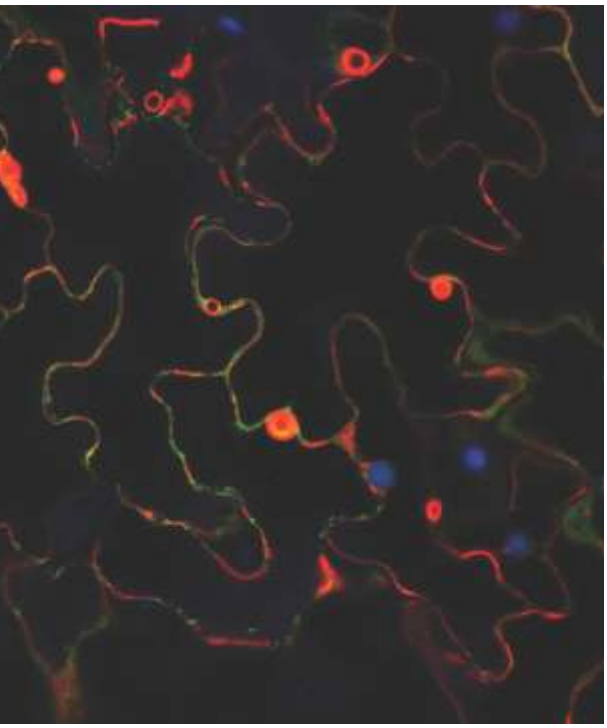
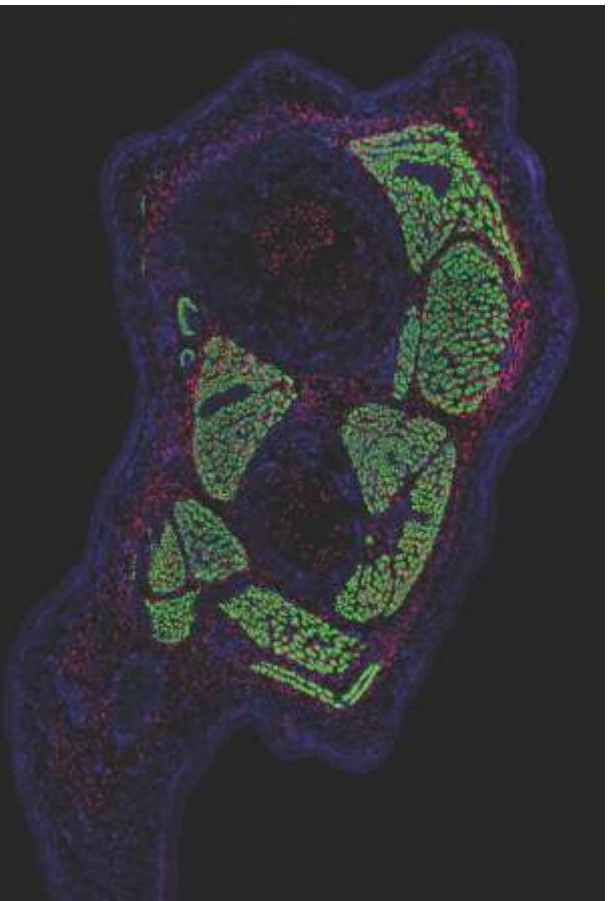
ANNUAL REPORT

2019-2020





United Nations
Educational, Scientific and
Cultural Organization

क्षेत्रीय जैव प्रौद्योगिकी केन्द्र
Regional Centre
for Biotechnology


EGIONAL C


RCB
CENTRE FOR BIOTECHNOLOGY

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

Regional Centre for Biotechnology (RCB) has continued to march towards achieving its goals and fulfilling the key mandates of imparting education and training, and conducting research in the broad area of biotech sciences. RCB is a category-2 institution of the UNESCO. This linkage provides an international reach to our academic and training programs. The members of RCB have been striving hard to achieve the various RCB objectives. Provided below is a summary of RCB's progress in the academic and research spheres.

RCB's academic programs are tailored such that the students have an opportunity to work and train with researchers in our state-of-the-art research laboratories. RCB offers structured degree programs as well as short-term training programs in highly specialized areas of biotechnology and life sciences. Around 100 students are pursuing doctoral degree programs in Biotechnology, Bioinformatics, and Biostatistics in different RCB laboratories. RCB also has an integrated MSc-PhD degree program where students with bachelor's degrees are admitted. This year 16 students (including an international student) were admitted to the program. The RCB Act 2016 empowers the Centre to recognize higher learning institutions for their various academic programs. In this direction, after the due diligence, RCB has granted recognition to the MSc, MSc-PhD (integrated), or PhD programs at eight such centers. These include the Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad; National Institute of Animal Biotechnology (NIAB), Hyderabad; National Agri-Biotechnology Institute (NABI), Mohali; Centre for Innovative and Applied Biotechnology (CIAB), Mohali; Institute of Life Sciences (ILS), Bhubaneshwar; Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram; Translational Health Science and Technology Institute (THSTI), Faridabad; and National Institute of Biomedical Genomics (NIBMG), Kalyani. A total of 218 students from these recognized centers are registered for their degrees with RCB.

RCB offers short-term innovative training programs and organizes national and international scientific meetings for young scientists towards human resource development in the advanced areas of life sciences and biotech sciences. In this direction, RCB conducted a 6-days' long workshop on molecular neurobiology. A variety of topics relating to the neurobiology of smell and taste, Autism, Epilepsy, and Parkinson's and Alzheimer's disease were discussed. RCB hosted an international conference on calcium signaling, which held sessions on calcium homeostasis, organellar calcium dynamics, and the role of calcium microdynamics in physiology and disease. A workshop on high content imaging trained researchers in advanced techniques for drug screening was also conducted. Besides, RCB continues to provide the 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 various scientific programs of RCB can be broadly grouped under the following heads: Infectious Disease Biology, Molecular Medicine, Structural Biology, 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 important research highlights of this year.

Parkinson's disease is a multifactorial malady and the second most common neurodegenerative disorder, characterized by the formation of intracellular protein inclusions, termed Lewy bodies (LBs). OTUB1, a deubiquitinating enzyme, is enriched together with α-synuclein in LBs. Our studies show that OTUB1 aggregates were associated with severe cytoskeleton damage, rapid internalization inside the neuronal cells, and mitochondrial damage, all of which contribute to neurotoxicity, indicating that OTUB1 may contribute to LB pathology through its amyloidogenic properties.

Missense mutations in the MYH3 gene encoding myosin heavy chain-embryonic (MyHC-embryonic) cause two skeletal muscle contracture syndromes, Freeman Sheldon Syndrome (FSS) and Sheldon Hall Syndrome (SHS). Our scientists generated transgenic Drosophila expressing myosin heavy chain (MyHC) transgenes with the FSS mutations. The mutant Mhc transgenes lead to structural abnormalities in the muscle, which increase in severity with age and muscle use. Functionally, the mutation led to significantly reduced climbing capability in adult flies. This fly model of FSS will be handy for studying muscle physiology and biochemistry.

MicroRNAs (miRNAs) released from the activated microglia upon neurotropic virus infection may exacerbate the neuronal damage. Our scientists identified let-7a and let-7b (let-7a/b) as one of the essential miRNAs over-expressed upon Japanese Encephalitis virus (JEV) infection, and released in the culture supernatant of the JEV-infected microglial cells through extracellular vesicles. Exosomes secreted from virus-infected or let-7a/b over-expressed microglia when co-incubated with mouse neuronal (Neuro2a) cells or primary cortical neurons facilitated caspase activation leading to neuronal death, thus providing evidence for the multifaceted role of let-7a/b miRNAs in JEV pathogenesis.

Inflammatory bowel disease (IBD) is a complex autoimmune disorder associated with SUMOylation, a post-translational modification mechanism. Our scientists have identified a link between epithelial deSUMOylases and inflammation in IBD. DeSUMOylase SENP7 was upregulated specifically in intestinal epithelial cells in both human IBD and a mouse model. The upregulation led to an expansion of localized proinflammatory γδ T cells. Strong correlations between upregulated SENP7 and high clinical disease indices were observed in IBD patients. These data reveal that epithelial SENP7 is necessary and sufficient for controlling gut inflammation, thus highlighting its importance as a potential drug target.

Interkingdom polymicrobial biofilms formed by Gram-positive *Staphylococcus aureus* and *Candida albicans* pose serious threats of chronic systemic infections. Our scientists conducted the structure-activity relationship (SAR) study of membrane-targeting cholic acid-peptide conjugates (CAPs) against Gram-positive bacterial and fungal strains. These studies revealed that valine-glycine dipeptide-derived CAP 3 was the most effective broad-spectrum antimicrobial against *S. aureus* and *C. albicans.* Murine wound and catheter infection models further confirmed the equally potent bactericidal and fungicidal effect of CAP 3 against bacterial, fungal, and polymicrobial infections. These results demonstrate that CAPs, as potential broad-spectrum antimicrobials, can effectively clear the frequently encountered polymicrobial infections and can be fine-tuned for future applications.

Tunneling nanotubes (TNTs) are membrane conduits that mediate long-distance intercellular cross-talk in several organisms and play vital roles during development, pathogenic transmission, and cancer metastasis. The protein MSec is essential for TNT formation in multiple cell types. Our scientists found that MSec interacted with the endoplasmic reticulum (ER) chaperone ERp29 for maintaining MSec protein stability. The ERp29-MSec interaction appeared to require other bridging protein(s), perhaps triggered by post-translational modification of ERp29. The study implicates MSec as a target of ERp29 and reveals an indispensable role for the ER in TNT formation, suggesting new modalities for regulating TNT numbers in cells and tissues.

Additionally, RCB continues to participate in a multi-institutional research program 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. 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 the development of antivirals against Chikungunya and Japanese encephalitis viruses also got underway this year.

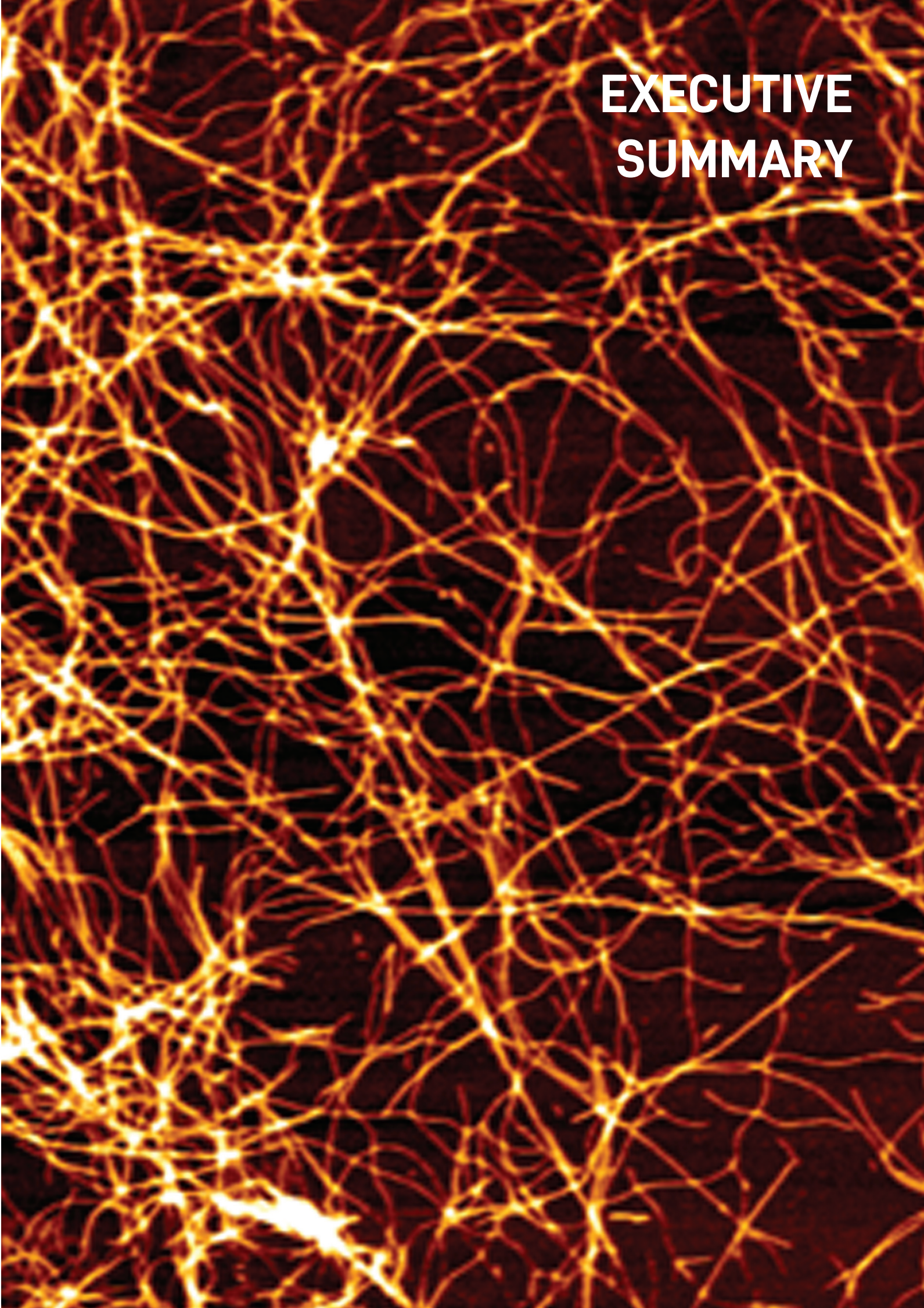
RCB has established a Bio-Incubator with financial support from the BIRAC under the BioNEST (Bio-Incubators Nurturing Entrepreneurship for Scaling Technologies) scheme. The Bio-Incubator has been established to foster innovation, research, and entrepreneurial activities in biotechnology-related areas. Around 15 start-up companies are now 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 the 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

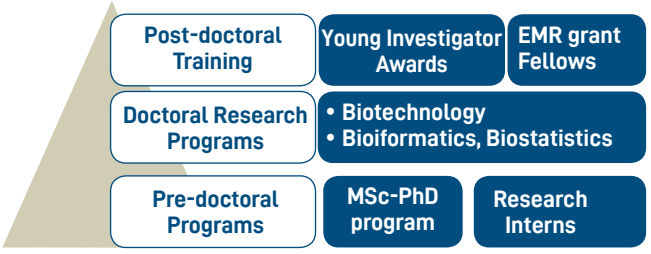


EXECUTIVE SUMMARY

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

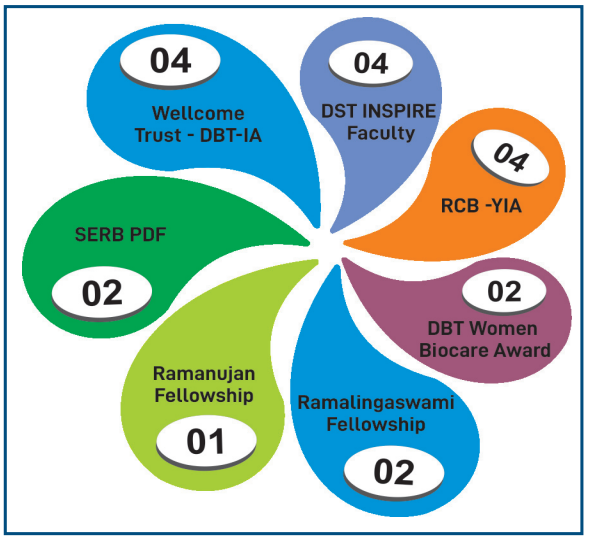
Academic and Training Activities



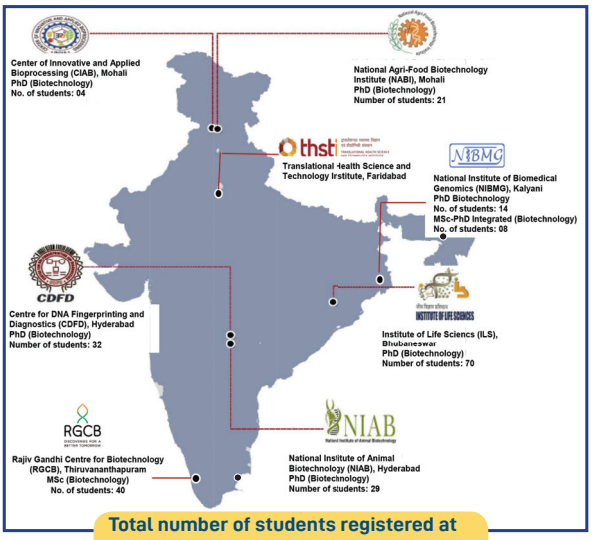
No. of Students studying at RCB

92	PhD (Biotechnology)	MSc-PhD (Biotechnology)	26
04	PhD (Bioinformatics)	PhD (Biostatistics)	01
42	Research Interns	PhD awarded	10

Awards and Fellowships



RCB Recognized Centres

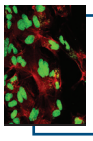


Total number of students registered at RCB: 218

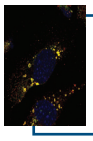
Date	Event Organized
2 March, 2020	RCB Day Lecture by Dr. Chandrima Shaha on "Celebrated Ideas in Biology: Influence on Future of Life Science Research"
28February, 2020	RCB Open Day (National Science Day)
24-29 February, 2020	Workshop on Molecular Neurobiology: From Genes, Neurons to behavior in health and disease
January 31-February 01, 2020	International conference on Calcium Signaling
21-22 January, 2020	Workshop on Science Communication and Careers
25-27 November, 2019	Workshop on High Content Imaging
5 November, 2019	RCB in collaboration with UNESCO conducted an Event at RCB campus to commemorate World Science Day
16 October, 2019	RCB Open Day

Research Areas

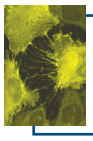
Structural Biology



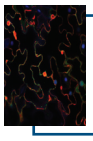
Molecular Medicine



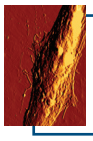
Infectious Disease Biology



Cancer & Cell Biology



Agricultural Biotechnology



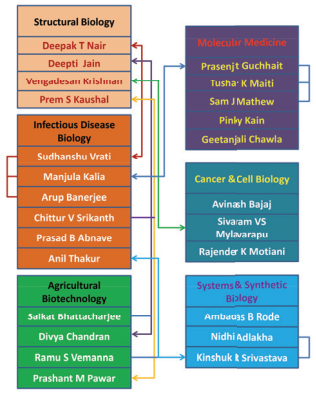
Systems & Synthetic Biology

Publications : 47
Patent Applications : 02

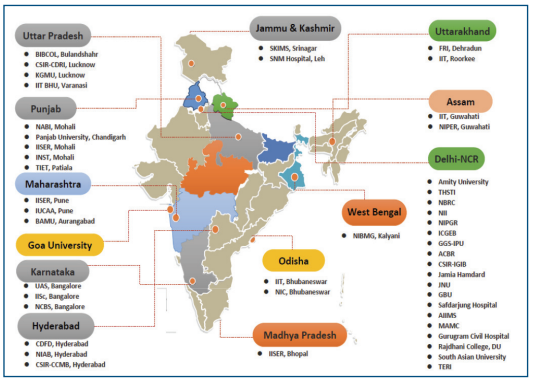
Research Highlights

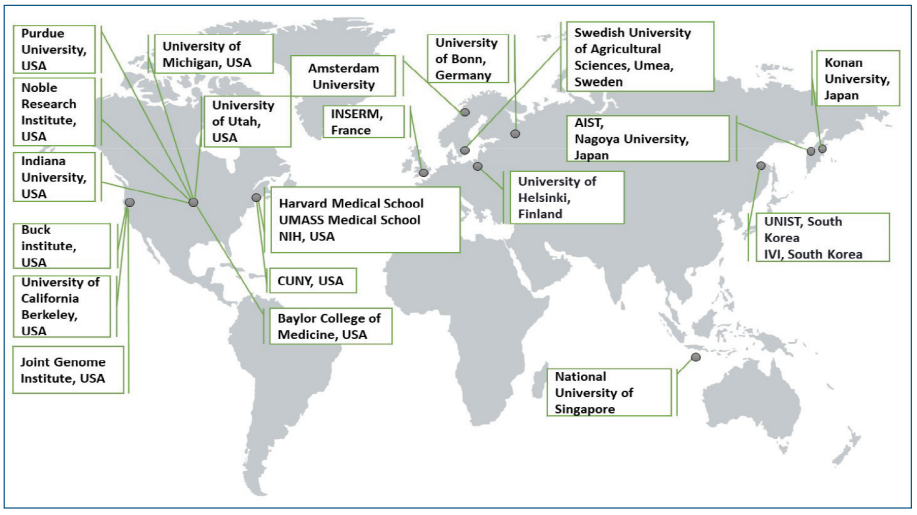
- Developed a natural bile acid peptide conjugate to eradicate the biofilms formed by fungus and gram-positive bacteria.
- A natural bile acid-derived Amphiphile-6 eradicated *S. aureus* from the infected catheter implants and skin wound infections, and showed a broad range of inhibitory activity against multiple drug-resistant clinical strains.
- The structure of a transcription factor that regulates biofilm formation from *Pseudomonas aeruginosa* was determined and demonstrated that the moderate activity of the protein is essential for rapid motility to biofilm transition.
- Identified from the Lewy body of Parkinson's disease (PD) a deubiquitinating enzyme OTUB1 that shows amyloid behavior in vitro and in redox stress condition, demonstrating it to be a critical regulator of PD pathology.
- Identified the role for epithelial deSUMOylase SENP7 in triggering expansion of proinflammatory Υδ T cells in distal gut during inflammatory bowel disease.
- Quantitative proteome analysis of fibroblasts that lack a functional autophagy pathway (*Atg5* knock-out) indicated a crucial role of autophagy for signaling, cell adhesion, development and immunity.
- A novel, essential and conserved crosstalk was identified between the endocytic and exocytic molecular machineries in mediating cytokinesis, revealing new molecular targets for therapeutic intervention against cancer and certain developmental disorders.
- The role of the endoplasmic reticulum resident chaperone protein ERp29 was defined in forming tunneling nanotubes from the surface of animal cells that may spread microbial pathogens and cancers.
- The first animal model to study the congenital muscle disorder Freeman-Sheldon Syndrome was successfully generated providing new insights to understand this disease and develop potential therapies.
- Produced and crystallized a recombinant pilus adhesin from an early colonizer *Streptococcus oralis* of dental plaque for its structure determination towards understanding and targeting pili-mediated interaction in combating infections.
- Developed insights into potential resistance and susceptibility mechanisms employed by the forage legume *Medicago truncatula* against the pea powdery mildew pathogen during an early infection event.
- Described the role of platelets in activating immune cells such as neutrophils and in turn triggering pro-inflammatory complication in haemolytic diseases such as paroxysmal nocturnal hemoglobinuria (PNH) and sickle-cell disease (SCD).
- Developed novel insights into the role of microglial cells released extracellular vesicles in Japanese encephalitis virus (JEV) infection providing a new dimension to extracellular vesicle-mediated events that may cause neuronal damage and JEV pathogenesis.

Intra-institutional collaborations



National Collaboration





Infrastructure and Support Services

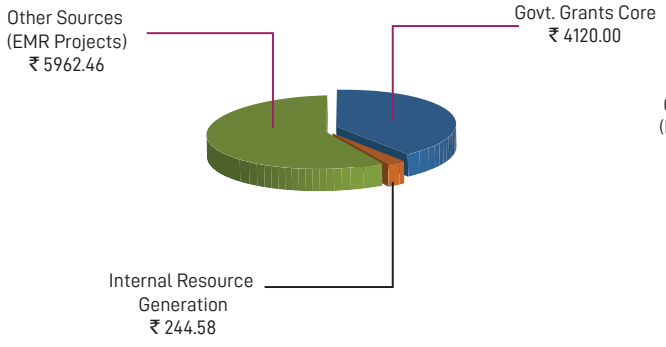
Advanced Technology Platform Centre

Biosafety Support Unit

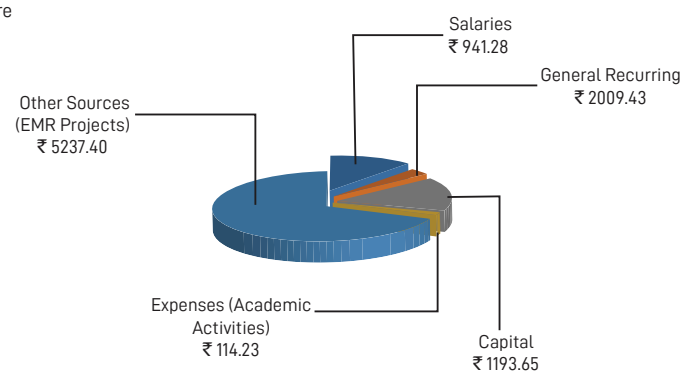
BSC BioNEST BioIncubator

Financial Figures

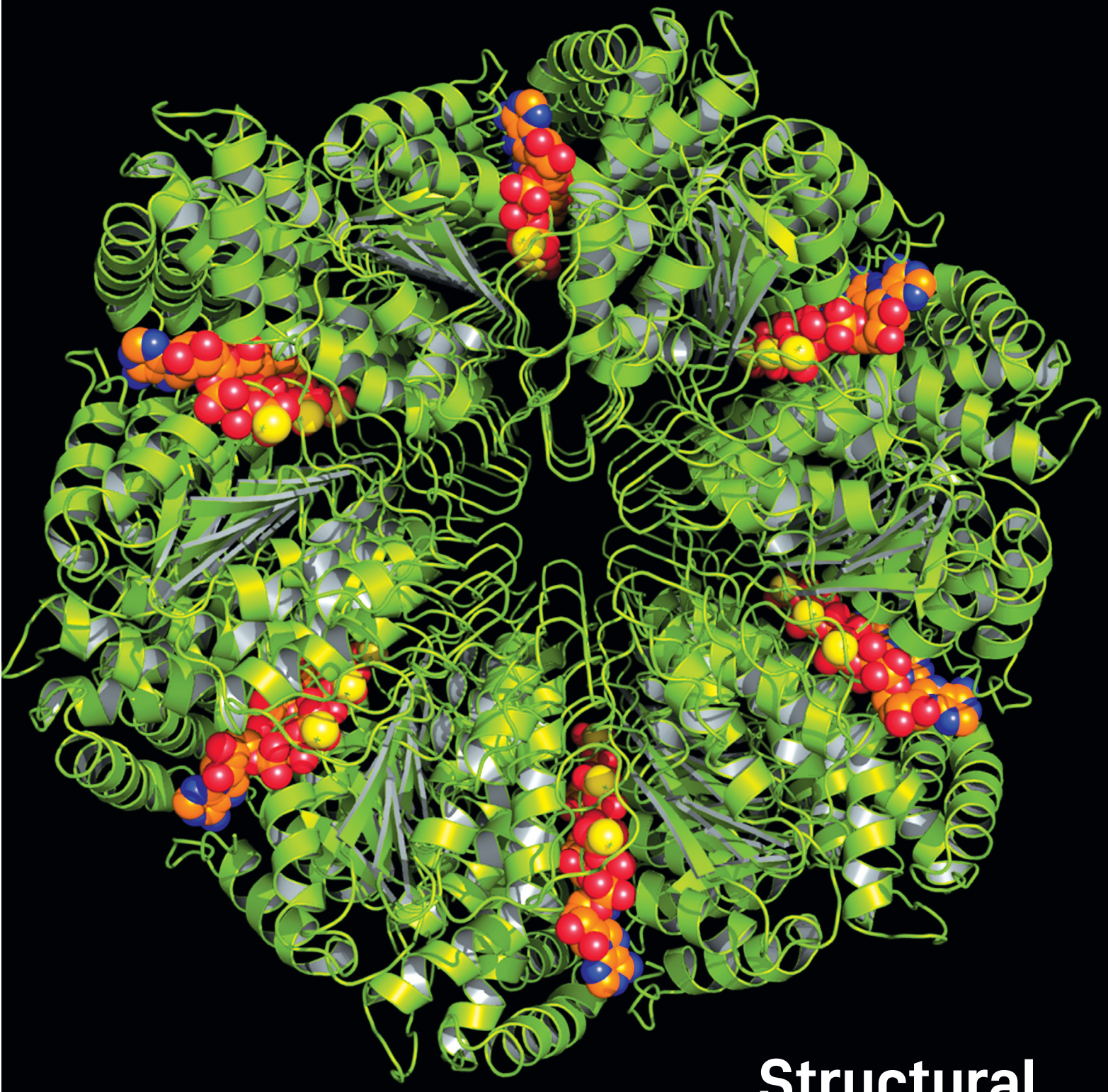
Total Income (Rs. In lakhs) 2019-2020



Total Expenses (Rs. In lakhs) 2019-2020



SCIENTIFIC REPORTS



Structural Biology

Deepak T Nair
Principal Investigator

Lab Members
Rahul Sharma
Shilpi Nagpal
Minakshi Sharma
Patterson Clement
Dalchand
Thangaraj V
Bhawna Mawri
Naveen Narayanan
Mary K Johnson
Naveen Kumar
Mayank Mamgain
Rashmi Joshi

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. Within this broad aim, some of the biological processes under scrutiny in our laboratory are DNA replication, stress-induced epigenetic modification and viral genome replication. The insights gained from these studies shed light on how organisms evolve and also provide a robust platform for the development of novel therapeutic strategies against pathogenic bacteria and viruses..

DNA Replication

DNA-dependent DNA polymerases (dPols) are the primary enzymes responsible for duplication of the genome. We study different dPols from various organisms to understand the chemical mechanism utilized to achieve their role in replication and evolution. Ribonucleotide incorporation during DNA synthesis by DNA polymerases leads to genomic instability and cellular lethality. To prevent the addition of rNTPs, a majority of DNA polymerases possess a steric filter in the form of a bulky aromatic residue that stacks against the ribose sugar. MsDpo4 from Mycobacterium smegmatis naturally lacks this steric filter and hence can incorporate ribonucleotides. In comparison to MsDpo4, DNA polymerase IV from Escherichia coli (PolIV) exhibits stringent selection of deoxyribonucleotides during DNA synthesis. A rigorous comparison of MsDpo4 and PolIV using structural, biochemical tools and growth assays led to the discovery of an additional polar filter utilized by DNA polymerases to prevent ribonucleotide incorporation. Overall our studies show that the polar and steric filter acts in

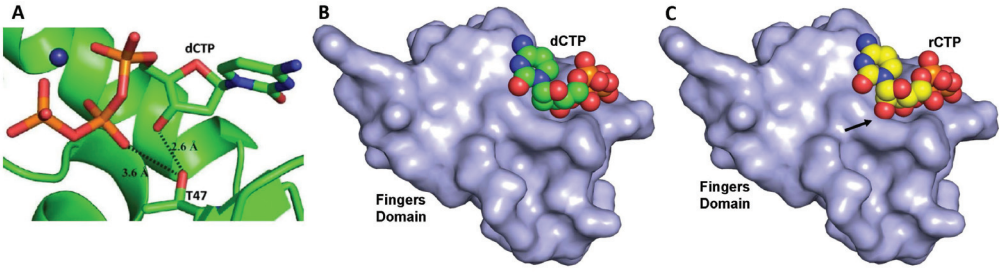


Figure 1: *Polar filter aids sugar selectivity. A) The crystal structure of the MsDpo4-C47TDNA(dG):dCTP complex shows that the 3' -OH and the β-phosphate of the incoming nucleotide form interactions with the engineered T47 residue. B) The surface of the fingers domain from the structure of the MsDpo4-C47TDNA(dG):dCTP complex along with the space-filling representation of the incoming dCTP is displayed. The figure shows that the dCTP molecule is accommodated in the catalytic site cavity without any steric clashes. C) The surface of the fingers domain from the structure of the MsDpo4-C47TDNA(dG):dCTP complex along with the space-filling representation of incoming rCTP modelled in the catalytic site is displayed. The 2'-OH of the modelled rCTP forms steric clashes with the surface of the fingers domain (highlighted by an arrow). The engineered residue (Thr47) therefore represents a polar filter that aids sugar selectivity.*

concert to avert adventitious rNTP addition by DNA polymerase. (Johnson et al., 2019, Nucleic Acids Res., 47:10693).

Stress-induced epigenetic modification

The pathogen *Helicobacter* pylori is responsible for stomach ulcers and gastric cancer. Restriction modification (RM) systems are abundant in this bacterium, and these RM systems

regulate natural transformation and consequent genomic plasticity of this microbe. Some DNA Methyltransferases (dMTases) that are part of these RM systems exhibit activity only in adverse conditions such as the highly acidic environment in the human stomach. Methylation of cognate sequences by these enzymes results in the swift alteration of transcriptional profiles to respond rapidly to environmental stress. We aim to elucidate the regulatory mechanisms that permit these enzymes to act only under specific environmental conditions. The expression of the dMTase coded for by the *hp0593* gene- named M.HpyAXI, is upregulated when the pathogen encounters low pH. M.HpyAXI is a Type III dMTase that belongs to the ß-class of these enzymes. The enzyme exhibits optimal activity at pH 5.5 and is predicted to modulate the expression of different genes to relieve acid stress and thus aid the survival of *H. pylori* in the human stomach.

