mol Cell Res.;1867(6):118680.

35. Preksha G, Yesheswini R, Srikanth CV. Cell culture techniques in gastrointestinal research: Methods, possibilities and challenges. Indian J Pathol Microbiol. 2021; 64(Supplement):S52-S57.

36. Sharma G, Dang S, K Aruna, Kalia M, Gabrani R (2020) Synergistic antibacterial and anti-biofilm activity of nisin like bacteriocin with curcumin and cinnamaldehyde against ESBL and MBL producing clinical strains. Biofouling 2020 Aug 9;1-15. doi: 10.1080/08927014. 2020.1804553.

37. Sarkar R, Sharma KB, Kumari A, Asthana S, Kalia M (2020) Japanese encephalitis virus capsid protein interacts with non-lipidated MAP1LC3 on replication membranes and lipid droplets. Journal of General Virology. 2021 Jan;102(1). doi: 10.1099/jgv.0.001508. Epub 2020 Oct 23.

38. Klinosky DJ et al., (2021) Guidelines for the use and interpretation of assays for monitoring autophagy (4th edition) Autophagy 2021 Jan;17(1):1-382. doi: 10.1080/15548627.2020. 1797280. Epub 2021 Feb 8

39. Kangale LJ, Raoult D, Fournier PE, Abnave P, Ghigo E (2021). Planarians (Platyhelminthes)—An Emerging Model Organism for Investigating Innate Immune Mechanisms. Frontiers in cellular and infection microbiology. 11:619081.

40. Thakur A, Gaikwad S, Vijjamari AK, Hinnebusch AG (2020). eIF2a interactions with mRNA control accurate start codon selection by the translation preinitiation complex.Nucleic Acids Res 9;48(18):10280-10296.

41. Agarwal M*, Sharma A*, Kumar P*, Kumar A*, Bharadwaj A, Saini M, Kardon G and Mathew SJ (2020). Myosin heavy chain-embryonic regulates skeletal muscle differentiation during mammalian development.Development 147(7). pii: dev184507. [*equal contribution]

42. Kumar S and Bajaj A (2020). Advances in Self-assembled Injectable Hydrogels for Cancer Therapy Kumar. Biomaterials Sci. 8, 2055-2073.

43. Gupta R, Thakur J, Pal S, Mishra D, Rani P, Kumar S, Saini S, Singh A, Srivastava A, Prasad R, Gupta S, Bajaj A (2021). Cholic Acid-Derived Amphiphiles can Prevent and Degrade the Fungal Biofilms. ACS Appl Bio Mater, https://doi.org/10.1021/acsabm.9b01221

44. Sreekanth V, Kar A, Kumar S, Pal S, Yadav P, Sharma Y, Komalla V, Sharma H, Shyam R, Sharma R.D, Mukhopadhyay A0, Sengupta S, Dasgupta U, & Bajaj A (2021). Bile Acid-tethered Docetaxel-based Nanomicelle Mitigates Tumor progression through Epigenetic Changes. Angew Chem Int Ed 60:5384.

45. Pal S, Mehta D, Dasgupta U and Bajaj A (2021). Advances in engineering of low molecular weight hydrogels for chemotherapeutic applications. Biomed Mater 16: 024102.

46. Verma P, Srivastava A, Srikanth CV, Bajaj A (2021) Nanoparticle-mediated Gene Therapeutic Strategies for Mitigating the Inflammatory Bowel Disease. Biomater Sci 9: 1481.

47. Medatwal N, Ansari MN, Kumar S, Pal S, Jha S.K, Verma P, Rana K, Dasgupta U and Bajaj A (2020) Hydrogel-mediated delivery of celastrol and doxorubicin induces a synergistic effect on tumor regressionviaupregulation of ceramides. Nanoscale, 12:18463

48. Dagar S, Pushpa K, Pathak D, Samaddar S, Saxena A, Banerjee S and Mylavarapu SVS (2021). Nucleolin regulates 14-3-3Zeta mRNA and promotes cofilin phosphorylation to induce tunneling nanotube formation.FASEB Journal, 35(1): e21199. doi: 10.1096/fj.202001152R.

49. Sharma A, Dagar S, Mylavarapu SVS (2020). Transgelin-2 and Phosphoregulation of the LIC2 Subunit of Dynein Govern Mitotic Spindle Orientation. J Cell Sci, doi: 10.1242/jcs.239673.

50. Sharma N, Arora S, Saurav S, Motiani RK (2020). Pathophysiological Significance of Calcium Signaling at Mitochondria-Associated Endoplasmic Reticulum Membranes (MAMs). Current Opinion in Physiology. 17:234.

51. Tanwar J, Singh JB, Motiani RK (2021). Molecular machinery regulating mitochondrial calcium levels: The nuts and bolts of mitochondrial calcium dynamics. Mitochondrion. 57: 9-22.

52. Tanwar J, Arora S, Motiani RK. (2020) Orai3: Oncochannel with therapeutic potential. Cell Calcium, 90:102247

53. Ingole KD, Dahale SK, Bhattacharjee S (2021). Proteomic analysis of SUMO1-SUMOylome changes during defense elicitation in Arabidopsis. J Proteomics 232: 104054.

54. Gupta M, Dubey S, Jain D, Chandran D (2021). The Medicago truncatula sugar transport protein 13 and its Lr67res variant confer powdery mildew resistance in legumes via defense modulation. Plant Cell Physiol (advance article).

55. Bhatnagar A, Singh S, Khurana JP, Burman N (2020). HY5-COP1: the central module of light signaling pathway. J Plant Biochem Biotechnol 29:590–610.

56. Burman N, Chandran D, Khurana JP (2020). A rapid and highly efficient method for transient gene expression in rice plants. Front Plant Sci 11:1564.

57. Karthika V, Babitha KC, Kiranmai K, Shankar AG, Udayakumar M, Vemanna RS (2021). Disruption in DNA mismatch repair gene MSH2 by CRISPR-Cas9 in Indica rice can create genetic variability. J Agri Food Chem 69(14): 4144–4152.

58. Vidya N, Akshay UR, Sujitha D, Akashata D, Ashwin V, Udayakumar M, Vemanna RS (2021). Stress-induced detoxification enzymes in rice have broad substrate affinity. ACS Omega 3399-3410.

59. Vemanna RS, Oh S, Lee HK, Nandety RS, Oh Y, Lee S, Nakashima J, Tang Y, Senthil-Kumar M, Mysore KS (2021). A novel role of salt and drought induced RING 1 protein in modulating plant defense against hemibiotrophic and necrotrophic pathogens. Mol Plant Microbe Interact 34(3):297-308.

60. Vemanna RS, Akashata D, Lee S, Oh S, Lee HK, Sun L, Senthil-Kumar M, and Mysore KS (2020) Ribosomal protein QM/RPL10 positively regulates defense and protein translation mechanisms during nonhost disease resistance. Mol Plant Pathol 21:1481–1494.

61. Vemanna RS, Preethi V, Nisarga KN, Srivatsava KR , Sheshshayee MS, KS Mysore and Udayakumar M (2020). Carbonyl cytotoxicity affects plant cellular processes and detoxifying enzymes scavenge these compounds to improve stress tolerance. J Agri Food Chem 68(23): 6237–6247.

62. Preethi V, Nagashree N. Vemanna RS, Raviswamy GH, Dhananjay DS, Xinyou Y, Struik PS, Udayakumar M, Sheshshayee MS. Metabolome profiling reveals impact of water limitation on grain filling in contrasting rice genotypes. Plant Physiol Biochem (2021) 162:690-698.

63. Lekshmy VS, Preethi V, Nagashree AN, Vemanna RS, Ramegowda V, Makarla U and Sreeman S (2021). Induction of acquired tolerance through gradual progression of drought is the key for maintenance of spikelet fertility and yield in rice under semi-irrigated aerobic conditions. Front Plant Sci 11:632919.

64. Prasannakumar MK, Parivallal BP, Manjunatha C, Pramesh D, Narayan KS, Venkatesh G, Banakar SN, Mahesh HB, Vemanna RS, Rangaswamy KT (2021). Rapid genotyping of bacterial leaf blight resistant genes of rice using loop-mediated isothermal amplification assay. Mol Biol Rep 48:467.

65. Kaundal A, Vemanna RS, Mysore KS (2020). The ATPase activity of Escherichia coli expressed AAA+-ATPase protein. Bio-Protocol. 10(15):e3705.

66. Ahmed F, Senthil-Kumar M, Dai X, Vemanna RS, Lee S, Mysore KS, Zhao PX. (2020). pssRNAit-a web server for designing effective and specific plant siRNAs with genome-wide off-target assessment. Plant Physiol 184 (1):65-81.

67. Preethi V, Vemanna RS, Xinyou Y, Paul CS, Udayakumar M, and Sheshshayee S. (2020). Acquired traits contribute more to drought tolerance in wheat than in rice. Plant Phenomics doi: 10.34133/2020/5905371.

68. Thapliyal G, Vemanna RS, Pawar PM, Barthwal S, Meena KR, Pandey S, Bhandari MS (2020). First record of off-season flowering in Populus deltoides from India: paradigm of climate change indicator. Int J Biomet 64:1629–1634.

69. Karthika V, Babitha KC, Kiranmai, K, Shankar AG, Vemanna RS, Udayakumar M (2020). DNA mismatch repair systems involvement in genetic diversity in plants for speed breeding programs for crop improvement. Plant Physiol Rep. 25(2):185–199.

70. Derba-Maceluch M, Amini F, Donev EN, Pawar PMA, Michaud L, Johansson U, Alberectsen BR, Mellerowicz EJ (2020). Cell wall acetylation in hybrid aspen affects field performance, foliar phenolic composition and resistance to biological stress factors in a construct dependent fashion. Front Plant Sci 11:651.

71. Singh N, Sunny, Gupta A, Srivastava KR (2021). Revolutionizing enzyme engineering through artificial intelligence and machine learning. Emerging Top Life Sci 5:113-125.

72. Periwal N, Rathod SB, Paul R, Sharma P, Nebhnani L, Barnawal R P, Arora P, Srivastava, KR, Sood V (2021). In silico characterization of mutations circulating in SARS-CoV-2 structural proteins. J Biomol Struct Dyn 1-16 doi: 10.1080/07391102.2021.1908170.

73. Newmister S, Srivastava KR, Espinoza R, Haatveit KC, Khatri Y, Martini R, Garcia-Borràs M, Podust L, Houk K, Sherman D (2020). Molecular basis of iterative C-H oxidation by TamI, a multifunctional P450 monooxygenase from tirandamycin biosynthetic pathway. ACS Catal 10:13445-13454.

74. Pani T, Rajput K, Kar A, Sharma H, Basak R, Medatwal N, Saha S, Dev G, Kumar S, Gupta S, Mukhopadhyay A, Malakar D, Maiti TK, Aneeshkumar AG, Deo SVS, Sharma RD, Bajaj A, Dasgupta U (2021). Alternative Splicing of Ceramide Synthase 2 Alters Levels of Specific Ceramides and Modulates Cancer Cell Proliferation and Migration in Luminal B Breast Cancer Subtype. Cell Death Dis 12: 171.

Pre-prints

1. Verma R, Saha S, Kumar S, Mani S, Maiti TK, Surjit M (2021). RNA-protein interaction analysis of SARS-CoV-2 5'- and 3'-untranslated regions identifies an antiviral role of lysosome-associated membrane protein-2. bioRxiv, doi.org/10.1101/2021.01.05.425516

2. Navalkar A, Pandey S, Singh N, Dey AK, Saha S, Patel K, Mohanty B, Jadhav S, Chaudhari P, Maiti TK, Maji SK (2020) Induction of intracellular wild-type p53 amyloids leading to cellular transformation and tumor formation in mice. bioRxiv, doi.org/10.1101/2020.06.04.133124.

3. Pandey M, Bansal S, Bar S, Sokol NS, Tennessen JM, Kapahi P and Chawla G. miR-125-chinmo pathway regulates dietary restriction dependent enhancement of lifespan in Drosophila. bioRxiv 2020.09.01.277772; doi: https://doi.org/10.1101/2020.09.01.277772.

4. Walia Y, Kasera M, Ingole KD, Peddiraju S, Roy A, Laha D, Schaaf G, Bhattacharjee S (2020). Arabidopsis inositol polyphosphate kinases regulate COP9 signalosome deneddylase functions in phosphate-homeostasis. bioRxiv, doi: https://doi.org/10.1101/2020.10.02.323584.

5. Gulabani H, Goswami K, Walia Y, Noor JJ, Ingole KD, Roy A, Laha D, Schaaf G, Bhattacharjee S (2021). Arabidopsis inositol polyphosphate kinases IPK1 and ITPK1 modulate crosstalks between SA-dependent immunity and phosphate-starvation responses. bioRxiv, doi: https://doi.org/10.1101/2021.01.27.428180.

6. Laha NP, Dhir YW, Giehl RFH, Schäfer EM, Gaugler P, Shishavan ZH, Gulabani H, Mao H, Zheng N, Wirén NV, Jessen HJ, Saiardi A, Bhattacharjee S, Laha D, Schaaf G (2020). ITPK1-Dependent

Inositol Polyphosphates Regulate Auxin Responses in Arabidopsis thaliana. bioRxiv, doi: https://doi.org/10.1101/2020.04.23.058487.

7. Ingole KD, Kasera M, van den Burg H, Bhattacharjee S (2020). Contrasting functions of Arabidopsis SUMO1/2 isoforms with SUMO3 intersect to modulate innate immunity and global SUMOylome responses. bioRxiv, doi: https://doi.org/10.1101/2020.05.15.097535.

8. Garg T, Singh Z, Dwivedi AK, Varapparambathu V, Singh RS, Yadav M, Chandran D, Prasad K, Jain M, Yadav SR (2020). Genome-wide high resolution expression map and functions of key cell fate determinants reveal the dynamics of crown root development in rice. bioRxiv, doi.org/10.1101/2020.06.11.131565.

9. Lee S, Vemanna RS, Oh S, Rojas CM, Oh Y, Kaundal A, Kwon T, Lee HK, Senthil-Kumar M, Mysore KS (2020). Formate dehydrogenase (FDH1) localizes to both mitochondria and chloroplast to play a role in host and nonhost disease resistance. Preprints doi:10.20944/preprints202007.0272.v1.

Book chapters

1. Sadaqat Z, Kaushik S and Kain P (2021). Gut feeding the Brain: Drosophila gut an animal model for medicine to understand mechanisms mediating food preference. IntechOpen | DOI: http://dx.doi.org/10.5772/intechopen.96503.

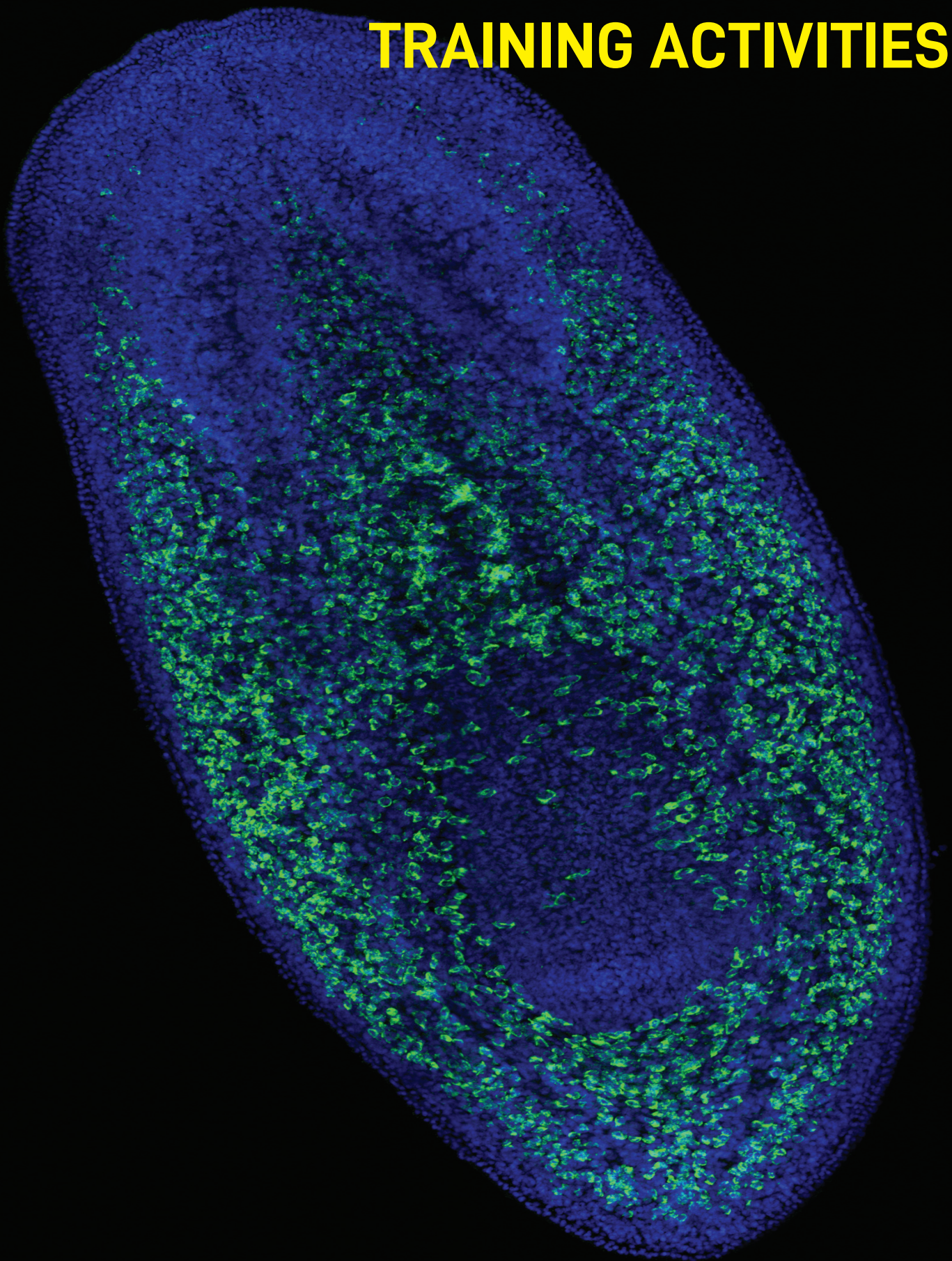
2. Pandey M, Bansal S, Chawla G (2021). Genomic DNA isolation from Drosophila. In: H. A. Ranganath, S.C. Lakhotia (Eds.) Experiments with Drosophila for Biology Courses. Indian Academy of Science, Bengaluru, India: 329-335.