We have determined the structure of M.HpyAXI in complex with the inhibitor sinefungin (SFG). The structure along with biochemical and biophysical analysis of site-specific mutants of M.HpyAXI suggests that the functional form of this enzyme is an oligomer that is formed only at low pH (Fig.1). This property of M.HpyAXI ensures that it is licensed to act only when the organism is subjected to acid stress (Narayanan et al, 2020, J. Mol. Biol. 432:24).

Viral Genome Replication

SARS-CoV-2 is the causative agent for the COVID19 pandemic, and this virus belongs to the Coronaviridae family. Like other members of this family, the virus possesses a positive-sense single-stranded RNA genome. The genome encodes for the nsp12 protein, which houses the RNA-dependent-RNA polymerase (RdRP) activity responsible for the replication of the viral genome. A homology model of nsp12 was prepared using the structure of the SARS nsp12 (6NUR) as a model. The model 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 vitamin B12 (methylcobalamin) may bind to the active site of the nsp12 protein (Fig. 2). A model of the nsp12 in complex with substrate RNA and incoming NTP showed that Vitamin B12 binding site overlaps with that of the incoming nucleotide. A comparison of the calculated energies of binding suggested that the vitamin may bind to the active site of nsp12 with affinity comparable to that of the natural substrates. It is, therefore, possible that methylcobalamin binding may prevent association of nsp12 with RNA and NTP and thus inhibit the RdRP activity. Overall, our computational studies suggest that methylcobalamin form of vitamin B12 may serve as an effective inhibitor of the nsp12 protein

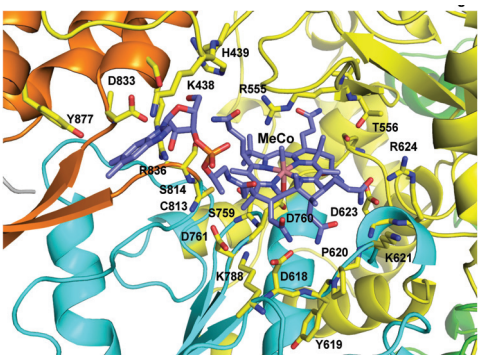


Figure 2: *Computational model of nsp12 in complex with methylcobalamin. The Vitamin B12 (MeCo) molecule is shown in stick representation and coloured according to element. The N-terminal extension region and the palm, fingers and thumb domains are shown in green, cyan, yellow and orange, respectively. The interacting residues are coloured according to element and shown in stick representation.*

Deepti Jain
Principal Investigator

Lab Members
Rohit Ruhal
Vineet Kumar
Aruna Rani
Chanchal
Priyajit Banerjee
Pankaj Kumar Sahoo
Shikha Raghav
Keshav Gupta
Sheenu
Sumit Kumar

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 an essential process responsible for gene expression. 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. The mechanistic insights obtained are exploited for the development of novel therapeutic agents against pathogenic bacteria and development of novel inducible recombinant expression systems. Following model systems are being employed

Regulation of flagellar and biofilm genes in Pseudomonas aeruginosa

Pseudomonas aeruginosa is an opportunistic human pathogen and is the primary cause for nosocomial infections. It also has a remarkable ability to form biofilms in a variety of environmental conditions. Biofilms are surface attached sessile communities of bacteria that are encapsulated in an extracellular polymeric substance or EPS. Biofilms are protective for the bacteria and allow them to survive in the hostile conditions such as antibiotic challenge or the host immune response. *Pseudomonas* is known to transition from a motile to a biofilm phenotype and this ability is regulated by transcription modulators called bacterial enhancer binding proteins. These transcription factors belong to AAA+ (ATPase associated with various cellular activities) family of proteins. FleQ protein from *Pseudomonas aeruginosa* is responsible for planktonic to biofilm transition. The activity of FleQ is regulated by anti-activator FleN. Recent studies from our laboratory have delineated the structural mechanism of anti-activation of transcription factor. We have determined the crystal structure of the complex and characterized the interactions between the transcription activator and its anti-activator (Fig. 3). We have shown that the anti-activator inhibits the catalytic activity of the activator and also prevents the formation of its functional form. Our lab is currently exploiting this finding for in silico screening of database of small molecules that can directly or allosterically inhibit ATP binding to the transcription factor. These molecules will be further examined for their ability to bind and inhibit the ATPase activity of FleQ through in vitro assays and eventually for their ability to inhibit biofilm.

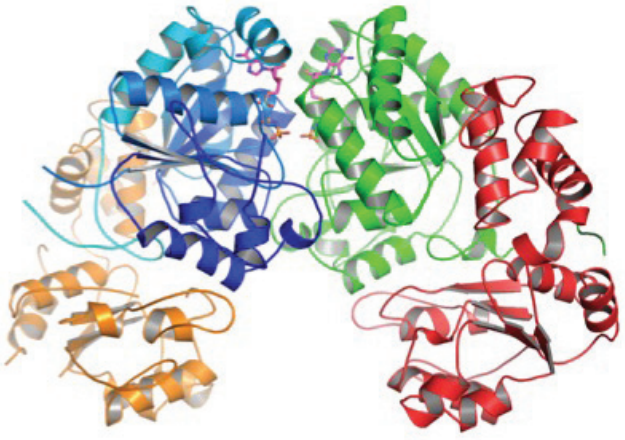


Figure 3: *Crystal structure of the activator and anti-activator complex*

Regulation of Antibiotic Resistance in Staphyloccocus aureus

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 very essential. The GraXSR (Glycopeptide Resistance Associated) regulon, is essential for antibiotic resistance in *S. aureus*. We have determined the crystal structure of the adaptor protein whose knockout results in downregulation of the genes necessary for resistance to antibiotics. Additionally, it was observed that the knockout of the adaptor protein results in increased

susceptibility to vancomycin indicating that this protein is an important target against development of antibiotic resistance. The in vitro and in vivo work is currently ongoing. This work will aid in deciphering the putative network responsible for the increase in glycopeptide tolerance in *Staphyloccocus.* The insights obtained from this study will be used to design and test small molecule inhibitors.

Establishing the mechanism of action of Bg_9562 a broad spectrum antifungal protein

This project is being carried out in our laboratory in collaboration with Gopaljee Jha from NIPGR. A prophage tail-like protein (Bg_9562) was shown to be essential for the fungal eating property of *Burkholderia gladioli* strain NGJ1. The purified protein causes hyphal disintegration and inhibits the growth of several fungal species. In our laboratory, we aim to understand the molecular basis of antifungal activity of the protein through structural analysis. A BLAST search reveals that Bg_9562 (110 aa) with a molecular weight of 11.3KDa, did not show any homology to proteins whose structures have been determined. The BLAST search also shows that Bg_9562 belong to Phage tail assembly chaperon (or TAC) family of proteins. A homology based model of the Bg_9562 was made (Fig. 4A). Based on model, it is predicted that the protein forms oligomers through the unstructured N-terminus (Fig. 4B). These oligomers are of variable length. Thus, in order to increase the homogeneity of the protein which will facilitate crystallization, various constructs were designed, cloned and expressed and purified in *E. coli.* These constructs were designed on the basis of structure prediction of Bg_9562, homology modelling and sequence alignment with the other members of TCA family of proteins. All the constructs were purified and screened for crystallization. Crystals were obtained for one of the protein constructs. An appropriate cryo-protectant for freezing was optimized and frozen crystals were diffracted in X-ray beam and the diffraction pattern was recorded. The crystals diffracted to about 7.8 Å at home source. The preparation of seleno-methionine labeled protein is under progress, which is required to determine the structure of Bg_9562.

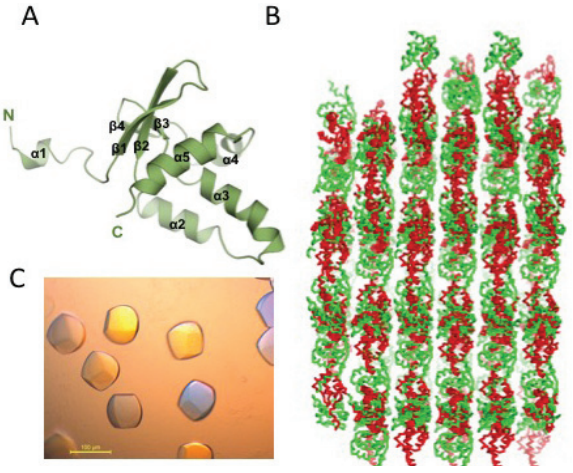


Figure 4: *A) Homology Based model of Bg_9562 B) Predicted oligomerization of the protein C) Crystals of Bg_9562 for structural analysiscomplex*

Vengadesan Krishnan
Principal Investigator

Lab Members
Shivendra Singh
Vijay Kumar
Abhiruchi Kant
Abhin Kumar Megta
Rajnesh Kumari Yadav
Amar Prajapati
Smita Yadav
Vinay Sharma

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 probiosis are highly dependent on the initial interaction or adherence. Interfering with the host-microbial interface (e.g. anti-adhesion therapy) is considered as one of the attractive approaches 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 host, and how the adhesive strategies differ among microbes. Towards providing the essential foundations for this approach and understanding the mechanism by which 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 called pili that enable the bacteria to establish the initial contacts with the host surfaces for colonization and biofilm formation. Our ongoing structural investigation programme covers certain beneficial and pathogenic strains for getting insights into tissue tropism and microbial interaction strategies in health and diseases. We have begun a structural investigation programme with strains from human gut and oral cavity which harbor largest and diverse microbiota.

Beneficial strains from gut microbiota

Lactobacillus rhamnosus GG (LGG) is one of the well-researched and widely-used probiotic strains for its various health-promoting effects. Its genome contains two different pilus operons (*spaCBA* and *spaFED*) for sortase-mediated pili formation. The *spaCBA* encodes a major/backbone pilin (SpaA), two minor pilins (SpaB and SpaC) and a pilin-specific C-type sortase (SrtC1). Similarly, the *spaFED* encodes a major pilin (SpaD), two minor pilins (SpaE and SpaF) and a C-type sortase (SrtC2). While the C-type sortase catalyzes the pilus polymerization, a housekeeping A-type sortase (SrtA) attaches the assembled pilus to cell-wall. The pili in LGG are the major contributing factors in human gut adherence and colonization. The LGG pili play a key role in persistence and immunomodulation in providing beneficial health effects. The LGG utilizes pili to mediate interaction with intestinal mucus and components of the extracellular matrix (ECM). Towards understanding the molecular mechanism by which this bacterium assembles pili and adheres to host surfaces, we began the structural investigation for the pilus constituents and sortases. Our earlier work on SpaA, SpaD and SpaE, has revealed new insights about pilus shaft formation

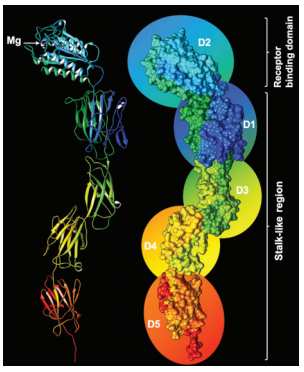


Figure 5: *Structure of pilus adhesin SpaC from L. rhamnosus GG. Ribbon (left) and surface (right) representation show the full-length SpaC crystal structure with five domains (D1, D2, D3, D4 and D5). The N-terminal binding domain (D1) is with MIDAS (metal ion-dependent adhesion site) containing vWFA (von Willebrand factor type A) module. The C-terminal stalk (D2, D3, D4, and D5) region contains immunoglobulin-like domains. An arrow marks magnesium ion (pink) in the MIDAS motif of vWFA domain (D2). The blend through color indicates the chain direction (N-terminal in blue and C-terminal in red).*

and ancillary pilin incorporation for the first time from a probiotic strain [Sci.Rep. 6:28664(2016), Comm.Biol. 1:94(2018) and J.Struct.Biol. 207:74(2019)].

The SpaB shows mucin-binding capacity in addition to its typical role as a basal pilin. Obtaining SpaB crystal remained particularly challenging until we implemented a three-pronged approach involving C-terminal tail truncation, surface lysine methylation and magnesium

additives. Ultimately, we obtained hexagonal crystals of SpaB and its structure determination is in progress. We have recently determined the structure of SpaC, and also crystallized the sortases (SrtC1 and SrtA). The SpaC structure shows multiple domains with exciting features. The SpaC, which is primarily responsible for the pili-mediated adhesion, shows the receptor-binding and immunoglobulin-like domains at the N- and C-terminal region, respectively (Fig. 5). Our initial analysis indicates that the N-terminal region is responsible for attachment with ECM components like collagen and mucin, while the C-terminal region act as stalk to facilitate the attachment. The imaging analysis further shows the presence of SpaC at the pilus tip (Fig. 6). Our ongoing interaction analysis of SpaC with ECM components would reveal more structural and mechanistic insights about attachment.

Lactobacillus ruminis (LRU) is an indigenous microbiota present in the gut of humans and other animals. In addition to its probiotic effects (immunomodulation, inhibition of pathogens, and maintenance of gut flora), the LRU is an indispensable agent in the fermentation of foods and feed. Its pilus operon (*lrpCBA*) encodes three pilins (LrpA, LrpB and LrpC) and one sortase (SrtC). In contrast to LGG pili, the LrpCBA lacks mucus-binding but shows affinity to collagen and fibronectin. Since LrpCBA pilus structure and mechanism of interaction could be different from that of LGG pili, it likely represents a third sortase-mediated pilus type in Lactobacillus species. The LRU pilus constituents were recombinantly produced, and their structure determination is in progress.

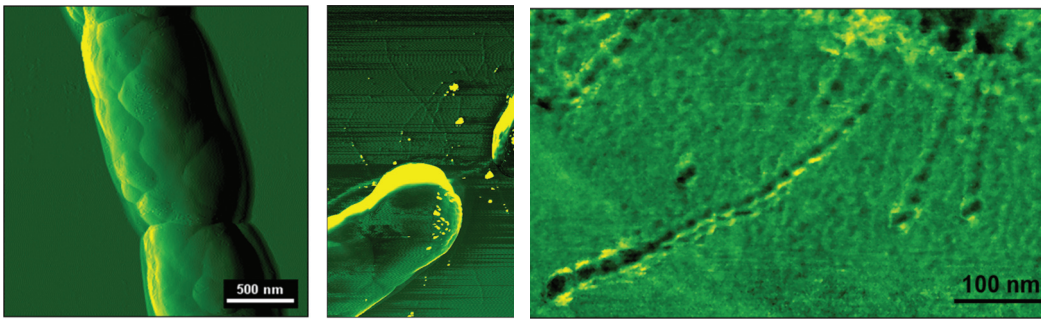


***Figure 6**: Atomic force microscopy (AFM) image of L. rhamnosus GG cells. Lock-in phase image of ΔSpaC a mutant (left) and wild type (middle) L. rhamnosus GG cells. The wild type cells show pili with different lengths while the mutant cells have no pilus extension. Enlarged view (right) of SpaCBA pili show beads-like pilus backbone (shaft) with bulky SpaC at the pilus tip.*

Pathogenic strains from the oral cavity

The oral cavity harbors 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 provide sites for other bacteria (secondary colonizers) to develop oral biofilms (plaque). The plaque damages teeth and gums and leads to several periodontal diseases such as carries and gingivitis. Pilus components from these primary colonizers were produced for structural characterization. Recently, we have crystallized pilus adhesin PitA from a primary colonizer *Streptococcus oralis* and X-ray diffraction data were collected.

We have initiated collaborative projects to study key molecules from *Mycobacterium* through structural investigation.

Prem S. Kaushal
Principal Investigator

Lab Members
Wahab Khan
Niraj Kumar
Sheenam
Shivani Sharma

Structural aspects of translation regulation and ribosome assembly

Translation, the process of protein synthesis, in which genetic information present in mRNA is decoded into a polypeptide, is a key step in central dogma of molecular biology. Our laboratory's research goal is to unravel the structural basis of the functioning of macromolecular complexes involved in translation regulation and in ribosome assembly, thereby, identifying the potential drug targets. We are focusing on the structural aspects of protein synthesis in Mycobacterium tuberculosis (Mtb) in dormancy, and to understand how a mega Dalton protein synthesis machinery, the ribosome, assembles inside the cell.

Understanding the translation strategies M. tuberculosis adopts in dormancy

MTb the causative agent of tuberculosis (Tb), is one of humankind's deadliest disease. MTb becomes dormant, nonreplicating and phenotypically drug resistant when it encounters multiple stress within the host macrophages. This condition is also known as latent tuberculosis infection (LTBI) or the dormancy. Nearly, one third of world population possesses LTBI out of which ~10% people develop acute Tb infection. In order to mimic the host macrophage stress environment, different models have been developed. The most widely accepted models are: (1) Wayne hypoxia model, (2) Lobel nutrient starvation model and (3) Multi stress condition model in which MTb are grown in low oxygen, low nutrient and different stress conditions, respectively. We were able to grow *M. smegmatis* under hypoxia by following Wayne hypoxia model in our laboratory. It took 45 days to achieve hypoxia at room temperature (25°C). The literature suggests that it should take two weeks' time at 37°C. We are in process of growing mycobacteria in bacterial incubator at 37°C. We also tried to grow *M. smegmatis* under nutrition starvation, following Loebel model of starvation. After a week it was observed that culture started aggregating because of very low agitation. We will next grow the cells in the roller bottle to attain nutrient starvation condition and prevent aggregation. We have also started the ribosome isolation and purification from *M. smegmatis* and were able to partially resolve the ribosomal 70S, 50S and 30S, fractions. Further optimization is in progress (Fig. 7A). We were also able to standardize the protocol for electron microscopy (EM) and were able to collect negative stained EM images (Fig. 7B) and cyo- EM images (Fig. 7C).

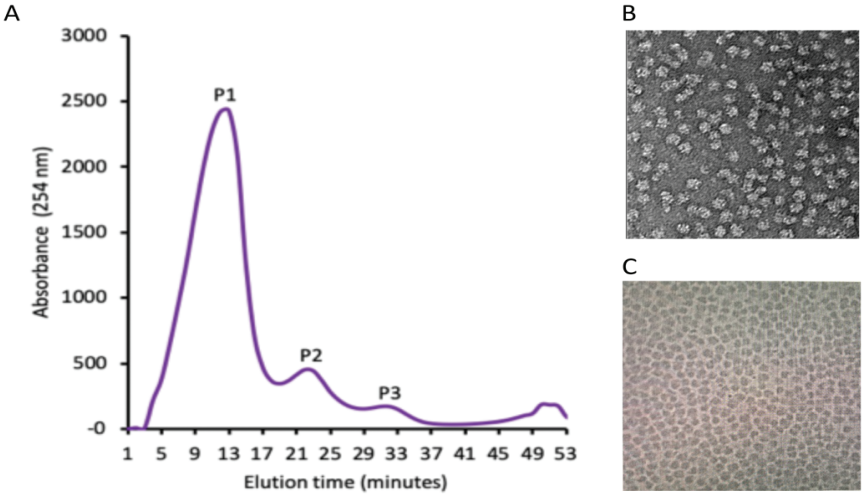


Figure 7: *Ribosome purification and electron microscopy. A) Fractionation of crude ribosome in 10% - 40% sucrose gradient using BIORAD FPLC system, peaks P1, P2 and P3 corresponds to 70S, 50S and 30S subunits, respectively. B) Negatively stained electron microscopy Image and C Cryo- electron microscopy image of 70S ribosome. The negative stained EM images were collected in JEOL 14400 microscope and cyo- EM images were collected in JEOL 2200FS microscope equipped with K2 submit direct detector camera at Advance Technology Platform Centre (ATPC), RCB, Faridabad.*

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

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

We were able to overexpress, and purify RafH by Ni-NTA his tag purification (Fig. 8A) and gel filtration (Fig. 8B). The crystallization attempts were made and crystal were checked in X-ray beam at home source. To our disappointment all crystal obtained so far turned out to be salt crystals.

Role of a DEAD box helicase, RhlE, in ribosome assembly

Ribosomes are the ribonucleoprotein (RNP) complexes of mega Dalton (mDa) size and are responsible for protein synthesis in the cells. Each ribosome is composed of two subunits, a large subunit (LSU), where peptidyl transference takes place and a small subunit (SSU) which is responsible for decoding mRNA. Prokaryotic ribosome is composed of 52 ribosomal proteins (RPs) and 3 rRNAs. The formation of functional ribosome is a complex process, and defects in ribosome assembly is associated with various diseases such as Diamond-Blackfan anemia, Cartilage hair hypoplasia and cancer etc.

The DEAD-box helicase family of proteins are ATP dependent RNA helicases that cause local melting of the dsRNA by introducing a bend in the bound RNA strand and acts as ribosome maturation factors. The RhlE, a DEAD-box helicase, is shown to modulate the activity of SrmB and DeaD by regulation of 23S precursor accumulation in ΔSrmB or ΔDeaD mutants, resulting in formation of 40S particles instead of 50S particle. Therefore, a thorough understanding of the RhlE would provide insights in its role in ribosome assembly. We were able to overexpress and purify *M. tuberculosis* RhlE by using His tag Ni-NTA affinity (Fig. 8C) and gel filtration (Fig. 8D) techniques. Further, effort for crystallization is in progress.

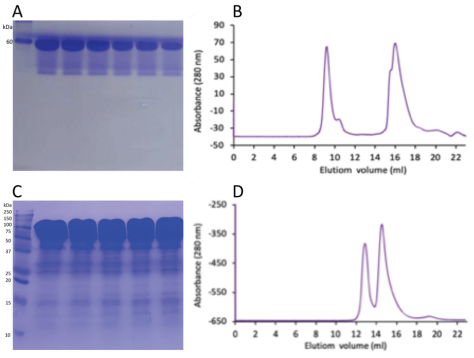
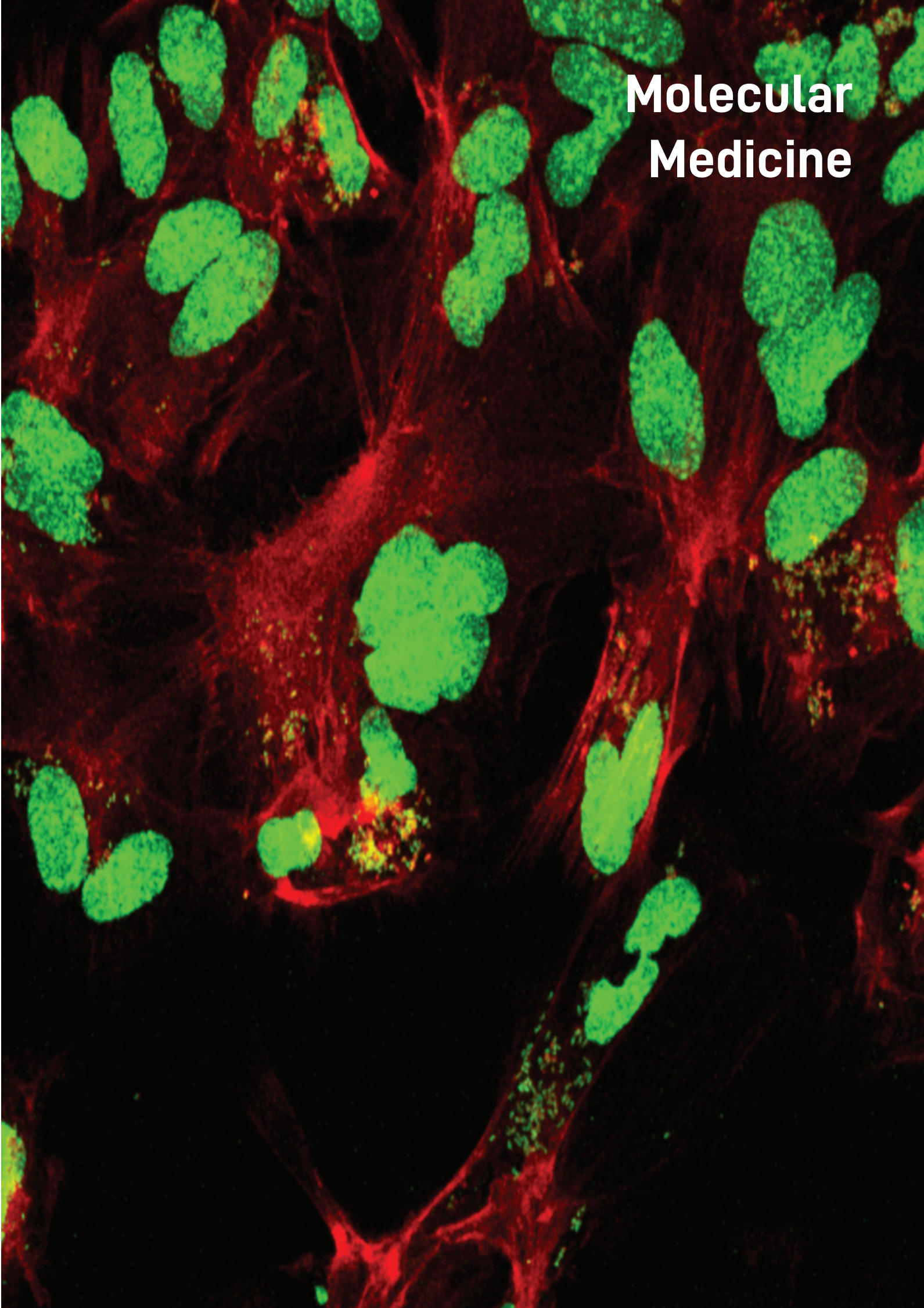


Figure 8: *Protein overexpression and purification. A) RafH purification by using His-tag, Ni-NTA affinity chromatography and B) further purification by gel filtration using Superdex 200 10/300 GL column. C) RhlE purification by using His-tag, Ni-NTA affinity purification D) gel filtration using Superdex 75 10/300 GL column. First and second peaks correspond to the void volume and protein of interest, respectively.*



Molecular Medicine

Prasenjit Guchhait
Principal Investigator

Lab Members

Sulagna Bhattacharya
Nishith Shrimali
Sakshi Agarwal
Anamika Singh
Kishan K Gaur
Simrandeep Kaur
Riya Ghosh
Piyush Bisht

Inflammation and Thrombosis in Human Diseases

This research program is designed to understand the: 1) Molecular mechanism of inflammation and thrombosis in acute mountain sickness (AMS) and high-altitude pulmonary edema (HAPE) in mountain travellers to high altitudes; also to investigate, how the Tibetans with genetic adaptation are protected from these hypoxia-driven disorders at high altitudes; 2) To examine inflammation and thrombosis in metabolic (type 2 diabetes), hemolytic (PNH and SCD) and autoimmune (aHUS and SLE) disorders; 3) To study the host inflammatory response to viral infections including Dengue, JEV and SARS-CoV-2. The program also aims to find biomarkers and molecular targets to develop potential therapeutics for prophylaxis of these complications.

AMS and HAPE

Recently, we have shown that the Tibetan specific mutation (C12G and G380C) in *EGLN1* gene [which encodes Prolyl hydroxylase-2 (PHD2), the negative regulator of hypoxia inducible factor (HIF)1α] or $PHD2^{D4E/C127S}$ variant protects them from polycythaemia (elevated RBCs and hemoglobin). Further, we show that the variant protects Tibetan highlanders 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. This suggests the use of αKG in the prophylaxis of systemic as well as lung inflammation, commonly observed in AMS and HAPE.

Metabolic, hemolytic and autoimmune disorders

Although the pathophysiological mechanisms of inflammation and thrombosis are different, we focus on investigating the crosstalk of leukocytes-platelet, a common mechanism associated with the severity of these diseases. We are investigationg the: 1) Mechanism of elevated activation of platelets/leukocytes and its association with systemic/local (organ) inflammation and pulmonary fibrosis in patients and mice with type-2 diabetes (T2D). 2) Association between intravascular hemolysis and inflammation/thrombosis in hemolytic disorders including paroxysmal nocturnal hemoglobinuria (PNH) and sickle cell disease (SCD); 3) The activation of complement factor-H (FH) in conjunction with FH-related proteins (FHR), and their association with systemic and organ inflammation in patients with autoimmune disorders including atypical hemolytic uremic syndrome (aHUS) and systemic lupus erythematosus (SLE).

Dengue, JEV and SARS-CoV-2

Recently, we have shown that elevated plasma PF4 is associated with increased replication of Dengue virus (DV) and Japanese encephalitis virus (JEV) in monocytes, and also decreased Interferon (IFN) synthesis in Dengue patients and JEV-infected mice. Our further investigation gives insights into the molecular mechanisms of the PF4-mediated elevation in viral replication in monocytes. We show a significantly less colocalization of LAMP1 (lysosomal marker) and NS1

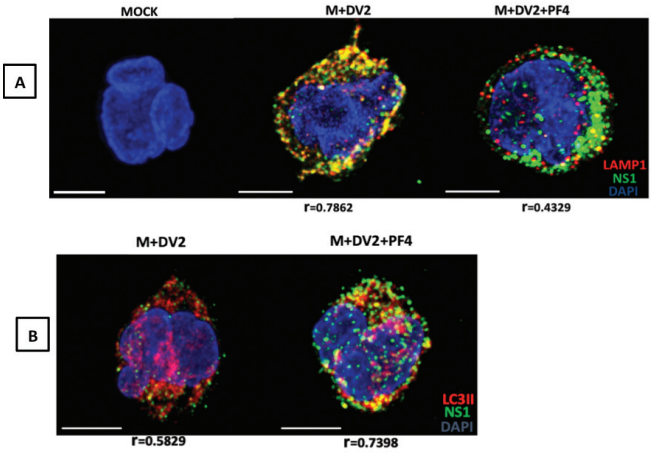


Figure 9: *Monocytes isolated from healthy individuals, were infected with Dengue virus-2 (DV2, MOI~3) for 24 hrs and stained for viral NS1 and human LAMP1 and LC3II, and image was taken using confocal microscopy. The colocalization of the proteins is presented as r ~ correlation coefficient. Image bar, 5μm.*

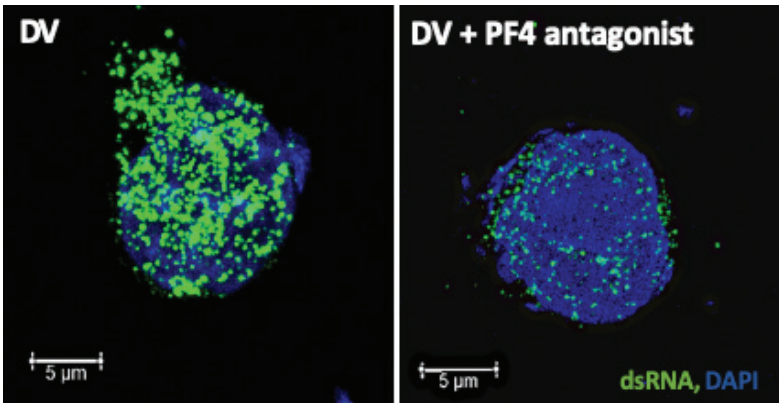


Figure 10: *Monocytes isolated from healthy individual, were infected with Dengue virus-2 (DV2, MOI~3) for 24 hrs with and without PF4 antagonist and stained for viral dsRNA and image was taken using confocal microscopy.*

(viral protein), Fig.9A, and higher colocalization of LC3II (autophagy marker) and NS1, Fig. 9B, in monocytes in presence of PF4 *in vitro*, suggesting the involvement of autophagy-lysosomal pathways. We are investigating the role of PF4 - IFNα/β axis in the infection of above viruses.

Current focus

1) We are investigating the anti-inflammatory potential of αKG in the prophylaxis of HIF-driven inflammatory disorders using inflammatory mice models. 2) We are working on the role of collagen-platelet and platelet-leukocytes in developing lungs fibrosis using mice (genetic as well as induced) models of T2D. 3) We are testing small molecule inhibitors for PF4 *in vitro* and in mice model of JEV and DV infections. As outlined in Fig. 10, one the drugs from our library (screened through MTT assay) is showing significant inhibition of DV replication in monocytes *in vitro*. 4) We are also assessing the lungs inflammation, cytokine storm and hypoxemia (less oxygen in arterial blood) in hACE2-transgenic mice or hamster models of SARS-CoV-2 infection. In addition, we are focued on developing treatment against hypoxia-triggered inflammation in SARS-CoV-2 infected mice.

Tushar Kanti Maiti
Principal Investigator

Lab Members
Amit Kumar Dey
Bhoj Kumar
Sanghati Bhattacharya
Sanjay Kumar
Raniki Kumari
Manisha Kumari
Sandhini Saha
Sushanta Majumder
Krishna Singh Bisht

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 the abnormal accumulation of intracellular or extracellular protein aggregates in different parts of the brain. The impairment of protein quality control leads to the 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.