3. Pandey M and Chawla G. Total RNA isolation from Drosophila using TRIzol based reagent. In: H. A. Ranganath, S.C. Lakhotia (Eds.) Experiments with Drosophila for Biology Courses. Indian Academy of Science, Bengaluru, India: 341-350.

Patent granted

Adlakha N, Munjal N (June 2020). Microorganisms for enhanced production of 2,3 butanediol and uses thereof; Indian patent application number 337873.

ACADEMIC & TRAINING ACTIVITIES



Academic Programmes

1. PhD Programme in Biotechnology

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

Currently, 104 students are working at RCB for the PhD degree in Biotechnology. During the current reporting period, 15 students were awarded the PhD degree.

2. PhD Programmes in Biostatistics & Bioinformatics

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

In addition to the core 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. The faculty members holding an adjunct 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, 11 students are registered with RCB for PhD in the above collaborative programmes.

3. PhD (Integrated) 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 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, 23 students are registered in the programme.

4. Research & Training Programme at RCB

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

Short-term summer trainings/ internships are also offered to students interested in research areas of specialization in RCB. Selection is based on the strength of resume and evaluation of write-up on their research interests. Selected candidates undergo research training under the mentorship of RCB faculty. They learn to carry out their own research projects in collaboration with other group members. Trainees get a realistic experience of several facets of conducting modern biological research and embarking on a research career. The training programmes range from two to six months' duration. During 2020-21 one student completed short-term internship while 28 students were imparted research training for six months' duration.

5. Academic Programmes at RCB's Recognized Centers

RCB has provided 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 the recognized programmes are registered at RCB for the award of their respective degrees. Currently, following institutions and their academic programmes are recognized by RCB. The details of various programmes are provided below:

Name of Recognized Centre	Courses Recognized	No. of students Registered
Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad	PhD (Biotechnology)	31
Center of Innovative and Applied Bioprocessing (CIAB), Mohali	PhD (Biotechnology)	4
National Institute of Animal Biotechnology (NIAB), Hyderabad	PhD (Biotechnology)	37
National Agri-Food Biotechnology Institute (NABI), Mohali	PhD (Biotechnology)	25
Institute of Life Sciences (ILS), Bhubaneswar	PhD (Biotechnology)	68
Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram	Msc (Biotechnology) PhD (Biotechnology)	71 8
Translational Health Science and Technology Institute (THSTI) Faridabad	PhD (Biomedical Sciences)	0
National Institute of Biomedical Genomics (NIBMG), Kalyani	MS-PhD (Integrated) Biotechnology (Specialization: Biomedical Genomics) PhD (Biotechnology) (Specialization: Biomedical Genomics)	17 20
Christian Medical College (CMC), Vellore	PhD (Medical Biotechnology; Specialization: Hematology) PhD (Medical Biotechnology; Specialization: Endocrinology)	6 1
National Centre for Cell Science (NCCS), Pune	PhD (Biotechnology)	3

Meet our Alumni

S. No.	Name of Student	Date of Award	Current Designation	Current Affiliation
1.	Abha Jain	09.02.2017	Post-doctoral Fellow	UNC Eshelman School of Pharmacy
2.	Jithesh Kottur	14.07.2017	Post-doctoral Fellow	Icahn School of Medicine at Mount Sinai, New York
3.	Gowtham Kumar Annarapu	29.11.2017	Post-doctoral Fellow	University of Pittsburg Medical school, USA
4.	Somanath Kundu	29.11.2017	Post-doctoral Fellow	Upstate Medical University, New York
5.	Sagar Pralhad Mahale	19.02.2018	Post-doctoral Fellow	University of Gothenburg, Sweden
6.	Pranita Hanpude	15.06.2018	Post-doctoral Fellow	Ohio State University
7.	Vedagopuram Sreekanth	10.07.2018	Post-doctoral Fellow	Harvard Medical School, Boston
8.	Roshan Kumar	26.10.2018	Post-doctoral Fellow	Michigan State University
9.	Rashi Singhal	07.01.2019	Post-doctoral Fellow	Michigan State University
10.	Shivlee Nirwal	11.01.2019	Post-doctoral Fellow	International Institute of Molecular and Cell Biology, Warsaw, Poland
11.	Gayatree Mohapatra	05.03.2019	Post-doctoral Fellow	Wiezmann Institute, Israel
12.	Priyanka Chaurasia	10.04.2019	Post-doctoral Fellow	Biomedicine Discovery Institute,
13	Amit Sharma	29.04.2019	Post-doctoral Fellow	Monash University, Clayton campus
14.	Salman Ahmed Mustafa	01.05.2019	Post-doctoral Fellow	Yale University, USA
15.	Rahul Kumar Sharma	27.05.2019	Post-doctoral Fellow	EMBL-Grenoble, 71 avenue des Martyrs, CS 90181, 38042 Grenoble Cedex 9, France
16.	Amrita Ojha	25.10.2019	Post-doctoral Fellow	Scripps Institute, Florida, USA
17.	Pregu Rajaih	01.11.2019	Post-doctoral Fellow	Amit Choudhary Lab, Brigham and Women's Hospital, Harvard Medical School and the Broad Institute of MIT and Harvard, Cambridge USA.
18.	Harsh Kumar	04.11.2019	Post-doctoral Fellow	All India Institute of Medical Sciences, New Delhi

Sr. No.	Name of Student	Date of Award	Current Designation	Current Affiliation
19.	Angika Bhasym	06.12.2019	Post-doctoral Fellow	National Institute of Health, Bethesda, USA
20.	Harmeet Kaur	17.01.2019	Data Scientist IV	Genetech, Franklin Park, New Jearsy, USA
21.	Tanu Johari	19.11.2019	Scientist	Smart Analyst, Gurugram, India
22.	Sanjay Kumar	30.06.2020	Post-doctoral Fellow	Mayo Clinic, USA
23.	Sandeep Kumar	17.07.2020	Post-doctoral Fellow	Johns Hopkins University, USA
24.	Naveen Narayanan	28.08.2020	Project Field Operating Officer	Regional Centre for Biotechnology
25.	Sheenam Verma	14.10.2020	Post-doctoral Fellow	Benaroya Research Institute at Virginia Mason
26.	Zaid Kamal Madni	13.11.2020	Project-RA	ICGEB, New Delhi
27.	Sarita Chandan Sharma	18.12.2020	Post-doctoral Fellow	Indian Institute of Science Education and Research (IISER), Tirupati
28.	Abhiruchi Kant	21.01.2021	Post-doctoral Fellow	Rutgers University, USA
29.	Nihal Medatwal	01.02.2021	Post-doctoral Fellow	University of Pennsylvania
30.	Syed Mohd. Aamir Suhail	03.02.2021	Post-doctoral Fellow	Harvard Uuniversity
31.	Sanjay Pal	10.02.2021	Post-doctoral Fellow	National Institute of Health, Bethesda, USA
32.	Raniki Kumari	11.02.2021	Post-doctoral Fellow	Johns Hopkins University, USA
33.	Meha Shikhi	12.02.2021	Post-doctoral Fellow	The European Molecular Biology Laboratory, Germany
34.	Ingole Kishor Dnyaneshwar	27.02.2021	Post-doctoral Fellow	University of Bonn, Germany
35.	Priyajit Banerjee	05.04.2021	Project SRF	Regional Centre for Biotechnology

Webinars/ Seminars

Speaker	Title	Date
Prof. Sanjeev Galande Indian Institute of Science Education and Research (IISER), Pune	Multimodal functional activity of SATB2 during early vertebrate embryogenesis: From genome organizer to regulator of tissue specification	March 19, 2021
Prof. Craig Montell, Distinguished Professor, University of California, Santa Barbara, USA	Cellular and molecular basis of taste sensation in Drosophila	March 19, 2021
Prof. Manzoor Bhat, Cellular and Integrative Physiology, UT Health San Antonio TX, USA	Molecular Principles of Saltatory Action: Potential Propagation in Myelinated Axons	March 19, 2021
Prof. Peter Dayan, Director, Max Planck Institute of Biological Cybernetics, Tubingen, Germany	Neural Reinforcement Learning	March 18, 2021
Prof. Richard Benton, Center for Integrative Genomics, University of Lausanne, Switzerland	Olfactory evolution: receptors, circuits and behaviors	March 18, 2021
Prof. Nancy Bonini, Department of Biology, University of Pennsylvania, USA	Drosophila as a model for human neurodegenerative disease	March 18, 2021
Prof. Sophie Scott, Institute of Cognitive Neuroscience, University College of London, UK	Laughter on the brain	March 17, 2021
Prof. Sanjay Sane, National Centre for Biological Sciences, TIFR, Bengaluru	Behavioral coordination in flying insects	March 17, 2021
Prof. Simon Sprecher, Department of Biology, University of Fribourg, Switzerland	Resolving neural circuits and functions at the single cell level	March 16, 2021
Prof. Ed Boyden, Departments of Brain and Cognitive Sciences, Massachusetts Institute of Technology, Cambridge, USA	Tools for Understanding and Repairing the Brain	March 16, 2021
Prof. Sandhya Koushika, Department of Biological Sciences, TIFR, Mumbai	Making & moving synaptic vesicles	March 15, 2021
Prof. Shubha Tole, Department of Biological Sciences, TIFR, Mumbai	Circuits of Sensation: How we Perceive the World	March 15, 2021
Dr. Steve Decker National Renewable Energy Laboratory, USA	Enzyme Engineering at NREL: Learning from Nature to Build a Better Cellulase	March 05, 2021
Dr. Rajan Sankaranarayanan CSIR - Centre for Cellular and Molecular Biology, Hyderabad	Chiral chekpiont during protein biosynthesis and their evolutionary implications	February 26, 2021
Dr. Dasaradhi Palakodeti Institute of Stem Cell Science and Regenerative Medicine, Bengaluru	Understanding body axis formation during regeneration in planarians	February 19, 2021
RCB Webinar Series: Commemorating 75th year of independence as part of Science Setu Programme	Celebrating the glory of Indian Science: Showcasing the life and works of Eminent Indian scientists - Dr. Janaki Ammal	February 19, 2021

Speaker	Title	Date
Dr. Prabodh Kumar Trivedi CSIR- Central Institute of Medicinal & Aromatic Plants, Lucknow	Interactions of small molecules play a bigger role in plant growth and development	February 12, 2021
RCB Webinar Series: Commemorating 75th year of independence as part of Science Setu Programme	Celebrating the glory of Indian Science: Showcasing the life and works of Eminent Indian scientists - Dr. Asima Chatterjee	February 12, 2021
Prof. Matthew D. Disney, Department of Chemistry, Florida Campus, Scripps Research, USA	Sequence-Based Design of Small Molecules Targeting RNA.	January 29, 2021
Prof. Purnananda Guptasarma, Department of Biological Scienes, Indian Institute of Science Education and Research (IISER), Mohali	The pleasures and annnoyances of three++ decades in science: Two and a half as a PI, and one as a professor.	January 29, 2021
RCB Webinar Series: Commemorating 75th year of independence as part of Science Setu Programme	Celebrating the glory of Indian Science: Showcasing the life and works of Eminent Indian scientists - Dr. V. Ramalingaswami	January 29, 2021
Dr. Thomas Pucadyil, Indian Institute of Science Education and Research (IISER), Pune	Membrane Fission: Insights From Reconstituting Organelle Form and Chemistry.	January 22, 2021
Prof. Paul Freemont, Faculty of Medicine, Department of Infectious Disease, Imperial College London	In vitro synthetic Biology – using cell free systems to prototype parts and pathways to enzymatic conversions in a test – tube.	January 15, 2021
Dr. Santosh Chauhan Institute of Life Sciences, Bhubaneswar	IRGM connects autophagy to inflammation and autoimmunity	December 18, 2020
Prof. Oliver Ebenhoeh CEPLAS – Cluster of Excellence on Plant Sciences, Dusseldorf, Germany	Thermodynamics aspects of metabolism and microbial growth	December 11, 2020
Dr. Shubhadeepn Chaterjee, Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad	Understanding the social language of bacteria : Speak or not to speak?	December 04, 2020
Dr. Andrew M. Lynn Professor School of Computational and Integrative Sciences, Jawaharlal Nehru University, Delhi	Looking Ahead!	November 30, 2020
Prof. Umesh Varshney, Department of Microbiology and Cell Biology, Indian Institute of Science, Bengaluru	A tRNA - centric view of translation initiation and its regulated by one- carbon metabolism in bacteria	November 27, 2020
Vivek T Natarajan, Principal Scientist, Skin and Pigment Cell Biology, CSIR-Institute of Genomics and Integrative Biology, Delhi	Deciphering cell fate transitions in melanocyte lineage	November 20, 2020
Mr. Angshuman Sarkar Head - Statistics, Biostatistics (India) GSK Pharmaceuticals Ltd	Quantitative Decision-Making in Clinical Development Plan	November 12, 2020

Speaker	Title	Date
Prof. Sayantan Banerjee Professor Operations Management & Quantitative Techniques, Indian Institute of Management (IIM), Indore	Merging science with Computing	October 30, 2020
Dr. P V Shivaprasad National Centre for Biological Science, TIFR, Bengaluru	Biogenesis and functions of small RNA regulators in plants	October 23, 2020
Dr. Sanghamitra Bandyopadhyay* JC Bose National Fellow Professor Machine Intelligence Unit Indian Statistical Institute Calcutta	Evolving Science with Data	October 15, 2020
Dr. B. Jayaram Professor, Department of Chemistry & School of Biological Sciences, Indian Institute of Technology, Delhi	Bioinformatics and Biostatistics 101	September 30, 2020
Dr. Maria Kowalczuk, Research Integrity Manager, Springer Nature, London	Ethics in Publishing	September 16 2020,
Ms. Sonal Shukla, Head - Abstracting and Indexing (A&I), Springer Nature, New York	Abstracting & Indexing – How to get indexed and how to increase the research impact	September 9, 2020
1. Dr. William Curtis, Executive Vice President, Medicine & Life Sciences (MLS) Journals 2. Dr. Jacco Flipsen, Vice President, MLS Journals 3. Ms. Pooja Aggarwal, Editorial Director, MLS Journals 4. Mr. Peter Butler, Editorial Director, MLS Journals 5. Dr. Mamta Kapila, Executive Editor, MLS Journals	Trends in Biomedicine & Life Sciences Publishing and Nuances & Tools of Scientific Publishing	September 2, 2020

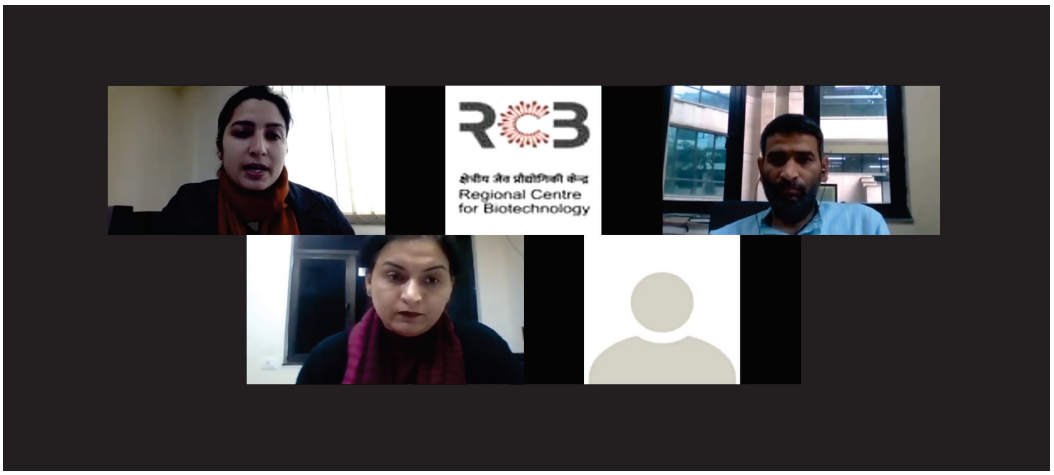
Events organized

Virtual Workshop On Mass Spectrometry Based Proteomics

ATPC organized an online workshop on Mass Spectrometry Based Proteomics on 04th & 18th February, 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. Towards this, online lectures and virtual demonstrations were organized on the following key themes:

- Basics of Mass Spectrometry and proteomics
- Routine Workflows for MS- based proteomics
- Sample preparation for IDA and iTRAQ
- Data Analysis: Protein pilot, Mascot
- Virtual demonstration on Triple TOF 5600

A total of 127 candidates attended the workshop.



RCB Foundation Day 2021

In 2016, RCB was ordained with the status of an "Institution of National Importance" through an Act of the Indian Parliament. It was brought into effect by a Gazette notification on 1st March, 2017. To commemorate this momentous occasion, 1st March has been adopted as the RCB Day.

The program began with a welcome address by Prof. Sudhanshu Vrati, Executive Director, RCB. Dr. Renu Swarup, Secretary, DBT, Guest of Honour for the day, joined through Skype and gave the RCB Day message. The RCB Day oration was given by Dr. Anurag Agarwal, Director, CSIR-IGIB.

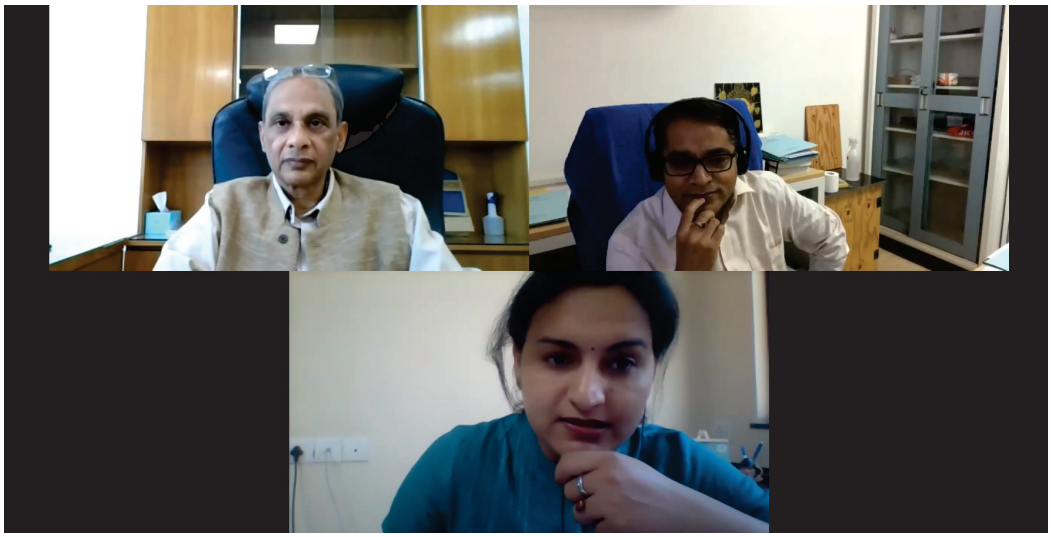
A mini research symposium presentation was also organised for the final year PhD students. The students presented their work before a panel of distinguished judges and award for the best scientific presentation was distributed to the winners.

Virtual Workshop on Basics of Electron Microscopy

ATPC organized a virtual workshop on Basics of Electron Microscopy on 03rd March, 2021. The main aim of the workshop was to introduce the participants to the basics of electron microscopy including, transmission electron microscopy, scanning electron microscopy and cryo-electron microscopy. The participants were familiarised with experimentation, technology, imaging parameters and troubleshooting primarily focussing on biological samples. The lectures and virtual practical demonstrations via in-house recorded videos focussed on the following:

- Basics of Transmission Electron Microscopy
- Sample Preparation for Transmission Electron Microscope
- Recent advances in single particle cryo-electron microscopy (cryo-EM) to determine the structure of biological macromolecules
- Sample preparation for Cryo-TEM
- Basics of Scanning Electron Microscopy
- Sample Preparation for Scanning Electron Microscopy

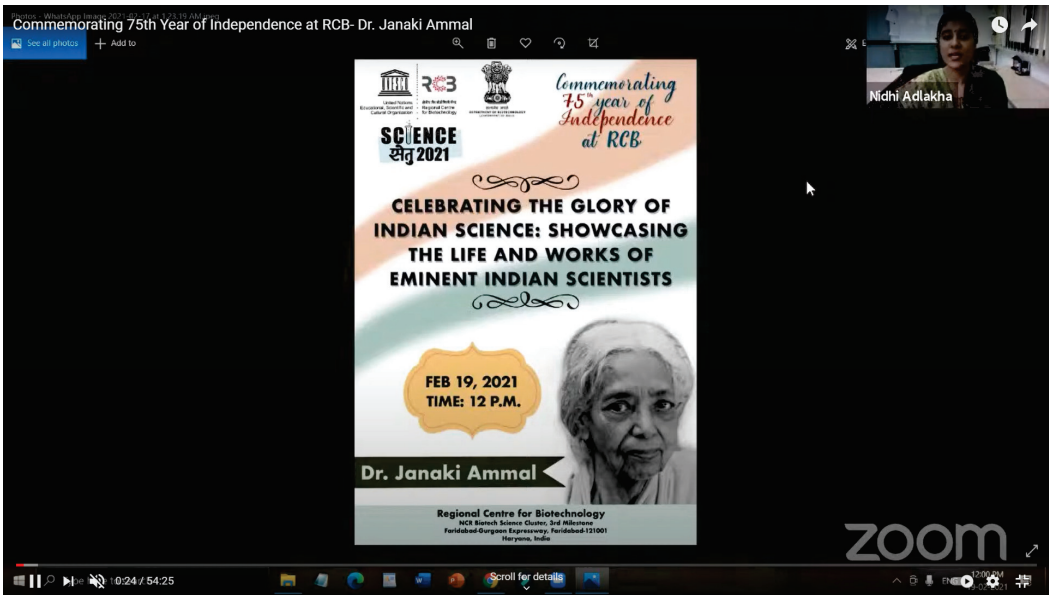
The workshop was attended by 110 candidates.



ID-75 Science Setu Webinar Series

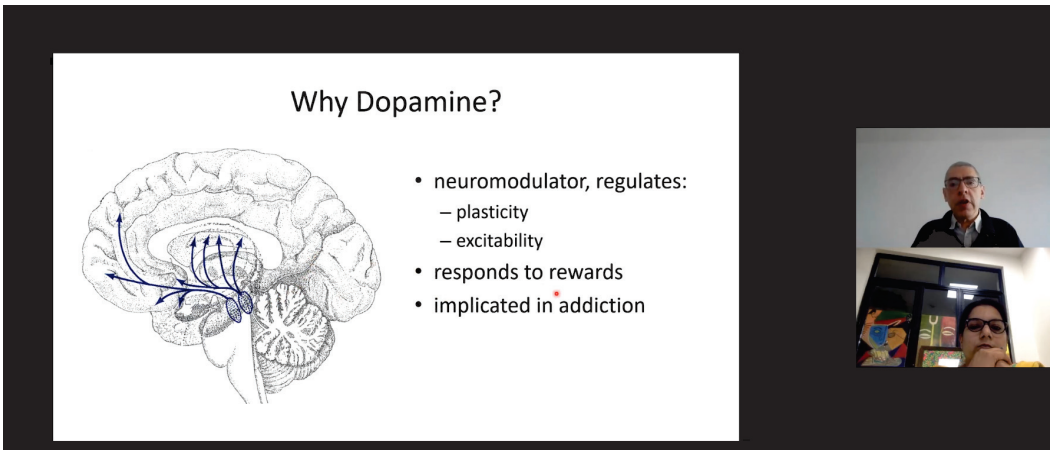
As a part of Science Setu and to commemorate 75th Year of Indian Independence, RCB is organizing webinar series (till August 2022) where the life and works of eminent Indian scientists who have made a difference to science and lives of people, and who have furthered science to its current glory in India and around the world are being showcased:

S.No.	Date	Theme/ Subject	Activity Details	Venue
1	29.01.2021	Celebrating the Glory of Indian Science: Showcasing the Life and Works of Eminent Indian Scientists	Dr. V. Ramalingaswami	Presentations delivered through RCB's YouTube channel
2	12.02.2021		Dr. Asima Chatterjee	
3	19.02.2021		Dr. Janaki Ammal	



Brain Awareness Week

An international webinar series was conducted and organized by Dr. Pinky Kain to celebrate the "Brain Awareness Week" from March 15-21, 2021. During this event, various speakers (international and national) were invited to discuss and unite on one platform to increase the awareness about nervous system disorders, its implications on mental health and diseases. The science on circuits of sensation; synaptic vesicles; neural circuits at single cell level; tools for repairing brain; anxiety and addiction in adolescence; laughter on the brain; behavioral coordination; neural reinforcement and learning; olfactory evolution; various neurodegenerative diseases; taste sensation; molecular principles of myelination were discussed. The overwhelming participation by students and researchers (Bachler's, Master's, PhD, Post–Docs and Scientists) made brain awareness week a big success. The exciting question and answer session after the talks throughout the webinars series helped participants to discuss their excitement about wonders of brain in a one to one manner. The webinars series also offered not only knowledge sharing but also availability of tools and reagents that could be shared between international scientific community to help each other.



Scientific events conducted

Deepti Jain

1. Organizer of celebratory event each month (ID75 series of webinars) as a part of DBT Science Setu program to commemorate India's 75th year of independence from Jan 2021-August 2021

CV Srikanth

1. Coordinated the RCB's Contemporary Webinar Series

Sam Mathew

1. Co-organized the online conference titled "Muscle and Diseases" on November 6-7, 2020.

Pinky Kain

1. Organized "Brain Awareness Week"- an international webinar series at Regional Centre for Biotechnology, NCR Biotech Science Cluster, Faridabad, India from March 15-21, 2021.

Divya Chandran

1. Organizer of celebratory event each month (ID75 series of webinars) as a part of DBT Science Setu program to commemorate India's 75th year of independence from Jan 2021-August 2021

Prashant Pawar

1. Supervised students to prepare a documentary on Dr V. Ramalingswami as a part of the RCB Science Setu ID75 program.

Nidhi Adlakha

1. Organizer of celebratory event each month (ID75 series of webinars) as a part of DBT Science Setu program to commemorate India's 75th year of independence from Jan 2021-August 2021

Membership of Professional/Academic bodies

Deepak T Nair

1. Member, Academic Management Committee, Regional Centre for Biotechnology
2. Member, Board of Studies, Regional Centre for Biotechnology
3. Co-opted Member, Interdisciplinary Science PAC, SERB
4. Member, Task Force on Research Resource Service Facility and Platforms (RRSFP) of DBT
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, Technical Committee to review proposals submitted to the European Synchrotron Radiation Facility Access Program of the Regional Centre for Biotechnology
7. Life Member, Indian Crystallographic Association
8. Life Member, Indian Biophysical Society
9. Life Member, Society of Biological Chemists
10. Elected Member, Guha Research Conference
11. Member, Purchase Finalization Committee of IIT-Delhi for procurement of 300 KV Cryo-Electron Microscope

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

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

Prem S Kaushal

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

Prasenjit Guchhait

1. Member of the Board of Study of the Apeejay Stya University, Gurugram (2019-2021).
2. Member, Steering committee of the Good Clinical Practice Professional Certification Scheme (GCPPCS), CDSA, THSTI, Faridabad (2020).

Tushar K Maiti

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

Sam Mathew

1. Member, Institutional Stem Cell Research Committee, THSTI, Faridabad
2. Member, Indian Society for Developmental Biology (InSDB)

Pinky Kain

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

Geetanjali Chawla

1. Member, American Medical Writers Association (AMWA)
2. Associate Editor, Journal of Experimental research on human growth and Aging (JERHA).

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, Klayani.
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, Scientific Advisory Group, INSACOG

CV Srikanth

1. Member of American Society for Microbiology
2. Member of Area Review Panel (ARP)-Therapeutics Meeting on Covid 19 Research Consortium (DBT)
3. Member of TEC of Infectious Disease Biology of DBT

Manjula Kalia

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

Arup Banerjee

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

Prasad Abnave

1. Member, Institutional Stem Cell Research Committee, THSTI, Faridabad
2. Review Editor for Frontiers in Cellular & Infection Microbiology
3. Review Editor for Frontiers in Cell and Developmental Biology

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

Sivaram Mylavarapu

1. Life Member, Indian Society for Cell Biology (ISCB)
2. Member, Review committee, Ramalingaswami re-entry fellowship annual progress, December 14, 2020
3. Member, Institutional Stem Cell Research Committee, THSTI Faridabad

4. DBT nominee, Institutional Biosafety Committee, Vyome Therapeutics Limited, Delhi

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

Saikat Bhattacharjee

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

Divya Chandran

1. Member, Fulbright-Nehru Postdoc Selection Committee (STEM-I), January 28-29, 2021
2. Member, Review Committee, Ramalingaswami re-entry fellowship annual progress, December 16, 2020
3. Council Member, Haryana Science & Technology Council, Women's Indian Chamber of Commerce and Industry, 2021
4. Member, International Society for Molecular Plant-Microbe Interactions (IS-MPMI)
5. Member, British Society for Plant Pathology (BSPP)
6. Associate Editor, Plant Molecular Biology Reporter

Nidhi Adlakha

1. Review Editor, Frontiers in Bioengineering and Biotechnology

Kinshuk Srivastava

1. Review Editor, Frontiers in Bioengineering and Biotechnology
2. Review Editor, Frontiers of Physics
3. Editorial Board Member, International Journal of Advanced Biotechnology Research

Distinctions, Honours and Awards

Sudhanshu Vrati

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

Sam Mathew

1. Article highlighted and interviews with first and corresponding authors published in Development: Agarwal M, Sharma A, Kumar P, Kumar A and Mathew SJ (2020). The people behind the papers. Development 147(7). pii: dev190025

Pinky Kain

1. Mentorship award by CSIR-Summer Research Training Program (SRTP) 2020

Geetanjali Chawla

1. India Alliance DBT/Wellcome Intermediate Fellowship (2018-2022)
2. Mentorship award by Freedom Employees Authority (FEA) 2020
3. Mentorship award by CSIR-Summer Research Training Program (SRTP) 2020

Prasad Abnave

1. DST-INSPIRE Faculty Fellowship Award

Anil Thakur

1. Ramalingaswami Fellowship, DBT, India

Shivram Mylavarapu

1. Article highlighted and interview of first author published in Journal of Cell Science: "First person-Amit Sharma." Journal of Cell Science (2020) 133(12):jcs249623

Rajender Motiani

1. India Alliance DBT/Wellcome Trust Intermediate Fellowship

Karthigeyan Dhanasekaran

1. Ramalingaswami Re-entry Fellowship

Ramu S Vemanna

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

Prashant Pawar

1. DST INSPIRE Faculty
2. DBT - Energy Bioscience Overseas Fellowship (Relinquished)

Nidhi Adlakha

1. INSPIRE Faculty Fellowship, DST

Lectures, Visits and Outreach

Deepak T Nair

1. Delivered an invited talk online titled "New answers to old questions regarding DNA synthesis by DNA polymerases" at IISER-Trivandrum on 16th October, 2020.
2. Delivered an invited talk titled "DNA synthesis by DNA polymerases: Old questions and new answers" as part of the webinar series titled Progress and Prospects in Biology on 2nd August, 2020.
3. Delivered an invited talk titled "An overview of the COVID19 pandemic" at the Colloquium organized by the IUCAA Centre for Astronomy Research and Development, Delhi University on 19th May, 2020.
4. Delivered an invited talk titled "Computational drug discovery and a potential antiviral for SARS-CoV-2" at the Global Online Conference on "Combating COVID-19: Through Bio-based Technologies" on 16th April, 2020 organized by Bennet University.
5. Delivered an invited talk online titled "DNA Replication: New answers to old questions" at Sukshjeev Society, Dept. of Microbiology, Bhaskaracharya College of Applied Sciences, University of Delhi on 19th March, 2021.