Role of novel deubiquitinating enzyme OTUB1 in Parkinson disease pathogenesis

Parkinson's disease (PD) is the second most common neurodegenerative disorder, which is characterized by the death of dopaminergic neurons in the midbrain. Lewy body (LB) formation is the hallmark of PD pathology. PD is accompanied by shaking, rigidity, slowness of movement, difficulty with walking and ultimately death. Genetic factors, ageing and excessive exposure to environmental toxins contribute to the etiology of PD. Recent studies have shown that more than 500 proteins are present in the LB and many of them are co-enriched with α-synuclein. These proteins belong to the family of kinases, deubiquitinases, ubiquitin ligases, chaperones and oxidative stress regulators. The functional role of a few proteins has been studied. However,

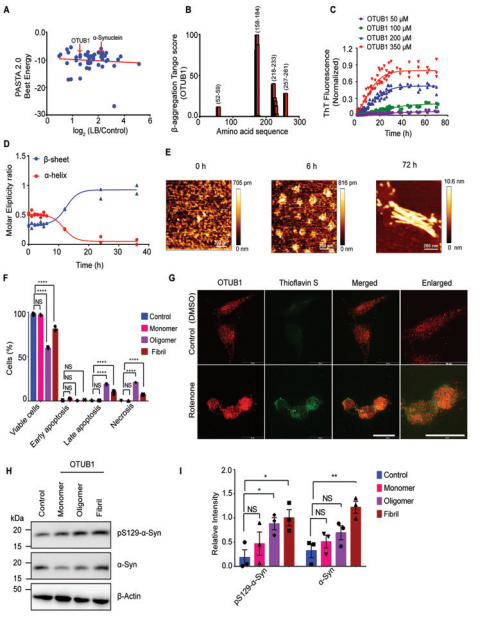


Figure 11: *A) Correlation plot of PASTA 2.0 energy of 27 proteins. Blue dot, PASTA 2.0 best energy of each protein. PASTA 2.0 best energy of OTUB1 and α-synuclein, which are -8.0 and -7.0, respectively. B) Prediction of amyloidogenicity of OTUB1 by Tango score. Amino acid residues 158–184 show the highest scores in Tango analysis. C) ThT fluorescence intensity shows the amyloid property of OTUB1 at different concentrations during aggregation (mean ± S.E., n ≥ 3).D) CD spectroscopy, showing the molar ellipticity ratio of α-helix (208/218 nm) and β-sheet (218/208 nm) at different time points (mean ± S.E., n ≥ 2). E) The structural topology of OTUB1 at each time point was monitored by AFM. OTUB1 changes morphology from the OTUB1 monomer, oligomers to the mature fibrillary structure during the aggregation cycle. F) Quantification of flow cytometry (Annexin V FITC/PI). A scatter plot of quantified flow cytometry data shows the cell percentage of the viable cell, early apoptotic cell, late apoptotic cell, and necrotic cell after treatment with OTUB1. Values are mean ± S.E. (error bars), n ≥ 3. G) Cells were exposed to 500 nM rotenone for 24 h. Images show the OTUB1 (red) aggregated inside the cell and co-localized with Thioflavin S (green). Scale bar, 20 µm. H) Cells were exposed to OTUB1 in Opti-MEM medium. Immunoblot showing the expression level of pS129-α-synuclein and α-synuclein. β-Actin was probed for total protein loading control. I) Scatter plot showing the quantification of immunoblotting.*

In summary, our study demonstrates OTUB1 as a novel amyloidogenic protein in the LB and provides its aggregation in vitro and in mice model. Oligomeric structure of OTUB1 is a specific molecular form which potentiates neuronal toxicity, cytoskeleton disruption, the abrupt release of ROS and damage of mitochondria. OTUB1 co-localizes with the pS129-α-synuclein in neuronal cells and PD mice model. This study is published in Journal of Biological Chemistry and has been illustrated in the schematic model (Fig.12). Apart from its deubiquitination activity and negative regulator of Ubc13, amyloid aggregation of OTUB1 provides a new mechanism in synucleinopathies which can be further studied.

the precise role of these proteins in PD pathogenesis is still limited. Many of the identified proteins have not been investigated yet in the context of PD. Thus, it is pertinent to study their role in PD mechanism.

OTUB1, a deubiquitinating enzyme of the OTU family, is enriched with α-synuclein in LB of Parkinson's patients. However, its role in neuronal function and neurodegenerative diseases has not been investigated. OTUB1 is also majorly expressed in brain and its presence in Lewy Body is intriguing to us. We have reanalyzed the reported mass spectrometry data and found that 52 proteins have shown a significant differential expression in Lewy bodies of PD than control. We also analyzed the aggregation propensity of these 52 proteins using different bioinformatics pipelines and observed a high degree of aggregation propensity of OTUB1 like many reported amyloidogenic proteins. Further, we checked the amyloidogenicity of OTUB1 in the *in-vitro* condition. ThT is a dye that binds with the amyloid proteins and shows an increase in ThT fluorescence. Here, we observed that OTUB1 strongly binds with ThT dye at heat-induced condition. We also tested the secondary structural change upon heat induction using circular dichroism spectroscopy and observed a gradual conversion of α-helical structure to β-sheet structure upon 37°C incubation. The heat-induced aggregates of OTUB1 showed a fibrillar morphology in atomic force microscopy at 72 h. However, at 6 h time point, we observed an oligomer of annular ring-like geometry (Fig.11). Many amyloid proteins like Huntington protein, Ataxin3Q82, and Amylin peptide are shown to have an annular-like structure and they exhibit strong cytotoxicity.

We measured the toxicity of different forms of OTUB1 (monomer, oligomers, and fibrils) in SH-SY5Y using Annexin-FITC assay. The OTUB1 oligomers showed more toxicity than the fibril species. We also analyzed the inclusion formation of OTUB1 in confocal microscopy by staining SH-SY5Y cells with Thioflavin S and anti-OTUB1 antibody upon rotenone exposure. Thioflavin S is a fluorescent dye that binds with amyloid protein in cells or tissue. Rotenone-treated cells showed strong co-localization of Thioflavin S with OTUB1. However, control cells did not show any signal of Thioflavin S. These results provide evidence for cellular aggregation of OTUB1 in redox stress conditions. Cell-to-cell propagation of aggregated protein plays an important role in the progression of α-synucleinopathies. The enhanced accumulation of pS129-α-synuclein in the neurons is considered to be an important pathological hallmark of PD progression. We exposed the different forms of OTUB1 (monomer, oligomers, and fibrils) to SH-SY5Y cells and checked the expression of α-synuclein and pS129-α-synuclein. Both OTUB1 oligomers and fibrils showed an increase in pS129-α-synuclein and α-synuclein expression (Fig.11).

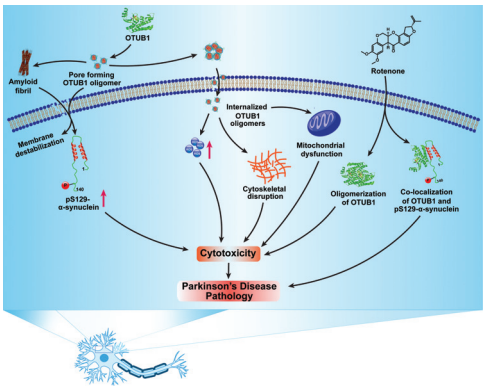


Figure 12: *Schematic model of OTUB1 mediated PD pathogenesis.*

Sam J Mathew
Principal Investigator

Lab Members
Masum Saini
Bhargab Kalita
Megha Agarwal
Pankaj Kumar
Akashi Sharma
Shreyasi Das
Anushree Bharadwaj
Subhashni Sahu
Nimisha Mishra
Shashank Khare

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 skeletal muscle is able to carry out these critical functions due to its ability to contract, a crucial property mediated by actin and myosin proteins. Formation of the mammalian skeletal muscle occurs in distinct phases during embryonic, fetal, neonatal and adult stages. We are studying how different myosin proteins regulate skeletal muscle development, maintenance and regeneration, and how their absence lead to muscle diseases using animal models. We are also studying signaling events that result in a cancer type called rhabdomyosarcoma, where the tumor cells exhibit properties of muscle cells.

Myosins in skeletal muscle development and disease

Myosins are proteins that are present in all cell types, essential for fundamental cellular functions such as cell movement, cell division and transport of cargoes within cells. A specialized set of myosin proteins known as muscle myosins, which are required for muscle contraction, are expressed by the skeletal muscle. While most muscle myosin proteins are expressed in the adult muscle, two are expressed only during embryonic development. Very little is known about these developmentally expressed muscle myosins except that mutations in the gene encoding one of the myosins, *MYH3,* leads to Freeman-Sheldon Syndrome (FSS) in humans, a genetic disease causing severe musculoskeletal abnormalities including joint deformities, bent fingers, club feet, curved spine and facial anomalies. FSS patients have compromised movement, respiratory, speech and feeding problems and delayed growth and development.

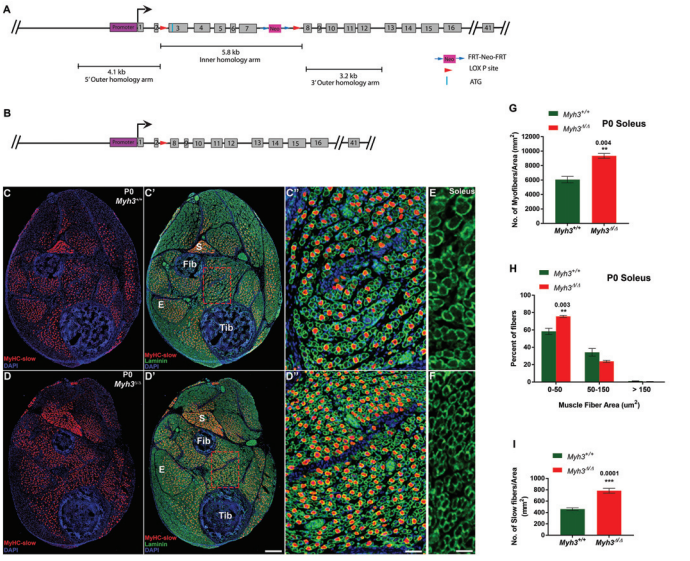


Figure 13: *Loss of MyHC-embryonic leads to neonatal myogenic defects. A-B) Schematics depicting Myh3fl3-7 allele, where LoxP sites (red arrowheads) flank exons 3-7 A) and the Myh3Δ allele lacking exons 3-7 of Myh3 (B). C-D'') Confocal microscopy images of cross sections through the hind limbs of P0 Myh3+/+ (C-C') and Myh3Δ/Δ (D-D') mice labeled by immunofluorescence for MyHC-slow (red), Laminin (green) and DAPI (blue); ('E' and 'S' denote EDL and soleus muscles respectively and 'Tib' and 'Fib' denote tibia and fibula bones respectively in C' and D'; C'' and D'' are magnifications of boxed areas of the flexor digitorum longus (FDL) muscle from C' and D' respectively). E-F) Laminin (green) labeling through the soleus muscles of P0 Myh3+/+ E) and Myh3Δ/Δ F) mice. G) Quantification of myofiber number through the soleus muscle of P0 Myh3+/+ and Myh3Δ/Δ mice. H) Quantification of myofiber area through the soleus muscle of P0 Myh3+/+ and Myh3Δ/Δ mice, grouped into area bins of 0-50 µm2, 50-150 µm2 and above 150 µm2. I) Quantification of MyHC-slow+ fibers from P0 Myh3+/+ and Myh3Δ/Δ shank whole cross section normalized to total area. (Scale bar in D' is 200 microns, D'' is 40 microns and F is 20 microns).*

Laboratory mouse have been used to understand the functions of the *Myh3* gene (which codes for MyHC-embryonic protein) during embryonic, fetal and neonatal development. We generated targeted mouse models for *Myh3* using which we found that the loss of MyHC-embryonic leads to muscle abnormalities including alterations in muscle fiber type, fiber number and fiber size (Fig. 13). We also found that MyHC-embryonic is required to regulate the rate of differentiation of the muscle stem cells during development, and that this effect is mediated by fibroblast growth

factor (FGF) signaling (Fig. 14). Interestingly, although MyHC-embryonic is expressed in all muscles, we find that loss of MyHC-embryonic has differential effects on distinct muscles. We also observed that adult mice lacking MyHC-embryonic exhibit scoliosis (abnormal curved spine), an abnormality seen in individuals with Freeman-Sheldon Syndrome (Fig. 14).

MyHC-embryonic leads to scoliosis in adult mice, a defect seen in FSS patients, and this mouse model could thus be a valuable tool in understanding the defects underlying this congenital disorder. We are also investigating the function of MyHC-embryonic in adult muscle regeneration.

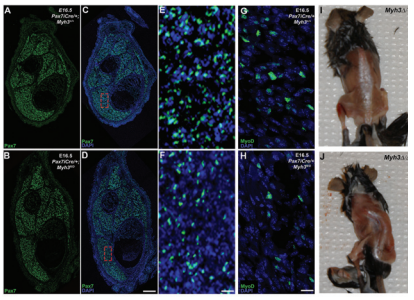


Figure 14: *MyHC-embryonic non-cell autonomously regulates myogenic progenitor differentiation during embryonic and fetal myogenesis. A-F) Immunofluorescence for Pax7 (green), and DAPI (blue) on cross sections through E16.5 control (A, C, E) and Pax7iCre/+;Myh3Δ/fl3-7 (B, D, F) embryo hind limbs; E and F are magnifications of boxed areas from C and D respectively. G-H) Immunofluorescence for MyoD (green), and DAPI (blue) on cross sections through E16.5 control (G) and Pax7iCre/+;Myh3Δ/fl3-7 (H) embryo hind limbs. I-J) 6-week old Myh3Δ/Δ mice exhibit scoliosis (I), compared to control Myh3Δ/+ animals (H). (Scale bar in D is 200 microns, and in F and H are 20 microns)*

Signaling pathways that regulate rhabdomyosarcoma

Rhabdomyosarcoma (RMS) is a tumor type predominantly seen in children, where the tumor cells exhibit skeletal muscle characteristics and are thought to arise from muscle stem cells that undergo uncontrolled cell division. However, unlike the skeletal muscle, the RMS tumor cells do not differentiate terminally. RMS tumors can occur in different regions of the body and are currently treated by radiotherapy, surgery and chemotherapy. We are investigating signaling pathways that are mis-regulated in RMS tumors, which could be used as targets to facilitate terminal differentiation of RMS cells. This could lead to improved strategies to treat patients with RMS tumors.

Modulation of MET signaling and its role in myogenesis

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

Cell signaling, including cascades transduced by receptor tyrosine kinases (RTKs), is the cornerstone of regulated physiological processes. Abnormal cellular communication, therefore, skews the physiological balance towards pathological states. MET is a proto-oncogenic RTK crucial to embryonic development, particularly critical for migration of skeletal muscle precursors during muscle development (myogenesis). MET signaling is vital for post-injury muscle regeneration and is deranged in several cancers including Rhabdomyosarcoma (RMS), a pediatric soft-tissue cancer where tumor cells resemble muscle precursors and fail to differentiate. Therefore, to ascertain the mechanistic regulation of MET signaling that is a connecting thread between muscle development, regeneration and disease, I am using mouse genetics and in vitro tools. We are generating mouse models to first characterize MET expression during embryonic development and muscle regeneration in adult mice. Further, we are also planning to ablate MET in the myogenic lineage in the mouse, to understand its role in developmental and regenerative myogenesis.

Geetanjali Chawla
Principal Investigator

Lab Members
Sakshi Bansal
Manish Pandey

RNA Biology of Aging and Dietary Restriction

The complex process of 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)-reduced nutrient intake that does not incur 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 diverse 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. Regulatory RNAs include a variety of evolutionarily conserved classes of small noncoding RNAs [small interfering RNAs (siRNAs), microRNAs (miRNAs), small nuclear RNAs (snRNAs) and piwi interacting RNAs (piRNAs)] as well as the relatively newly evolved long noncoding RNAs (lnRNAs). Despite growing evidence that ncRNAs are altered during aging, there is little evidence on dietary restriction dependent positive effects on ncRNAs and their targets or the pathophysiological consequences of these alterations. This research program combines the genetically amenable fruit fly model with high throughput technologies such as RNAseq, proteomics and metabolomics to identify conserved miRNA-mediated networks that operate during aging and dietary restriction. This study is of direct relevance to the study of human age-associated diseases, as the inappropriate expression of miRNAs has been linked to a number of 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.

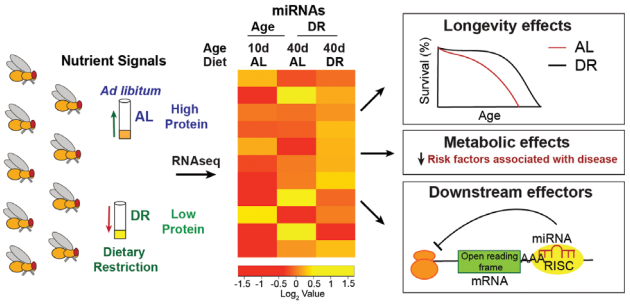


***Figure** 15: Working model for identification and characterization of age- and diet-modulated miRNA networks. (Left panel) Fruit flies were fed Ad libitum (AL) or nutrient restricted (DR) diet and total RNA extracted from young (10 d) and aged (40 d) flies was used to perform small RNAseq. (Middle panel) Heat map showing miRNA abundances in adult fruit flies exposed to AL diet for 10 days (column 1), AL diet for 40 days (column 2) and DR diet for 40 days (column 3). (Right panel) The identified age- and diet-modulated miRNAs and their downstream targets are being characterized for their ability to extend lifespan and reduce risk factors associated with diseases.*

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 interested in using the fruit fly, *Drosophila melanogaster* as a model to study miRNA-mediated post-transcriptional networks that operate during aging and late onset diseases. 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 assess whether miRNAs can mimic the effects of DR in animals that are fed a normal diet, we performed high throughput

RNA sequencing of small RNAs isolated from fruit flies exposed to dietary restricted and nutrient-rich diets (Fig. 15). Since mutations in 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 will aid in defining miRNA mediated mechanisms that operate during aging and determine how targeted disruption, competitive inhibition or overexpression of miRNA network components modulates aging.

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

Human neurodegenerative diseases are characterized by the progressive and widespread loss of neurons in the central nervous system, with aging being the major risk factor for disease onset. Recent studies have found that miRNAs are mis-regulated 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 mechanisms underlying miRNA-mediated neurodegeneration and to explore miRNA-mediated therapies designed to ameliorate neurodegenerative symptoms. We have identified a few conserved miRNAs that are altered in a diet-dependent manner in AD models (Fig. 16) and are currently examining the effects of modulating these miRNAs on disease progression. Together these studies are aimed at developing RNA based therapeutic strategies to fine-tune conserved pathways that are able to provide broad spectrum health improvement and can aid in the development of treatments for late onset diseases simultaneously.

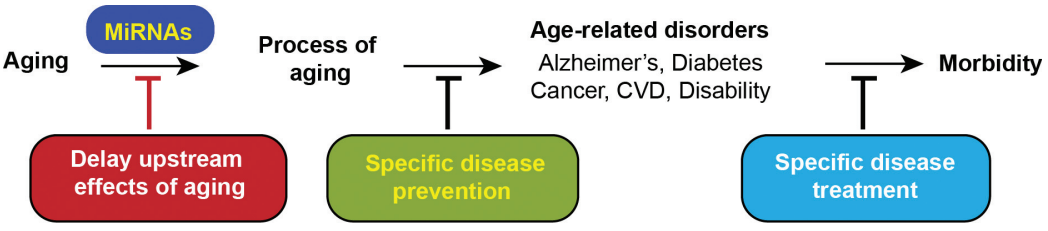


Figure 16: *Slowing the rate of aging as a strategy to delay onset of multiple diseases. Schematic representing the various stages at which therapeutic strategies can be designed for treatment of age-related degenerative diseases. We are testing the efficacy of miRNAs to slow down the rate of aging and prevent multiple diseases simultaneously.*

Pinky Kain
Principal Investigator

Lab members
Shivam Kaushik
Banwari Lal
Srishti Sanghi

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 the 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.

Activity and state dependent modulation of salt feeding behavior in Drosophila melanogaster

Table salt (NaCl) is a key component of many tasty foods. Sodium present in the salt is a fundamental nutrient that is required for many physiological processes, the most important ones includes electrolyte homeostasis and neuronal activity in the animal body. In animals including mammals and *Drosophila*, the detection of NaCl produces two different behaviors in a concentration dependent manner: low-salt concentration <100 mM acts as an attractive cue and induces attraction, whereas high-salt concentrations >200 mM evoke aversive behavior. A complex code for salt taste at the periphery has been proposed recently in flies. However, how feeding on high salt modulates the feeding behavior, especially how it affects the preferred level of salt and other taste preferences is a yet-to-be-identified area and has not been explored earlier. In one of our studies, we identified that pre-exposing adult flies to high salt concentration (200 mM) in the fly media for three days maintains their preferences towards high salt even later, and enhances taste sensitivity for selective sugars. Wild type mated female flies show high feeding preferences towards high salt diet and show increase in body weight, probably to get enough sodium during the reproductive phase. Wild type flies also show developmental delay, have shorter life spans and lay less number of eggs when grown on high salt media throughout. Under starvation, high salt pre-fed flies with silenced neuronal activity of peripheral sweet (Gr5a+) or bitter neurons (Gr33a+) (pharyngeal neurons are still active in these cases) show enhanced feeding responses and consume more salt. Our results suggest a role of intact active pharyngeal LSO (Labral Sense Organ) neurons irrespective of what receptor they express in decision making and regulating high salt intake in flies, where sensitivity of LSO neurons increases towards salt, particularly when exposed to high salt previously. Our

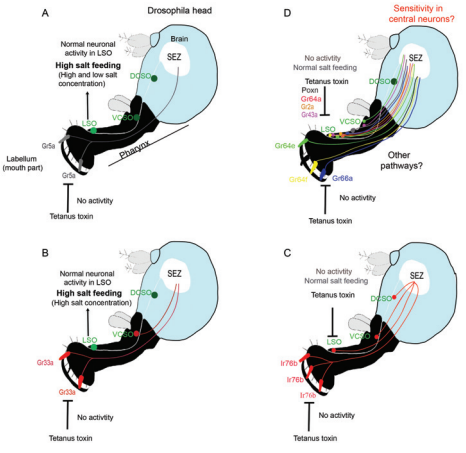


Figure 17: *Role of activity and starvation state in pharyngeal LSO neurons. A and B. The pharynx of flies consists of LSO (labral sense organ), VCSO (ventral cibarial senses organ) and DCSO (dorsal cibarial sense organ). Silencing peripheral sweet and bitter (labellum) neurons with tetanus toxin causes increased feeding on salt in high salt sensitized flies due to intact LSO neurons. Pre-feeding of flies on high salt sensitize pharynx LSO neurons and cause amplified feeding responses. Under starvation silencing LSO neuronal activity specifically bring down these increased feeding responses to normal (C and D).*

study reveals that neuronal activity and the starvation state in salt-sensitized pharyngeal LSO neurons play important roles in regulating salt intake and present a complex code at the level of the internal taste organ. Our results suggest that reciprocal regulatory mechanisms may exist for regulating salt intake between the peripheral and pharyngeal taste organs like LSO and play an important role in sodium homeostasis. Furthermore, the linkage between salty and sweet taste modulations may optimize sodium and calorie intakes. Understanding the mechanism of high salt feeding and its effect on feeding behavior, longevity, mating and egg laying behavior in insects like *Drosophila* could help in preparing inexpensive and effective pesticidal salt baits for pest control.

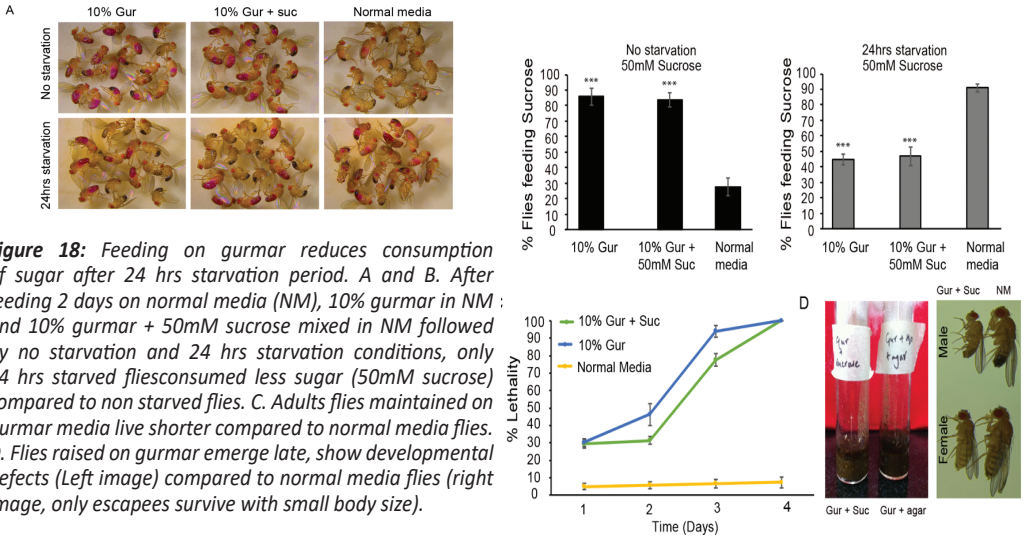
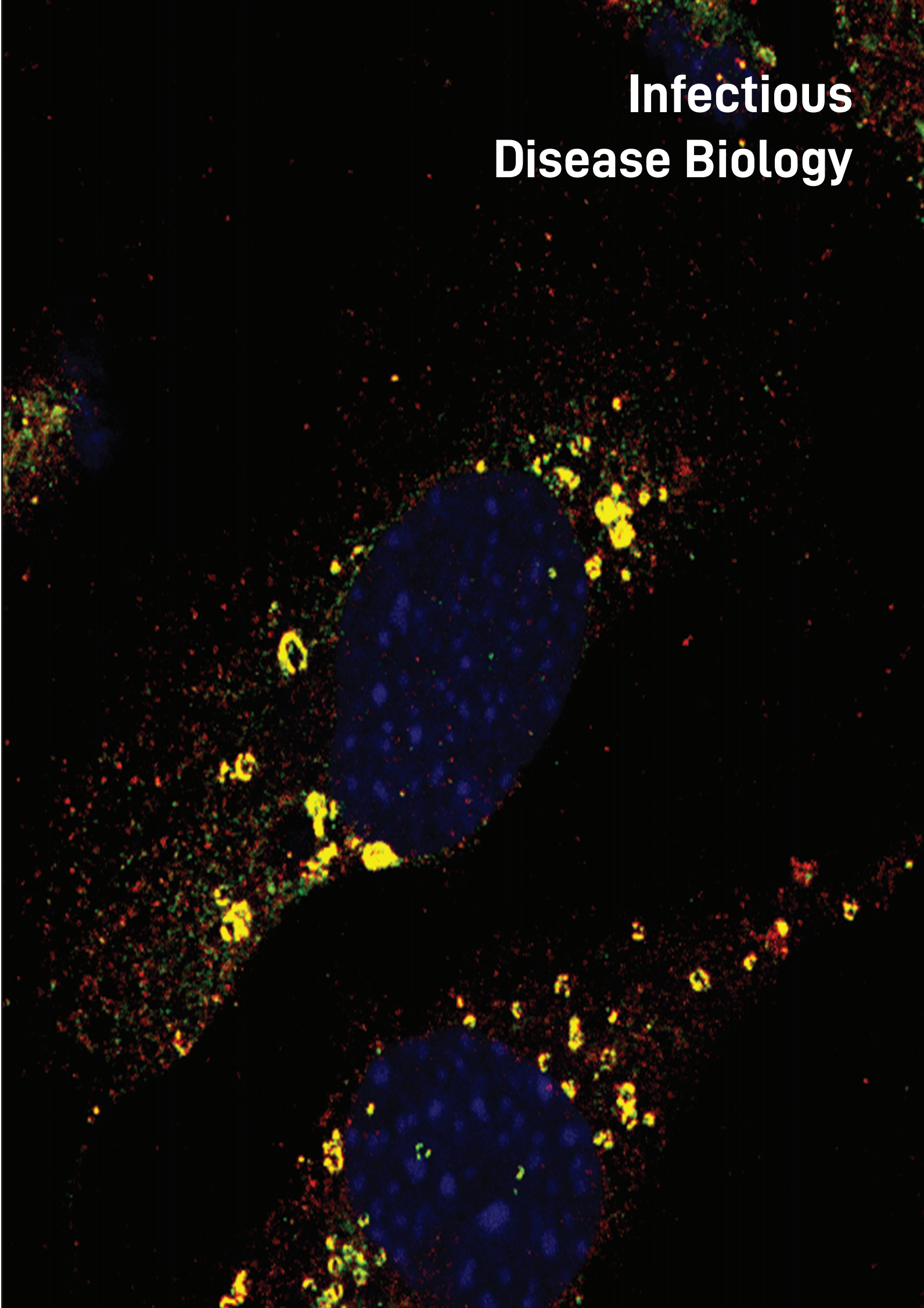


Figure 18: *Feeding on gurmar reduces consumption of sugar after 24 hrs starvation period. A and B. After feeding 2 days on normal media (NM), 10% gurmar in NM and 10% gurmar + 50mM sucrose mixed in NM followed by no starvation and 24 hrs starvation conditions, only 24 hrs starved fliesconsumed less sugar (50mM sucrose) compared to non starved flies. C. Adults flies maintained on gurmar media live shorter compared to normal media flies. D. Flies raised on gurmar emerge late, show developmental defects (Left image) compared to normal media flies (right image, only escapees survive with small body size).*

Modulation of taste behavior by Gymnema sylvestre in Drosophila melanogaster

Sugar is the main source of energy for nearly all animals. However, consumption of high amount of sugars can lead to many metabolic disorders including obesity, diabetes and cardiovascular diseases, hence balancing calorie intake in the form of sugar is required. Taste helps in evaluating and choosing food rich in calories and avoiding compounds that are toxic to the body. Like humans, *Drosophila melanogaster* can sense and differentiate between all taste modalities. Various herbs are in use to control the body weight, cure diabetes and control elevated blood sugar levels. One such herb is *Gymnema sylvestre*, commonly called as Gurmar (destroyer of sugar), is shown to selectively inhibit sugar sensation and curb the cravings for sugar. Using *Drosophila*, we are trying to understand the effect of gurmar on the feeding behavior of flies. Our data demonstrate that gurmar causes early lethality, developmental defects and is aversive to flies. Our data also suggest that gurmar acts on taste neurons or receptors to reduce the consumption of sugar in flies only if they are starved for at least 24 hours. Our study has the potential to be useful in developing cost effective strategies for pest control using a raw powdered form of gurmar and save agricultural crops from insects.

Infectious Disease Biology



Sudhanshu Vrati
Principal Investigator

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

Lab Members
S. Chandru
Shweta Duggal
Priyanka Sharma
Sapna Sehrawat
Arundhati Deb
Brohmomoy Basu
Shivani Balyan
Chetna Mathur

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. This program aims to study the biology of mosquito-driven viruses relevant to India, such as Chikungunya (CHIK), Dengue (DEN) and Japanese encephalitis (JE) viruses, to understand their replication and pathogenesis with a view to design novel antiviral strategies. 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 2560 compounds that includes all drug molecules, we have identified lead compounds that show inhibition of CHIK virus infection in 3 different cell types at 1 micromolar concentration. A mouse model of CHIK virus infection in mice has been established where at least a couple of these compounds have shown antiviral potential. Attempts are underway to understand the mechanism of antiviral action of these compounds.

A 96-well plate high throughput assay has been developed to test the DEN virus antivirals. A collection of compounds obtained from the AIST is currently being screened for anti-DEN virus activity in this assay.

Valosin-containing protein plays critical roles in the JE virus life cycle

Host factors provide critical support for every aspect of the virus life cycle. We previously identified the valosin-containing protein (VCP)/p97, an abundant cellular ATPase with diverse cellular functions, as a host factor important for JE virus replication. In the cultured cells, using siRNA-mediated protein depletion and pharmacological inhibitors, we showed that VCP was crucial for the replication of three flaviviruses: JE, Dengue, and West Nile viruses. An FDA-approved VCP inhibitor, CB-5083, extended the survival of mice in the animal model of JE infection. While VCP depletion did not inhibit flavivirus entry, it delayed the JE virus capsid degradation, potentially through the entrapment of the endocytosed virus in an early endocytic compartment. Early during infection, VCP-depleted cells showed an increased colocalization of JE virus capsid with clathrin, and also higher viral RNA levels in early endosome fractions. We show that VCP interacts with the JE virus nonstructural protein NS5 and is an essential component of the virus replication complex. Mechanistically, thus, VCP affected two crucial steps of the JE virus life cycle – nucleocapsid release and RNA replication. This study establishes VCP as a common host factor with a broad antiviral potential against flaviviruses

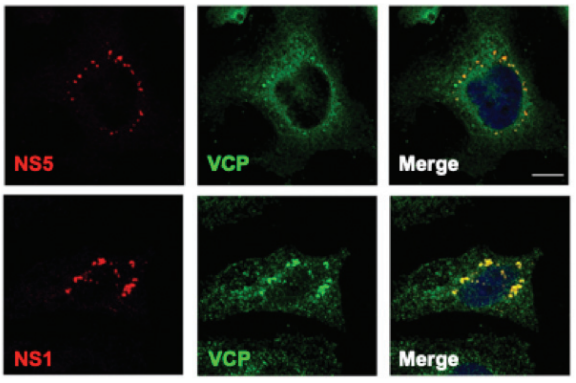


Figure 19: *Colocalization of VCP with JE virus non-structural proteins NS1 and NS5.*

Dengue virus infection impedes megakaryopoiesis in MEG-01 cells

DEN virus infection causes dengue fever in humans, which can lead to thrombocytopenia showing a marked reduction in platelet counts, and dengue hemorrhagic fever. The virus may cause thrombocytopenia either by destroying the platelets or by interfering with their generation via the process of megakaryopoiesis. MEG-01 is the human megakaryoblastic leukemia cell line that can be differentiated in vitro by phorbol-12-myristate-13-acetate (PMA) treatment to produce platelet-like-particles (PLPs). We have studied DEN virus infection of MEG-01 cells to understand its effect on megakaryopoiesis and the generation of PLPs. We observed that DEN virus could infect only naive MEG-01 cells, and differentiated cells were refractory to virus infection/replication. However, DEN virus-infected MEG-01 cells, when induced for differentiation with PMA, supported an enhanced viral replication. Following the virus infection, the MEG-01 cells showed a marked reduction in the surface expression of platelet markers (CD41, CD42a, and CD61), a decreased polyploidy, and significantly reduced PLP counts. DEN virus infection caused an enhanced Notch signaling in MEG-01 cells where the virus envelope protein was shown to interact with TAL-1, a host protein important for megakaryopoiesis. These observations provide a new insight into the role of DEN virus in modulating the megakaryopoiesis and platelet production process.