Deepti Jain

1. Nominated to represent RCB at the Mega Science Expo held as a part of India International Science Festival organized by DBT held virtually from December 22-25, 2020.
2. Delivered an invited talk titled "Antibiotic Resistance: Science is the key to fight the war" held online to Class IX students of Manav Rachna International School, Sector 14, Faridabad, 1st May 2020.
3. Delivered an invited talk titled "Regulation of motility to biofilm transition in Pseudomonas aeruginosa" held online to India Biofilm Society on 25th July, 2020.

4. Delivered an invited talk titled "Transcription Regulation of biofilm gene expression in Pseudomonas aeruginosa" held online in UK-India joint symposium organized by India Biofilm Society and NBIC on 5th September, 2020.

5. Participated in an invited panel discussion on "Biofilm related scientific and health challenges in India" at the Biofilm Baithak organized on 20th Feb. 2021 by the Biofilm society of India.

Vengadesan Krishnan

1. Attended and delivered an invited talk on 'How do pili in probiotic Lactobacillus rhamnosus GG enhance its persistence in the human gut for providing potential beneficial effects? - A Structural Biology Perspective' at the '5th Biennial Conference of PAi and International Symposium on Probiotics and Immunity: way forward to microbial theraphy' organized by Probiotic Association of India in association with ICAR-National Dairy Research Institute, Karnal, India, November 19-20, 2020.

2. Attended and delivered an invited talk on 'How do pili help to enhance the persistence of probiotic Lactobacillus rhamnosus GG in the gut for beneficial effects?' at virtual submit on 'Pre and Probiotics: A shift from pharmaceuticals to nutraceuticals', held on November 09, 2020.

3. Attended and participated in the following webinar series organized by DeLCON with publishers during April 2020 – September 2020.

    i. Attended a workshop on 'Fine tuning research planning using Scopus, ScienceDirect & Mendeley' organized by the DeLCON and Elsevier on 28th April 2020.

    ii. Attended a training session on 'How to publish with Oxford Journals' organized by the DeLCON and Oxford University Press on 24th July 2020.

    iii. Attended webinar on 'Open Research Publishing' organized by the DeLCON and Taylor and Francis on 11th August 2020.

    iv. Participated on training session on 'How to run effective searches on Wiley online library' organized by DeLCON and Wiley on 11th August 2020

    v. Attended webinar on 'Accessing T&F Journal & Open Access Features' organized by the DeLCON and Taylor and Francis on 19th August 2020.

    vi. Attended webinar on 'Publishing in academic journals and how to succeed with your publication' organized by the DeLCON and Taylor and Francis on 26th August 2020.

    vii. Attended webinar on 'Open Access options in Microbiology Society Journals' organized by the DeLCON and Microbiology Society on 30th August 2020.

    viii. Attended webinar on 'Trends in Biomedicine & Life Sciences Publishing and Nuances & Tools of Scientific Publishing' organized by the DeLCON and Springer Nature on 2nd September 2020.

    ix. Attended webinar on 'Abstracting & Indexing – how to get indexed and how to increase research impact' organized by the DeLCON and Springer Nature on 9th September 2020.

    x. Attended webinar on 'Publishing Ethics in Biomedicine & Life Sciences Research' organized by the DeLCON and Springer Nature on 16th September 2020.

Prem S Kaushal

1. Delivered a webinar on "Opportunities & fellowships in India to pursue research as a career option" organized by the Department of Higher Education, Kullu, HP, on September 27, 2020.

2. Showcased the research activity of structural biology at RCB, Faridabad, through virtual mode, in Vigyan Yatra as a part of the 6th India International Science Festival 2020 (IISF 2020) on December 21, 2020.

3. Delivered a Lecture on "Recent advances in single particle cryo- electron microscopy (cryo-EM) to determine the structure of biological macromolecules" at the virtual

Workshop on Basic of Electron Microscopy organized by ATPC, RCB Faridabad on March 3, 2021.

4. Demonstrated sample preparation for cryo- electron microscopy at the virtual Workshop on Basic of Electron Microscopy organized by ATPC, RCB Faridabad on March 3, 2021.

Sam Mathew

1. Delivered a talk titled "Myosins in muscle development" in the "Muscle and Diseases" online conference organized by Ashoka University, Sonepat, Haryana on November 6, 2020.

Pinky Kain

1. Seminar delivered on "Understanding the current pandemic-The biology behind Covid-19" in international Webinar organized by Pt. L. M. S. GOVERNMENT PG COLLEGE RISHIKESH (Sridev Suman Uttarakhand University) on "Science behind Covid-19 and its prevention, on October 17, 2020.

2. Seminar delivered on "Understanding salt taste modulation using Drosophila as a model system" in an international Webinar series on Arthropod Sensory organs organized by Department of Life Sciences, National Institute of Technology, Rourkela, India during October 12-16th, 2020.

3. Served as a mentor in the Council of Scientific and industrial Research (CSIR)-Summer Research training program (SRTP) (online), during 2020 July-August, 2020.

Geetanjali Chawla

1. Attended and presented poster titled 'miR-125 regulates dietary restriction dependent enhancement of lifespan in Drosophila' at the virtual meeting on Mechanisms of Aging organized by Cold Spring Harbor Laboratory, USA, during September 22-25, 2020.

2. Attended Webinar on India EMBO Lecture Courses on December 15, 2020.

3. Attended and showcased achievements of Regional Centre of Biotechnology at the Vigyaan Yatra program organized by India International Science Festival 2020 (virtual), on December 21, 2020.

4. Serving as a volunteer in the Evidence synthesis team of the Lancet Commission for Reimaging healthcare in India, since February, 2021.

5. Attended online protocol development workshop organized by Christian Medical College, Vellore, during March 8-April 9, 2021.

6. Serve as a mentor in the Freedom Employability academy since 2018.

7. Visited the Buck Institute for Research on Aging, Novato, California, USA, as part of a collaboration for the Wellcome-DBT India Alliance Intermediate fellowship project titled "Post transcriptional regulators of aging and dietary restriction", from February 1-September 6, 2021.

Sudhanshu Vrati

1. Delivered an invited talk on "Development of antivirals against SARS-CoV-2" in the Webinar series titled 'Response of the DBT's Autonomous Institutes to COVID-19 (Part-III)', organized by DBT on October 16, 2020.

2. Invited speaker in the DBT-Elsevier webinar on "Strengthening research capabilities remotely: Empowering Indian Research on COVID-19" on 22 May 2020.

3. 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 invited talk on the theme 'COVID-19: A Status on the development of Vaccine & Therapeutics' for the 'AFOB BioEconomy Webinar 2021' organized by AFOB, India Chapter (North Zone) in Association with RCB, Faridabad and GIET University, Gunupur (Odisha) on

26.03.2021.

CV Srikanth

1. Participated as a mentor in EMBO | IndiaBioscience Workshop on Oral Communication in Science, on January 12, 2021.

Manjula Kalia

1. Delivered an invited talk titled 'Proteome landscape of Japanese Encephalitis Virus' at the 2-day (online mode) conference entitled 'Host-pathogen interaction: present and future perspective' organized by Department of Life Science, NIT Rourkela, Odisha, on September 24-25, 2020.

Prasad Abnave

1. Participated in 13th Young Investigators' Meeting (YIM 2021) from March 17-19, 2021.

Anil Thakur

1. Attended a conference on "Candida and Candidiasis 2021" organised by Microbial Society, UK, during March 21-27, .2021

Avinash Bajaj

1. Delivered an invited talk titled 'Strengthening the pillars of Nanomedicine to Combat Cancer' at Indian Institute of Technology Delhi, on March 12, 2021.

Sivaram Mylavarapu

1. Delivered an invited colloquium talk titled "Tunneling Nanotubes: Secret Channels that Smuggle Cargo between Cells in Health and Disease" at the Department of Zoology, Deshbandhu College, University of Delhi, on October 01, 2020.

Rajender Motiani

1. Delivered a talk on the "Cell and Cancer Biology" research program at RCB. It was part of RCB Vigyan Yatra conducted for school students, college scholars and common layman audience under the umbrella of the 6th India International Science Festival (IISF), on December 21, 2020.

Karthigeyan Dhanasekaran

1. Delivered an invited talk titled 'Nup188, an inner PCM protein, functions in centriole duplication' at the Adichunchanagiri Institute of Molecular Medicine, BG Nagara, Adichunchanagiri University, on September 4, 2020.

Saikat Bhattacharjee

1. Delivered a virtual Seminar titled ' Arabidopsis inositol polyphosphate kinases regulate COP9 signalosome deneddylase functions in phosphate-homeostasis: Tale of a central Signalosome in (a)biotic stress responses' at the 'IISF, YSC' organized by Ministry of Earth Sciences, Ministry of Science and Technology, Ministry of Health & Family Welfare and Vijnana Bharati (VIBHA), on December 23, 2020.
2. Delivered an invited Seminar titled 'Functional Modulation of COP9 Signalosome in stress responses of Plants: Dancing to the tunes of Inositol Polyphosphates' at the 1st International Inositol Phosphate: The more the merrier' Conference, on January 11, 2021.

Divya Chandran

1. Delivered an invited talk titled 'Effectoromics-based identification of molecular targets for powdery mildew disease control' at the 'Recent Trends in Modern Biology Webinar' organized by P.D. Patel Institute of Applied Sciences, Charotar University of Science and Technology (CHARUSAT), Changa, Gujarat, on December 12, 2020.
2. Showcased RCB's research, training and education-related activities at the Mega Science,

Technology & Industry Expo, India International Science Festival, New Delhi, during December 22-25, 2020.

3. Delivered an invited lecture titled 'Single-cell and spatial transcriptomics using laser microdissection' as part of the 25th Refresher Course in Life Sciences and Biotechnology organized by JNU New Delhi, on January 06, 2021.

4. 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, Science Setu and Women's day, January-March 2021.

5. Delivered an invited lecture titled 'Unravelling legume-powdery mildew interactions by RNA-Seq' as part of the Webinar on 'Next-generation sequencing for deciphering host-pathogen interactions' organized by the Indian Phytopathological Society and Bionivid, on February 04, 2021.

6. Delivered an invited lecture titled 'Omics-based identification of molecular targets for powdery mildew disease control' as part of the Webinar organized by Department of Microbiology, Institute of Home Economics, University of Delhi, on March 26, 2021.

Ramu S Vemanna

1. Delivered a virtual talk in Vigyan Yatra, as a part of 6th India International Science Festival (IISF) 2020 organized by Regional Centre for Biotechnology, on December 21, 2020.

Prashant Pawar

1. Delivered talk at the International Virtual Conference of Plant Specialised Metabolism & Metabolic Engineering at CSIR-CIMAP, Lucknow, on October 15, 2020.

Ambadas Rode

1. Attended 'The RNA Institute Mini Symposium (Virtual), organized by University at Albany, State University of New York, during March 3-4, 2021.

2. Attended the '5th Annual Cell and Gene Therapy Symposium (Virtual)', organized by Centre for Stem Cell Research, Christian Medical College Campus, Bagayam, Vellore, during September 3-4, 2020.

Nidhi Adlakha

1. Delivered an invited talk titled 'Understanding metabolic networks as a tool to engineer the microorganisms' organised by Institute of Home Economics, University of Delhi, on March 26, 2021.

2. Attended 13th Young Investigators' Meeting (YIM 2021) held virtually, during February 17-19, 2021.

3. Participated as Mentor in MinSpar3.0 Ideathon organised by Venkateshwara College, University of Delhi, on March 21, 2021

Kinshuk Srivastava

1. Delivered a talk titled 'Synthetic biology: A programme at RCB' in IISF-RCB Vigyan Yatra, on December 21, 2020.

Reviewer of proposals/thesis/research articles

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 the journals Nucleic Acids Research, DNA Research, Journal of Structural Biology, Computational and Structural Biology Journal, and Scientific Reports
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 thesis from JNU, Manipal Academy of Higher Education, University of Calcutta and AcSIR

Deepti Jain

1. Examiner for PhD thesis from CDRI, IISER-Mohali, ILS and University of Calcutta
2. Reviewer for journals Nucleic Acids Research, Biochemistry, Scientific Reports, PLoSOne and Environmental Microbiology

Vengadesan Krishnan

1. Reviewer for thesis from University of Madras and JNU
2. Examiner for PhD viva-voce at CDRI
3. Reviewer for research articles from International Journal of Biological Macromolecules, Microbial Pathogenesis, and International Journal of Data Mining and Bioinformatics

Prem S Kaushal

1. Reviewer for research proposals for SERB-IRHPA Cryo-electron microscopy for macromolecular structure and complexes
2. Reviewer for research grants of DST-SERB

Prasenjit Guchhait

1. Reviewer for US-India Fulbright-Nehru Fellowship for postdoctoral research abroad 2020
2. Reviewer for Indo-Australia Biotechnology Fund (IABF), DBT, Govt. of India 2020
3. Reviewer for research proposals for BIRAC, DBT, Govt. of India, IIT Kanpur Innovative Centre, 2020
4. Reviewer for research proposals for BIRAC, DBT, Govt. of India, NCL Pune Incubator, 2020
5. Reviewer for research proposals for BIRAC, DBT, Govt. of India, CCAMP Bangalore Incubator, 2019-2020
6. Reviewer for Scientific Journals: Frontier in Immunology, 2021

Tushar K Maiti

1. Reviewer for Biochemical J, Biomacromolecules, J Proteomics, Bioscience Report, International Journal of Biological Macromolecules
2. Reviewer, DST-CRG grant proposal
3. Reviewer, PhD thesis entitled "Studies on role of wild type and spliced isoform of metadherin in breast cancer progression, IICT Hyderabad, AcSIR

Sam Mathew

1. Reviewer for research proposals for DBT, CSIR, Israel Science Foundation, Medical Research Council (UK), and INSERM-CNRS (France)
2. Reviewer for PhD thesis from Manipal University, Sastra University and AcSIR
3. Reviewer for Scientific Journals: Cell Death and Disease, Developmental Biology, FASEB J, Molecular Therapy-Nucleic Acids, IUBMB Life and Scientific Reports

Pinky Kain

1. Reviewer for Scientific Journals: Science Progress, Scientific reports, Neuroscience Insights
2. Reviewer and thesis committee member of Saba Ashfeen (Jamia Hamdard University, Delhi, Department of toxicology)
3. Reviewer for research grants of CSIR EMR-II

Geetanjali Chawla

1. Reviewer for Scientific Journals: eLife, Scientific Reports, MicroRNA

Manjula Kalia

1. Reviewer for Scientific journals: Autophagy, Journal of Virology, Brain Research, Journal of Neurochemistry, Virology, Virus Disease, Veterinary Microbiology
2. Reviewer for SERB-CRG scheme proposals
3. Examiner for PhD thesis from CSIR-CDRI, Lucknow
4. Examiner for M.Biotech thesis from AIIMS, New Delhi

Prasad Abnave

1. Reviewer for Scientific journals: Open Life Sciences. Pathogens

Anil Thakur

1. Reviewer for Scientific reports

Sivaram Mylavarapu

1. PhD thesis examiner for Mr. Vipin Kumar, National Institute of Immunology, Jawaharlal Nehru University, New Delhi
2. Reviewer for Journal of Cell Science

Rajender Motiani

1. Reviewer for research proposals/grants for SERB, DST
2. Reviewer for Journal of Biological Chemistry, Scientific Reports, Frontiers in Cell & Developmental Biology, Mitochondrion and Cell Calcium
3. Ph.D. Thesis Examiner of Ms. Akansha Rai, Institute of Genomics and Integrative Biology (IGIB), New Delhi

Karthigeyan Dhanasekaran

1. Reviewer for IEEE Access

Ambadas B. Rode

1. Reviewer for Scientific journals: Progress in Molecular Biology and Translational Science (Elsevier); Engineering in Life Sciences (Wiley); and Frontiers in Genetics
2. Reviewer for research grants of DST

Saikat Bhattacharjee

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

Divya Chandran

1. Reviewer for Scientific journals: BMC Molecular and Cell Biology, Phytopathology, Genes, Plant Methods, Scientific reports, Genomics

Ramu S Vemanna

1. Reviewer for SERB-CRG scheme proposals
2. Reviewer for Scientific journals: Plant Physiology, Plant Biotechnology, Canadian Journal of Plant Pathology, Frontiers in Plant Science, Plant Physiology and Biochemistry, Scientific Reports, 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

Prashant Pawar

1. Reviewer for Scientific journals: Frontiers in Bioengineering and Biotechnology, Frontiers in Energy Research, Plant Physiology and Biochemistry

Nidhi Adlakha

1. Reviewer for research grants of DBT and CSIR
2. Reviewer of PhD thesis from ICT Mumbai
3. Reviewer for Scientific journals: Applied and Microbial Technology and Infections and Biotechnology for Biofuel

Kinshuk Srivastava

1. Reviewer for Scientific journals: Nature Catalysis, Frontiers of Physics, RSC, OMICS journals

EXTRAMURAL ACTIVITIES & NETWORKING

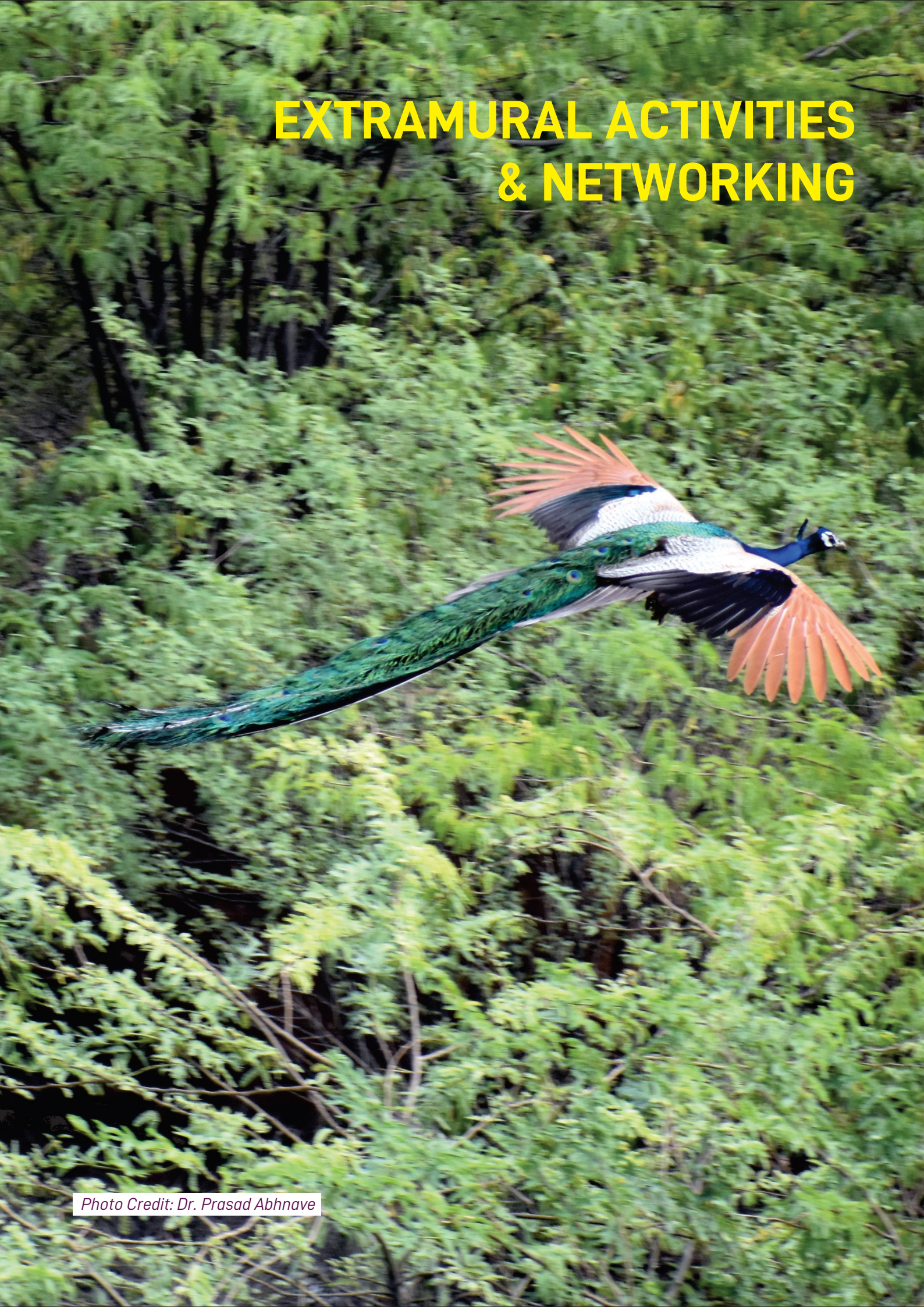


Photo Credit: Dr. Prasad Abhnave

ESRF Access Program

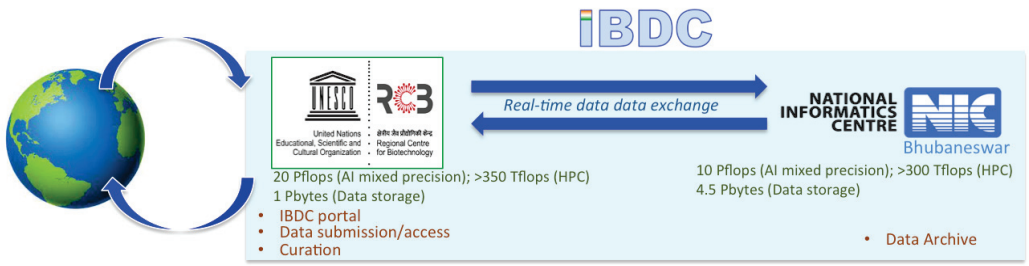
Regional Centre for Biotechnology (RCB) and European Synchrotron Radiation Facility (ESRF) have entered into an agreement concerning the medium-term use of synchrotron for non-propriety research for the benefit of the Indian scientific community as a whole, and notably the structural biology research groups. The program provides access to Indian investigators to high intensity macromolecular crystallography, small angle X-ray scattering experimental stations and the Cryo-Electron Microscopy Facility located in ESRF. The initial agreement was renewed recently by Prof. Vrati and Dr. Francesco Sette (Director General, ESRF) for another three years till January, 2023 and this endeavor was supported by the present DBT Secretary, Dr. Renu Swarup. ESRF has undergone an extensive upgrade recently and is, at present, the only fourth generation synchrotron in the world. The DBT-supported ESRF access program of the RCB helps Indian researchers to carry out experiments at this unique facility located in Grenoble, France.

Since the start of this arrangement, researchers from 25 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 (Bhubaneswar), 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 (Bhubaneswar), 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) and National Chemical Laboratory (Pune).

The ESRF access program has enabled Indian researchers to publish several research papers in International peer-reviewed journals involving basic and applied research. 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 (IBDC)

The Indian Biological Data Center (IBDC) is a national facility established at RCB with support from the Department of Biotechnology, Govt. of India. The Centre is mandated to archive all publically funded life science data generated at national level. This is in accordance to the 'National Biological Data Access Policy' that is being actively discussed at cabinet level and is expected to be implemented soon. Housed at RCB, the IBDC is being developed under active collaboration with NIC, NII and ICGEB, New Delhi. The computational infrastructure including a High Performance Computation (HPC) cluster and archival data storage will be jointly hosted at RCB and NIC, Bhubaneswar. RCB will house a compute power of about 20 PetaFlops (AI mixed precision), >350 TeraFlops (HPC) along with a 1 PB (PetaByte) of storage, while NIC (Bhubaneswar) would house about 10 PetaFlops (AI mixed precision), >300 TeraFlops (HPC) along with a 4.5 PB of data storage. The two sites will be connected by high band-with internet connectivity through NKN. The biological data generated by researchers in India will be curated at RCB and hosted by NIC, Bhubaneshwar for seamless access by users. Owing to the magnitude and complexity of the expected data, IBDC is being developed in a modular nature. The first two sections being developed are the 'Indian Nucleotide Data Archive' (INDA) and the 'Structure Biology Database, India' (SBDi). User-friendly portals are being developed for data submission and access. These data portals are based on internationally accepted data formats thus ensuring seamless exchange of data. IBDC shall have a clearly defined and transparent data access policy primarily based on the provisions provided in the 'National Biological Data Access Policy'.



Diagrammatic schema of IBDC storage & compute infrastructure

Active efforts are being made to establish collaborations with international repositories such as European Nucleotide Archive (ENA), European Molecular Biology laboratory (EMBL) and Protein Data Bank (PDB) to ensure global recognition of IBDC. Besides, archiving life science data, IBDC shall also indulge in developing highly curated data sets. Consequently, IBDC shall also develop interfaces with national research groups/consortiums etc. for domain specific expertise.

The IBDC team include personnel with diverse background including IT experts, biocurators and biologists. A total of 12 personnel have been recruited so far and more are expected to join in near future.

The IBDC will host conferences and workshops to increase the number of manpower skilled in data sciences in the country. The data stored at the IBDC will enable big data analytics to identify emergent properties in biological systems and thus aid the development of novel solutions for problems faced by Indians in the areas of health, agriculture and the environment.

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 (Department of Biochemistry, Indian Institute of Science, Bangalore) Dr. S. Batra, (CSIR-Central Drug Research Institute) Dr. Debasisa Mohanty, (National Institute of Immunology), Dr. Dinesh Gupta, (International Centre for Genetic) Engineering and Biotechnology-New Delhi) Mr. Sudhir Chandra, (National Informatics Institute) Dr. Dinakar M. Salunke, International Centre for Genetic Engineering and Biotechnology-New Delhi)
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's group (University of Helsinki, Finland), Dr. Partha Roy (IIT, Roorkee)
Dr. Prem S. Kaushal	Dr. Rajesh Prakesh Ringe, IMTECH, Chandigarh, and Dr. Anil Thakur, RCB, Faridabad
Prof. Prasenjit Guchhait	Prof. Josef T Prchal (Univs of Utah, Salt lake city, USA), Prof. Perumal Thiagarajan (Baylor College of Medicine, Houston, USA), Dr. Navaneetha Rao (RythRx Therapeutics, Ann Arbor, USA), Prof. Tulika Seth, Prof. Rajesh Khatgawat, Prof. Naval Vikram, (AIIMS, New Delhi), Prof. Parvaiz Kaul (SKIMS, Srinagar), Prof. Ramandeep Singh, Dr. Sankar Bhattacharyya, Dr. Shailendra Asthana, Dr. Milan Surjit (THSTI, Faridabad), Prof. Anirban Basu (NBRC, Manesar), Dr. Sanjay Banerjee (NIPER, Guwahati), Prof. S. Eswaran (TERI, Gurugram), Dr. Surajit Karmakar (INST, Mohali), Dr. Soumen Basak (NII, New Delhi), Prof. Sudhanshu Vrati, Prof. Avinash Bajaj, 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, Delhi), Dr. Palanimurugan Rangasamy (CSIR-CCMB, Hyderabad)
Dr. Pinky Kain	Prof. S.V. Eswaran (TERI, Delhi), Prof. Suhel Parvez (Jamia Hamdard University, Delhi), Prof. Monalisa Mishra (NIT, Rourkela, India), Prof. Axel Brockmann (NCBS-TIFR, Bangalore, India), Prof Teiichi Tanimura (Nagoya Japan), Prof. Pankaj Kapahi (Buck Institute, California, USA), Dr. Nisha N Kannan (IISER Thiruvananthapuram)
Dr. Geetanjali Chawla	Prof. Pankaj Kapahi (The Buck Institute for Research on Aging, CA, USA), Dr. Nick Sokol (Indiana University), Dr. Jason Tennessen (Indiana University), Dr. Monika Garg (NABI, Mohali)
Prof. Sudhanshu Vrati	Dr. Milan Surjit (THSTI), Dr. Renu Wadhwa (AIST, Japan), Dr. Anirban Basu (NBRC, Manesar), Dr. Arup Banerjee (RCB), Dr. Gulam Seyed (ILS, Bhabaneshwar)

Dr. CV 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
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)
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 and Dr. Arnab Mukhopadhyay, 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. Rajender K. Motiani	Dr. Rajesh S Gokhale (NII, New Delhi), Dr. Sridhar Sivasubbu (IGIB, New Delhi) and Dr. Vivek Natarajan (IGIB, New Delhi)
Dr. Ambadas B. Rode	Prof. Naoki Sugimoto (FIBER, Konan University), Prof. Sheshnath Bhosale (Goa University), Dr. Deepak Salunke (Panjab University), Dr. Ramandeep Singh (THSTI, Faridabad).
Dr. Saikat Bhattacharjee	Dr. SV Eswaran (TDNBC, Faridabad), Dr. Nimisha Sharma (GGSIPU, New Delhi), Dr. Ramu Vemanna (RCB, Faridabad), Dr. Debabrata Laha (IISc, Bengaluru), Dr. Walter Gassmann (University of Missouri-Columbia, USA, 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. Igor Grigoriev, Dr. Sajeet Haridas (Joint Genome Institute, USA), Dr. Shri Ram Yadav (IIT, Roorkee), Dr. Atul Goel (CDRI, Lucknow), Dr. Yashwant Kumar (THSTI, Faridabad), Dr. Vineet Ahuja (AIIMS, New Delhi), Dr. Bonamali Pal (Thapar Institute of Engineering and Technology, Patiala), Dr. Senjuti Sinharoy, Dr. Senthil Kumar Muthappa (NIPGR, New Delhi), Dr. Deepti Jain, Dr. Sivaram Mylavarapu (RCB, Faridabad), Dr. Nirpendra Singh (ATPC, NCR Biotech Science Cluster, Faridabad)
Dr. Ramu S. Vemanna	Prof. Udayakumar M, 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, New Delhi), Dr. Maneesh Bhandari (Forest Research institute, Deharadun), Dr. Saikat Bhatacharjee, Dr. Avinash Bajaj (RCB, Faridabad)
Dr. Prashant Mohan Pawar	Dr Ewa J Mellerowicz (UPSC, Sweden), Dr Clint Chapple (Purdue University, USA), Dr Lakshmi Kasirajan (SBI, Coimbatore), Dr Yashwant Kumar (THSTI, Faridabad), Dr Kinshuk Srivastav, Dr Nidhi Adlakha, Dr Ambadas Rode, Dr Nidhi Adlakha (RCB, Faridabad).