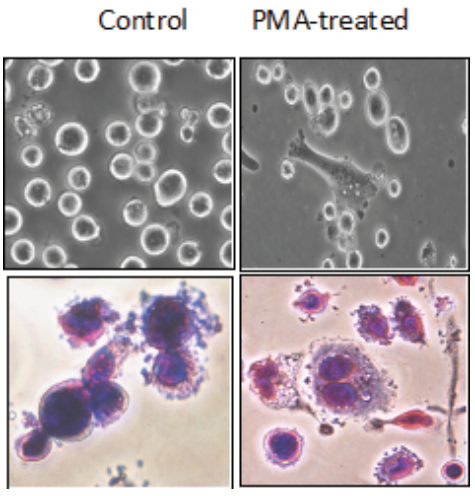


Figure 20: *PMA treatment of MEG-01 cells induces differentiation and enhanced production of platelet-like particles.*

Characterization of distal gut virome through metagenome sequence analysis

Dr. Kanchan Bhardwaj
DBT Biocare Awardee

We have sequenced metagenomes of free viruses (dsDNA and ssDNA) and lysogenized bacteriophages that are present in fecal samples collected from a "healthy" population of Indian individuals. Data analysis has shown that majority of the identified viruses are bacteriophages. A significant proportion of sequences belong to a recently identified new family of bacteriophages, crAss-like phages. We are classifying them to understand their relationship with the strains found in other geographical locations and ecosystems as well as investigating their functional potential. In addition, focus of our analysis is also to provide support for the presence or absence of a core virome in human gut. Further, we are applying various bioinformatics approaches to assemble complete genomes for better understanding of the gut viruses as well as to identify candidates for bio prospecting.

Chittur V Srikanth
Principal Investigator

Lab members
Aamir Suhail
Sarika Rana
Pharvendra Kumar
Hridya Chandrasekhar
Preksha Gaur
Sonalika Maurya
Rohan Babar

Molecular biology of infectious and idiopathic inflammation of the gut

Uncontrolled inflammation is a major culprit in a number of gut illnesses including inflammatory bowel disease (IBD). IBD includes two major forms, ulcerative colitis (UC) and Crohn's disease (CD), both accompanied by chronic inflammation in the gut leading to a severely compromised life. In CD the inflammation may be anywhere in the gut, while in UC it is restricted to the colon. Notably, gastroenteritis caused by gastric pathogens such as *Salmonella* predispose individuals for IBD. Efforts of our group is directed at understanding novel molecular mechanisms that shape intestinal inflammation and autoimmune disorders. Using a mutli-pronged methodology involving a range of different model systems, we are studying SUMOylation pathway and other post-translational modification pathways that may be crucial in both IBD and *Salmonella* pathogenesis. The results of our studies are expected to provide novel insights into intestinal inflammations and facilitate possibilities of development of strategies for fighting such autoimmune diseases.

Intestinal epithelial-immunocyte crosstalk involving DeSUMOlase SENP7

IBD represents chronic remittent disorders that have been characterised by alarmingly increasing incidence in the recent decades. Intestinal epithelial cells (IECs) act as sentinels as they sample luminal contents and orchestrate optimal immune response. However, the molecular determinants of IEC-immune compartment interaction are not well understood. Recent publications from our own group and others has highlighted the importance of SUMOylation, a reversible PTM mechanism, in governing IEC signalling. Specifically, upregulation of deSUMOlase (SUMO-deconjugase, SENP7) in IBD was seen in initial experiments. We hypothesised that SENP7 may contribute to IEC signalling and intestinal inflammation. In the current work, we have investigated the possible involvement of epithelial deSUMOylases in IBD.

We carried out dextran sulphate sodium treatment of mice for 7 days that resulted in development of intestinal inflammation, mimicking human IBD. Analysis revealed a significantly upregulated expression of SENP7 protein in gut of DSS treated animals (DSS mice), but not control animals. Notably, increase in SENP7 expression was seen in intestinal epithelial cells, crypts and villi (Fig. 21). In line with this, SENP7 expression analysis in human patient biopsy samples revealed a significant increase UC and CD patients. These changes were also accompanied with a decrease in global SUMO-conjugation and a rise in free SUMO in these samples. Together these data suggested that the expression of deSUMOylase enzyme SENP7 is altered in human and murine colitis.

Using high-resolution mass spectrometry, SENP7 interactome was probed. The analysis revealed several interesting regulatory proteins and substrates of SENP7. A key finding was SIAH2, an E3-ubiquitin ligase, known to participate in protein turnover. Furthermore, the primary amino acid sequence of SENP7 harbors a motif (PxAxVxP), known to be present in substrates of SIAH2. Co-immunoprecipitation experiments and imaging experiments revealed a strong and specific interaction of SIAH2 and SENP7 occurring via PxAxVxP motif. Biochemical tests revealed that SIAH2 ubiquitinated SENP7 and thereby controlled its stability.

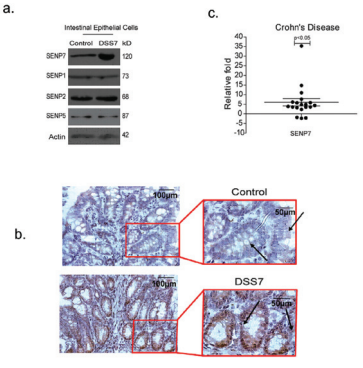


Figure 21: *Upregulated expression of SENP7 in intestinal tissues of murine and human IBD. a. Expression analysis of deSUMOylases by immunoblotting from whole colonic tissue lysates of mock treated and 2.5% DSS treated mice (labeled as DSS7) (n=3). ß-Actin was used here as a loading control. b. Immunohistochemistry of SENP7 from colonic sections. Cell nuclei blue, scale bar 100 µm. c. Quantitative RT PCR-based fold change expression of SENP7 from human CD (n=19) and UC (n=19) patients colonic epithelium relative to averaged control values (baseline zero) (n=19) are plotted. Each dot represents data from one sample. Expression values of GAPDH were used for normalization. Statistical test was performed between control and IBD (UC and CD) group using Mann-Whitney U-test (p-value as indicated).*

Next, SENP7 was experimentally perturbed in epithelial cells followed by co-culturing with immunocytes. To see the effect of SENP7 perturbation on immune cells, we used flow cytometry. The co-culturing resulted in no other change, except an increase in the number of Υδ T cells, a category of T lymphocytes. Furthermore, higher Υδ T cells correlated with a massive increase in proinflammatory cytokines. These data allowed us to conclude that epithelial SENP7 activation is sufficient for triggering inflammatory signaling via expansion of Υδ T cells.

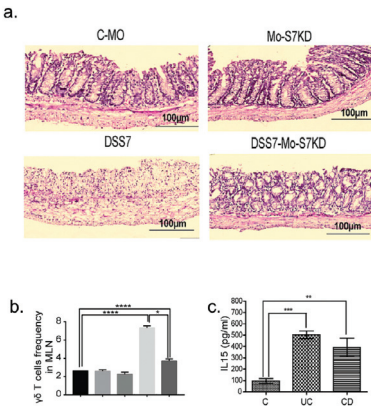


Figure 22: *Intestinal epithelial SENP7 triggers intestinal inflammation by recruiting γδ T cells. A) Histopathology of colonic sections of SENP7-customised morpholino injected mice and the other groups (C-MO: control morpholino treated, MO-S7KD: SENP7 morpholino treated, DSS: DSS treated, MO-S7KD-DSS: SENP7 morpholino treated and DSS treated). b) Bar graphs showing frequency of γδ T cells in the presence of morpholino-mediated SENP7 knockdown treated with DSS compared to other groups in Mesenteric Lymph Nodes (MLNs). Flow cytometry done in a BD FACS Canto, analyzed using Flow jo and represented in the form of a bar graph (mean + SEM values) c) ELISA of IL-15 from mucosal extracts of UC and CD (n=8 each) and control patient endoscopic samples (n=5). Statistical differences were calculated using Prism by two-way ANOVA with Tukey's test. *p,0.05, **p,0.01, ***p,0.001.*

To understand the specific role of SENP7 in the gut, we developed an *in vivo* knock-down mice model of SENP7 using a commercially available customized morpholino-based technology (Gene Tools, LLC). The knock-down of SENP7 rescued the animals from DSS induced colitis (Fig. 22). The histopathology of the ceca and colon of SENP-7 knock-down mice revealed no signs of inflammation. Furthermore, they were devoid of Υδ T cells. This was in stark contrast to control DSS mice which showed epithelial disruption, crypt abscess, PMN infiltration and ulceration. Analysis of cytokines in the intestine of control DSS mice revealed elevated levels of several pro-inflammatory cytokines such as IFN-Υ, TNF-αand IL17A. However, the SENP7 knock-down mice were completely devoid of these cytokines.

Since our results point towards a role for Υδ T cells, we investigated the cytokines, IL15 and KGF that control these immunocytes using human patient samples. Significantly elevated levels of both these cytokines were seen in UC and CD samples compared to the control group. We also analyzed profiles of SIAH2 and SENP7 expression with relation to CD and UC disease severity. Interestingly both CD and UC samples with moderate disease indices were always associated with high SENP7 expression. Furthermore, patients with mild disease indices displayed a low SENP7. These differences were also statistically significant as revealed by a strong correlation by strata analysis. We have shown crucial involvement of SENP7 in epithelial signaling and immune cell recruitment in IBD (Suhail et al., 2019 Cell reports 29:3522). We are currently involved further dissecting this mechanism and in devising strategies to curtail SENP7 function in the gut to combat inflammation.

Manjula Kalia
Principal Investigator

Lab Members
Surendra Kumar Prajapat
Puja Sharma
Sakshi Khera
Renu Khasa
Kiran Bala Sharma

Host-Pathogen Interactions of Flaviviruses

Japanese encephalitis virus (JEV) is a major public health concern for India and every year several cases are reported. The virus is spread by mosquito bites and several children succumb to the disease every year. The virus infection leads to acute brain fever (encephalitis). Though vaccines are available, no drugs or therapeutics against JEV have been developed. Treatment for the disease is only supportive and hence there is an urgent need for the development of effective anti-virals or therapeutics. During a 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.

Our lab research focuses on how JEV intersects with the cellular pathways such as endocytosis and autophagy, and with cellular organelles such as the endoplasmic reticulum (ER), and how this impacts the immune response and virus pathogenesis. This year we have made progress on understanding changes in the cellular proteome during virus infection, and how the virus exploits lipid droplets (LDs) for its propagation. We are also working towards understanding how pharmacological modulation of autophagy can be exploited as a potential therapeutic target for JE.

Proteome landscape of JEV infection

We have recently completed and validated a based mass spectroscopy study to elucidate the proteome landscape of JEV infection. This was done by comparing the level of protein abundance between uninfected/mock and JEV infected cells. We observed that JEV infected condition displayed a 2.96% change in the cellular proteome of fibroblasts. Pathway enrichment analysis of up and down regulated proteins showed that several proteins involved in defense response to virus, response to interferons (IFN), positive and negative regulation of innate immune responses, regulation of proteolysis, antigen processing and presentation, cytokine mediated signaling, inflammatory responses and positive regulation of programmed cell death were enhanced in JEV infected condition (Fig. 23). These proteins had diverse molecular functions such as RNA binding, ubiquitin-like protein ligase binding, ubiquitin-protein transferase activity, cytokine activity, exonuclease activity and MHC protein binding etc. These data suggest that fibroblasts activate a robust immune response against JEV infection and are likely to generate an anti-viral state during infection.

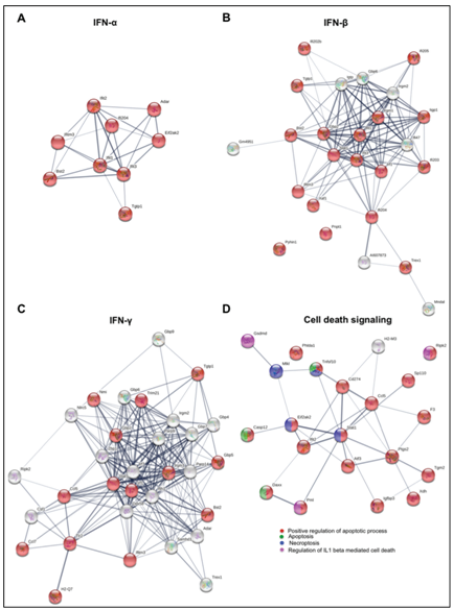


Figure 23: *JEV infection activates the host response to type-I and type-II interferon and cell death signaling in fibroblasts.Functional protein association network of JEV activated IFN-α A), IFN-β B) and IFN-Y C) mediated signaling proteins was generated using STRING 11.0. D) A functional protein association network of cell death-related signaling proteins was generated using STRING 11.0. The line thickness (-) indicates the strength of data support.*

Characterization of the JEV replication complex and the role of host factors

Virus genome replication takes place in virus induced specialised intracellular membranous structures described as convoluted membranes (CMs) and vesicle packets (VPs). The VPs are composed of both viral and host proteins, and confine viral RNA replication to specific cytoplasmic locations. Viruses hijack a diverse array of host proteins to induce the formation of these replication complexes. Virions are assembled in close proximity to the ER and LDs.

We have characterized the role of a host-factor, the Microtubule-associated protein 1 light chain 3 (MAP1LC3, and henceforth LC3) for virus replication. LC3 is an ubiquitin-like protein and its lipidated form (LC3-II) is a defining characteristic of autophagosomes. However, the non-lipidated LC3 (LC3-I) also has autophagy independent roles and a part of the virus replication complex.

We have observed that the JEV capsid protein associates with LC3-I in infected cells. This association was also observed on lipid-enriched membranes and is likely to be essential for ribonucleoprotein and subsequent infectious virus particle formation. The number of lipid droplets decreased significantly in JEV infected cells highlighting a link of virus replication with lipid droplet metabolism. A detailed molecular modelling study identified a putative LC3-interacting region in the capsid protein and key residues that are likely to be involved in LC3-capsid interaction.

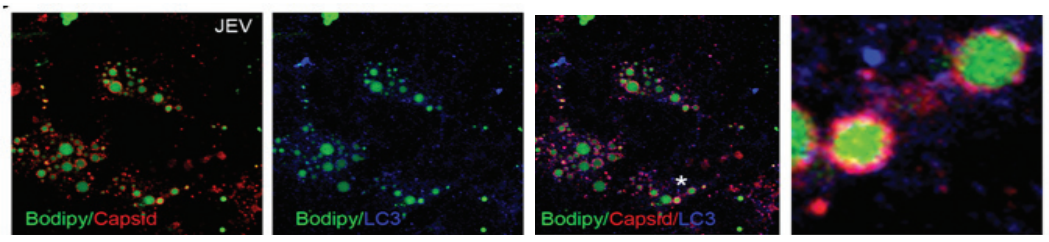


Figure 24: *JEV capsid colocalizes with endogenous LC3 around lipid droplets. Huh7 cells were JEV infected (5MOI) for 24 h and were stained using Bodipy (green), capsid (red), LC3 (blue) antibodies. Extreme right image in the panel shows a magnified view of the region corresponding to the asterisk.*

Drug repurposing for JE

Several FDA approved drugs have been shown to enhance autophagy, and this has the potential to be repurposed for treatment of infectious diseases. A high-throughut screening platform for measuring autophagy flux was successfully established. A panel of FDA-drugs was tested for its effect on autophagy flux, JEV induced neuronal cell death and JEV replication. Several drugs were found to be potent autophagy inducers. A total of 10 drugs showed moderate reduction in virus induced cell death and some of these showed inhibition of virus replication.These drugs have been short-listed for further studies on JEV induced neuroinflammation, innate and adaptive immune responses in JEV infected human monocyte derived dendritic cells.

This research project will establish the effect/ potential of autophagy modulation in determining the pathology of JE. Advances made in this project are also likely to have direct application for understanding the pathogenesis of other acute viral infections.

Arup Banerjee
Principal Investigator

Lab members
Surender Rawat
Jaya Saini
Sharda Kumari
Aarti Tripathi
Naina Soni

Understanding Viral Pathogenesis and Development of Therapeutics Measures against the Flaviviruses prevalent in India

Our research group investigates the immunopathogenic mechanisms of two important viruses prevalent in India 1) Dengue virus (DV) 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 immune cells. Neutrophils are the first immune cell population recruited to sites of viral infections. While neutrophil activation has been recently shown to be associated with DV infection, there is a gap in understanding the mechanism that warrants detailed investigation. Therefore, we wish to understand the DV induced neutrophil activation and their interaction with other immune components (e.g. Platelet, T cells). Our work encompasses studying the modulation of immune responses and their impact on the development of disease severity. Simultaneously, the identification of novel prognosis markers for dengue severity is our research priority. Knowledge gained from these studies could be directly exploited towards strategies for the amelioration of disease conditions.

Neutrophil activation in dengue pathogenesis

Neutrophil extracellular traps (NETs) formation is a novel mechanism through which hosts restrict the spread of infiltrating pathogens into our bodies. Several studies suggested that NETs releasing neutrophils are phenotypically different and can interact with immune cells, modulating their functions. The NET release, also known as NETosis, is a process through which dsDNA containing several cytoplasmic toxic granules comes out from the cells and form a sticky, web-like structure. NETosis is initially considered as an essential part of host defense mechanisms, however, excess NETs deposit on the blood vessel and increase capillary damage, hemorrhagic lesions, and can cause irreversible tissue damage, leading to plasma leakage. This phenomenon is particularly important in context to DV infection. Neutrophils can also regulate platelet function by direct adhesion and/or by paracrine effects of secreted factors.

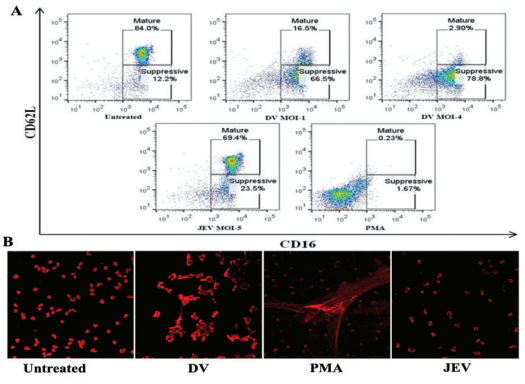


Figure 25: *Effect of Dengue virus on neutrophils. Neutrophils were isolated from healthy volunteer and were either untreated or separately treated with Dengue virus (DV) , PMA and Japanese Encephalitis virus (JEV) for 3 hours. The expression of Neutrophil specific Cell surface markers (CD16, CD62L) were determined by FACS. A) The representative contour plot showing the different neutrophil subsets- mature (CD16BrightCD62LBright) and suppressive (CD16BrightCD62LDim). B) Cells were permeabilized after 3h treatment and nucleus were stained by Sytox Orange Dye.*

In our ongoing study, we are planning to address several key questions relevant to disease manifestation. Is dengue virus capable to induce phenotypic and functional differentiation in Neutrophils or requires other triggers (e.g. interaction with activated platelet)? If yes, how does it affect other immune cells function? The answer to this question will provide knowledge on

how and what extent neutrophils shapes adaptive immune response during DENV infection. Interestingly, we observed that incubation of DV with neutrophils can induce changes on the cell surface marker expression and the nuclei of these neutrophils mostly undergo decondensation (Fig. 25), suggesting that these neutrophils are primed towards NETs release. Based on the preliminary data, further studies are in progress understanding the in-depth mechanisms of virus-induced NET formation and their effect on immune modulation.

Insights into the circulating microRNAs in the plasma of patients with dengue infection

Micro RNAs (miRNAs) are small (~19-21 nt. in length), non-coding RNAs, extremely stable and easily detectable in the plasma; thus, have biomarkers potential for diagnosing and monitoring human diseases. The circulating miRNAs profile has been widely used for identifying potential biomarkers against viral infections. However, data on circulating microRNA expression patterns in dengue patients is scanty. Considering the impact of severity caused by dengue infection, circulating miRNAs profiles in plasma of dengue patients may prove to be valuable for developing early prognostic markers for the disease severity. We conducted a study to identify the differentially expressed miRNAs in the plasma of 39 dengue patients using the high-throughput small RNA sequencing technology. MiRNAs expression pattern analysis compared with the follow-up samples, revealed nine miRNAs, which were found to exhibit an altered expression that could be distinguished between the severe dengue and the convalescent patients. To understand the abundance and specificity of the differentially expressed miRNAs in context to dengue infection and disease progression, four of these miRNAs (hsa-miR-486-5p, hsa-miR-92a-5p, hsa-miR-320a, and hsa-miR-191-5p) were further validated in the dengue virus-infected cell lines as well as in the patient's plasma and PBMCs using the qRT□PCR method. Our study provides a comprehensive analysis of miRNAs circulated in plasma of dengue infected patients and provides a precious resource of candidate miRNAs with biomarker potential involved in the dengue infection and disease progression.

Effect of adult stem cells extracellular vesicles (EVs) in ameliorating viral pathogenesis

Human adult stem cells can release extracellular vesicles (EVs) (also known as exosomes). These EVs can have the cell-free therapeutic potential against virus infection. In collaboration with AIIMS, New Delhi, and NBRC, Manesar, we have started to explore the effect of adult stem cells derived exosomes against JEV infection and replication. We are using adult stem cell-derived exosomes and explore their ability (in vitro as well as in animal model) to inhibit JEV replication. The study is also addressing the effect of EVs on inducing neurogenesis in the brain. So far, we have isolated adult stem cells EVs from Bone Marrow (BM), Adipose Tissue (AD) as well as Wharton's Jelly (WJ) and characterized the content of bioactive molecules in the exosomes using Proteomics and RNA-seq methods. We have observed that bone marrow-derived exosomes when incubated with primary neuronal stem cells in the presence of the JEV, enhances neurogenesis, indicating that BM-derived exosomes have neurogenic property. Further study is in progress to check its ability to inhibit virus replication in the JEV infected animal model.

Prasad Abnave
Principal Investigator

Investigating Adult Stem Cells Dynamics in the Infection Scenario

Adult stem cells (ASCs) 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 help to improve the ASCs tolerance to infection burden and thus has profound biomedical importance.

Following are our strategic objectives and broad plan of action:

Study adult stem cells dynamics during bacterial/ viral 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 and viral 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. 26).

We would be using planarian flatworms for the in vivo investigations. Planarian Schmidtea mediterranea has an extraordinary regeneration ability. They possess a pool of pluripotent adult stem cells (known as neoblasts) which allows them to grow an entire body from a tiny tissue fragment (Fig. 27). The genetic machinery essential for the stemness in mammalian stem

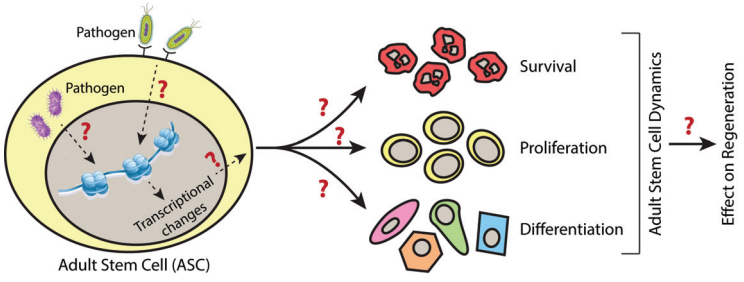


Figure 26: *The schematic of research questions we are trying to address*

cells is conserved considerably within planarian ASCs. Moreover, planarian ASCs can be easily studied in vivo or isolated by flow 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. Our preliminary observations suggest that planarian ASCs function and regeneration ability remains unaffected during bacterial

infections, but thorough investigations need to be performed to get detailed insights. We will also be studying ASCs from a vertebrate system, i.e. mice. We will examine different types of ASCs from both the planarian and mammalian (mice) systems for their function after various bacterial/ viral infections. It will be the first comprehensive study providing meticulous insights about ASCs behaviors during infections.

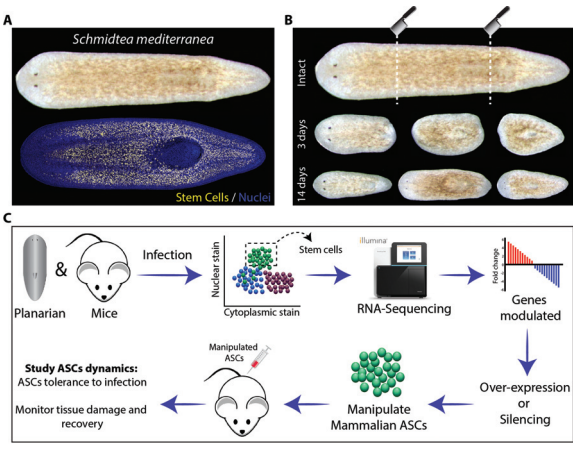


Figure 27: *The planarian Schmidtea mediterranea and schematic of the workflow. A) Bright-field image of Schmidtea mediterranea and in-situ hybridization image of planarian showing the distribution of adult stem cells (yellow) throughout the animal. B) The planarian cut into three pieces give rise to three whole animals in less than 14 days. C) Schematic of the workflow to identify genetic machinery governing the ASCs dynamics during infections and attempt to enhance mammalian ASCs tolerance to infection.*

Identify the molecular mechanisms governing the ASCs dynamics during infections

By next-generation sequencing (RNA-Seq), we will identify the transcriptional response of both planarian and mammalian ASCs to infections (Fig. 27). 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 bacterial/ viral infections. We will also perform RNA-Seq on the mammalian ASCs in response to infection. By comparing it with the planarian ASCs transcriptome, we will reveal the conserved genetic response in both the systems. The comparison may also highlight some gene regulatory changes responsible for the difference in the ASCs behaviour in both the systems.

Attempt to enhance the tolerance of mammalian ASCs to infection stress

The genes emerged from RNAi screening in planarians will be further tested *in vitro* (by overexpression and down-regulation) 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 will transplant ASCs with overexpressing/ silencing the gene of interest into the mice, and examine their tolerance to infection (Fig. 27). We will periodically monitor the recovery of various infected tissues. We envision to increase 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.

Anil Thakur
Principal Investigator

Lab member
Aishwarya Rana

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 events in translation and it determines the reading frame to be decoded. However, little is known about the translatome employed by human fungal pathogens during infection. Transcriptional profiling of fungal cells exposed to phagocytes have indicated major influences on ribosome biogenesis and protein synthesis. However, the translational regulation that fine tunes the translation of 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 and 40S subunit that promote the high-fidelity selection of AUG start codons

Accurate identification of the translation initiation codon is critical to ensure the synthesis of the correct 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 stimulated by factors eIF1, eIF1A, and eIF3. The resulting 43S preinitiation complex (PIC) attaches to the 5' end of mRNA and scans the mRNA leader 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 relatively 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

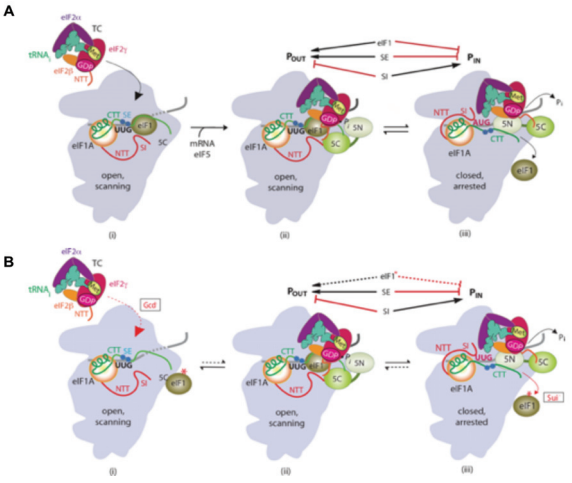


Figure 28: *Model describing conformational rearrangements of the PIC during scanning and start codon recognition and the consequences of Sui- substitutions in eIF1. A) Assembly of the PIC, scanning and start codon selection in WT cells. (i) eIF1 and the scanning enhancer (SE) elements in the CTT of eIF1A stabilize an open conformation of the 40S subunit in the 43S PIC to which TC rapidly loads. (ii) After joining with mRNA, the 43S PIC in the open conformation scans the mRNA for the start codon with Met-tRNAi bound in the POUT state. The unstructured NTT of eIF2β interacts with eIF1 to stabilize eIF1•40S association in the open PIC conformation. (iii) On AUG recognition, the Met-tRNAi moves from the POUT to PIN state, eIF1 dissociates from the 40S subunit. (Adapted from Hinnebusch Lorsch 2012, Nanda et al. 2013, Martin-Marcos et al. 2014.) B) Mutations in eIF1 that disrupt physical interaction between eIF1 and eIF2β (i) An eIF1 substitutions decreases the rate of TC loading to confer the Gcd- phenotype (red dotted arrow). (ii) While the decreased rate of TC loading slows formation of the scanning complex from the 43S PIC, once TC eventually binds and scanning commences, an increased frequency of mutant eIF1 dissociation from the open/POUT conformation enables more frequent rearrangement to the PIN state at UUG codons (iii), conferring the Sui- phenotype (red solid line).*

in the closed state "P_{IN}" (Fig.28A). Subsequently joining of 60S subunit and formation of an 80S initiation complex ready to commence protein synthesis.

eIF1 plays a dual role in translation initiation. It promotes the open conformation (P_{OUT}), while clashing with Met-$tRNA_i$ in the P_{IN} state. Hence, eIF1 dissociation from the 40S subunit is required for start codon recognition. Using *Saccharomyces cerevisiae* as a model organism we have shown mutations in eIF1 that disrupt physical interaction between eIF1 and eIF2β confer dual defects *in vivo*: (i) they reduce the rate of TC loading; (ii) they increase initiation at near cognate codons by destabilizing the open/P_{OUT} state and favoring rearrangement to the closed/P_{IN} state. A reduced rate of TC loading resulting from such eIF1 mutations confers derepressed translation of *GCN4* mRNA *in vivo* (the Gcd^- phenotype). Increased initiation at near-cognate codons in such eIF1 mutants also restores translation of *his4-303* mRNA, lacking the AUG start codon, by elevating initiation at an in-frame UUG triplet at the third codon (the Sui^- phenotype) (Fig. 28B). These results indicate that eIF1-eIF2β contacts important for recognition of correct initiation codon. Still many mechanistic aspects of the translation initiation process remain unclear. Currently we are identifying the role of translation initiation factors and 40S subunit to determine the high-fidelity selection of AUG initiation codons.

Delineate the translational mechanisms that play important role in controlling virulence and drug resistance in human fungal pathogens

The most important virulent trait of human fungal pathogen *Candida albicans* is to undergo a reversible morphological transition from yeast to hyphal filaments in the host environment. The virulence genes are least expressed in yeast form, but expression of virulence genes are increased in formation of hyphae (Fig. 29). These fungal pathogens infect host tissues by adapting to stressful micro environmental conditions which reduces general protein translation rates and redirects protein synthesis toward a selective set of stress-responsive proteins. This mechanism reduces the energy expenditure of the cell, and targets translation initiation step that is prime center of translation, so actively translated mRNAs are often differs from the transcriptome. It suggests that the fidelity of initiation codon recognition is a point of translational control efficiency mechanisms that may play an important role in controlling morphology and virulence of fungal pathogens. We hypothesized the changes in fidelity of start codons selection could change the proteome to combat with different stresses. It is plausible that translation initiation dynamics may fine tune the expression of virulent factors those are responsible for pathogenesis. We are systematically analysing near cognate codons initiation and differential expression of genes *in vivo* under several stresses. The endeavor of study is to unravel a novel translation regulatory mechanism harnessed by fungal pathogens to survive in the hostile environments of the host.