Dr. Nidhi Adlakha	Dr. Syed Shams Yazdani, Dr. Charanpreet (ICGEB, New Delhi), Dr. Tarun Sharma (THSTI, Faridabad), Prof. Rakesh Bhatnagar (JNU, New Delhi)
Dr. Kinshuk R. Srivastava	Prof. S. K. Khare (IIT Delhi), Dr. V. Sood (Jamia Milia University, New Delhi), Dr. Prashant Pawar, Dr. Ramu S. Vemanna, Dr. Anil Thakur (RCB, Faridabad), Prof. David Sherman (University of Michigan, USA), Prof. B. Ruotolo (University of Michigan, USA)

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 lakhs	2018-21
2.	Prof. Deepak T. Nair	Mechanism of mutagenic & translesion DNA synthesis by a mycobacterial Y-family DNA polymerase	Science & Engineering Research Board	57.9 lakh	2017-20
3.	Prof. Deepak T. Nair (Co-PI)	Molecular Interactions critical for DNA Mismatch Repair	Science & Engineering Research Board	Total grant: 59.6 lakhs Grant for RCB: 24.9 lakhs	2017-21
4.	Prof. Deepak T. Nair (Co-PI)	Access to Macromolecular Crystallography Beamlines, France	Department of Biotechnology	1749.4 lakhs	2017-21
5.	Dr. Deepti Jain	Insights into the signal transduction mechanism of GraXSR regulon required for antibiotic resistance in *Staphyloccocus aureus*	Science & Engineering Research Board	43.8224 lakhs	2019-22
6.	Dr. Deepti Jain	Structure and mechanism of FleQ, master regulator of transcription of flagellar and biofilm genes in *Pseudomonas aeruginosa*	Department of Biotechnology	68.088 lakhs	2018-21
7.	Dr. Deepti Jain	Establishing the mechanism of action of Bg_9562, the broad spectrum antifungal protein	NCR BioCluster Grant	20 lakh	2019-21
8.	Dr. Vengadesan Krishnan	Structural studies on pilus proteins from *Lactobacillus ruminis*	Department of Biotechnology	44.5 lakh	2018-22
9.	Dr. Vengadesan Krishnan (Co-PI)	Investigating Functional Role of Polyketide Modifying Enzymes in Mycobacterial Biology	Science & Engineering Research Board	46.7 lakh Grant for RCB: 8.1 lakh	2019-22
10.	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

11.	Prof. Prem S. Kaushal	Understanding the translation strategies adopted by *M. tuberculosis* during dormancy	Science and Engineering Research Board	46.33 lakh	2019-21
12.	Prof. Prasenjit Guchhait	Mechanism of rapid propagation of dengue virus during infection	Department of Biotechnology	100.1 lakh	2018-21
13.	Prof. Prasenjit Guchhait	Identification of small molecule inhibitors of PF4 and CXCR3 to prevent Dengue and JEV infection in host	Science and Engineering Research Board	57.08 lakh	2019-22
14.	Prof. Prasenjit Guchhait	Role of platelet activation in the development of systemic inflammations in patients with type-2 diabetes.	Department of Biotechnology	71.59 lakh	2019-22
15.	Dr. Tushar Kanti Maiti	Inter-institutional programme for Maternal, Neonatal and Infant Sciences: a translational approach to studying PTB	Department of Biotechnology	613 lakh	2013-21
16.	Dr. Tushar Kanti Maiti	A "bench to bedside" model for clinical and translational science between academic research institutes and hospitals focused on fetal growth restriction and preterm birth."	Department of Biotechnology	23.13 lakh	2018-23
17.	Dr. Tushar Kanti Maiti	Multi-Omics Signatures of Human Placenta: Real time assessment of underlying mechanisms for prediction of birth outcomes and development	Department of Biotechnology	64.77 lakh	2020-23
18.	Dr. Tushar K. Maiti	MOMI: Biorepository local analysis- INDIA	BMGF	61.85 lakh	2021-22
19.	Dr. Sam J. Mathew	The role of Transducin-like Enhancer of Split 3 (TLE3) in regulating myogenesis.	Science and Engineering Research Board	64 lakh	2017-21
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.	India Alliance DBT/Wellcome Trust Early Career Fellowship	167 lakh	2018-22
21.	Dr. Sam J. Mathew	Functional characterization of skeletal muscle myosin heavy chain-embryonic in adult muscle regeneration and disease.	Department of Biotechnology	77 lakh	2020-23

22.	Dr. Pinky Kain Sharma	Understanding taste and its modulation using *Drosophila melanogaster*	India Alliance DBT/Wellcome Trust Intermediate Fellowship	350 lakh	2016-21
23.	Dr. Geetanjali Chawla	Post-transcriptional regulators of aging and dietary restriction	India Alliance DBT/Wellcome Trust Intermediate Fellowship	359 lakh	2018-22
24.	Prof. Sudhanshu Vrati	DBT-AIST International Center for Translational and Environmental Research (DAICENTER)	Department of Biotechnology	145 lakh	2018-21
25.	Dr. Kanchan Bharadwaj (Mentor: Prof. Sudhanshu Vrati)	Metagenome Sequence Analysis of the Distal Gut Virome in Healthy Indian Adults	Department of Biotechnology	58.21 lakh	2017-20
26.	Prof. Sudhanshu Vrati	DBT-HRD Project & Management Unit at RCB, Faridabad	Department of Biotechnology	414 lakh	2020-21
27.	Prof. Sudhanshu Vrati	Sub-Network1: Studies on anti-SARS-CoV2 activity of selected medicinal plants and formulations in cell culture model of virus infection	Department of Biotechnology	39.24 lakh	2020-21
28.	Dr Chittur V. Srikanth & Dr Girish Ratnaparkhi	From the gut SUMO cycles its way into gastrointestinal disorders	MHRD	93.34 lakh	2020-23
29.	Dr. Aamir Suhail (mentor Dr CV Srikanth)	Studies on understanding the role of E3 Ubiquitin ligase Siah2 in inflammatory bowel disease	Department of Health Research	27.83 lakh	2020-23
30.	Dr. Manjula Kalia	Pharmacological Modulation of Autophagy as a Potential Therapeutic for Japanese encephalitis	Department of Biotechnology	81.2 lakh	2019-22
31.	Dr. Arup Banerjee	Understanding the therapeutic role of adult stem cell-derived exosome in combating virus-induced neurodegenerative disease	Department of Biotechnology	Total grant: 81.38 lakh Grant for RCB: 29 lakh	2018-21
32.	Dr. Arup Banerjee	Investigating the molecular modulators of microglial activation and their effect on JEV pathogenesis	Science and Engineering Research Board	41.12 lakh	2018-21

33.	Dr. Prasad Abnave	Investigating molecular mechanisms governing the proliferation-differentiation balance in adult stem cells during chronic infections.	Department of Science & Technology	35 lakh	2019-24
34.	Dr. Prasad Abnave	Investigating histone methylation changes induced in adult stem cells during bacterial infections.	Science and Engineering Research Board	28.32 lakh	2020-22
35.	Dr. Anil Thakur	Translation dynamics govern fungal virulence and drug resistance in Candida species	Department of Biotechnology	42.50 lakh	2020-25
36.	Dr. Anil Thakur	Characterization of translation initiation codons dynamics to determine pathogenicity of Candida albicans	Science and Engineering Research Board	23.46 lakh	2020 -22
37.	Dr. Avinash Bajaj	Targeting Molecular Probes for Diagnosis of Mycobacterial Infections	Science and Engineering Research Board	50.446 lakh	2019-22
38.	Dr. Avinash Bajaj	Combating Topical and Medical Device Related Multidrug Resistant Fungal Infections Using Molecularly Engineered Anti-Fungal Hydrogels	Department of Biotechnology	92.39 lakh	2019-22
39.	Dr. Avinash Bajaj	Spatiotemporal Targeting of Multiple Pathway using Engineered Polymer Gatekeepers in Porous Nanomaterials for Cancer Combination Therapy	Department of Science & Technology	60.77 lakh	2018-21
40.	Dr. Avinash Bajaj	Engineering of membrane targeting molecular probes for diagnosis of mycobacterial infections	Science and Engineering Research Board	50.45 lakh	2019-22
41.	Dr. Avinash Bajaj	Temporal targeting of siRNA therapeutics to the gastrointestinal tract (GIT) using chimeric nanogels	Department of Biotechnology	84.3 lakh	2017-20
42.	Dr. Avinash Bajaj	Investigating the role of BLM Helicase as a global tumor suppressor: understanding its regulatory loops and using the knowledge for therapeutic and clinical applications in cancer biology	Department of Biotechnology	29.4 lakh	2015-20

43.	Dr. Avinash Bajaj	Deciphering the Impact of Time-Restricted Feeding (TRF) as a Neoadjuvant Intervention with Chemotherapy for Cancer Treatment, and its Regulatory Mechanisms	NCR BioCluster Grant	20 lakh	2020-22
44.	Dr. Avinash Bajaj	Towards development of a potent antiviral against the SARS CoV2 by targeting the interaction between nucleocapsid protein and viral RNA	Science and Engineering Research Board	9.72 lakh	2020-23
45.	Dr. Sivaram V. S. Mylavarapu	Prolyl Isomerization of Dynein Light Intermediate Chain Subunits as a Regulatory Driver in Mitosis	Science & Engineering Research Board (SERB)	22 lakh	2018-21
46.	Dr. Pushpa Kumari (mentor Dr. Sivaram V. S. Mylavarapu)	Understanding the role of Exocyst complex in cell division and development in *Caenorhabditis elegans*	India Alliance DBT Wellcome Trust Early Career Fellowship	144 lakh	2014-20
47.	Dr. Rajender K Motiani	Role of ER and Mitochondria in Pigmentation: Organellar Calcium signaling perspective.	India Alliance DBT/ Wellcome Trust	360 lakh	2020-25
48.	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	2019-21
49.	Dr. Saikat Bhattacharjee	Investigating a key regulatory defense assembly and pathogen effector-induced perturbations during innate immune signaling of plants	Department of Biotechnology	92.01 lakh	2018-21
50.	Dr. Saikat Bhattacharjee	The identification and characterization of defense signaling pathways primed by Sea6 Energy products	Sea6 Energy Pvt. Ltd., Bengaluru	8.13 lakh	2020-21
51.	Dr. Divya Chandran	Elucidation of the functional interactome of legumes with the fungal pathogen *Erysiphe pisi* as keys to powdery mildew disease resistance	Science and Engineering Board	43.98 lakh	2020-23

52.	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
53.	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)	52.91 lakh	2019-22
54.	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
55.	Dr. Ramu S Vemanna	Disruption of genome integrity to create genetic variability by editing (Using CRISPR Cas9) the genes associated with DNA mismatch repair and characterization of their relevance in crop improvement	Department of Biotechnology	70.168 lakh	2017-20
56.	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
57.	Dr. Prashant Mohan Pawar	Understanding plant cell wall biosynthesis to optimize lignocellulosic biomass	Department of Science and Technology (INSPIRE)	35 lakh	2018-23
58.	Dr. Prashant Mohan 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)	26.70 lakh	2020-21
59.	Dr. Ambadas B. Rode	Rationally targeting & tuning riboswitch mediated gene regulation for therapeutic and synthetic biology application	Department of Biotechnology	88 Lakhs	2018-23
60.	Dr. Ambadas B. Rode	Design and synthesis of small molecules to target nucleic acids structures for therapeutic applications: Targeting riboswitches for antibacterial therapy	SERB-SRG	19.324 lakh	2019-21

61.	Dr. Nidhi Adlakha	Understanding mechanism underlying plant invasion and survival by *B. cinerea* using temporal secretome mining approach	Science and Engineering Research Board	27.03 lakh	2019-21
62.	Dr. Nidhi Adlakha	Development of *Paenibacillus polymyxa* as a platform for the production of branched chain alcohols	DBT-Mission Innovation- IC4 grant	*Total grant:* 89.58 lakh *Grant for RCB:* 0 lakh	2019-22
63.	Dr. Nidhi Adlakha	Unravelling transcriptional regulation of cellulase gene overexpression in *Talaromyces* sp. NA01	NCR Biotech cluster grant	20 lakh	2020-22
64.	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
65.	Dr. Kinshuk R. Srivastava	Biocatalytic combinatorial synthesis of cyclic dipeptides for diverse biological activity	Department of Biotechnology	42.5 lakh	2019-24
66.	Dr. Kinshuk R. Srivastava	Development of imine reductase based biocatalytic technology for the synthesis of chiral amines and amino acids for diverse industrial application	Department of Science & Technology	25 lakh	2021-23
67.	Dr. Rajendra P. Roy	Semisynthetic histones with defined chemical marks for interrogation of eraser specificity	Science and Engineering Research Board	40.73 lakh	2020
68.	Prof. Sudhanshu Vrati (Co-ordinator) Dr. Deepak Nair (PI)	Setting up of the Indian Biological Data Centre Phase-I	Department of Biotechnology	7578 lakh	2020-22
69.	Prof. Sudhanshu Vrati (PI) Dr. Arup Banerjee (Co-PI)	Covid-19 Bioresource at the NCR Biotech Science Cluster	Department of Biotechnology	94.43 lakh	2020-22
70.	Prof. Sudhanshu Vrati (Co-ordinator) Prof. Deepak 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

71.	Prof. Deepak T. Nair Dr. Deepti Jain Dr. Vengadesan Krishnan Dr. Prem Singh Kaushal	Bioinformatics Centre for Computational Drug Discovery at Regional Centre for Biotechnology- BIC at Regional Centre for Biotechnology, Faridabad	Department of Biotechnology	197.31 lakh	2021-26

RESEARCH & INNOVATION INFRASTRUCTURE

Photo Credit: Jaya Bharti Singh

BSC BioNEST Bio-Incubator (BBB)

BSC BioNEST Bio-Incubator (BBB) is a leading Bio-Incubator located in the National Capital Region on Faridabad-Gurugram Expressway, with a vision to foster innovation, research and entrepreneurial activities in biotechnology related areas. The mission of BBB is to stimulate the establishment and growth of biotechnology based startup companies. BBB is funded by BIRAC under the BioNEST (Bioincubators Nurturing Entrepreneurship for Scaling Technologies) scheme, managed and operated by Regional Centre for Biotechnology (RCB). BBB is now recognized as 'Associate BIG Partner' by BIRAC.

BBB is one of the largest Bio-Incubator of NCR region. Uniquely designed technology and incubation facility of BBB supports all kind of startups working towards improving healthcare. The best thing about BBB is its unique infrastructure and vibrant ecosystem that offers flexibility to choose from shared or independent wet labs with seating capacity of 3, 4, 8 or 12 as per need. The facility is available to the startups at very affordable cost. BBB is the only Bio-Incubator in NCR region which is dedicated to support healthcare based startups.

BBB provides globally competitive superior incubation facilities & infrastructure, spread across 35000 sq. ft. covered area which includes lab Space, office Space, professional business suites, culture facility and Instrumentation facility. It also provides Technical, IP and Mentoring support to the young startups.

Incubatees have access to the Advanced Technology Platform Centre (ATPC), which is the state-of-the-art advanced instrumentation facility. In addition, startups also have access to the pool of expert faculties on the premise for collaboration. Incubatees can also get access to Small Animal Facility (SAF) to conduct animal studies in collaboration with cluster faculty.

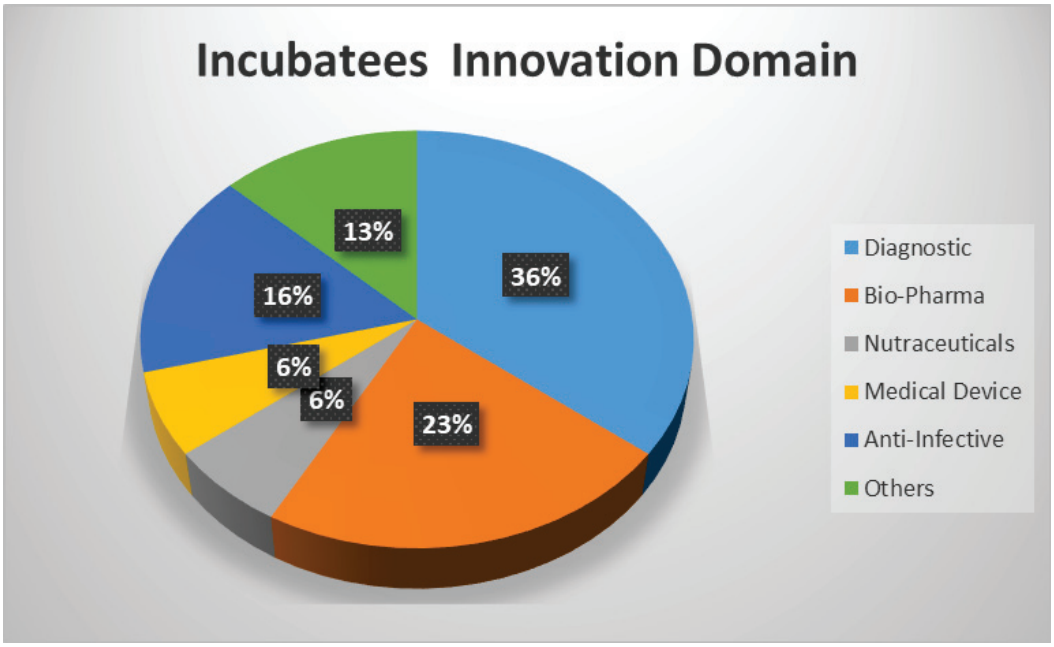
BBB has successfully supported 31 startups till date, out of which 16 startups were on-boarded during the pandemic year of FY 2020-21. Major thrust area is diagnostics with 36% of the total companies working towards it. It is followed by Biopharma which accounts for 23%. Three startups (InnoDx Solutions Pvt. Ltd, TechInvention Lifecare Pvt. Ltd and Vanguard Diagnostics Pvt. Ltd) have also won national awards for their innovative ideas in healthcare domain in FY2020-21.