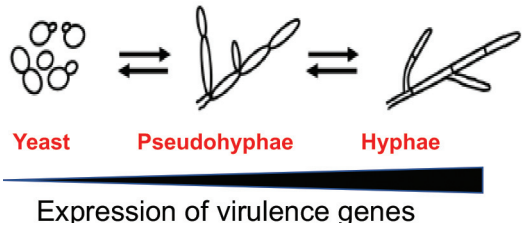
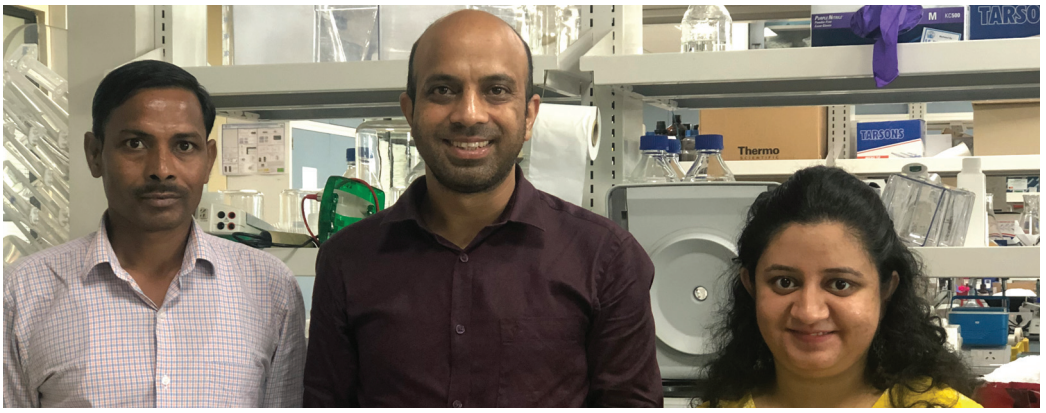
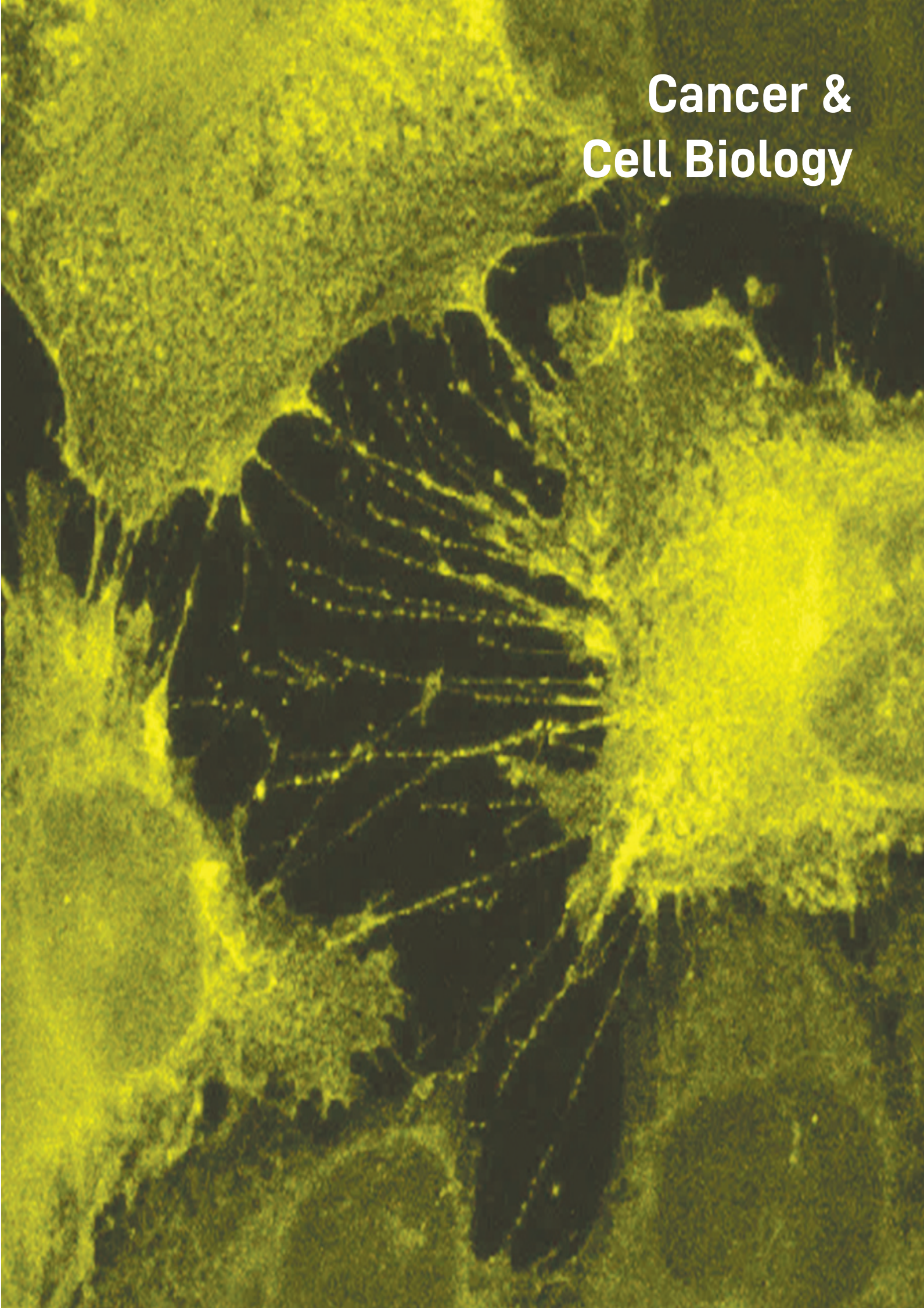


Figure 29: *The expression of virulence genes of Candida albicans from yeast to hyphae*




Cancer &
Cell Biology

Avinash Bajaj
Principal Investigator

Co-Principal Investigators
Ujjaini Dasgupta, Amity University
Sagar Sengupta, NII

Lab Members
Siddhi Gupta
Sandeep Kumar
Nihal Medatwal
Sanjay Pal
Animesh Kar
Priyanka Verma
Poonam Yadav
Kajal Rana
Dolly Jain
Varsha Saini
Somesh K Jha
Mohd. Nafees Ansari
Trishna Pani
Devashish Mehta
Yamini Sharma

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.

Cancer progression involves chronic proliferation of tumour cells assisted by the recruitment of endothelial and inflammatory cells at the tumor microenvironment (TME) causing angiogenesis and inflammation. These associated phenomena, along with proliferating tumor cells, make the current therapeutic regimes ineffective. We synthesized twenty lithocholic acid-dipeptide conjugates where the C-termini of dipeptides were conjugated to the 3'-OH of benzylated lithocholic acid. The dipeptides contained glycine at the C-terminal, and any one of the twenty-natural amino acids conjugated at the N-terminal (Fig. 30A). Screening of these amphiphiles and rheology studies confirmed that Glycine-Glycine (LCA-GG) forms the most stable hydrogel that is injectable. *In vivo* implantation of the fluorescent (1% Rhodamine entrapped) LCA-GG hydrogel revealed that the hydrogel remained intact for 20 days in BALB/c mice, and for 32 days in Sprague Dawley rats (SD rats). H&E stained sections for the tissue-LCA-GG hydrogel interface from BALB/c mice did not reveal any infiltration of neutrophils or macrophages. Comparison of IR-820-doped hydrogels with direct subcutaneous injection of IR-820 revealed sustained and localized release of the dye at the injection site for 20 days (Fig. 30B).

We hypothesized that the sequential and sustained release of the anticancer drug Doxorubicin (DOX, topoisomerase inhibitor), anti-angiogenic Combretastatin A-4 (CA4), and anti-inflammatory corticosteroid Dexamethasone (DEX) from a chimeric hydrogel depot would help in targeting tumour cell proliferation, angiogenesis and inflammation of solid tumors that are critical phenomena happening at the tumour site (Fig. 30C). Rheology experiments showed successful entrapment of these three drugs into the gel (TRI-Gel) without losing gel integrity. Drug release kinetics showed the sequential release of DOX, CA4 and DEX, while maintaining the sustained concentration of the drugs over a period of 20 days (Fig. 30D). Anticancer activities of the TRI-Gel on the syngeneic Lewis Lung Carcinoma (LLC) model in C57/BL6 mice showed minimal progression of tumour growth on TRI-Gel treatment, as compared to untreated mice and mice with tumour site injection of these drugs (without hydrogel, TRI-TS), and intravenous/oral delivery (TRI-IV) of these drugs (Fig. 31A). We observed 2-, 4-, and 10-fold reduction in tumour volume on TRI-Gel treatment as compared to TRI-IV, TRI-TS and untreated mice respectively. TRI-Gel enhanced mice survival by 18 days without any change in body weight of the mice (Fig. 31B).

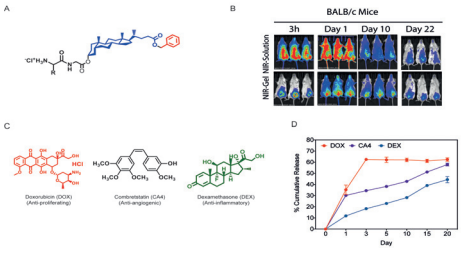


Figure 30: *A) Molecular structures of lithocholic acid-peptide conjugates. B) Bioluminescence imaging of mice after injection of NIR dye solution and NIR-Gel suggesting the sustained release of the dye over 20 days. C) Molecular structures of chemotherapeutic drugs that were entrapped in the hydrogel for tumor regression studies. D) Drug release kinetics of Doxorubicin (DOX), Combretastatin A4 (CA4) and Dexamethasone (DEX) from drug-entrapped hydrogel.*

Sphingolipid profiling in response to TRI-Gel therapy showed an upregulation in all ceramide species, with short chain C16 species showing significant alterations (Fig. 32C). Remarkably, there was a down regulation of glucosyl ceramides in TRI-gel treated tumours with significant decrease in C16 Glucosyl ceramide (GluCer), demonstrating that TRI-Gel combination has the potential to circumvent GluCer induced multi-drug resistance, a prime obstacle for sustained

therapy and recurrence. Ceramide-1-phosphate (C-1-P), generated by direct phosphorylation of ceramide, is an anti-apoptotic lipid with distinct roles in cell growth, inflammation, macrophage proliferation and migration. TRI-Gel treatment resulted in significant reduction of C20, C22 and C24 species with respect to untreated tumors. The alteration in sphingolipids in response to TRI-Gel treatment supports its anti-proliferative, anti-inflammatory and anti-angiogenic roles.

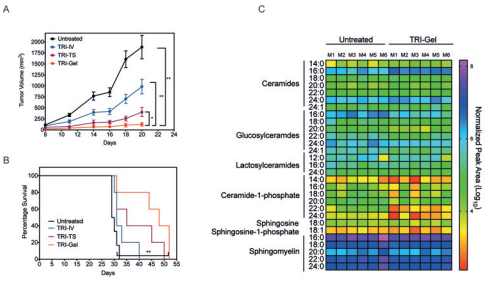


Figure 31: *A) Tumour growth kinetics of LLC tumour-bearing mice on treatment with combination of anti-proliferating, anti-angiogenic and anti-inflammatory drugs using hydrogel (TRI-Gel), without hydrogel at tumour site (TRI-TS), and using intravenous/oral routes (TRI-IV). B) Percentage median survival of tumour-bearing mice on different treatments. C) Heat map showing alterations in different sphingolipid species as normalized peak area (Log10) on TRI-Gel treatment as compared to untreated tumors.*

RNA-sequencing and pairwise comparative analysis showed 351 differentially expressed genes in TRI-Gel treated tumours as compared to untreated tumours, with 76 genes significantly upregulated (≥1.5, *p*-value ≤ 0.05) and 91 genes significantly downregulated (≥1.5, *p*-value ≤0.05). However, no sphingolipid gene showed any significant alteration of gene expression in response to TRI-Gel. We therefore systematically investigated the transcriptome-wide AS events in single and TRI-Gel treated tumours to explore the mechanism by which TRI-Gel could alter the levels of bioactive sphingolipids and enhance tumour cell apoptosis. We observed 351 significant cassette exon (CE) events (in 285 unique genes) and 1762 intron retention (IR) events (in 1140 unique genes) upon TRI-Gel treatment. Interestingly, there are multiple genes of the sphingolipid biosynthetic pathway that are targets for AS events in single and TRI-Gel treated tumours, indicating that sphingolipid genes are subject to post-transcriptional regulatory control in response to chemotherapy.

Isoform-specific PCR showed significantly lower level of Gba1 transcript with I8 intron retention (Intron between exon 8 & 9) in TRI-Gel tumor as compared to UT and a corresponding increase in the normal protein coding transcript. We also observed a higher Gba1 protein level and a significantly higher Gba1 enzyme activity in the TRI-Gel tumour. This elevated Gba1 level in tumour cells increases ceramide levels and reduces glucosylceramide levels, paving the way for cancer cell to undergo apoptosis and circumvent drug resistance as validated by *p*-glycoprotein (pGp) expression. Silencing of Gba1 in the TRI-Gel treated tumour reverses the drug effect and identifies Gba1 as a potential target for cancer therapy.

In summary, our studies showed that chimeric hydrogels targeting the tumor microenvironment help in regression of cell proliferation along with control of angiogenesis, inflammation and an immunosuppressive microenvironment. This treatment alters sphingolipid metabolism using post-transcriptional (alternative splicing) regulatory mechanisms, and helps in combating drug resistance.

Sivaram V S Mylavarapu
Principal Investigator

Collaborators
Mahak Sharma
IISER Mohali
Jayanta Bhattacharya
THSTI-IAVI
Divya Chandran, RCB
Sourav Banerjee, NBRC
Megha Kumar, CSIR-CCMB
Anjana Saxena,
CUNY New York

Lab Members
Pushpa Kumari
Harsh Kumar
Rajaiah Pergu
Amit Sharma
Amrita Kumari
Sunayana Dagar
Chandan Kumar
Diksha Pathak
Neeraj Wasnik
Monika Rawat

Molecular mechanisms of cell division, intercellular communication and cellular dynamics

Our research group studies the molecular regulation of cell division and intercellular communication, two vital and highly dynamic cellular processes essential for cell survival and organism development. These processes are subverted in both infectious and non-infectious diseases, making such efforts vital for future therapeutic exploitation. As part of this broad objective, we wish to understand the regulation of cell division by the intracellular transport motor dynein and the mechanisms of organelle traffic during cytokinesis, the final step of cell division. We also aim to elucidate the mechanisms of formation and function 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. 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 directly exploited towards strategies for the amelioration of disease conditions.

Transgelin-2 is a novel dynein interactor that governs mitotic spindle orientation

The animal cell mitotic spindle consists of the two centrosomes (spindle poles) that nucleate kinetochore-directed microtubules, inter-polar microtubules and the astral microtubules that engage with the cortex to anchor the spindle, thus positioning and orienting it properly within the cell. Proper positioning and orientation of the mitotic spindle decides the plane of cell division within a tissue, and hence governs several fundamental physiological functions impacting embryonic and tissue development, body axis elongation and asymmetric division of stem cells leading to self-renewal or differentiation. The mechanisms of spindle orientation are important to understand both from a fundamental standpoint and also from a therapeutic angle, since spindle mis-orientation leads to several disease conditions.

The molecular motor dynein is essential for mitotic spindle orientation, which defines the axis of cell division. The light intermediate chain subunits, LIC1 and LIC2, define biochemically and functionally distinct vertebrate dynein complexes, with LIC2-dynein playing a crucial role in ensuring spindle orientation. We reveal a novel, mitosis-specific interaction of LIC2-dynein with the cortical actin-bundling protein transgelin-2. Transgelin-2 is required for maintaining proper spindle length, equatorial metaphase chromosome alignment, spindle orientation and timely anaphase onset. Mechanistically, we show that transgelin-2 stabilizes the cortical recruitment of LGN-NuMA, which together with dynein is required for spindle orientation. The opposing actions of transgelin-2 and LIC2-dynein maintain optimal cortical levels of LGN-NuMA (Fig. 32).

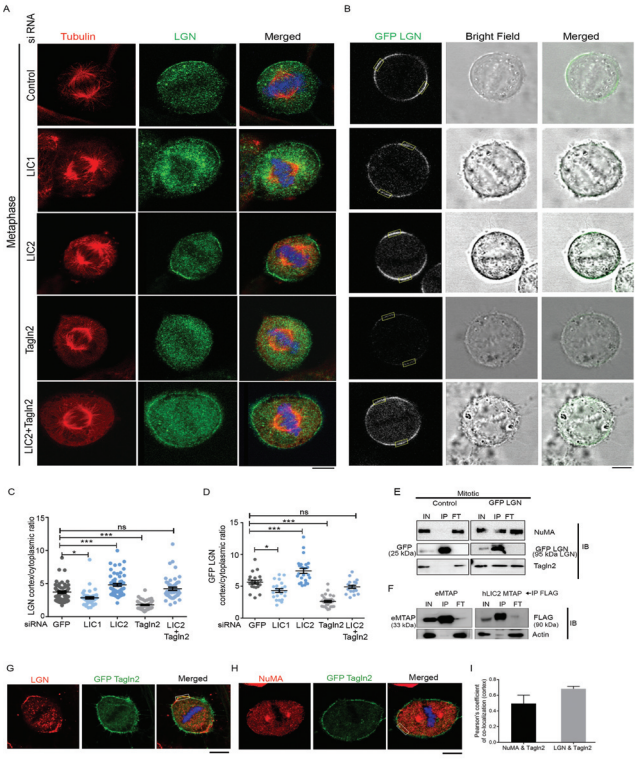


Figure 32: *Transgelin 2 is required for spindle orientation through proper recruitment of LGN at the cortex in mitosis. Figure adapted from J Cell Sci, 2020.*

Phosphorylation of dynein LIC2 at a conserved residue is required for spindle orientation

In addition, we probed whether the mitosis-specific phosphorylation of the LIC2 subunit of dynein is required for spindle orientation. LIC2, one of the main determinants of the cargo binding ability of the dynein complex, undergoes hyperphosphorylation by the master mitotic kinase cdk1 at the interphase to mitosis transition at three conserved sites, namely S194, S383 and S391.

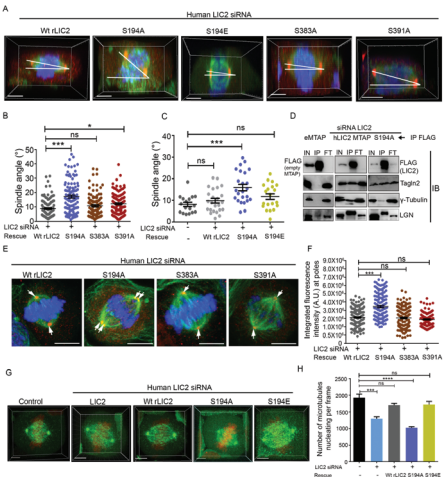


Figure 33: *Phosphorylation of LIC2 at residue S194 regulates spindle orientation. Figure adapted from J Cell Sci, 2020.*

We show that the highly conserved S194 phosphorylation of LIC2 is required for proper spindle orientation, by maintaining mitotic centrosome integrity to ensure optimal astral microtubule nucleation. Our study uncovers distinct contributions of the N-terminal phosphorylation (S194, in metaphase functions including chromosome congression, pole-mediated microtubule nucleation, spindle orientation and timely anaphase onset), and of the clustered C-terminal phosphorylations (S383 and S391, during cytokinesis) (Fig. 33). These observations reveal finely tuned regulation of the mitotic functions of LIC2, depletion of which has been shown to impede the progression of both metaphase and cytokinesis.

Overall, the work reveals two specific mechanisms through which LIC2-dynein regulates mitotic spindle orientation, namely, through a new interactor transgelin-2 required for engagement of LGN-NuMA with the actin cortex, and also through mitotic phospho-regulation of LIC2 to control microtubule nucleation from the poles.

Distal tip cell (DTC) plexus: an in vivo model for tunneling nanotubes (TNTs)?

Dr. Pushpa Kumari
Wellcome-DBT, IA Early Career Fellow

Tunneling nanotubes (TNTs), a novel mode of intercellular-communication, have been identified in multiple animal cell types in both cultured and *in-vivo* environments. The field is expanding rapidly to understand both the biogenesis and physiological functions of these nano-structures in both health and disease. This calls for the identification and development of an *in vivo* model for TNTs that is both genetically tractable and amenable to high resolution imaging, preferably in live tissue. We have identified the distal tip cell (DTC), the somatic niche for germline stem cells (GSCs) in the round worm *Caenorhabditis elegans*, as a potential *in vivo* model for TNTs. The DTC projects several cytoplasmic protrusions that can reach up to tens of micrometers in length to form an intricate network called the DTC-plexus, which enwraps the GSCs in a canopy-like meshwork essential for niche-stem cell signaling and stem cell survival. Our morphometric analyses revealed that these cellular projections are nanoscale. Depletion of orthologs of mammalian proteins required for TNT biogenesis impeded the length, density and functional signaling of the DTC plexus. Our work uncovers a potential *in vivo* model system for studying the structure-function correlates of TNTs.

Rajender K Motiani
Principal Investigator

Lab members
Nutan Sharma
Samriddhi Arora
Suman Sourav
Jyoti Tanwar
Jaya Bharti Singh

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 an integral role in maintaining tissue homeostasis and health. Perturbation in Ca^{2+} dynamics causes impairment of cellular physiology eventually leading to diseases. The focus of our group is to understand the role of Ca^{2+} signaling in skin pigmentation, tumorigenesis and cancer metastasis. We are aiming to: 1) Delineate the role of organellar Ca^{2+} dynamics in these pathophysiological conditions; 2) Elucidate detailed molecular mechanisms connecting dysregulated Ca^{2+} signaling to cancers and pigmentary disorders; 3) Eventually, 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 the Ca^{2+} homeostasis in these cells (Fig. 34).

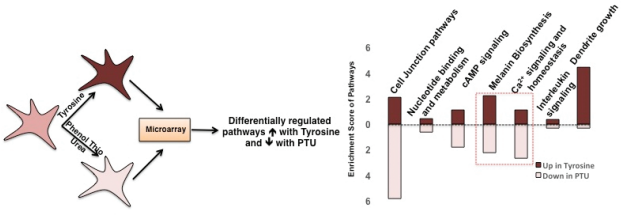


Figure 34: *Microarrays on hyperpigmented and hypopigmented primary human melanocytes. Primary melanocytes were treated with either tyrosine (substrate for rate limiting enzyme in melanogenesis pathway i.e. tyrosinase) to enhance pigmentation or phenol thio-urea (PTU, tyrosinase inhibitor) for decreasing pigmentation. RNA samples from these hyper and hypopigmented melanocytes were subjected to microarrays. DAVID tool was used for analysis of differentially regulated pathways that were upregulated with tyrosine and suppressed with PTU. Ca2+ homeostasis emerged as one of the most differentially regulated signaling modules in response to pigmentation changes (adapted from Motiani et al. EMBO J, 2018).*

However, the functional relevance of Ca^{2+} handling proteins in pigmentation biology remains largely unappreciated. Therefore, we aim to delineate their role in skin pigmentation.

One of the ongoing projects under the ambit of this program is focused on understanding further molecular details of the unique function of STIM1 in melanocytes. An interesting observation from our earlier work was that STIM1 expression is increased in melanocytes when they proliferate and pigment simultaneously. This observation raised a number of thought-provoking questions: 1) Is the increase in STIM1 levels unique to either melanogenesis or melanocyte cell proliferation? 2) Is this enhanced STIM1 expression essential for driving pigmentation and/or proliferation? 3) What is the status of STIM1 expression under physiologically relevant conditions and in primary melanocytes of varying genetic origin? 4) What are the molecular mechanisms that regulate STIM1 expression in primary human melanocytes?

Our preliminary data suggests that STIM1 overexpression is specific to melanogenesis. We will perform an array of experiments for validating our initial observations. Further, we will evaluate the significance of STIM1 overexpression in more physiological experimental setups. Finally, we will determine the molecular choreography driving STIM1 expression. This knowledge will

empower us with the possibility of targeting the molecular players regulating STIM1 expression and thereby, could lead to the development of strategies for calibrating pigmentation.

Targeting calcium signaling for curtailing tumor growth and metastasis

During the transformation of normal healthy cells to cancerous cells, there are perturbations in the expression and function of Ca^{2+} handling proteins such as Ca^{2+} channels, pumps and transporters. This, in turn, leads to enhanced proliferation, invasion and resistance to apoptosis. Therefore, we are currently generating a knowledge base that in the future could be used for targeting tumorigenesis.

To start with, we are focusing on the highly selective Ca^{2+} channel Orai3. It is a unique Ca^{2+} channel that, during the course of evolution, came into existence in mammals only. We have previously reported that: a) Orai3 forms a functional Ca^{2+} influx channel in breast cancer; b) it regulates breast cancer development in mice models and c) its expression is higher in cancerous tissues in comparison to patient matched non-cancerous tissues. Our current efforts are directed towards understanding the mechanisms regulating Orai3 expression in cancerous tissue, because Orai3 becomes functional only upon its overexpression, while its homolog Orai1 mediates Ca^{2+} influx in healthy, non-cancerous tissue. Thus, Orai3 can be selectively targeted in cancerous tissue without any significant side effects on healthy tissues. Please refer to Fig. 35 for brief overview of role of Orai3 in tumorigenesis.

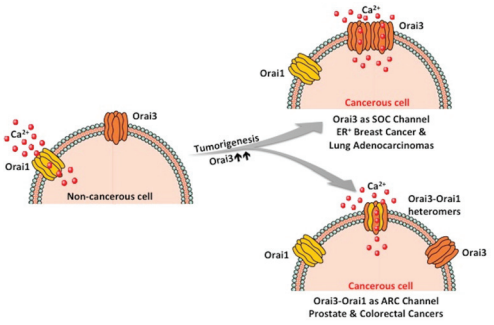
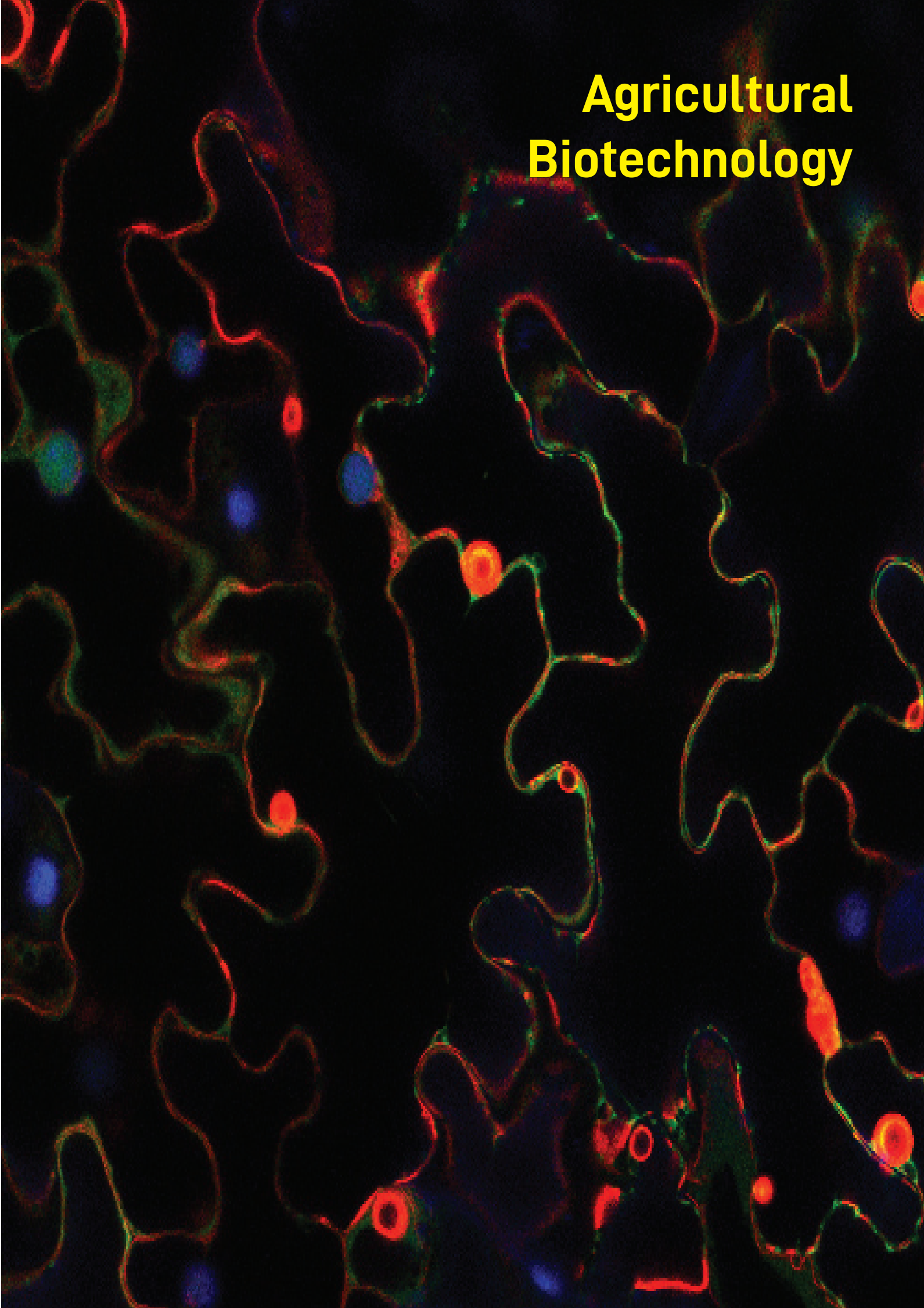


Figure 35: *Orai3 and tumorigenesis. Cancer progression is associated with enhanced Orai3 expression. Increase in Orai3 levels results in the formation of either Orai3 encoded SOC channels or Orai3-Orai1 constituted heteromultimeric ARC/LRC channels. The Ca2+ influx through these SOC or ARC/LRC channels regulates hallmarks of cancers, thereby driving tumorigenesis (adapted from Tanwar et al., Cell Calcium, 2020).*

We have further initiated studies in other cancers, wherein we started with extensive bioinformatics and integrative data mining from "The Cancer Genome Atlas (TCGA)". We identified that aberrant Orai3 expression is associated with a highly prevalent cancer. Intriguingly, there are no studies on Orai3 in this cancer type. Further, our preliminary data corroborates a unique Orai3 expression profile in these cancerous cells. Our current efforts are directed towards understanding the role of Orai3 in regulating cancer hallmarks in these cells. In the future, we aim to perform *in vivo* animal studies for delineating the precise role of Orai3 in cancer progression.

Agricultural Biotechnology



Saikat Bhattacharjee
Principal Investigator

Lab members

Yashika Walia Dhir
Dwaipayan Ghosh
Hitika Gulabani
Ingole Kishor Dnyaneshwar
Krishnendu Goswami
Mritunjay Kasera
Shraddha Dahale
Sakshi Rampuria
Abhisha Roy
PNVSJ Swaroop

Molecular mechanisms of signal transduction in innate immune responses of plants

Under constant threats from pathogens, plants have evolved a sophisticated defense system that meets transitory immune requirements without irreparable compromises on overall growth. Versatile players that functionally intersect on defensive and developmental signaling routes facilitate these balances. With a broad aim to improve durable resistance in plants, our research program utilizes *Arabidopsis thaliana* and *Pseudomonas syringae pv* tomato (*PstDC3000*) pathosystem to dissect immune crosstalks at three essential nodes: Regulation, Trigger and Signaling. Broadly, we elucidate post-translational modifications (PTMs) of central immune players that influence their strategic deployment and provide regulatory modes to defense signaling routes. Counter-evolving pathogen effectors are a constant challenge in engineering plant immunity. In our efforts to enhance broad-spectrum resistance, we characterize functions and perceptions of newly acquired effectors that cause alarming expansion in disease on crops. With our program, we envision deeper understanding of immune networks that will channel improved approaches to boost plant defenses.

Functional intersections of SUMO isoforms regulate global SUMOylome adjustments during stress

Covalent linkage of SUMO (Small-Ubiquitin like Modifier) on substrate proteins affects its fate or function. A plant maintains strict control over its pool of SUMOylated proteins (termed SUMOylome) which upon biotic or abiotic stresses are altered to facilitate appropriate responses. *Arabidopsis* mutants with disturbed steady-state SUMOylome display stronger immunity. However, most often these mutants incur growth penalties. These observations suggest that SUMOylation adjustments during immunity is tightly regulated to prevent developmental costs. In *Arabidopsis,* four SUMO isoforms are expressed namely SUMO1, SUMO2, SUMO3 and SUMO5. Simultaneous knockout of *SUM1* and *SUM2* is embryonic lethal suggesting at least one isoform is essential for survival. In response to the defense hormone salicylic acid (SA), *SUM3* but not *SUM1/2* is upregulated. Since SUMOs self-regulate SUMOylation efficiencies, existence of multiple isoforms introduces possibilities of their functional intersections which remain unexplored. Using well-established defense responses elicited against *PstDC3000*, we investigated crosstalks in individual and combinatorial *Arabidopsis sum* mutants. We identified that while *SUM1* and *SUM2* additively, but not equivalently suppress defenses, *SUM3* promoted immunity. Growth of *PstDC3000* is drastically reduced in both *sum1-1* and *sum2-1* (with *sum1-1* immunity > *sum2-1*) in comparison to wild-type (Col-0) plants (Fig. 36A) The *sum3-1* plants however are more susceptible to *PstDC3000* allowing more bacterial colonization than Col-0. We noted that basal SA levels are enhanced in *sum1-1* or *sum2-1* and diminished in *sum3-1,* respectively in comparison to Col-0 (Fig. 36B). This results in elevated or deficient levels of PATHOGENESIS ASSOCIATED PROTEIN 2 (PR2) in *sum1-1* or *sum2-1* and *sum3-1*, respectively thus accounting for their altered immunity (Fig. 36C). Through combinatorial mutants with deficient defenses followed by extensive measurements of kinetics of defense-associated

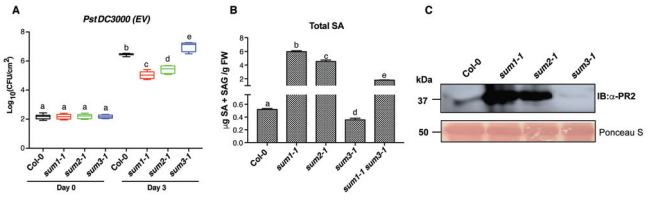


Figure 36: *SUM1/2 function as negative whereas SUM3 is a positive regulator of basal immunity in Arabidopsis. A) PstDC3000 growth on wild-type (Col-0), sum1-1, sum2-1 and sum3-1 plants determined at Day0 and Day3 post-infection. Whisker Box plot with Tukey test; n=12; ANOVA was performed to measure statistically significant differences (at p-value <0.001) in growth of bacteria in Log10 scale. B) Total salicylic acid (SA) in Col-0 and mutants in 4-week-old plants measured by biosensor Acinetobacter method. Data is representative of three biological replicates. Statistical significance calculated by Student t-test. Different alphabets indicate significance at p<0.001. C) Anti-PR2 immunoblot of total protein extracts from 4-week-old Col-0 and indicated sum mutants. Ponceau S stain of Rubisco subunit indicative of equal protein loading between samples is shown. Migration position of molecular weight standards (in kDa) are indicated.*

marker expressions, we further reveal that *SUM1/2* suppress whereas *SUM3* promotes SA-signaling routes. Overall, our results provide the first in depth molecular insights that place SUM1/2 as *bona fide* negative and *SUM3* as a positive regulator of immunity.

With first evidence of antagonistic roles of selective SUMO isoforms, we investigated their functional intersections in modulating immune amplitudes. We observed that mild growth defects in *sum1-1* plants that included stunted phenotype, tapered, and narrow leaves *are partially alleviated by the loss of SUM3 (Fig. 37A). This clearly implicated SUM1-SUM3* intersections on developmental processes. Enhanced immunity of *sum1-1* to *PstDC3000* is also toned-down in the *sum1-1 sum3-1* double mutant supporting that *SUMO1* is partly responsible for suppressing *SUM3* role in potentiating defenses (Fig. 37B). Remarkably, we also observed that optimal increase in global SUMO1/2 SUMOylome as a response to *PstDC3000* challenges require *SUM3* involvement since a *sum3-1* plant accumulates relatively lower SUMO1/2-conjugates than Col-0 (Fig. 37C). We further confirmed these crosstalks by measuring differences in accumulation kinetics of defense-associated markers upon *PstDC3000* infections. To investigate whether SUMO isoform crosstalks impact other stress responses, we investigated *SUM3* role in hyper-elevation of SUMO1/2-conjugates in response to heat-shock exposures. As observed for *PstDC3000* infections, loss of *SUM3* not only severely reduced enhancement of SUMO1/2 SUMOylome but also suppressed induction of several heat-shock responsive transcripts. Our results hence expand SUMO isoform crosstalks on adaptations to both biotic and abiotic stresses. Functions of SUMOylation-associated proteins are self-regulated by SUMOs. To explore molecular insights into protein platforms where SUMO isoforms may functionally intersect, we determined the efficiency of formation of SUMO-conjugates. In a heterologous expression system, we detected reciprocal increases in conjugation efficiencies when SUMO3 and SUMO are co-expressed (Fig. 37D). Curiously, these enhancements were independent of SUMOylation-proficiency of the co-expressed SUMO isoform suggesting that in addition to covalent attachments, SUMOs may regulate global SUMOylome changes non-covalently. Overall, our investigations reveal novel insights into auto-regulatory mechanisms of host SUMOylome maintenance and adjustments to environmental challenges. We are currently pursuing the identification of differentially SUMOylated candidates in response to pathogen challenge. Further elucidation of their functional modulation via SUMO will improve our understanding of immune signaling networks.

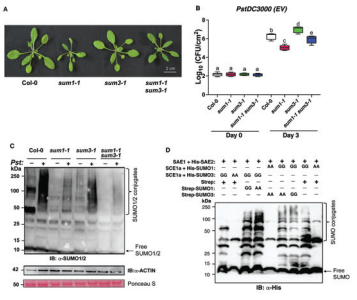
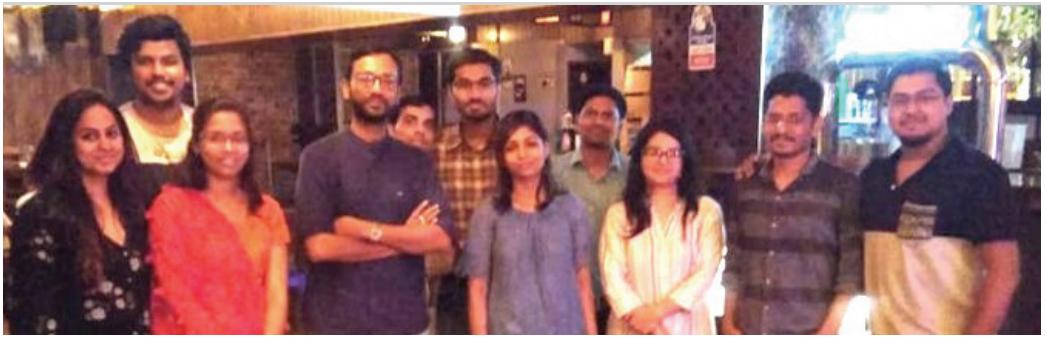


Figure 37: *Loss of SUM3 alleviates developmental defects and enhanced defenses in sum1-1 plants. A) Developmental phenotypes of 4-week-old Col-0, sum1-1, sum3-1 and sum1-1 sum3-1 plants. B) Growth of PstDC3000 in indicated plants at Day0 and Day3 post-infiltration. Whisker Box plot with Tukey test; n=12; ANOVA was performed to measure statistically significant differences (at p-value <0.001) in growth of bacteria in Log10 scale. C) Reduction in SUM1/2-conjugates due to loss of SUM3. Total protein extracts from indicated plants 24 h post-infection were immuno-blotted with anti-SUMO1/2 antibodies. Approximate positions of SUMO1/2-conjugates are shown. Anti-actin immunoblot or Ponceau S staining demonstrate comparable protein loading between samples. Relative positions of molecular weight standards (in kDa) are indicated. D) Reciprocal enhancements in SUMO-conjugates in E. coli SUMOylation-reconstitution system. Cell lysates from bacteria expressing the indicated SUMOylation components were probed with anti-His or anti-Strep antibodies. Relative position of SUMO-conjugates is depicted. Position of molecular weight standards (in kDa) is indicated.*



Divya Chandran
Principal Investigator

Lab Members
Raghavendra Aminedi
Naini Burman
Babitha K C
Megha Gupta
Arunima Gupta
Akriti Sharma
Debashish Sahu
Shubam Dubey
Poonam Ray
Diksha Mehta

Investigations into the molecular mechanisms underlying legume-powdery mildew interactions

Powdery mildews are significant biotrophic fungal pathogens that cause yield losses of ~25-60% in agriculturally relevant grain legumes, such as pea, lentil, and mung bean. The broad goal of our research program is to develop legume crops with durable resistance to the pea powdery mildew pathogen *Erysiphe pisi (Ep)*. To achieve this, we use functional genomics and molecular genetics tools to uncover the molecular interplay between *Ep* and two legume hosts, *Medicago truncatula* and pea.

Dual RNA-Sequencing provides new insights into legume-PM interactions

Dual RNA-Seq is an attractive transcriptomics approach to decipher host-pathogen crosstalk at the genome-wide level. We used this approach to delineate the molecular mechanisms underlying incompatible and compatible legume-PM interactions. Host and pathogen transcriptomes were simultaneously profiled at 1 day post-inoculation of resistant (A17) and susceptible (DZA) *Medicago* genotypes with the *Ep* isolate Palampur-1 (Fig. 38). At this early infection stage, 99% of the dual transcriptome was represented by *Medicago* transcripts and 0.5% by *Ep* transcripts. The number of differentially expressed genes (DEGs) was higher in A17 than in DZA, indicating that powdery mildew resistance is associated with extensive transcriptional reprogramming. Functional enrichment of host DEGs and *in silico* analysis of co-regulated promoters revealed that amplification of PTI, activation of salicylic acid and jasmonic acid signaling networks, and regulation of growth-defense balance correlate with resistance. By contrast, processes that favour biotrophy, such as suppression of plant defense signaling, cell death, and cell wall defenses, appear to be important susceptibility factors. These findings are significant because components of pathogen perception and defense signaling, such as pattern-recognition receptors and transcription factors, can be exploited to provide broad-spectrum and potentially durable resistance in legumes. Another significant outcome was the identification of seven *Ep* effector candidates with infection stage-specific expression patterns. Of these, four are novel whereas three show sequence similarities to effectors identified in other powdery mildews, suggesting that *Ep* deploys unique and conserved mechanisms to overcome host defenses.

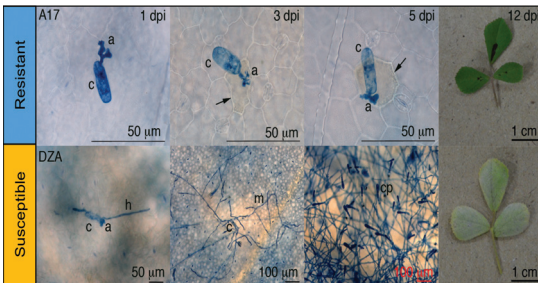


Figure 38: *Powdery mildew disease progression on resistant and susceptible Medicago genotypes. Trypan blue stained images of Ep isolate Palampur-1 on A17 and DZA leaves at 1, 3 and 5-days post inoculation (dpi) with an image of representative leaves at 12 dpi. c, conidia; a, appressorium; h, primary hypha; m, mycelium; cp, conidiophores. Arrows point to infected epidermal cells showing cytoplasmic disorganization and browning, indicative of cell death.*

Cross-kingdom RNA interference identifies key pea powdery mildew pathogenicity determinants

To establish biotrophic relationships with their host, powdery mildews secrete an arsenal of effector proteins primarily through specialized infection structures termed haustoria. RNA-Seq of enriched *Ep* haustoria identified 622 candidate secreted proteins (CSPs) and 167 candidate secreted effector proteins (CSEPs). The functional role of two *Ep*CSEPs and one *Ep*CSP was probed via double-stranded (ds) RNA-based RNA interference, a process in which plant cells transfer small interfering RNAs to invading pathogens to mediate the transient silencing of target genes. Foliar application of individual *EpCSEP/CSP*-dsRNAs resulted in gene silencing and a marked reduction in disease symptoms (Fig. 39), indicating that these genes play significant roles in powdery mildew pathogenesis. Homology modeling revealed that the two *Ep*CSEPs are analogous to fungal ribonucleases. The residues responsible for catalysis

are partially conserved in these proteins suggesting that they may possess RNA cleavage activity. This is in contrast to similar effectors from the barley powdery mildew which lack all catalytic residues and only exhibit RNA binding activity. Localization studies revealed that these *Ep*CSEPs localize to different host subcellular compartments. Future investigations will focus on the identification of their host targets.

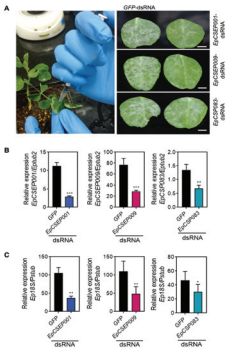


Figure 39: *dsRNA-mediated cross kingdom RNA interference of EpCSEP001, 009 and EpCSP083. A) Foliar infiltration of individual EpCSEP/CSP-dsRNA but not GFP-dsRNA in pea results in marked reduction in visible powdery mildew disease symptoms at 72-hours post inoculation (hpi). Bar, 1 cm. B) EpCSEP/CSP transcript levels measured in pea leaves infiltrated with EpCSEP/CSP- or GFP-dsRNA at 72 hpi with Ep. Data represent mean ± SEM of expression values normalized to that of the reference gene Eptub2 from at least ten biological replicates from two independent experiments. Significant differences in mean expression values were computed using the non-parametric Wilcoxon matched-pairs signed-rank test (**p<0.005, ***p<0.001). C) Ep18S rRNA transcript levels measured in pea leaves infiltrated with EpCSEP/CSP- or GFP-dsRNA at 72 hpi. Data represents mean ± SEM of expression values normalized to that of the reference gene Pstubulin from at least four biological replicates. Significant differences between means were computed using paired t-test (*p<0.05, **p<0.005).*

Functional characterization of HY5 homolog in rice

Dr. Naini Burman
DST Inspire Faculty

Light is an important environmental signal which is perceived by plants to adapt to ambient conditions. Photoreceptors perceive the light signal and pass on this signal to master regulators, which in turn bring about changes in downstream components, leading to changes in gene expression. One of these master regulators is HY5 transcription factor. We have identified that there are three orthologs in rice based on presence of COP1-binding and bZIP domains. One ortholog, OsbZIP48, was functionally characterised by us. We are now looking into how these three genes work in tandem as well as independent of each other. A repressor domain was attached to OsbZIP1 and the construct was overexpressed in rice and *Arabidopsis*. To identify the residues that abolish OsbZIP48-OsCOP1 interaction, mutational studies are being carried out.

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

Dr. Babitha K.C.
DBT Women BioCARe Awardee

Plants adapt to drought by synthesizing the ABA hormone, which not only limits water loss through stomatal regulation but also induces the synthesis of osmoprotectants and ROS scavengers. The dehydration control by stomatal regulation usually limits the uptake of CO_2, and thus, growth and productivity. Hence, we aim to minimize ABA-induced stomatal closure without affecting ABA-regulated cellular tolerance mechanisms to improve carbon gain under moderate stress conditions. Genes encoding anion channels that regulate stomatal aperture, such as ALMT12 and SLAC1, will be modulated using CRISPR-Cas9 technology in rice. The guide RNAs targeting exon regions of these genes were designed and cloned into pRGEB32 binary vector, and transformation in rice is underway. Further, to regulate the function of these genes through a chemical genomics approach, protein structures were deduced and small molecule interactors were identified through docking studies using the Schrödinger software. Evaluation of the predicted interactions is in progress.

Ramu S Vemanna
Principal Investigator

Lab Members
Chanchal Kumari
Akashata Dawane
Garima Pal
Chetan Chauhan
Pooja

Improving stress adaptation of crops

Plant adaptation to changing climatic conditions is crucial to improve productivity. Under stress, many cytotoxic compounds are generated that affect cell metabolic processes and reduce crop yield. We characterized aldo-keto reductases and identified natural chemical molecules that scavenge cytotoxic compounds under stress and confer improved resistance in different crops. Protein turnover mechanisms are affected under stress conditions, including protein synthesis and degradation. We aim to identify genes and genetic networks associated with protein turnover mechanisms and functionally characterize relevant genes. Ribosomal proteins were identified from RNA-sequencing (RNA-seq) analysis and functional characterization of a few genes were done in Arabidopsis and in *Nicotiana benthamiana* for disease resistance. The salt and drought induced Ring box1 (SDIR1), an E3 ligase, was characterized for disease response in a model system. These studies provide promising leads for the development of stress tolerant crops.

Enzymatic and non-enzymatic detoxification of reactive carbonyl compounds improves the oxidative stress tolerance in cucumber, tobacco and rice seedlings

Plants are constantly exposed to stress, and oxidative stress is ubiquitous. The downstream effects of oxidative stress in terms of generation of reactive carbonyl compounds (RCC) and glycation products were underexplored in plant biology. We have explored both enzymatic and non-enzymatic mechanisms to prevent cell damage caused by RCC generated in cucumber, tobacco and rice seedlings under stress conditions. Oxidative stress was induced by exposing the seedling systems to glucose, sodium chloride, and methyl viologen. RCC damage and degrade proteins and phospholipids that are vital for normal growth and development of plants, and adversely affect the activity and performance of seeds during germination. Plants have evolved mechanisms to detoxify and repair the damage caused by such reactive molecules. In tobacco and rice, the enzyme aldo-keto reductase-1 (AKR1) caused detoxification of RCC, malondialdehyde, and methylglyoxal and improved seedling growth under stress conditions. Small molecules such as acetylsalicylic acid, aminoguanidine, carnosine, curcumin and pyridoxamine neutralized RCC non-enzymatically and rescued the cucumber seedling growth during stress conditions. Besides the detoxification process, small molecules also prevent cell damage caused by RCCs. The study highlights the significance of small molecules in neutralizing the harmful effects of RCC and promoting seedling growth (Fig. 40). These molecules can be used in seed treatment processes in agriculture and the enzyme encoding genes may be used as molecular markers and candidates for gene editing in crop improvement programs.

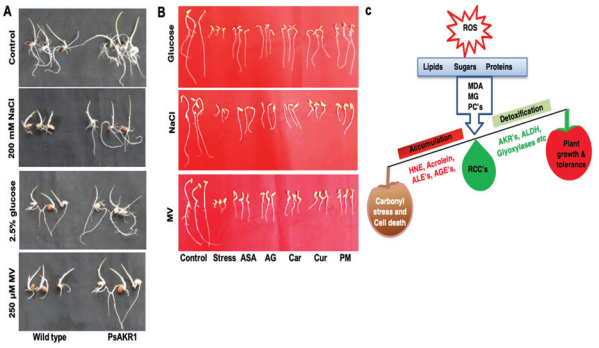


Figure 40: *Enzymatic and non-enzymatic detoxification of reactive carbonyl compounds (RCCs) generated under stress. A) Overexpression of Aldo keto reductase (AKR1) in rice improves seedling growth under NaCl, glucose and methyl viologen induced oxidative stress. B) Non-enzymatic mediated detoxification of RCCs in cucumber seedlings exposed to stress. (Control = water; ASA = 50 µM acetylsalicylic acid; AG = 10 µM aminoguanidine; Car = 10 µM carnosine; Cur = 1 µM curcumin; PM = 10 µM pyridoxamine). C) Model showing that the oxidative stress mediated damage on macromolecules leading to generation of RCCs. Under stress, RCCs accumulated at higher levels and the detoxification enzymes could scavenge these molecules to improve stress tolerance of crops.*

Ribosomal protein QM/RPL10 positively regulates defense and protein translation mechanisms

Ribosomes play an integral part in plant growth, development and defense responses. We report the role of ribosomal protein large (RPL) subunit QM/RPL10 in nonhost disease resistance. *RPL10*-silenced *N. benthamiana* plants showed compromised disease resistance against the nonhost pathogen *Pseudomonas syringae* pv. tomato T1 that generally cannot cause disease. RNA-seq analysis revealed that many genes involved in defense and protein translation

mechanisms were differentially affected due to *NbRPL10* silencing. Arabidopsis *AtRPL10* RNAi and *rpl10* mutant lines showed compromised nonhost disease resistance to *P. syringae* pv. tomato T1 and *P. syringae* pv. tabaci. Overexpression of *AtRPL10A* in Arabidopsis resulted in improved disease resistance against the host pathogen *P. syringae* pv. tomato (DC3000). RPL10 interacts with the RNA recognition motif protein and ribosomal proteins RPL30, RPL23 and RPS30 in a yeast two-hybrid assay. Silenced lines or mutants of genes encoding these RPL10 interacting proteins in *N. benthamiana* or Arabidopsis, respectively, also showed compromised disease resistance to nonhost pathogens (Fig. 41). Collectively, these results suggest that

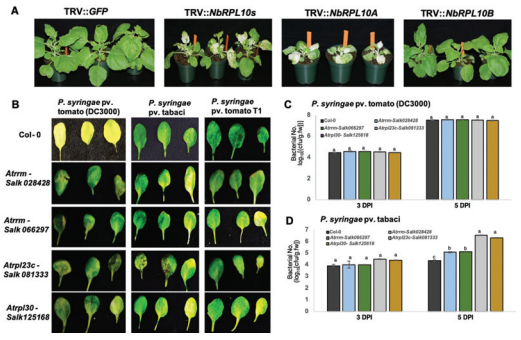


Figure 41: *Silencing NbQM/NbRPL10 in N. benthamiana and response of Arabidopsis RPL10A interacting ribosomal protein encoding gene mutants to host and nonhost pathogens. A) Visualization of developmental changes in N. benthamiana plants individually inoculated with TRV::NbRPL10s (silences both NbRPL10A and NbRPL10B), TRV::NbRPL10A, TRV::NbRPL10B and TRV::GFP (control; GFP does not have any sequence similarity to plant DNA and therefore will not cause gene silencing). B) Leaves of host and nonhost pathogen inoculated Arabidopsis mutants and wild-type (Col-0) were detached three days after inoculation and photographed. Four-weeks-old Arabidopsis mutants rrm, rpl23 and rpl30 were flood inoculated with nonhost pathogens P. syringae pv. tabaci, P. syringae pv. tomato T1 and host pathogen P. syringae pv. tomato (DC3000) at 1 x 105 cfu mL-1 concentration. C& D) Bacterial accumulation at 3- and 5-days post inoculation (dpi) was measured from leaves that were flood inoculated with P. syringae pv. tomato (DC3000) or P. syringae pv. tabaci. Bars represent average of three biological replicates in three independent experiments. Error bars represent the standard error. Different letters above the bars indicate a significant difference from Two-way ANOVA at $p < 0.05$ with Tukey's HSD means separation test ($\alpha = 0.05$) within a time point among respective wild-type and mutant lines.*

QM/RPL10 positively regulates the defense and translation-associated genes during nonhost pathogen infection.

We identified differentially expressed ribosomal genes in drought, pathogen and combined stress in rice using transcriptome profiling. Based on *in-silico* analysis from the rice genome annotation project, we have identified several different copies of RPL10 in rice. There are two *RPL10A* genes, and one each for *RPL10B* and *RPL10C* in rice. To assess the role of each independent copy of RPL10 in plant growth, development and stress conditions, all full-length *RPL10* genes were cloned into entry vectors. Further work in rice is in progress.

Plant E3 Ligase SDIR1 degrades JAZ9 to modulate plant defense against hemibiotrophic and necrotrophic pathogens

Pathogens target the ubiquitin systems of plants to suppress their innate immunity. We report a novel role of E3 ligase Salt- and Drought-Induced Ring finger1 (SDIR1) in plant immunity. The silencing of *SDIR1* in *N. benthamiana* reduced the multiplication of the virulent bacterial pathogen *Pseudomonas syringae* pv. tabaci. The Arabidopsis *sdir1* mutant is resistant to virulent pathogens whereas *SDIR1* overexpression lines are susceptible to both host and nonhost hemibiotrophic bacterial pathogens. However, *sdir1* mutant and *SDIR1* overexpression lines showed hypersusceptibility and resistance, respectively, against the necrotrophic pathogen, *Erwinia carotovora*. We demonstrate that SDIR1 interacts with and degrades JAZ9 through the proteasome-mediated pathway. Our results show the role of SDIR1 in plant defense gene expression modulation and immunity.

Prashant Pawar
Principal Investigator

Lab Members
Lavi Rastogi
Deepika Singh
Aniket Chaudhari

Elucidating the role of the GDSL lipase/esterase family in plant cell wall biosynthesis and modification

The focus of our research program is to understand the molecular mechanism of polysaccharide assembly, and to explore novel ways to alter the plant cell wall for its effective conversion to value-added products. One of the critical factors that plays a vital role in wall assembly and disintegration is acetyl, which is substituted on the polysaccharide backbone or side chain. It plays a vital role in polysaccharide maintenance, stability, and interactions with other components of the cell wall. However, the mechanism of polysaccharide acetylation is poorly understood. We are interested in the functional characterization of genes involved in polysaccharide acetylation. The knowledge gained can be used for the generation of tailor-made plant cell walls for various bioenergy applications.

In silico identification of putative Arabidopsis GDSL lipase/esterase gene members

According to the current polysaccharide acetylation model, acetyl-CoA is transported by Reduced Wall Acetylation from cytoplasm to Golgi. Altered Xyloglucan 9 and Trichome Birefringence Like proteins are transferases which recruit acetyl groups to polysaccharides. Recently, two members of the GDSL lipase/esterase family were characterized as Golgi-localized acetyl xylanesterases (AXE) in rice and shown to be necessary to maintain the balance of acetyl pool on polysaccharides; however, evidence for the presence of AXE in other plants was lacking. Thus, unravelling the role of GDSL lipase/esterases is necessary to understand the mechanism of polysaccharide acetylation.

There are a total of 100 gene members in the Arabidopsis GDSL lipase/esterase family. Only few members of this family have been functionally characterized in Arabidopsis and shown to possess diverse functions in plant growth, development, secondary metabolism and pathogen defense. To understand the role of the GDSL lipase/esterase family in cell wall biosynthesis, we have generated a phylogenetic tree using all Arabidopsis and characterized AXE rice protein sequences. Based on phylogenetic analysis, the GDSL genes cluster into two clades – orange and blue. The two characterized rice AXE genes group in the orange clade (Fig. 42A). In silico analysis suggests that most of the genes from the orange clade are co-expressed with plant cell wall biosynthetic genes. Further, co-expression analysis of four AtGDSL genes from this clade (Fig. 42B-E) revealed that they are co-expressed with genes encoding biosynthetic enzymes and transcription factors involved in xylan, lignin, cellulose, and pectin biosynthesis. This suggests that these fourAtGDSL genes have a role in cell wall biosynthesis or modification.

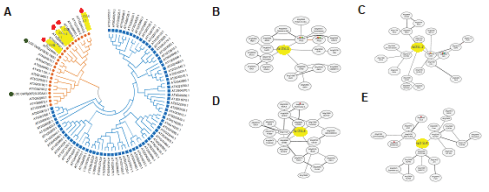


Figure 42:*Bioinformatics analysis of the GDSL lipase/esterase family. A) Phylogenetic tree was made using AtGELP protein sequences and known acetyl xylanesterases along with rice protein sequences BS1 and DAX1 which are characterisedxylanesterases in rice. The tree was built by Neighbour Joining method using MEGA X software. The tree is divided into two clades – shown in blue and orange. The green colour dots represent identified polysaccharide esterases from rice. The four red dots denote selected Arabidopsis GDSL members.B-D)Co-expression network analysis for AtGDSL1-4, generated by ATTED-II database (https://atted.jp/).*

Functional characterization of four Arabidopsis GDSL lipase/esterase family members

Since GDSL genes generally show esterase activity, our initial hypothesis is that they are involved in de-esterification of hemicellulosic polysaccharides. Hemicellulosic polysaccharides are assembled in Golgi, and enzymes such as transferases and esterases typically have one transmembrane domain at the N-terminal. We checked this by subjecting the amino acid

sequences to TMHMM, an in silico transmembrane domain analysis tool.None of the sequences were predicted to have transmembrane helices with probability of one, suggesting that AtGDSL proteins do not have a transmembrane domain (Fig. 43A-D) and probably do not function in the Golgi membrane. For further functional characterization ofAtGDSLgenes, we cloned all four genes under the control of the CAMV 35S constitutive promoter and transiently expressed them in Nicotianabenthamiana. Three days after agroinfiltration, we analysed esterase activity in soluble and wall bound protein fractions using the synthetic substrate 4-nitrophenyl acetate. The released product 4-nitrophenol was quantified by spectrophotometry. The empty vector (WT) was used as a negative control and acetyl xylan esterase (AnAXE) from Aspergillus niger as a positive control. We found 85% and 68% increase in soluble protein activity in AtGDSL1 and AtGDSL4 expressed tobacco tissues, respectively. Additionally, wall bound esterase activity was significantly higher in all GDSL expressed tobacco lines including AnAXE lines. This suggests that these proteins might be localized in the cell wall. This will be verified by localization studies where green fluorescent protein (GFP) will be attached to the N-terminus of the GDSL sequence and fluorescence monitored using confocal microscopy. Also, we observed that AtGDSL3 expressed tobacco tissues showed a 500% increase in esterase activity, higher than AnAXE expressed tobacco leaves. This suggests that AtGDSL3 has a prominent role in de-esterification of cell wall polysaccharides.

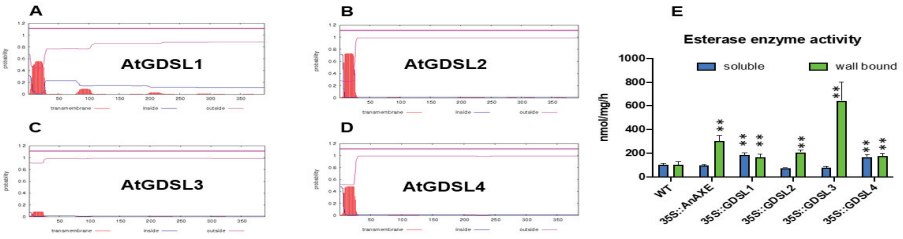
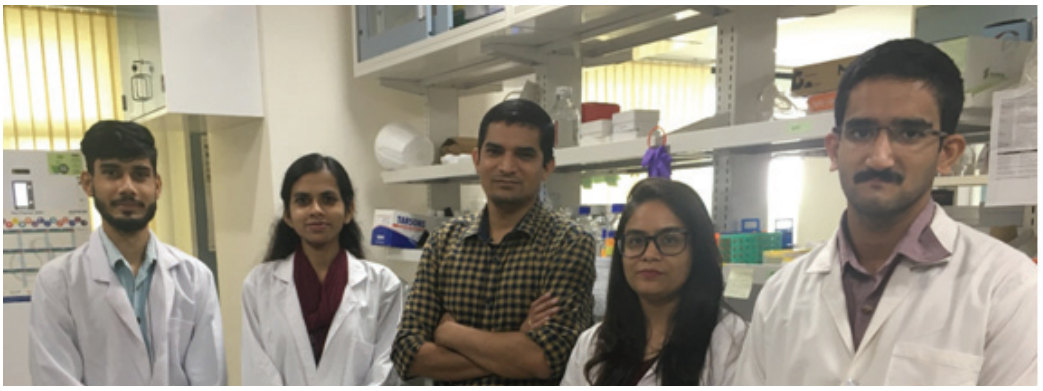
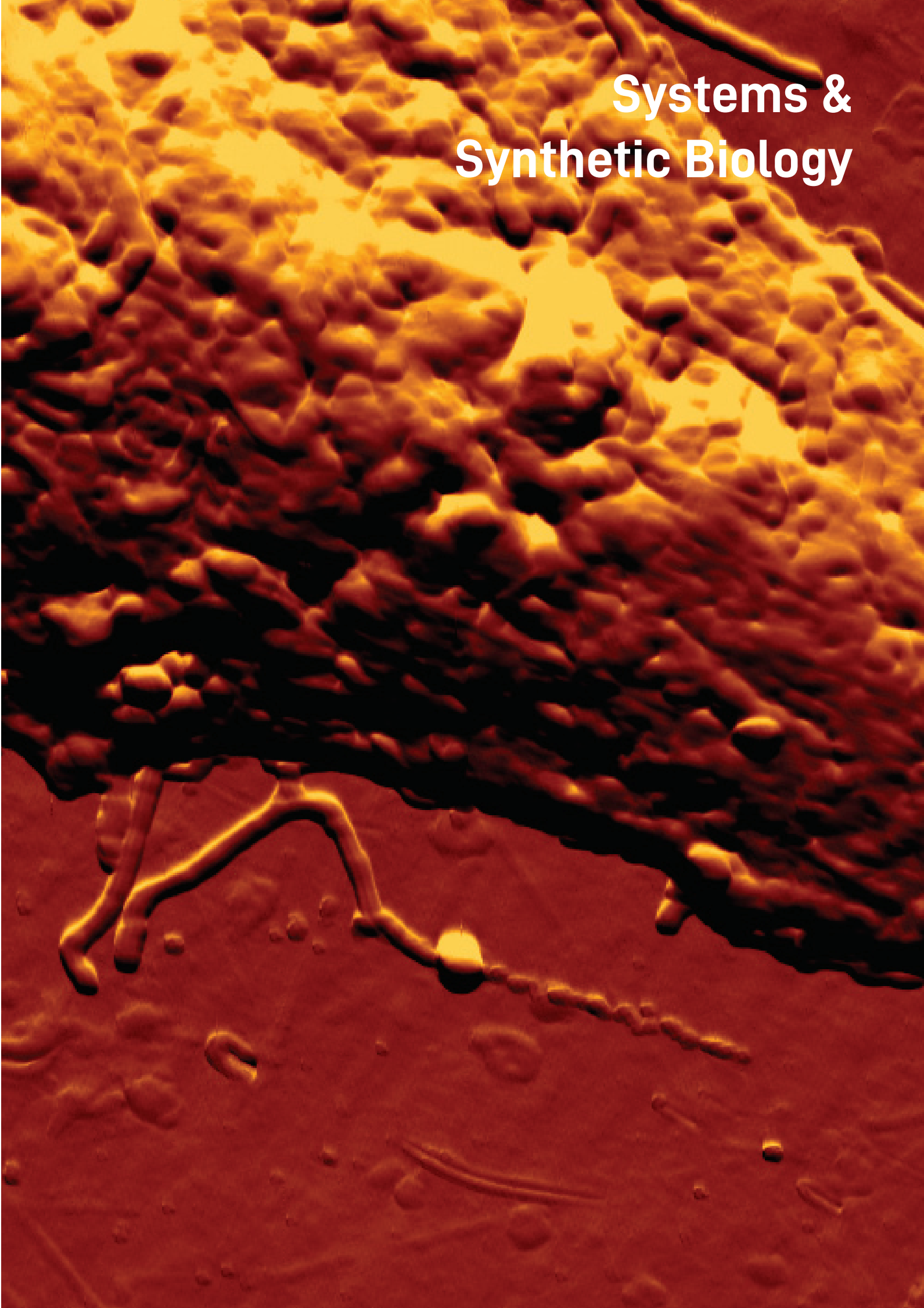


Figure 43: *Transmembrane domain prediction and esterase activity. A-D) Domain analysis was done using TMHMM server v. 2.0. Transmembrane (TM) helices prediction based on Hidden Markov Model (HMM) for AtGDSL1- 4. E) N. benthamiana leaves were infiltrated with agrobacterium carrying AnAXE, AtGDSL1, 2, 3 or 4 and assayed for esterase enzyme activity using 4-napthyl acetate as a substrate. The product 4-nitrophenol was analyzed at 410 nm. Data represents Mean ≤ SD. Asterisk represents significant difference between wild type and transgenic constructs, calculated using students t-test at p ≥ 0.05.*

For further functional characterization, we are in the process of generating Arabidopsis mutants and overexpression transgenic lines. Acetylation levels in xylan, pectin and xyloglucan polysaccharides will be checked in these transgenic lines and mutants. Additionally, we will monitor the growth phenotype of altered acetylation mutants because increase or decrease in polysaccharide O-acetylation has a negative impact on growth. We will investigate plausible reasons for these changes by examining several plant cell wall properties. We will use wet chemistry methods, Nuclear Magnetic Resonance (NMR), and Gas Chromatography-Mass Spectroscopy (GC-MS) to understand the plant cell wall structure in transgenic GDSL lines and mutants. The final goal of this project is to identify polysaccharide specific esterases that are either localised in Golgi or the plant cell wall, and comprehend the role of different polysaccharide O-acetylation in plant growth and development.