Startups Supported till date:

S.No	Company	Area
2018-19		
1	QbD Biosciences Pvt. Ltd.	Bio-Pharma
2	Bioheaven 360 Genotec Pvt. Ltd.	Molecular Diagnostic
3	NextGen InVitro Diagnostics Pvt. Ltd.	Diagnostic
2019-20		
4	shc Shine Biotech Pvt. Ltd	Diagnostic
5	VaxFarm Life Sciences LLP	Bio-Pharma
6	AIGen Therapeutics Pvt. Ltd.	Anti-Infective
7	InnoDx Solutions Pvt. Ltd.	Diagnostic
8	BioDva Life Sciences Pvt. Ltd.	Bio-pharma
9	Stellar Diagnostics India Pvt. Ltd.	Diagnostic
10	Vanguard Diagnostics (P) Limited	Diagnostic
11	Incredible Devices Pvt. Ltd.	Medical Device
12	BioCredence	Nutraceuticals
13	AptaBharat Innovation Pvt. Ltd.	Diagnostic
15	Biotide Solutions LLP	Anti-Infective
16	Organic 121 Scientific Pvt. Ltd.	Industrial Biotechnology
2020-21		
17	No Confusion Technologies Pvt. Ltd.	Environmental Biotech
18	Peptomer Therapeutics Pvt. Ltd.	Anti-Infective
19	Sleepiz India Pvt. Ltd.	Medical Device
20	Sunny Corporation Pvt. Ltd.	Diagnostic
21	Inte-e-Labs Pvt. Ltd.	Bio-Pharma
22	Genvynn Biologics Pvt. Ltd.	Bio-Pharma
23	Kantech Research Solutions	Anti-Infective
24	3CR Bioscience Ltd.	Diagnostic
25	TechInvention Lifecare Pvt. Ltd.	Bio-Pharma
26	Anziam Bio Pvt. Ltd.	Bio-Pharma
27	Celleome Biosciences LLP	Diagnostic
28	PriDignity Private Limited	Sanitation
29	Valetude Primus Healthcare Pvt. Ltd	Diagnostic
30	Ruhvenile Biomedical OPC Pvt. Ltd	Anti-Infective
31	Advinogen Innovations Pvt. Ltd.	Diagnostic

Incubatee companies at BBB

BBB Startups & Domain of work



Events Conducted during FY 2020-21

BBB is actively promoting the entrepreneurial aptitude among young innovators through its strategic programs & outreach activities (such as IDEA, EMPOWER, IDEATHON, LEARN etc.). It also regularly conducts workshops, seminars and facilitates the interaction between entrepreneurs.

S. No	STRATEGIC PROGRAMS	No.
1	IDEA	16
2	NETWORKING & CONFERENCES	5
3	BBB WEBINAR SERIES	6
4	EMPOWER	1
5	INNOVATION CHALLENGE FINE	2
6	LEARN	3
	Total	**33**

Awards won by startups during FY 2020-21

S. No.	Name of Startup	Award Received
1	InnoDx Solutions Pvt. Ltd.	SAMADHAN Award COVID-19
2	TechInvention Lifecare Pvt. Ltd	Time to Leap National Award
3	Vanguard Diagnostics Pvt. Ltd.	FICCI Healthcare Excellence Award

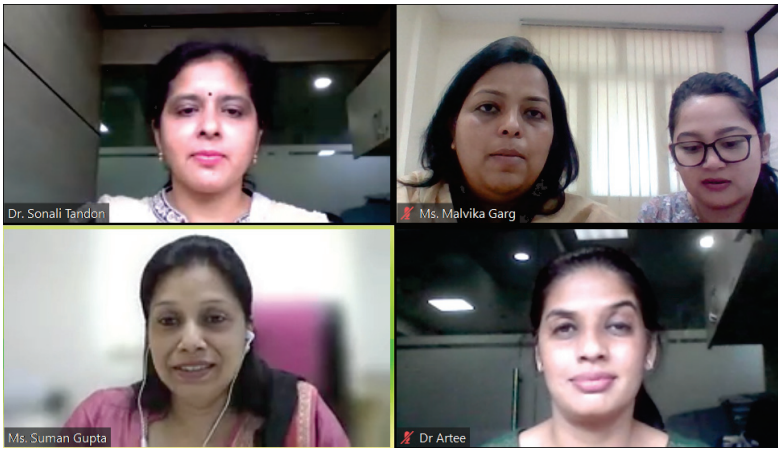
COVID related Products developed & commercialized by Startups at BBB

During the pandemic time, our startups rose up to the challenge and developed affordable products/technologies to combat COVID-19. These products included RT-PCR kits, Viral transport media kit, Viral lysis transport media kit, Rapid Anitgen test kit, Antibody ELISA kit, surface coating disinfectants etc.

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

Session by BIRAC Representatives

BBB has also ventured into pre-incubation services and launched a program **"SPROUT" (Special Program for University Technopreneurs)** that aims to promote entrepreneurship among university/college level. Under this program the University students can try their idea at BBB to generate the proof of concept.



AIM (Academia Industry Joint Mentorship), an internship connect program has also been designed to provide industrial internship to UG/PG students of Biotechnology and life sciences.

To promote networking among Incubatees, FUN@WORK initiative has been launched in Jan 2021. Few activities have been conducted under this program such as Republic day celebration and Women's Day celebration that provided ample opportunity for interaction with fellow incubatees and faculty from RCB.

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 2020-21 include:

- 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.
- Developed and updated a number of guidelines, Standard Operating Procedures and policy documents on emerging pandemic situation of COVID-19.
- 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.
- 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.
- 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.
- 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

I. RCGM/GEAC Related Activities

1. Review of applications:

BSU evaluated applications submitted to Review Committee on Genetic Manipulation (RCGM) for consideration in RCGM meetings (182nd to 202nd Meetings) during year 2020-21 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 633 applications in the field of Biopharma and a total of 108 Agri-Biotechnology related applications during the 2020-21.

2. Revision and updation of Biosafety Protocols and Guidelines

BSU has undertaken a major activity of revision/ updation of various guidelines related to biosafety of recombinant DNA research.

The BSU assisted different working groups in preparing following draft guidelines that are under RCGM consideration:

- Standard operating Procedures (SOPs) for exchange of infectious biosamples/ biospecimens from biorepository, 2021.
- Guidance Document on Genetically Engineered Plants Containing Stacked Events, 2021.

Further the updations of following guidelines are under consideration: 1. Updation of Regulations & Guidelines for Recombinant DNA Research and Biocontainment. 2. Updation of Guidelines on Similar Biologics. 3. Generic Protocols for BRL-I trial. 4. Document on Biosafety and Biosecurity issues arising from the research and environment release of GE insects including GM Mosquitoes.

3. Handbook for Institutional Biosafety Committees (IBSCs)

BSU has assisted in updating of IBSC handbook. The 2011 IBSC handbook has been revised taking into all reforms and online submission of applications.

4. Draft list of infective microorganisms corresponding to different risk groups

The Regulations & Guidelines for Recombinant DNA Research and Biocontainment, 2017 notified by the Department of Biotechnology listed infective microorganisms under different risk groups. The list was indicative but not exhaustive and needs to be updated periodically.

Accordingly, DBT undertook the task to review and update the risk group of microorganisms, for which Expert Committee was constituted under the Chairmanship of Dr. D. T. Mourya. Based on feedback received from IBSCs registered on the IBKP Portal and deliberations of the Sub Committees and Expert Committee, draft list of microorganisms was prepared. The list allows selection of appropriate biosafety level facilities for handling and carrying out research and development activities on the infective microorganisms. The Public Consultation on "Draft list of infective microorganisms corresponding to different risk groups" was completed on 15.03.2021. BSU assessed comments received on the same from stakeholders from industry and academia and revised the Draft list of microorganisms accordingly.

5. Draft General Principles, Regulatory Framework, and Data Requirements for Biosafety Assessment of Genome Edited Organisms

Stakeholder consultation meeting was held on 12.03.2020 to draft document Guidelines on Genome Editing wherein after extensive deliberations the Committee decided to segregate the guidelines and prepare guidelines on plants by a drafting group. RCGM in its 184th meeting held on 04.06.2020 deliberated on the "**Guidelines for the Safety Assessment of Genome Edited Plants**" and recommended to forward the same to GEAC for information and necessary actions.

6. Generic PCT protocol for assessing toxicity of recombinant DNA derived products in animal models

BSU assisted in drafting the generic PCT protocol as a step towards streamlining the regulatory approval process of biopharma products.

7. Commissioning of Indian Biosafety Knowledge Portal (IBKP)

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

8. Monitoring of IBSCs

DBT-RCGM has taken several reforms including empowering of IBSCs, hence stringent mechanism to monitor the IBSCs through their minutes & annual compliance reports has been started with IBKP portal. BSU is facilitating the RCGM in the monitoring of IBSCs.

9. Guidelines for the Establishment of Containment Facilities: BSL2 and BSL3 and Certification of BSL3 facility 2020

A need was felt to define the standards and specification for the certification of the new facilities or already existing BSL-3 & BSL-4 facilities. An expert committee was constituted for the purpose and BSU has extended help in the preparation of document on standards/ specification for certification and auditing of BSL-3 & 4 facilities.

10. Guidelines for Notified Field Trial Sites (NFTS) To Conduct Confined Field Trials of GE Crops

Draft Guidelines have been submitted to MoEFCC vide DBT letter dated 19.02.2020 and were considered in the 139th GEAC meeting held on 19.05.2020. The committee requested the GEAC Secretariat to examine the proposal which will be discussed in the subsequent meeting of GEAC for taking appropriate decision. In the meantime, the members were also requested to provide written comments on the above proposal.

11. Risk group updation

DBT through BSU routinely seeks stakeholder feedback on Guidelines and other documents before finalizing them through IBKP portal. For the updating of Risk Group for the microorganisms and inclusions of any new micro-organisms, stakeholder consultation through IBSCs was initiated on 18th July 20. BSU assessed feedback from (168) IBSCs registered on IBKP portal and subsequently coordinated sub-committees for finalizing the Draft List of microorganisms (including fungi, bacteria, virus, and parasites). Based on the IBSC response and expert committee deliberations, BSU compiled Draft list of microorganisms (Viruses, Bacteria, Fungi and Protozoa) for consideration of the Expert Committee.

Expert committee, in its 2nd meeting held on 06.01.2021, deliberated on the Draft list of microorganisms. Based on the deliberations, BSU modified the draft list of respective microorganisms, which now needs to be deliberated upon and approved by the Expert Committee.

12. Interactive sessions for awareness raising:

DBT along with BSU scientists provided training sessions to IBSCs. A total of 14 sessions (for Member Secretaries of IBSCs registered on IBKP and for researchers) have been organized. Further online Awareness Generation Sessions have been initiated.

13. Interim guidance document on laboratory biosafety to handle COVID-19 specimens for R&D purpose

BSU assisted DBT in drafting the interim guidance document as an immediate interim measure to handle COVID-19 specimens for R&D purpose.

14. Rapid Response Regulatory Framework for COVID-19 Vaccine development and Checklist for application to conduct pre-clinical toxicity (PCT) studies for recombinant vaccine for COVID-19

BSU assisted DBT in drafting the Checklist for the application to conduct pre-clinical toxicity (PCT) studies for recombinant vaccine for COVID-19 as a step towards Rapid Response Regulatory Framework for COVID-19 Vaccine development.

15. Press release

BSU has supported in framing the drafts for the following press release:

- Rapid Regulatory Frame Work for COVID -19. Press release posted on July 25, 2020 by PIB Delhi [https://pib.gov.in/PressReleseDetailm.aspx?PRID=1641140].
- Handbook for Institutional Biosafety Committees (IBSCs). Tweet posted on September 09, 2020 by BiotechIndia on Twitter [https://twitter.com/DBTIndia/status/1303571037494231041?s=20].

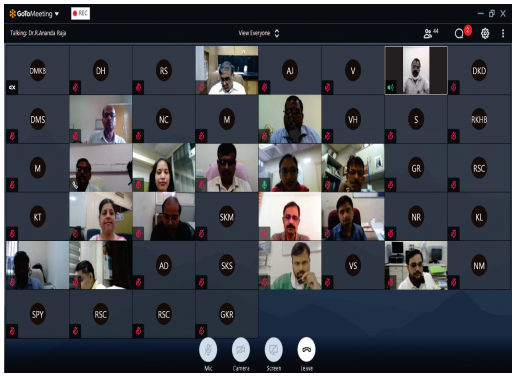
I. Other activities

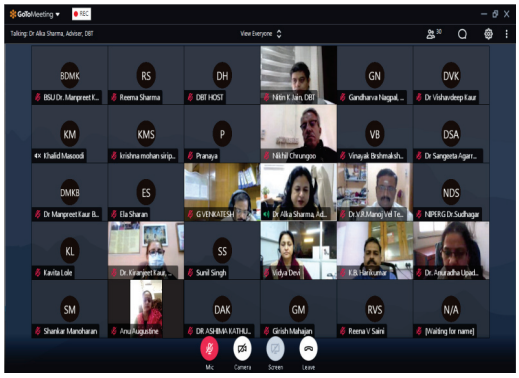
BSU has supported RCGM/GEAC for drafting affidavits/ replies for various Supreme Court cases and parliamentary questions.

II. Training and Capacity Building

a) Dr. Sangeeta Agarwal, CSO, BSU attended dialogue event "COVID-19 responses in India and the US: lessons learned and path forward"; Co-Hosted by the Johns Hopkins Center for Health Security and the Regional Centre for Biotechnology, Department of Biotechnology, on January 26 and 27, 2021.

b) Meeting for discussing proposed document on "Vaccine development and licensure for COVID 19" in line with guidance document issued by USFDA, held on 04.08.2020 through Video Conferencing (GoToMeeting).





Advanced Technology Platform Centre

The primary goal of the Advanced Technology Platform Centre (ATPC) is to accelerate innovation in biology and biotechnology and thus contribute towards improving the Indian economy.

The Centre plugs a huge gap in the innovation pipeline that has previously attenuated the ability of Indian researchers to realize their true potential. ATPC houses cutting edge technologies to enable researchers within all the constituent partner institutes to conduct experiments that will provide deep insight in biological processes and provides the best opportunity to translate these discoveries for commercialization.

At present the ATPC has six operational platform facilities equipped with the various high-end technologies for aiding biotechnology start-ups and researchers.

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.)
- Expression screening of the protein-of-interest by sub-cloning its gene in vectors with different tags.

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 been used by approximately 420 users and has processed 2200 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.

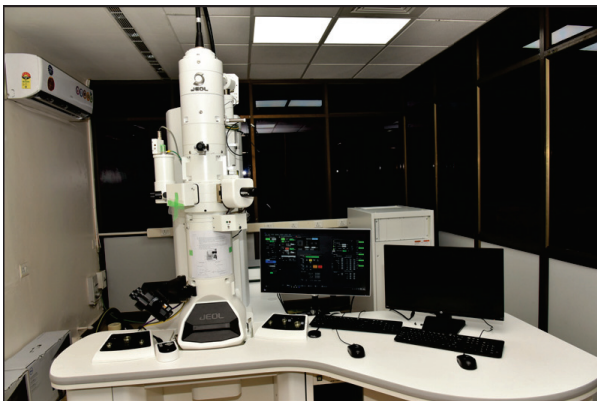
The facility has been providing its services to various internal and external investigators, from academia and industry such as NCR Biotech cluster, ICGEB-New Delhi, Premas biotech, PGI-Chandigarh, CDRI-Lucknow, JNU-New Delhi, Delhi University, AIIMS, NCL-Pune, ICT-Mumbai, Zydus Cadila-Ahmedabad, and many more. More than 3100 samples from 360 users 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. The electron microscopy facility has provided services to various institutes e.g. NCR Biotech cluster, JNU, and CSIR-IMTECH. The electron microscopy facility has analyzed 449 samples from 151 users. The services include high contrast imaging of biological samples (protein, viruses, bacteria, etc.) and material science samples (nanoparticles, micelles, etc.) using TEM and topographical analysis of bacteria, mammalian cells, and enzyme-treated plant biomass using FESEM.



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 approximately 7800 samples from more than 1300 users.

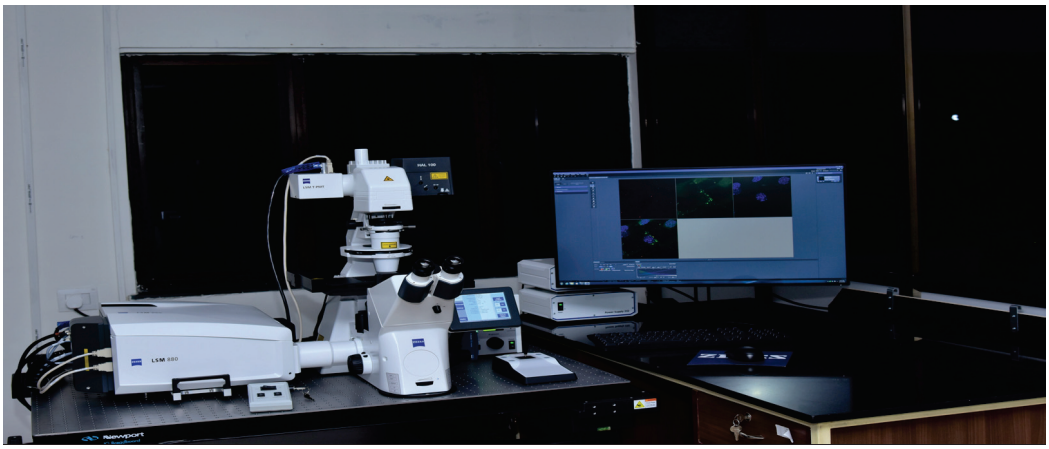
5. Optical Microscopy facility

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. Apart from the bio-cluster, we have been providing support and help to scientists from IIT-Delhi. Industrial Researchers from Acckamara Biomedicine Pvt. Ltd and Vyome Therapeutics Pvt. Ltd have been regularly availing the facility for their research work. This facility has supported approximately 130 users in their research



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).