Systems & Synthetic Biology

Ambadas B Rode
Principal Investigator

Lab Members
Nikita Verma
Dwarika Chavan
Bhaiyyasaheb Harale
Divya Ojha

Molecular engineering of functional nucleic acids for biomedical and biotechnological applications

Our research group focuses on targeting and tuning nucleic acid structure-mediated gene regulation in human and bacteria for therapeutic and biotechnology applications. The propensity of nucleic acids to control cellular processes, not only rely on their base-pair identities but also on the inherent ability to form tertiary 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 therapeutic targets. Besides this, the modular nature of nucleic acid structures makes them promising synthetic biology tools. Currently we are working on rational development of synthetic riboswitches for spatiotemporal control of gene expression for diverse applications. We also aim to design and synthesize new synthetic molecules to target riboswitches for antibacterial therapy.

Rational development of synthetic riboswitches for precise control of gene expression and its applications

Synthetic RNA switches (riboswitches) have the potential to program cellular functions. The key features of synthetic riboswitch-based gene regulation systems are its conditional, spatiotemporal and ligand-concentration dependent control over desired gene expression and 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. RNA aptamers for constructing artificial riboswitches have been mainly developed by using an iterative process called Systematic Evolution of Ligands by Exponential Enrichment (SELEX). Despite, generating aptamers with high binding affinities, SELEX generated aptamers have certain limitations to be used in synthetic riboswitches and at the same time is costly and time consuming. Hence, as an alternative reengineering of preexisting aptamer domains derived from natural riboswitches is emerging as a promising approach.

It has been shown that natural riboswitches bind to the same ligand with a wide range of binding affinities due to the variations present in the aptamer domain. This implies that nature itself has used these variations to 'fine-tune' the binding events, resulting in differential gene expression in different bacterial species. We envisaged that if this tuning mechanism is understood, ligand-dependent gene expression could be rationally tuned according to the application needs. In this direction we investigated the tuning mechanism, by studying the aptamer-ligand binding parameters of various riboswitches including Flavin mononucleotide (FMN) riboswitch (Fig. 44A). By using the insights gained from our biophysical studies, we identified the tuning regions that modulate ligand binding properties and eventually gene regulation. Using this novel approach, we constructed synthetic riboswitches using the orthogonal aptamer domain by rationally modifying the identified tunable regions. As a proof of concept, we evaluated ligand concentration-dependent suppression of eGFP gene expression (Fig. 44B) using our

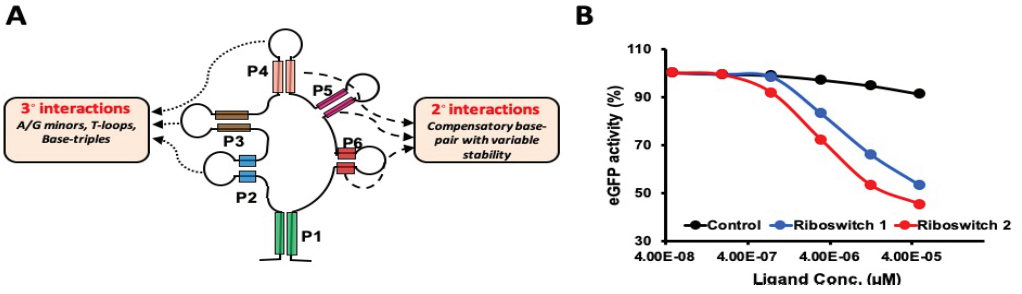


Figure 44: *A) The conserved secondary structure of FMN riboswitch showing crucial secondary and tertiary interaction for ligand recognition. B) In vitro coupled transcription/translation of artificial riboswitches consisting of orthogonal aptamer domains. In vitro experiments were performed for each riboswitch over a range of ligand concentration. Each data point is the average of four independent experiments.*

synthetic riboswitches. This suggests that a better understanding of the natural aptamers 'tuning regions' would enable researchers to rationally design controllable synthetic switches as per the application requirements.

Design and synthesis of small molecules to target riboswitches for antibacterial therapy

The widespread increase in bacterial resistance to conventional antibiotics has become a world-wide health concern. The emergence of antimicrobial resistance has brought the attention to the need for new validated cellular targets, that have not been explored much and are widespread in pathogenic bacteria. Recent advances in our understanding of how bacteria maintain physiological homeostasis reveals a promising class of potential antibiotic targets called riboswitches. The occurrence of riboswitches in pathogenic bacteria and its involvement in the regulation of genes essential for survival and pathogenesis makes it a promising target for the discovery of new leads. Towards this, we chose different classes of riboswitches such as cyclic-di-nucleotide riboswitch, S-adenosyl methionine (SAM) riboswitch and Flavin mononucleotide (FMN) riboswitch due to their prevailing occurrence in pathogenic bacteria. We used structure-based drug design strategy to design novel molecules that can bind to selected riboswitches similar to their cognate ligands. We performed a detailed structural analysis of free as well as ligand bound riboswitch structures. Based on the computational docking results, we selected the candidates with good docking score for further study (Fig. 45).

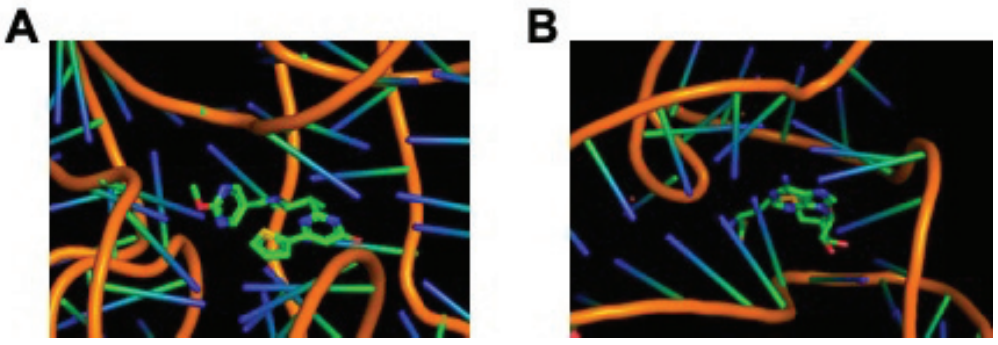


Figure 45: *Representative binding mode of synthetic analogs into the active site of A) FMN riboswitch, B) SAM riboswitch.*

We synthesized a series of synthetic analogs and characterized by using Nuclear Magnetic Resonance (NMR) and MALDI-TOF analysis. The antimicrobial activity was investigated for synthetic analogs in terms of Minimum Inhibitory Concentration (MIC), against a panel of gram-positive and gram-negative bacteria. The measured MIC_{99} values of the synthetic derivatives were found ranging from 20 µM to 100 µM, in particular effective against an antibiotic resistant strain of *S. aureus* and also *M. tuberculosis.* Further, we are working towards validating the interaction between the riboswitches and the synthesized derivatives, *in vitro*, using biophysical techniques. Our efforts are underway to establish the mode of action of these active compounds that would aid in the rational design of the new therapeutics.

Nidhi Adlakha
Principal Investigator

Lab Members
Sudipt Kumar Dalie
Aishwarya Srivastava
Manasa Hegde

Rational development of biocatalysts for production of value-added products

Our research program focuses on the development of biocatalysts for industrial and biomedical applications using a systems and synthetic biology approach. We aim to optimize existing microbial cell factories and improve cost economics of enzyme or bioproduct synthesis. Another goal of our program is to understand the underlying mechanism that biocatalysts employ, with the aim of augmenting yield and productivity of value-added products from engineered microbes. Our initial efforts will be directed at the following projects.

Investigation of cellulase induction system in industrial fungi leading to the development of a cost effective platform for polysaccharide degradation

The major goal of our research program is to develop superior biocatalysts for pharma, chemical, food, flavors, and agro-based industries. We intend to build a technology that is greener and economical, with improved sustainability. For agro-based industries, the lab aims to develop superior biocatalysts for cellulose degradation. In the present scenario, industries rely on cellulolytic fungi for production of biomass hydrolyzing enzymes wherein the secretion of enzymes by fungi needs the presence of an inducer in the medium. It has been suggested that oligosaccharides released from polymers function as the actual molecules that trigger enzyme induction. Hence, although the precise nature of the "true inducer" responsible for overexpression of cellulolytic enzymes is still unknown, complex polysaccharide is widely used an as inducer. In this context, we aim to investigate the cellulase induction system in cellulolytic fungi. The knowledge gained will not only help us understand the basic biology of the fungus, it will also allow us to develop a robust platform for better decomposition of lignocellulosic biomass. Further, to unravel the mechanism involved in regulation of the cellulase machinery, our group has performed transcriptomics of a cellulolytic fungus grown in the presence of cellulose and found putative transcription factors involved in mediating induction of cellulose depolymerizing enzymes. The study also led to the identification of carbohydrate active enzymes (CAZymes) that are expressed immediately after being exposed to cellulose, hinting at possible tailoring enzymes involved in inducer synthesis, which will eventually mediate production and secretion of cellulase disintegrating enzymes (Fig.46).

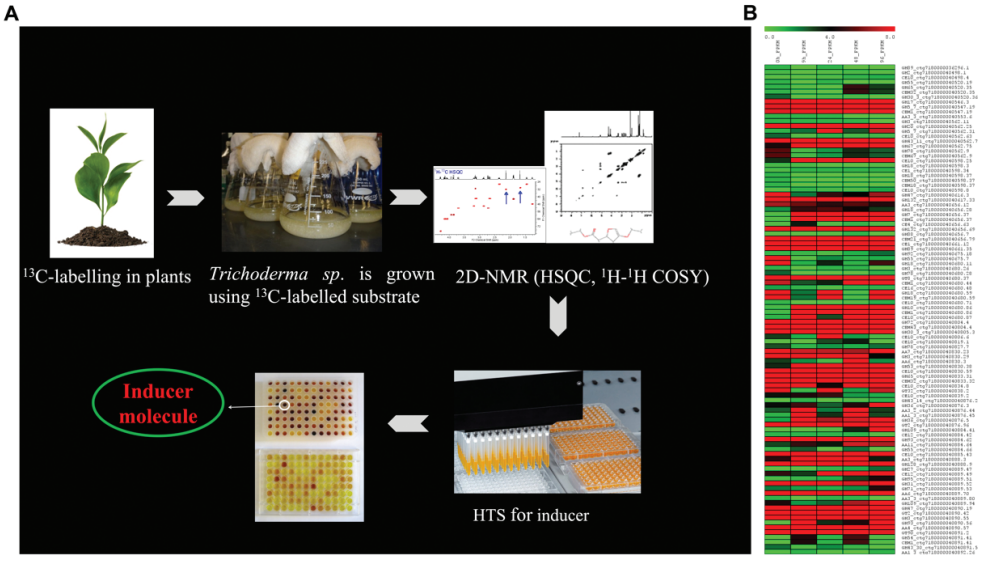


Figure 46: *Understanding the induction system in a cellulolytic fungus. A) Schematic of platform developed for inducer identification B) Dynamics of CAZymes (carbohydrate active enzymes) reflected in transcriptome of cellulolytic fungi grown in the presence of cellulose for 0h, 9h, 24h, 48h and 96h.*

Rational engineering of whole cell biocatalyst for bioproduct synthesis

We had previously 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 utilize this in-house developed enzyme system for fermentative production of other valuable bioproducts such as methyl ethyl ketone, which is widely used as an anti-freeze agent. This program aims at rational microbial engineering to improve cost economics for bioproduct synthesis. In this direction, we earlier identified *Paenibacillus polymyxa* from the gut of termites. This strain was found to ferment a range simple sugars, and thus utilized to ferment cellulosic hydrolysate into value-added products. Further, we are developing tools to engineer this natural isolate 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 water-absorbent. Thus, they can be utilized as very efficient drop-in fuel.

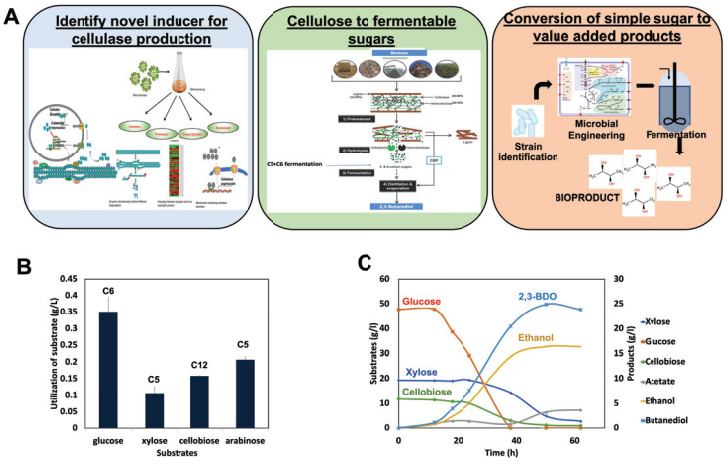


Figure 47: *Development of a platform for fermentation of lignocellulosic hydrolysate to value-added products. A) Three steps involved in rational microbial engineering for fermentation of complex sugars to bioproducts B) Utilization of mono- and di-saccharides by Paenibacillus polymyxa indicating that it harbors a pathway for consumption of a range of substrates C) Fermentative production of 2,3-butanediol (2,3-BDO) and ethanol by P. polymyxa.*

Future Plans

The research program aims at developing an economical platform for technology development and advanced bio-manufacturing using system and synthetic biology tools. It not only offers a way to reduce costs but also aims to produce new biocatalysts and bioproducts while protecting the environment.

Kinshuk Raj Srivastava
Principal Investigator

Lab Members
Nitu Singh
Bhupinder Singh
Sunny
Annu Chandra

Development of biocatalyst and synthetic biology approaches for the synthesis of high-value products

Nature has evolved enzymes to carry out complex chemical transformations in the biosynthesis of natural products. The rapid advancement of bioinformatics methods, genetic tools, and recombinant DNA technology enables researchers to discover and engineer enzymes from diverse biosynthetic pathways. Further, reconstruction of multienzyme cascades in a heterologous microbial host provides the handle to access the desired natural products and their novel analogues. Our research program is focused on developing biocatalytic/synthetic biology platforms for synthesis of natural product-derived therapeutics and other value-added compounds. We aim to achieve such a challenging goal by first developing a molecular level understanding of the factors governing an enzyme's stability and activity, as well as its spatio-temporal communications with other enzymes of biosynthetic pathways under consideration. The gained knowledge will be further exploited to develop synthetic biology platforms for combinatorial biosynthesis of desired compounds, followed by an assessment of their bioactivity and scale-up.

Biosynthesis of natural product derived therapeutics using synthetic biology

Cyclic peptides and flavonoids constitute large classes of natural products that display broad variety of biological and pharmacological activities, including antibacterial, antitumor, antifungal, antiviral, antitubercular, anti-cancer, etc. The exceptional stability and bioactivities of these natural products make them attractive structural scaffolds for medicinal chemistry and drug discovery applications. Recent advancements in molecular biology and recombinant technologies are enabling researchers to construct synthetic pathways in heterologous host systems for the production of these compounds, which have so far been intractable through chemical synthesis. The enormous potential of these compounds motivates us to develop synthetic biology approaches for combinatorial biosynthesis of cyclic peptide and flavonoid derived bioactive compounds by expressing single/multi-enzyme cascade in heterologous host systems such as *E. coli* and yeast. We began with database mining and chemo-informatics analysis of natural product/drug databases which enables us to deduce their structure-activity relationship i.e. addition of which particular group increases the degree of bioactivity and other properties in the compound. Next, mining of genome database for targeted natural product pathways provided critical information related to the necessary set of required biosynthetic enzymes for synthesis of core scaffold and late-stage tailoring to produce the bioactive compounds. We then designed synthetic pathways based on the mining/available literature knowledge about the biosynthetic gene cluster of targeted natural product. We have been routinely expressing the planned enzyme cascades in *E. coli* and/or yeast for production followed by isolation and assessment of their bioactivity. We will further generate structurally diverse compounds by engineering enzymes as well as by plug and play of enzymes from diverse pathways.

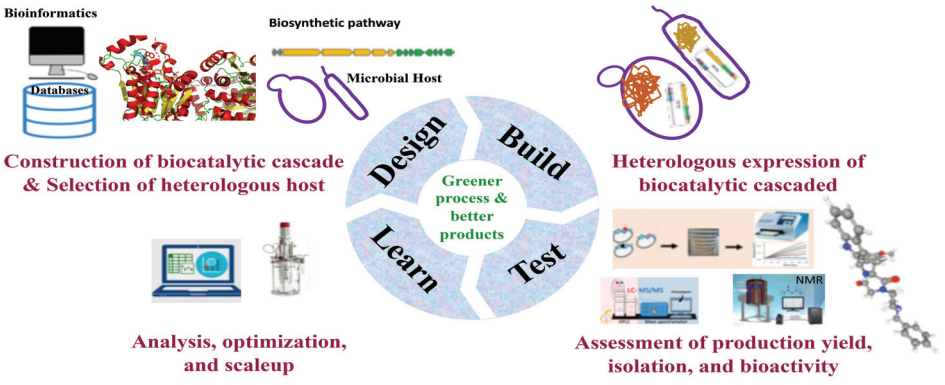


Figure 48: *Schematics of work flow for discovery and development of natural product derived therapeutics.*

Investigation of substrate channelling during biosynthesis of natural products

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 biology platforms and metabolic engineering. Towards this end, we have been probing enzyme-enzyme interactions and overall topology of multi-enzyme complexes (metabolons) from diverse natural product biosynthetic pathways. This effort will provide evidences and understanding about 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 value-added products such as active pharmaceuticals and fuels.

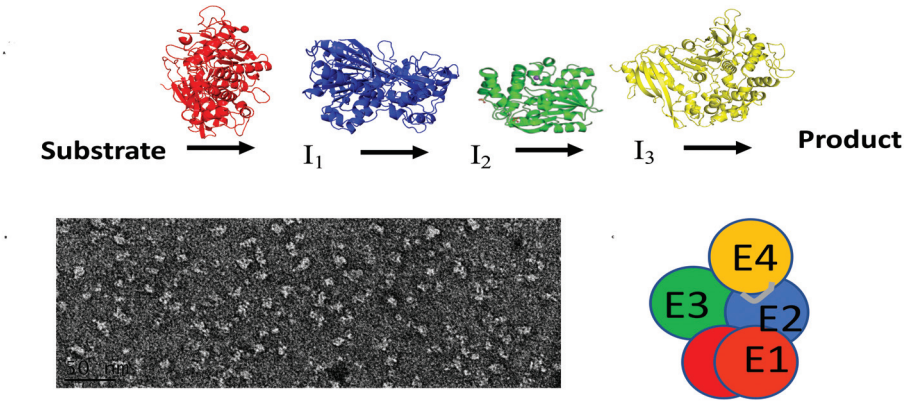
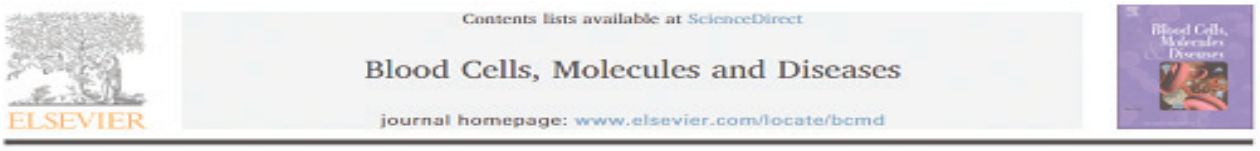


Figure 49: *A) Schematic representation of multi-enzyme cascade catalysis, B) EM image, and C) possible model of metabolons.*

Development of biocatalytic platforms for the synthesis of chiral amines for diverse industrial applications

Chiral amines are the most valuable building blocks in the pharmaceutical, fine chemicals and agrochemical industries. The majority of the drugs approved by FDA constitute amine intermediates, and about 40% of the APIs contain a chiral amine moiety. Chemical synthesis of chiral amines is very inefficient as it involves the application of expensive toxic metals, the stereoselectivity in chemical synthesis is difficult to control, and the product has to be purified as it contains a mixture of enantiomers. Enzymes such as transaminases (TA), monoamine oxidases (MAOs), amine dehydrogenases (AmDHs), phenylalanine ammonia lyases (PALs), imine reductases (IREDs), lipases, and monooxygenases are some of the classes of enzymes that are targeted for biocatalytic synthesis of chiral amines. We have begun the development of phenylalanine ammonia lyase (PALs) and imine reductase (IREDs) based biocatalytic technologies for the sustainable production of a diverse range of chiral amines of industrial interest.

Publications & Patents



Contents lists available at ScienceDirect

Blood Cells, Molecules and Diseases

journal homepage: www.elsevier.com/locate/bcmd

Elevated surface-bound complement FH alters the function of platelets and monocytes in *FHR1/3* null healthy individuals

frontiers in Microbiology

ORIGINAL RESEARCH

Ectopic Expression of Rv0023 Mediates Isoniazid/Ethionamide Tolerance via Altering NADH/NAD+ Levels in *Mycobacterium smegmatis*

Contents lists available at ScienceDirect

Genomics

journal homepage: www.elsevier.com/locate/ygeno

Original Article

Dual RNA-Seq analysis of *Medicago truncatula* and the pea powdery mildew *Erysiphe pisi* uncovers distinct host transcriptional signatures during incompatible and compatible interactions and pathogen effector candidates

ACS central science

Research Article

Cite This: ACS Cent. Sci. 2019, 5, 1648−1662

http://pubs.acs.org/journal/acscii

A Localized Chimeric Hydrogel Therapy Combats Tumor Progression through Alteration of Sphingolipid Metabolism

Cell Reports

Article

DeSUMOylase SENP7-Mediated Epithelial Signaling Triggers Intestinal Inflammation via Expansion of Gamma-Delta T Cells

The Plant Journal (2020) **102**, 340–352

doi: 10.1111/tpj.14627

Structural insights into the lipid transfer mechanism of a non-specific lipid transfer protein

Peer-reviewed Publications

1. Johnson MK, Kottur J, Nair DT (2019). A polar filter in DNA polymerases prevents ribonucleotide incorporation. *Nucleic Acids Res* 47: 10693-10705.
2. Narayanan N, Banerjee A, Jain D, Kulkarni DS, Sharma R, Nirwal S, Rao DN, Nair DT (2020). Tetramerization at low pH licenses DNA methylation activity of M.HpyAXI in the presence of acid stress. *J Mol Biol* 432: 324-342.
3. Jain A, Kumar A, Shikhi M, Kumar A, Nair DT, Salunke DM (2020). The structure of MP-4 from *Mucuna pruriens* at 2.22 A resolution. *Acta Crystallogr F* 76: 47-57.
4. Yadav AK, Sahoo PK, Goswami HN, Jain D (2019). Transcriptional fidelity of mitochondrial RNA polymerase RpoTm from *Arabidopsis thaliana. J Mol Biol* 431: 4767-4783.
5. Banerjee P, Chanchal, Jain D (2019). Sensor I regulated ATPase activity of FleQ is essential for motility to biofilm transition in *Pseudomonas aeruginosa*. *ACS Chem Biol* 14: 1515-1527.
6. Yadav RK, Krishnan V (2020). The adhesive PitA pilus protein from the early dental plaque colonizer *Streptococcus oralis*: expression, purification, crystallization and X-ray diffraction analysis. *Acta Crystallogr F* 76: 8-13.
7. Pratap S, Megta AK, Krishnan V (2019). Sortases from a Probiotic *Lactobacillus rhamnosus* GG: Cloning, Expression, Purification, Crystallization and Preliminary X-Ray Diffraction Study. *Crystallogr Rep* 64: 1117-1121.
8. Kumar MA, Palva A, von Ossowski I, Krishnan V (2019). SpaB, an atypically adhesive basal pilin from the lactobacillar SpaCBA pilus: crystallization and X-ray diffraction analysis. *Acta Crystallogr F* 75: 731-737.
9. Sood A, Dev A, Mohanbhai SJ, Shrimali N, Kapasiya M, Kushwaha A, Choudhury SR, Guchhait P, Karmakar S (2019). Development and targeting efficacy of disulfide bridged chitosan-Eudragit S-100 nanoparticles for colorectal cancer. *ACS Appl Nano Mater* 10: 6409-17.
10. Bhasym A, Bhakuni T, Guchhait P (2019). Elevated surface-bound complement factor-H alters the function of platelets and monocytes in FHR1/3-null healthy individuals. *Blood Cell Mol Dis* 79: 102349.
11. Bhasym A, Annarapu GK, Saha S, Shrimali N, Gupta S, Seth T, Guchhait P (2019). Neutrophils develop rapid proinflammatory response after engulfing Hb-activated platelets under intravascular hemolysis. *Clin Exp Immunol* 197: 134-140.
12. Bhakuni T, Singhal R, Aannarapu GK, Sharma A, Mahapatra M, Saxena R, Guchhait P (2019). Unique case of autoantibody mediated inactivation of ADAMTS13 in an Indian TTP patient. *Blood Cell Mol Dis* 77: 29-33.
13. Bhasym A, Gurjar BS, Sriharsha TM, Bhasym A, Prabhu S, Puraswani M, Khandelwal P, Saini H, Saini S, Verma AK, Chatterjee P, Bal V, George A, Sharma A, Hari P, Sinha A, Bagga A, Rath S, Guchhait P (2019). Altered Peripheral Blood Leucocyte Phenotype and Responses in Healthy Individuals with Homozygous Deletion of FHR1 and FHR3 Gene. *J Clin Immunol* 39: 336-345.
14. Kumari R, Kumar R, Kumar S, Singh AK, Hanpude P, Jangir D, Maiti TK (2020). Amyloid aggregates of the deubiquitinase OTUB1 are neurotoxic, suggesting that they contribute to the development of Parkinson's disease. *J Biol Chem* 295: 3466-3484.
15. Zaman NR, Kumar B, Nasrin Z, Islam MR, Maiti TK, Khan H (2020). Proteome analyses reveal Macrophomina phaseolina's survival tools when challenged by *Burkholderia contaminans* NZ. *ACS Omega* 5: 1352.
16. Kumar R, Kumar S, Hanpude P, Singh AK, Johari T, Majumder S, Maiti TK (2019). Partially oxidized DJ-1 inhibits primary and secondary nucleation through adhesive surface and remodels mature α-synuclein fibrils to toxic conformations. *Commun Biol* 2: 395.

17. Puraswani M, Khandelwal P, Saini H, Saini S, Gurjar BS, Sinha A, Shende RP, Maiti TK, Singh AK, Kanga U, Ali U, Agarwal I, Anand K, Padmaraj Rajendran NP, Sinha R, Vasudevan A, Saxena A, Agarwal SK, Hari P, Sahu A, Rath S, Bagga A (2019). Clinical and immunological profile of anti-factor H antibody associated atypical hemolytic uremic syndrome: A nationwide database. *Front Immunol* 10: 1282.

18. Das S, Kumar P, Verma A, Maiti TK, Mathew SJ (2019). Myosin heavy chain mutations that cause Freeman-Sheldon syndrome lead to muscle structural and functional defects in Drosophila. *Dev Biol* 449: 90-98.

19. Li H, Rai M, Buddika K, Sterrett MC, Luhur A, Mahmoudzadeh NH, Julick CR, Pletcher RC, Chawla G, Gosney CJ, Burton AK, Karty JA, Montooth KL, Sokol NS, Tennessen JM (2019). Lactate dehydrogenase and glycerol-3-phosphate dehydrogenase cooperatively regulate growth and carbohydrate metabolism during Drosophila melanogaster larval development. *Development* 146(17): dev175315.

20. Chawla G (2019). Healthy Aging Research in India. *Journal of Experimental research on human growth and Aging* 2(1): 1-2.

21. Krejcova G, Danielova A, Nedbalova P, Kazek M, Strych L, Chawla G, Tennessen JM, Lieskovska J, Jindra M, Dolezal T, Bajgar A (2019). Drosophila macrophages switch to aerobic glycolysis to mount effective antibacterial defense. *eLife* 8: e50414.

22. Pandey M, Bansal S, Chawla G (2020). Molecular approaches for analysis of Drosophila microRNAs. M. Mishra, editor: Springer, New York, NY.

23. Wu YC, Chawla G, Sokol N (1 April 2020). let-7-Complex microRNAs regulate Broad-Z3, which together with Chinmo maintains adult lineage neurons in an immature state. *G3: Genes Genom Genet* 10(4): 1393–1401.

24. Bawa S, Brooks DS, Neville KE, Tipping M, Sagar MA, Kollhoff JA, Chawla G, Geisbrecht BV, Tennessen JM, Eliceiri KW, Geisbrecht ER (2020). Drosophila TRIM32 cooperates with glycolytic enzymes to promote cell growth. *eLife* 9: e52358.

25. Kaushik S, Kain P (2019). Understanding taste using Drosophila melanogaster. In Drosophila-Little, but Powerful Tool for Discovery. *IntechOpen*.

26. Mukherjee S, Akbar I, Kumari B, Vrati S, Basu A, Banerjee A (2019). Japanese Encephalitis Virus-induced let-7a/b interacted with the NOTCH-TLR7 pathway in microglia and facilitated neuronal death via caspase activation. *J Neurochem* 149: 518-534.

27. Sharma KB, Sharma M, Aggarwal S, Yadav AK, Bhatnagar S, Vrati S, Kalia M (2019). Quantitative proteome analysis of Atg5-deficient mouse embryonic fibroblasts reveals the range of the autophagy-modulated basal cellular proteome. *mSystems* 4(6): e00481-19.

28. Suhail A, Rizvi ZA, Mujagond P, Ali SA, Gaur P, Singh M, Ahuja V, Awasthi A, Srikanth CV (2019). DeSUMOylase SENP7-mediated epithelial signaling triggers intestinal inflammation via expansion of Gamma-Delta T Cells. *Cell Rep* 29(11): 3522-3538.

29. 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.

30. Banerjee A, Tripathi A (2019). Recent advances in understanding Japanese encephalitis. *F1000Res* 8.

31. Awasthi AK, Gupta S, Thakur J, Gupta S, Pal S, Bajaj A, Srivastava A (2020). Polydopamine-on-liposomes: stable nanoformulations, uniform coatings and superior antifouling performance. *Nanoscale* 12: 5021-5030.

32 Gupta S, Thakur J, Pal S, Gupta R, Mishra D, Kumar S, Yadav K, Saini A, Yavvari PS, Vedantham M, Singh A, Srivastava A, Prasad R, Bajaj A (2019). Cholic acid-peptide conjugates as potent antimicrobials against interkingdom polymicrobial biofilms. *Antimicrob Agents Chemother 63*: e00520-19.

33. Pal S, Medatwal N, Kumar S, Kar A, Komalla V, Yavvari PS, Mishra D, Rizvi ZA, Nandan S, Malakar D, Pillai M, Awasthi A, Das P, Sharma RD, Srivastava A, Sengupta S, Dasgupta U, Bajaj A (2019). A localized chimeric hydrogel therapy combats tumor progression through alteration of sphingolipid metabolism. *ACS Cent Sci* 5: 1648-1662.

34. Kumar S, Thakur J, Yadav K, Mitra M, Pal S, Ray A, Gupta S, Medatwal N, Gupta R, Mishra D, Rani P, Padhi S, Sharma P, Kapil A, Srivastava A, Priyakumar UD, Dasgupta U, Thukral L, Bajaj A (2019). Cholic acid-derived amphiphile which combats gram-positive bacteria-mediated infections vial disintegration of lipid clusters. *ACS Biomat Sci Eng* 5: 4764-4775.

35. Ananthanarayanan V, Mylavarapu SVS (2020). Meeting report - the Microtubules, Motors, Transport and Trafficking (M2T2) 2019 meeting. *J Cell Sci* 133(8).

36. Kumar H, Pushpa K, Kumari A, Verma K, Pergu R, Mylavarapu SVS (2019). The Exocyst complex and Rab5 are required for Abscission by Localizing ESCRT III Subunits to the Cytokinetic Bridge. *J Cell Sci* 132 (14).