The facility provided valuable services, which included 635 hours of usage for the Flow Cytometry and supported the need of approximately 200 users. Apart from RCB, the institutions that utilized our services include CSIR-IGIB, ICAR-NBPGR, Jamia Hamdard, Shiv Nadar University, Ridge IVF Pvt. Ltd. and InnoDx Solutions Pvt. Ltd., BBB. This facility 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.

Number of trainings/workshops/seminars/etc. organized with details of titles/topics and number of attendees/participants

Manpower trained

S. No.	Facility	Name of Workshop	Duration	Year	No. of Participants
1.	Mass Spectrometry	Online workshop on Mass Spectrometry based Proteomics	4th & 18th February	2021	127
2.	Electron Microscopy Facility	Virtual workshop on Basics of Electron Microscopy	3rd March	2021	110

High Performance Computing Cluster & IT Infrastructure

A high performance computing (HPC) cluster with 8 nodes and a total of 128 processors is available for research in computational biology. The Information and Communication facilities at RCB are continuously evolving with state-of-the-art facilities. All the computers at RCB are provided with the latest updated software and hardware. Internet, printing and scanning facilities are also available throughout the network.

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

Computing Facilities

The Institute has three state of the art Computer facilities. All the computers facility in the Institute are provided with the latest updated software and hardware. Internet, printing and scanning facilities are also available through network. Desktops/ Laptops, multifunction printers have been provided to the staff with internet connectivity. There are about 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 already 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.

Graphics Lab

The graphics lab at RCB contains a HPC cluster with eight nodes, a Schrodinger suite server with 3 clients, and workstations for research in computational biology and structure-based drug design.

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 comprises about 1000 metres of fibre, with a 10Gbps backbone, 95+ wireless access points, and 35+ 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 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 7.4 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. RCB 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
- Vendor Registration portal etc.

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

Indian Biological Data Center (IBDC), a national facility established at RCB with support from the Department of Biotechnology, Govt. of India. Housed at RCB, the IBDC is being developed under active collaboration with NIC, NII and ICGEB, New Delhi. The computational infrastructure of IBDC include High Performance Computation (HPC) cluster and High capacity archival data

storage. The data will be curated at RCB and will be hosted by NIC, Bhubaneswar. The RCB IT-department will provide technical support for the development and day-to-day operations of the RCB component of IBDC.

Bioinformatics Center

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

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.

During FY 2020-21, Office of Connectivity has played a central role in completion of the following facilities of the NCR Bio-cluster:

a) Office of Connectivity Building
b) Biosafety Level-3 Facility
c) Vertical Extension of Hostel Building

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.

DBT HRD & Project Management Unit

Department of Biotechnology (DBT) has been running several programs to support the creation of the human resources in the area of Biotechnology. Of these, the Ramalingaswami Re-entry Fellowship (RRF) scheme, the DBT Junior Research Fellowship (JRF) scheme, and the Post Graduate Teaching Programs in Biotechnology and allied areas in the various universities, involve several hundred to several thousand candidates from post-doctoral, doctoral and masters level. Since the year 2020, DBT has entrusted RCB, Faridabad as the Nodal Implementation Agency for management of key human resource development programmes through DBT-HRD Project & Management Unit (DBT HRD PMU).

DBT HRD PMU has been established with necessary manpower to implement the following human resource development programs of DBT:

- Ramalingaswami Re-entry Fellowship (RRF) scheme
- DBT Junior Research Fellowship (JRF) scheme
- DBT Post Graduate Teaching Programs

DBT HRD PMU at RCB has organized national level entrance tests like Graduate Aptitude Test–Biotechnology (GAT-B 2020) and Biotechnology Eligibility Test (BET-2020) with approximately 22000 registered candidates in 59 cities across India during 2020-21 for selection of candidates to qualify for admission in the DBT supported PG programmes across 61 institutions in India and for the award of DBT Junior research fellowship to pursue PhD in Indian universities/institutions. For DBT RRF scheme, DBT HRD PMU had successfully organized the online Conclave during December 2020 and have processed the applications received for RRF–2020 for selection of new fellows under Ramalingaswami Re-entry Fellowship program. DBT HRD PMU at RCB has also successfully implemented the disbursement of fellowships to fellows under DBT JRF and RRF program through Public Financial Management System (PFMS).

FINANCIAL STATEMENTS

REGIONAL CENTRE FOR BIOTECHNOLOGY, FARIDABAD

BALANCE SHEET AS AT 31ST MARCH, 2021

Amount (In Rs.)

LIABILITIES	Schedule	31.03.2021	31.03.2020
Corpus / Capital Fund	1	6313,33,584	6281,95,531
Reserves and Surplus	2	504,72,628	225,53,878
Earmarked/Endowment Funds	3	-	-
Secured Loans and Borrowings	4	-	-
Unsecured Loans and Borrowings	5	-	-
Deferred Credit Liabilities	6	-	-
Current Liabilities and Provisions	7	23919,41,294	16552,89,308
Biotech Science Cluster (BSC)			
TOTAL		**30737,47,506**	**23060,38,717**
ASSETS			
Fixed Assets	8	5141,89,952	5375,63,927
Investment From Earmarked/Endowment Funds	9	-	-
Investment-Others	10	11294,13,171	6190,43,926
Current Assets, Loans, Advances etc.	11	3678,94,798	2742,51,864
Biotech Science Cluster (BSC)	8		
a. Capital Work in Progress		10622,49,585	8751,79,000
b. Advance to BSC Construction		-	
c. Funds in short term deposits		-	
d. Accrued interest & TDS		-	
Miscellaneous Expenditure		-	
(to the extent not written off or adjusted)			
TOTAL		**30737,47,506**	**23060,38,717**
Significant Accounting Policies and Notes on Accounts	24		
Contingent Liabilities	25		

Schedules 1 to 25 form an integral parts of Accounts

(C.B.YADAV)	(Dr. PRASENJIT GUCHHAIT)	(Dr. SUDHANSHU VRATI)
ADMINISTRATIVE OFFICER (F)	REGISTRAR	EXECUTIVE DIRECTOR

सी. बी. यादव, प्रशासनिक अधिकारी (वित्त व लेखा)
C.B. Yadav, Administrative Officer (F&A)
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

कुलसचिव / Registrar
क्षेत्रीय जैवप्रौद्योगिकी केंद्र / Regional Centre for Biotechnology
राष्ट्रीय महत्ता की संस्था / An Institution of National Importance
यूनेस्को के तत्वावधान में जैवप्रौद्योगिकी विभाग, भारत सरकार द्वारा स्थापित
Estd. by the Dept. of Biotechnology, Govt. of India under the auspices of UNESCO
एन.सी.आर बायोटेक साइंस क्लस्टर / NCR Biotech Science Cluster
तृतीय मील पत्थर, फरीदाबाद-गुड़गाव एक्सप्रेसवे
3rd Milestone, Faridabad-Gurgaon Expressway
फरीदाबाद - 121 001 (हरियाणा) / Faridabad - 121 001 (Haryana)

प्रो. सुधांशु व्रती / Prof. Sudhanshu Vrati
कार्यपालक निदेशक / Executive Director
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र / Regional Centre for Biotechnology
फरीदाबाद - 121 001 (हरियाणा), भारत/Faridabad - 121 001 (Haryana), India

Regional Centre for Biotechnology

Schedule 24: Accounting Policies and Notes Forming Parts of the Balance Sheet and Income & Expenditure Account for the Year Ended at 31st March, 2021

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

2. Since the RCB bill has been passed and notified on 1.3.2017 and thereafter the Statutes, Ordinances and regulations approved during September 2017, the liabilities on account of Gratuity & leave encashment of the Centre has been incorporated in the accounts for FY 2020-21 in accordance with the approved service conditions of the RCB, based on actuarial valuation.

3. (a) Recurring Grants have been recognised in the Income & Expenditure account and non-recurring Grants have been shown as part of capital.

   (b) Grants for core funds relatable 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). During the year income recognised in respect of such Grants amounts to Rs. 680,61,947.00

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. Rate of depreciation is annexed.

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

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

11. Expenses and Overheads incidental to construction of building of institute as well as other buildings in the NCR BSC, as reported by the Project Monitoring Consultant (Engineers India Limited), are added to the capital work in progress to be capitalized along with the building, only on submission of final accounts by the PMC. The project is being operated with an agreement which stipulates operation of an Escrow Account by NCR Biotech Science Cluster. The authorized signatories are Engineers India Ltd. (Project Management Consultant)

12. During the Financial Year, advance of Rs. 200 Lakhs was transferred to THSTI for construction of NCR Bio-tech Science Cluster Phase III construction work of NCR BSC, which relates to the work of Hostel and Utility Block (G Floor).

13. The Capital Work-in-progress booked in the accounts includes the construction of laboratory buildings of ATPC, Bio-incubator and hostels & faculty housing and common facilities etc. of THSTI, RCB, 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 shall be capitalised on receipt of occupancy certificate from MCF.

14. Interest earned on saving bank account and fixed deposits during the financial year 2020-21 of Rs.245.79 Lakhs has allocated to the respective projects on pro-rata basis.

Schedule 25: Contingent Liabilities

Purchase orders for consumables & equipment as per attached annexure are outstanding as on 31.3.2021 which have not been recognized in the books of accounts.

(C.B.YADAV)
ADMINISTRATIVE OFFICER (F)
सी. बी. यादव, प्रशासनिक अधिकारी (वित्त व लेखा)
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Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

(Dr. PRASENJIT GUCHHAIT)
REGISTRAR
कुलसचिव / Registrar
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राष्ट्रीय महत्ता की संस्था / An Institution of National Importance
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(Dr. SUDHANSHU VRATI)
EXECUTIVE DIRECTOR
प्रो. सुधांशु व्रती / Prof. Sudhanshu Vrati
कार्यपालक निदेशक / Executive Director
क्षेत्रीय जैवप्रौद्योगिकी केंद्र / Regional Centre for Biotechnology
फरीदाबाद - 121 001 (हरियाणा), भारत/Faridabad - 121 001 (Haryana), India

Place: Faridabad
Date: 11/06/2021

INSTITUTIONAL GOVERNANCE

Photo Credit: Viney Sharma

Board of Governors (BOG)

- **Dr. Renu Swarup (Chairperson)**
  Secretary
  Department of Biotechnology
  New Delhi - 110 003
- **Director (Ex-officio Member)**
  Rajiv Gandhi Centre for Biotechnology
  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
- **Dr. Y. K. Gupta (Permanent Invitee)**
  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

Programme Advisory Committee (PAC)

- **Dr. Y. K. Gupta (Chairperson)**
  Former Professor
  All India Institute of Medical Sciences
  New Delhi 110 029
- **Dr. Debashis Mitra (Member)**
  Professor of Eminence, National Centre for Cell Science
  Pune 411 007, Maharashtra
- **Prof. Saumitra Das (Member)**
  Director, National Institute of Biomedical Genomics
  Kalyani 741 251
  West Bengal
- **Dr. Rashna Bhandari (Member)**
  Staff Scientist
  Centre for DNA Fingerprinting and Diagnostics
  Hyderabad 500 039
- **Dr. Shrikumar Suryanarayan (Member)**
  Chairman
  Sea6 Energy
  Bengaluru 560 065
- **Dr. Paramjit Khurana (Member)**
  Professor & Head, Department of Plant Molecular Biology
  University of Delhi, South Campus
  New Delhi 110 021
- **Prof. Rakesh Bhatnagar (Member)**
  Vice-Chancellor
  Banaras Hindu University
  Varanasi 221 005
- **Dr. Joel Sussman (Member)**
  Professor, Dept. of Structural Biology
  The Weizmann Institute of Science
  Israel
- **Prof. Angelo Azzi (Member)**
  Vascular Biology Laboratory
  Tufts University, Medford, USA
- **Prof. R. Venkata Rao (Member)**
  Vice Chancellor
  National Law School of India University
  Bengaluru 530 072
- **Dr. Alka Sharma (Member)**
  RCB Coordinator
  Scientist-G, Department of Biotechnology
  Govt. of India
  New Delhi
- **Dr. Nitin K Jain (Special Invitee)**
  Scientist-F, Department of Biotechnology
  Govt. of India
  New Delhi
- **Prof. Sudhanshu Vrati (Member Secretary)**
  Executive Director
  Regional Centre for Biotechnology
  Faridabad 121 001

Executive Committee (EC)

- **Prof. Sudhanshu Vrati (Chairman, Ex-officio)**
  Executive Director
  Regional Centre for Biotechnology
  Faridabad 121 001

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

Finance Committee (FC)

- **Prof. Sudhanshu Vrati (Chairman, Ex-officio)**
  Executive Director
  Regional Centre for Biotechnology
  Faridabad 121 001
- **Additional Secretary & Financial Advisor (Member, Ex-officio)**
  Department of Biotechnology
  Govt. of India
  New Delhi 110 003
- **Dr. Alka Sharma (Member, Ex-officio)**
  RCB Coordinator
  Scientist-G, Department of Biotechnology
  Govt. of India
  New Delhi
- **Dr. Nitin K Jain (Member, Ex-officio)**
  RCB Nodal Officer
  Scientist-F, Department of Biotechnology
  Govt. of India
  New Delhi
- **Executive Director (Member, Ex-officio)**
  Translational Health Science &Technology Institute
  Faridabad 121 001
- **Mr. P.S. Rawat (Member)**
  Finance & Accounts Officer
  NII, New Delhi
- **Shri Pitambar Behera (Member)**
  Sr. Finance Officer
  Indian Institute of Foreign Trade
  New Delhi 110 016
- **Controller of Administration (Member, Ex-officio)**
  Regional Centre for Biotechnology
  Faridabad 121 001
- **Shri Vivek Agarwal (Member Secretary, Ex-officio)**
  Finance Officer
  Regional Centre for Biotechnology
  Faridabad 121 001

Scientific Personnel

Faculty

Executive Director and Professor
Prof. Sudhanshu Vrati

Dean
Dr. Rajendra Prasad Roy

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

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

Assistant Professor
Dr. Saikat Bhattacharjee
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

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

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

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

DBT Young Investigator Award
Dr. Siddhi Gupta
Dr. Shivendra Pratap
Dr. Yashika Walia Dhir
Dr. Raghavendra Aminedi

DBT Women BioCARe awardee
Dr. Kanchan Bhardwaj
Dr. Babitha Chandrashekhar

Ramalingaswami Fellowship
Dr. Kinshuk Srivastava
Dr. Ambadas Rode
Dr. Anil Thakur

Ramanujan Fellowship
Dr. Ramu S. Vemanna

SERB NPDF
Dr. Bhargab Kalita
Dr. Vijay Kumar
Dr. Archana Pant
Dr. Wahab Khan

DBT-RA
Dr. Nitu Singh
Dr. Sangeeta Yadav
Dr. Archana Prasad
Dr. Yashika Walia Dhir

Management

Office of the Executive Director

Executive Director
Prof. Sudhanshu Vrati

Staff Officer to Executive Director
Dr. Nidhi Sharma

Technical Assistant
Mr. Ramesh Chandiramouli

Academics, Administration, Finance and Purchase

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

Finance Officer
Mr. Vivek Agarwal

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

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

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

Documentation Assistants
Mr. Priyanshu Joshi
Mr. Amit Kumar Yadav

Technical

Executive Engineer
Mr. R.K. Rathore

System Administrator
Mr. Naveen Kumar

Instrumentation Engineer
Mr. Pankaj

Senior Technical Officer
Mr. Mahfooz Alam

Technical Officers
Mr. Deepak Kumar (On deputation)
Mr. Vijay Kumar Jha
Mr. Atin Jaiswal
Mr. Suraj Tewari

Technical Assistants
Mr. Madhav Rao M
Ms. Vishakha Chaudhary
Mr. Nagavara Prasad G.
Dr. Shaminder Singh
Mr. Dharmender Gupta
Mr. Manoj Kumar Soni
Dr. Reena Rani

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