37 Pergu R, Dagar S, Kumar H, Kumar R, Bhattacharya J, Mylavarapu SVS (2019). The chaperone ERp29 is required for tunneling nanotube formation by stabilizing MSec. *J Biol Chem* 294 (18): 7177-93.

38 Raja DA, Subramaniam Y, Aggarwal A, Gotherwal V, Babu A, Tanwar J, Motiani RK, Sivasubbu S, Gokhale RS, Natarajan VT (2020). Histone Variant Dictates Fate Biasing of Neural Crest Cells to Melanocyte Lineage. *Development* 147(5): dev182576.

39. Ojha D, Rode AB (2019). Recent Advances in Aptamer Generation for Synthetic Biology Applications. *Journal of the Japan Society of Nucleic Acids Chemistry* 3: 7-11.

40. Kauthale S, Tekale S, Rode AB, Patil R, Sangshetti J, Kótai L, Pawar R (2019). Eaton's Reagent Catalyzed Synthesis, In vitro, α-amylase inhibitory activity and molecular docking study of some Schiff's bases as diabetic-II inhibitors. *Eur Chem Bull* 8: 356-362.

41. Thakur SK, Goswami K, Bhattacharjee S, Soni U, Guchhait P, Eswaran SV (2019). A water soluble single walled carbon nanotube aryl aziridino carboxylic acid decorated Mn (II) complex increased root growth in *Arabidopsis thaliana. Chem Select* 4: 13604-13609.

42. Gupta M, Sharma G, Saxena D, Budhwar R, Vasudevan M, Gupta V, Gupta A, Gupta R, Chandran D (2020). Dual RNA-Seq analysis of *Medicago truncatula* and the pea powdery mildew *Erysiphe pisi* uncovers distinct host transcriptional signatures during incompatible and compatible interactions and pathogen effector candidates. *Genomics* 112: 2130-2145.

43. Sharma G, Aminedi R, Saxena D, Gupta A, Banerjee P, Jain D, Chandran D (2019). Effector mining from the *Erysiphe pisi* haustorial transcriptome identifies novel candidates involved in pea powdery mildew pathogenesis. *Mol Plant Pathol* 20(11): 1506-1522.

44. Kumar AN, Subbarao S, Vennapusa AR, Ashwin V, Banarjee R, Kulkarni MJ, Vemanna RS, Kumar MU (2020). Enzymatic and Non-enzymatic detoxification of reactive carbonyl compounds improves the oxidative stress tolerance in cucumber, tobacco and rice seedlings. *J Plant Growth Regul* 1-14

45 Wang Z, Pawar PMA, Derba-Maceluch M, Hedenström M, Chong S, Tenkanen M, Jönsson L and Mellerowicz EJ (2020). Hybrid Aspen expressing a carbohydrate esterase family 5 acetyl xylan esterase under control of a wood-specific promoter shows improved saccharification. *Front Plant Sci*. (In press).

46 Gupta M, Chauhan PS, Sopory SK, Singla-Pareek SL, Pareek A, Adlakha N, Kaur C (2019). Draft genome sequence of a potential plant growth-promoting Rhizobacterium, *Pseudomonas* sp. strain CK-NBRI-02. *Microbiol Resour Announc* 8: 43.

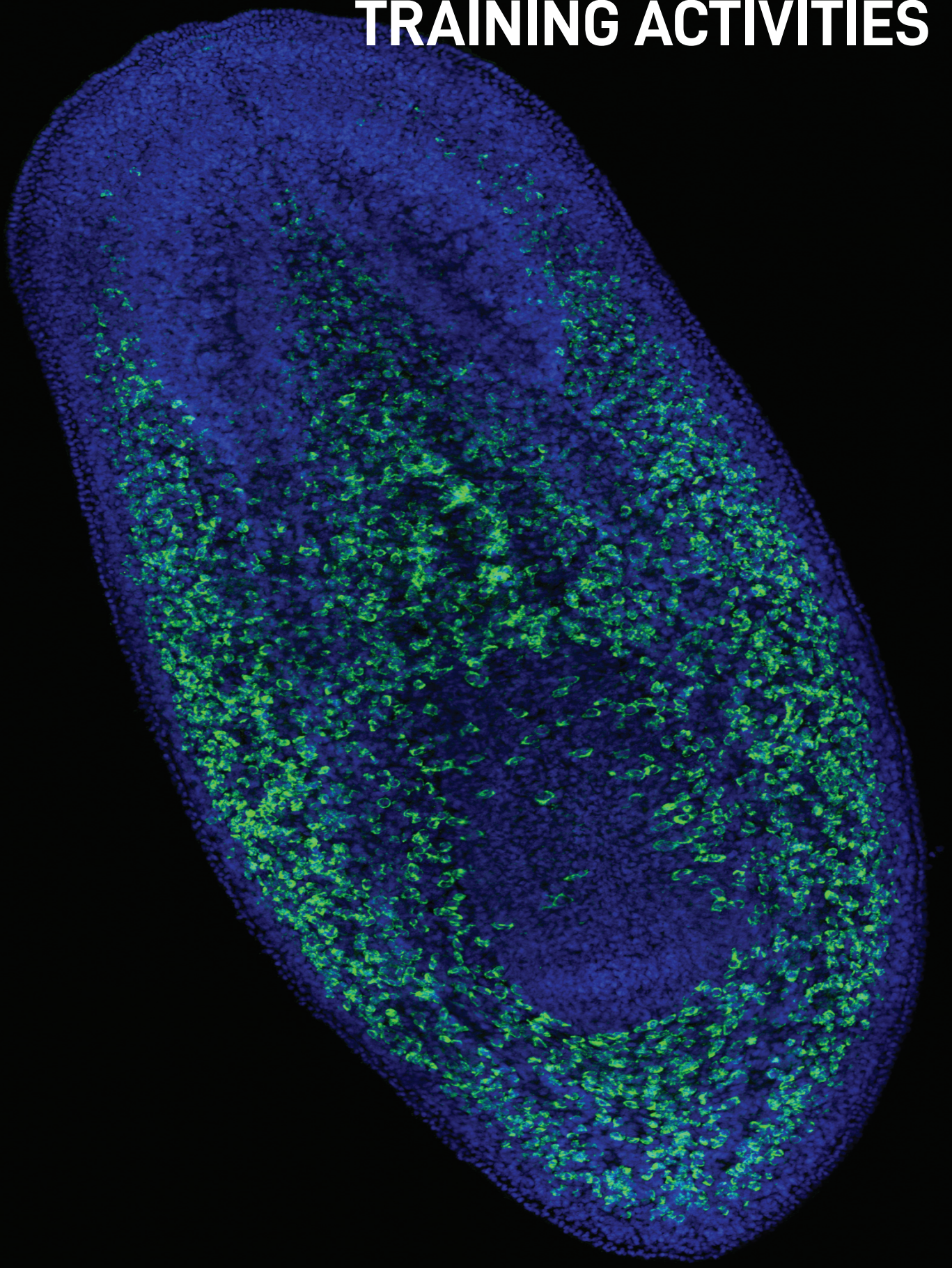
47. Malik A, Joshi H, Agarwal S, Adlakha N, Bhatnagar R (2019). In-vitro detection of phytopathogenic fungal cell wall by polyclonal sera raised against trimethyl chitosan nanoparticles. *Int J Nanomed* 14: 10023–10033.

Patent application

1. Guchhait P, Eswaran SV (June 2019) Water Soluble Fullerene C60 Adducts for Nano-Medicine & Materials Science; Application/Registration Number 201811020894.

2. Asthana S, Suri C, Kalia M, Awasthi A, Chande A, Rode AB, Prajapat SK, Shadhu S, Bhardwaj V and Ojha D (February 2020) m-Tor independent autophagy inducing small peptide and therapeutic uses thereof; Application No. 202011007117.

ACADEMIC & TRAINING ACTIVITIES



Academic Programmes

1. PhD Programme in Biotechnology

RCB offers a PhD programme in Biotechnology to students holding a post-graduate (or an equivalent) degree in any field of science, medicine or technology and having interest to work at the interface of multiple disciplines in the areas related (but not limited) to structural biology, molecular medicine, infectious disease biology, agricultural biotechnology, systems and synthetic biology, cancer & cell biology. Currently, 92 students are working at RCB for the PhD degree in Biotechnology. During the period of the report, 10 students were awarded PhD degree.

2. PhD Programme in Biostatistics and PhD Programme in Bioinformatics

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

In addition to RCB faculty members, a virtual faculty pool has been created with faculty from partner institutions like IIT Delhi, NII New Delhi, ICGEB New Delhi, NIBMG Kalyani, holding an adjunct faculty position with RCB, act as mentors for the students admitted to these programmes. Students receive a consolidated fellowship of Rs. 45000 per month for the first two years and Rs. 50000 for the next three years. Presently, 5 students are registered with RCB for PhD in these 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 in its first year provides extensive learning opportunities in the broad field of life sciences and biotechnology through rigorous class room study and hands-on laboratory experiments. In the second year, the students conduct research work under the supervision of a faculty member at RCB, in an area of mutual scientific interest, and submit a dissertation by the end of the fourth semester. The student may exit the programme with a Master's degree. Alternatively, the student may 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, 26 students are registered in the programme including 2 foreign students.

4. Research Internship & Training Programme at RCB

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

Short-term summer trainings/ internships are also offered to students interested in research areas of specialization at 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 2019-20, 29 research trainees joined RCB for six months' duration of training and 13 research interns joined for two months' research internship at RCB.

Academic Programmes at RCB's Recognized Centers

RCB has given academic recognition to the various institutions of excellence as per Clause 10(1) f of the RCB Act and RCB Ordinance for their academic programmes. Students admitted to these programmes are registered at RCB for their degrees. At present, following institutions and their academic programmes are recognized by RCB. The number of students registered under the 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)	32
Center of Innovative and Applied Bioprocessing (CIAB), Mohali	PhD (Biotechnology)	04
National Institute of Animal Biotechnology (NIAB), Hyderabad	PhD (Biotechnology)	29
National Agri-Food Biotechnology Institute (NABI), Mohali	PhD (Biotechnology)	21
Institute of Life Sciences (ILS), Bhubaneswar	PhD (Biotechnology) MSc-PhD Integrated (Biotechnology)	70 00
Rajiv Gandhi Centre for Biotechnology (RGCB), Thiruvananthapuram	MSc (Biotechnology)	40
Translational Health Science and Technology Institute (THSTI) Faridabad	PhD (Biomedical Science)	None
National Institute of Biomedical Genomics (NIBMG), Kalyani	PhD (Biotechnology) MSc-PhD Integrated (Biotechnology)	14 08

Distinguished Lectures

Date	Speaker	Title
July 29, 2019	Prof. Kiran Mysore Noble Research Foundation, USA	A Functional Genomics Approach Identifies Novel Genes Involved in Plant Immunity and Abiotic Stress
September 24, 2019	Dr. Shekhar C Mande Director General, CSIR	Networking in Biotechnology
November 11, 2019	Prof. Steve Busby University of Birmingham	Regulation at simple and complex bacterial promoters
March 2, 2020	Dr. Chandrima Shaha President, Indian National Science Academy	Celebrated Ideas in Biology: influence on Future of Life Sciences Research

Invited Seminars

Speaker	Title	Date & Time
Prof. B. V. Venkataram Prasad NBaylor College of Medicine, Houston, USA	Structural Biology of Rotavirus - from entry to exit	February 21, 2020
Prof. Teiichi Tanimura Nagoya University, Nagoya, Japan	Intelligent sugar searching behavior in *Drosophila*	December 19, 2019
Dr. Sangeeta Nath Manipal School of Regenerative Medicine, MAHE, Bengaluru	Amyloid-? induced membrane damage instigates tunnelling nanotubes and direct cell-to- cell transfer	December 18, 2019
Prof. Kartik Chandran Department of Microbiology & Immunology, Albert Einstein College of Medicine, Bronx, New York, USA	Unravelling and inhibiting the cell entry mechanisms of emerging RNA viruses	December 5, 2019
Prof. Amit Dhingra Genomics and Biotechnology, Department of Horticulture, Washington State University	Characterization of novel fruit ripening pathways	December 2, 2019
Dr. Anil Thakur Assistant Professor, Regional Centre for Biotechnology	Protein translation mechanism of gene expression in yeast and fungal pathogens	November 8, 2019
Dr. Prasad Abnave Assistant Professor, Regional Centre for Biotechnology	Investigating conserved gene regulatory mechanisms controlling adult stem cell dynamics in Planarians	August 30, 2019
Dr. Steve Xiaofeng Yu Senior VP, Model Development at Cyagen Biosciences	Turbo Knockout & CRISPR: Technologies for rapid generation of gene targeted mouse / rat models	August 8, 2019
Dr. Debojit Bose Free University, Germany	RNA Biology: Therapeutic potential and understanding	July 3, 2019
Prof. Sathees C. Raghavan Department of Biochemistry, IISc	'Repair of DNA double strand breaks in human cells: implications in oncogenesis & cancer therapy	May 27, 2019
Dr. Kavita Yadav University of Nottingham, UK	Metabolic engineering of Cupriavidus necator for isoprene production	May 7, 2019
Dr. Sandeep Saxena NII, New Delhi	Not- 'Çoding yet Compelling': The role of micro RNAs in human cancers	April 29, 2019
Dr. Shachi Gosavi NCBS-TIFR, Bangalore	Vignettes on protein assembly and design	April 5, 2019

Symposia, Conferences, Workshops and other Events

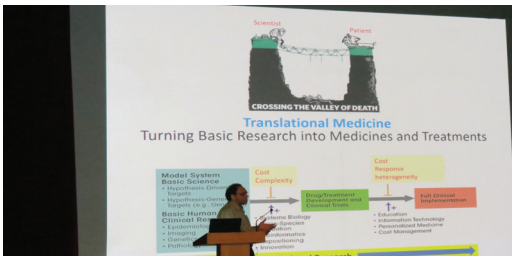
आरोहण-RCB OPEN DAY

RCB conducted its Open Day on 16th October, 2019 as an Outreach Program under the banner of India International Science Festival (IISF) on behalf of Ministry of Science & Technology and Ministry of Earth Sciences in association with Vijnana Bharati. The objective of this programme was to provide an insight into the work life of researchers and showcase the achievements of RCB scientists and research facilities at RCB.

The Open Day started with a popular science talk by Prof. Sudhanshu Vrati, Executive Director, RCB. RCB SciComm (Science Narratives from RCB laboratories) was organized for RCB students, which was followed by Science Declamation Contest for college students on "Achieving Sustainable Development Goals through Science".

A Sketching Competition was also organized for school and college students on "Biotechnological Innovations for Societal Development". This was followed by research displays by RCB students and faculty members. The attendees were taken for facility visits to RCB labs, ATPC, BBB & the Cluster.

Around 250 students from various schools and colleges visited RCB on the Open Day. The programme concluded with prize distribution ceremony and vote of thanks & concluding remarks by Dr. Deepti Jain, Associate Professor, RCB.



World Science Day

RCB in collaboration with UNESCO conducted an event on 5th November, 2019 at RCB campus to commemorate World Science Day. Every year World Science Day is celebrated on 10th of November for Peace and Development. It highlights the significant role of science in society and the need to engage wider public.

World Science Day was inaugurated with the opening remarks by Prof. Sudhanshu Vrati, Executive Director, RCB and Mr. Eric Falt, Director, UNESCO, Delhi. A Roadshow on Global Bio-India was organized, which was followed by panel discussion by distinguished guests. MindSpar Ideathon Competition was organized for PG students where students presented their ideas to be taken up as independent ventures. The students were taken for facility visits to RCB, ATPC and BBB. Declamation Contest on "Open Science to achieve Sustainable Development Goals" was conducted after the visits. The programme ended with the distribution of prizes.

Workshop on High Content Imaging

A workshop on basics of high content imaging was conducted from November 25-27, 2019. Fifteen selected candidates including PhD students, postdoctoral fellows, researchers and technical personnel from research institutions and industry across India attended this workshop. Lectures, discussions and hands on training were provided by in house experts from the Advanced Technology Platform Centre (ATPC), and industry specialists. Experiments on drug screening, spheroid culture, calcium imaging, cell migration, wound healing and cell cycle were carried out during the workshop. This workshop introduced participants to a cutting edge and powerful platform useful in large-scale investigations of biological parameters, with applications across multiple disciplines.

In addition to this workshop, ATPC has been regularly conducting various workshops/ training programs in the following areas:

1. Protein Production and Purification Workshop
2. Training Programme on FACSVerse
3. DNA Sequencing Technology & Droplet Digital PCR
4. Workshop on Biomolecular Interaction Study Technologies

Workshop on Science Communication and Careers

RCB and Wellcome Trust/DBT India Alliance organized a workshop on 'Science Communication and Careers' during January 21-22, 2020. The aim of the workshop was to train life science students to improve their writing skills and to communicate their discoveries in an effective way. The Editage-Cactus a Professional organization kindly agreed to send their trainers participate in the event to give lectures. The workshop was attended by about 30 candidates from the NCR.

The first day of the workshop was focused on 'Science communication'. The eminent speakers from Editage Cactus trained the participants in basics of Science communication, writing a manuscript, 'Ethics in Research', data falsification and fabrication, importance of grammar and language in scientific writing and responding to the reviewer's comments, writing grants etc.

The second day of the workshop was focussed on Careers options in Science, wherein accomplished science professionals from different scientific arenas shared their life journeys. The said professionals included Dr. Geetanjali Uppal, Dr. Suchita Markan, Dr. Geethavani Rayasam. Dr. Swathi Subodh, Dr. Anurag Varshney, Dr. Radhamani Anandalakshmi, Dr. Veena Kohli, Dr. Debjani Saha.

The poster session was also organized during the second day wherein, students were instructed to prepare a poster regarding their Curriculum Vitae to express their readiness for job/entrepreneurial market.

The session concluded with the remarks and prize distribution for poster presentation.

International Conference on Calcium Signaling

RCB organized an "International conference on Calcium Signaling" during January 31-February 01, 2020. The goal of this conference was to highlight latest scientific and technical advancements in the field of Ca^{2+} signaling and its role in physiology and disease. In the conference, sessions covering cellular Ca^{2+} homeostasis, organellar Ca^{2+} dynamics as well as Ca^{2+} microdomains and their role in physiology and disease were organized.

Another major objective of the meeting was to spur stimulating discussions with leaders in the field of Ca^{2+} signaling and drive new directions for related basic and medical research in India. This conference provided an invaluable opportunity for Indian students, postdocs and young faculty members to interact with, and gain knowledge from Eminent researchers from across the globe. The conference attracted participants at all levels i.e. Principal Investigators, postdocs and graduate students from research groups located all over the country. The conference provided a unique opportunity for the participants to interact in a relatively informal setting with the leaders of the Ca^{2+} signaling field.

Total 13 international and 8 national speakers delivered the talk and 27 participants presented poster in the meeting. Three best poster awards were given.

This meeting was highly appreciated by both the participants and the speakers.

Workshop on Molecular Neurobiology

RCB organized a workshop on Molecular Neurobiology: From Genes, Neurons to behavior in health and disease during 24-29th February, 2020. It explicitly focused on the current progress of neuroscience and neurobiology in India on health and disease issues and covered various model organisms used in the field. The workshop was organized to bring the Indian Neuroscience community together, to foster collaboration between institutes and possibilities of accessing available reagents and sharing great science.

In a 6-day's long workshop, leading Neurobiologists from institutes across India like NCBS (Bangalore), TIFR (Mumbai), IISc (Bangalore), NBRC (Manesar), JNCSAR (Bangalore), University of Delhi (Delhi), IISER (Pune), NCCS (Pune), IGIB (Delhi), NII (Delhi), IIT Kanpur, Jamia Hamdard (Delhi) mentored the students. Honourable guest speaker (Prof. Teiichi Tanimura) from Nagoya University, Japan also shared his science with students. A total of 55 participants including students and mentors actively participated in the workshop.

A variety of topics including wiring in the brain affecting smell and taste, neurodegeneration including Autism, Huntingtin disease, epilepsy, Parkinson's and Alzheimer's disease, olfaction, nutrition and memory were discussed.

The students were given hands on training on various model systems, which would help them choose the appropriate model system to address various neurobiology problems in future.

आरोहण-RCB OPEN DAY

The Regional Centre for Biotechnology conducted आरोहण-RCB OPEN DAY on 28th February, 2020 as a part of outreach activity on National Science Day, aiming at encouraging the youngsters for a career in research and science and contributing towards scientific and social responsibility of connecting with the society. A total of 152 students and 14 faculties from various colleges of Delhi-NCR visited RCB on the occasion.

RCB Open Day started with the display of RCB video, which provided the glimpse of activities and research work carried out in RCB. A science talk was delivered by Dr. Avinash Bajaj, Associate Professor, RCB on: "Defeating Cancer: Is India Ready to Take the Challenge?". RCB SciComm (Science Narratives from RCB laboratories) was presented by students of RCB explaining the complex mechanisms in various aspects of biotechnology in simple words to the young college students. Research Displays from various RCB labs were setup for the college students so that they get a hands-on experience of the various tools and techniques of biotechnology and interest areas of respective labs in RCB.

Students from participating colleges took part in sketching, debate and skit competitions organized by RCB. College students were taken in groups for facility visits, which included guided tour of RCB labs, Advanced Technology Platform Centre, Bioincubator & the NCR Cluster. It aimed at exposing the young scientific minds to the advanced technologies used in the field of biotechnology and help them in understanding the future prospects in this field. The event concluded with a prize distribution ceremony.

RCB Foundation Day

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

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

Prof. Sudhanshu Vrati, Executive Director, RCB welcomed the Chief Guest Dr. Chandrima Shaha and other dignitaries with a welcome address. An introductory video of RCB was shown to the gathering. Dr. Renu Swarup, Secretary, DBT, Guest of Honour for the day, joined through Skype and gave the RCB Day message highlighting the growth of RCB from a naive centre to an Institution of National Importance.

The event was presided over by Dr. Manju Sharma, Former Secretary, Department of Biotechnology. The Chief Guest, Dr. Chandrima Shaha, President, Indian National Science Academy, gave the RCB Day oration on "Celebrated Ideas in Biology: Influence on Future of Life Science Research". She enriched the audience on the developments/ discoveries made in the field of science and their importance in modern era.

The Executive Director, RCB felicitated Dr. Chandrima Shaha and Dr. Manju Sharma with a memento. The dignitaries presented the awards for the best scientific presentation to the winners. The session was followed by tree plantation by Dr. Manju Sharma and Dr. Chandrima Shaha. The RCB Day concluded with a cultural program presented by the first year Integrated PhD and PhD students.

Swachhata Hi Seva Campaign 2019

Responding to the Hon'ble Prime Minister's appeal for citizen's participation in Swachhata Movement, Swachhata Hi Seva (SHS) Campaign-2019 was celebrated at RCB and THSTI. In line with the mission of Swachhata Hi Seva Campaign, RCB has taken the following steps:

1. Ban Single use plastic
2. Active cleaning of labs, offices, lawns and open areas
3. Shramdaan

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

In furtherance to this, an outreach program was jointly conducted by RCB and THSTI on 1st October 2019 at Roshni Vidya Niketan, Faridabad, which is a school being run for children from underprivileged section of the society. A drawing competition on the theme, "SAY NO TO PLASTIC" was organized. for the school children. Students, scientists and staff of RCB and THSTI were actively engaged with the school children to guide and motivate them to convey the message to their respective families to stop the use of plastic and guided on alternate materials for daily requirements.

Sports Day 2020

Sports at RCB is a month-long activity which includes outdoor and indoor sports competitions like badminton, table tennis, cricket, volley ball, chess, carom etc., signifying the importance of physical and mental health being as important as intellectual health. The prize distribution for the winners of all the events was done on 29th February, 2020 during RCB-THSTI Family Get together.

Membership of Professional/Academic bodies

Prof. Deepak T Nair

1. Member, Guha Research Conference
2. Co-opted Member, Interdisciplinary Science PAC, SERB
3. Member, Screening committee to Review SAHAJ Proposals 2020 of DBT
4. Expert Member of the Selection Committee for the Faculty Recruitment in the discipline of Bioscience and Biomedical Engineering (BSBE) at Indian Institute of Technology Indore (IIT Indore) held in July, 2019
5. Member, Board of Studies, Regional Centre for Biotechnology
6. Life Member, Indian Crystallographic Association
7. Life Member, Indian Biophysical Society
8. Life Member, Society of Biological Chemists
9. Member, Expert Committee to review proposals submitted under the Niche Creating High Science and Focused Basic Research schemes for Healthcare theme of CSIR

Dr. Deepti Jain

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

Dr. Prem S Kaushal

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

Dr. Vengadesan Krishnan

1. Member, Indian Biophysical Society (IBS)
2. Member, Indian Crystallographic Association (ICA)
3. Member, Electron Microscopy Society of India (EMSI)
4. Member, International Union of Crystallography (IUCr)
5. Reviewer for International Journal of Biological Macromolecules, International Journal of Data Mining and Bioinformatics, Microbial Pathogenesis, Informatics in Medicine Unlocked, Molecular Microbiology

Prof. Prasenjit Guchhait

1. Reviewer for research proposals for BIRAC, DBT, IIT Kanpur Innovative Centre
2. Reviewer for research proposals for BIRAC, DBT, NCL Pune Incubator
3. Reviewer for research proposals for BIRAC, DBT, CCAMP Bangalore Incubator
4. Steering Committee member of the Good Clinical Practice Professional Certification Scheme (GCPPCS), CDSA, THSTI, Faridabad
5. Member of the Board of Study of the Apeejay Stya University, Gurugram
6. Scientific advisory committee member for reviewing new Platelet Research Center of ICMR
7. Reviewer for UGC Scheme for Trans-disciplinary research for India's Developing Economy
8. Review committee member for scientific proposals of Ramalingaswami Fellows, DBT
9. Reviewer for research grants of DBT and DST
10. Reviewer for *Emerging Microbes and Infections* and *Haematologica*

Dr. Tushar K Maiti

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

Dr. Sam J Mathew

1. Member, Indian Society for Developmental Biology (InSDB)
2. Member, Institutional Stem Cell Research Committee, THSTI, Faridabad
3. Reviewer for *Cell Death and Disease, Developmental Biology, FASEB J, Oncotarget, IUBMB Life and Scientific Reports*
4. Reviewer of grants for *Israel Science Foundation, Medical Research Council UK, and Inserm-CNRS France*

Dr. Geetanjali Chawla

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

Dr. Pinky Kain

1. Associate Editor, *Science Progress*
2. Editor, *Acta Scientific Neurology*

Dr. Sivaram V S Mylavarapu

1. Life Member, Indian Society for Cell Biology (ISCB)
2. Reviewer for Journal of Cell Science
3. External PhD thesis examiner and viva-voce examiner for Ms. Divya Pathak, TIFR Mumbai
4. Invited external member, 2019 PhD selection interviews for NBRC Manesar
5. Member, Institutional Stem Cell Research Committee, THSTI Faridabad
6. DBT nominee, Institutional Biosafety Committee, Akamara Biomedicine Private Limited, Delhi
7. DBT nominee, Institutional Biosafety Committee, Invictus Oncology Private Limited, Delhi
8. DBT nominee, Institutional Biosafety Committee, Vyome Therapeutics Limited, Delhi

Dr. Rajender Motiani

1. Reviewer for Journal of Biological Chemistry, Cellular Physiology and Biochemistry, Scientific Reports, Cell Calcium and Cancer Epidemiology
2. Ph.D. thesis examiner and external expert for the Ph.D. viva voce examination of Ms. Arijita Ghosh, Department of Biotechnology, IIT Madras, Chennai

Prof. Sudhanshu Vrati

1. Life Member, Indian Society for Cell Biology
2. Life Member, Society of Biological Chemists, India
3. Life Member, Association of Microbiologists of India
4. Life Member, Indian Immunology Society
5. Life Member, Indian Virology Society
6. Member, Scientific Advisory Committee, ILS, Bhubaneswar
7. Member, Scientific Advisory Committee, NIBMG, Kalyani
8. Member, Academic Council, South Asian University, New Delhi
9. Editorial Board Member, Therapeutic Advances in Vaccines (SAGE, UK)
10. Independent Director, BIBCOL, Bulandshahar

Dr. Chittur Srikanth

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

Dr. Manjula Kalia

1. Member, American Society for Microbiology
2. Member, American Society for Virology
3. Review Editor, *Frontiers in Cellular and Infection Microbiology*
4. Review Editor, *Frontiers in Neurology*
5. Reviewer for *Autophagy, Brain Research, Journal of Neurochemistry, Virology, Virus Disease, Veterinary Microbiology*

Dr. Arup Banerjee

1. Contributing member of the F1000 Faculty Infectious Diseases of the Nervous System Section in F1000Prime Member, American Society for Virology
2. Editorial Board member (Infectious Diseases) of *Scientific Reports*

Dr. Prasad Abnave

1. Reviewer for *Frontiers in Cellular & Infection Microbiology*, *Frontiers in Cell and Developmental Biology*, *Open Life Sciences*

Dr. Anil Thakur

1. Reviewer for Scientific Reports

Dr. Ambadas Rode

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

Dr. Saikat Bhattacharjee

1. Member, International Society- Molecular Plant Microbe Interactions (IS-MPMI)
2. Expert, Plant and Molecular Biology, Question Paper Setting, JNU Entrance Examination, National Testing Agency (NTA)

Dr. Divya Chandran

1. Member, International Society for Molecular Plant-Microbe Interactions (IS-MPMI)
2. Member, British Society for Plant Pathology (BSPP)
3. Associate Editor, *Plant Molecular Biology Reporter*
4. Reviewer for *BMC Molecular and Cell Biology*, *Phytopathology*, *Genes*, *Plant Methods*, *Scientific Reports*

Dr. Ramu S. Vemanna

1. Reviewer for *Frontiers in Plant Sciences*, *Applications in Plant Sciences*, *PNAS-India*, *Plant Physiology Reports*, *Plos One*, *Crop Science*

Dr. Prashant Pawar

1. Review Editor, *Frontiers in Bioengineering and Biotechnology*, *Frontiers in Energy Research*, *Plant Physiology and Biochemistry*

Dr. Nidhi Adlakha

1. Reviewer for *Biotechnology for Biofuels*, *Scientific Reports*, *Applied Microbiology and Biotechnology*

Dr. Kinshuk Raj Srivastava

1. Review Editor, *Frontiers of Physics*
2. Mentor, BSC BioNEST Bio-Incubator

Distinctions, Honours and Awards

Prof. Deepak T Nair

1. Nominated as Member, Executive Council, Indian Crystallographic Association

Dr. Geetanjali Chawla

1. Wellcome Trust-DBT IA Intermediate Fellowship

Dr. Pinky Kain

1. Wellcome Trust-DBT IA Intermediate Fellowship

Prof. Sudhanshu Vrati

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

Dr. Prasad Abnave

1. DST-INSPIRE Faculty Fellowship Award

Dr. Ramu S. Vemanna

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

Dr. Prashant Pawar

1. DST-INSPIRE Faculty Fellowship Award

Dr. Ambadas B. Rode

1. Ramalingaswami Fellowship, DBT

Dr. Nidhi Adlakha

1. DST-INSPIRE Faculty Award

Dr. Kinshuk Raj Srivastava

1. Ramalingaswami Fellowship, DBT

Lectures, Visits and Outreach

Prof. Deepak T Nair

1. Delivered an invited talk titled 'Chemistry & Biology of a DNA polymerase' at the Department of Bioinformatics, Savitribai Phule Pune University on October 9, 2019.
2. Delivered an invited talk titled 'New insight regarding long-standing questions about DNA synthesis by DNA polymerases' at the International Conference on Molecular Medicine held at CHARUSAT, Gujarat from September 25-27, 2019.
3. Delivered an invited talk titled 'New insights regarding old questions about DNA synthesis by DNA polymerases' at the Bangalore Structural Biology Symposium held at NCBS, Bangalore on May 15, 2019.
4. Attended EMBO practical course titled 'CEM3DIP 2020: Single particle Cryo-EM of macromolecular assemblies and cellular tomography' held at IISER-Kalyani and IICB-Kolkata during January 19-30, 2020.
5. Travelled to the Swiss Light Source, Paul Scherer Institute located in Villigen, Switzerland to collect X-ray diffraction data from macromolecular crystals during May 11-15, 2019.
6. Delivered an invited talk titled 'Structural Biology: Imaging at the Molecular Level' at the DST Sponsored Fourth Lecture Workshop on Trans-disciplinary Areas of Research and Teaching by Shanti Swarup Bhatnagar Awardees held at Deen Dayal Upadhayaya College in New Delhi from September 27-28, 2019.
7. Organized International Symposium titled "Multidisciplinary research at ESRF: An opportunity for Indian Science" held at the Regional Centre for Biotechnology on June 14, 2019

Dr. Deepti Jain

1. Nominated to represent RCB for the India International Science Festival and the Women Scientist Entrepreneur Conclave organized by DST held at Kolkata from November 5-8, 2019.
2. Delivered an invited talk titled 'Transcription Regulation of flagellar gene expression in *Pseudomonas aeruginosa*' at the Gordon Research Conference on Microbial Transcription held at Bates College, Maine, USA from July 28 - August 2, 2019.
3. Delivered an invited talk titled 'Structural basis of anti-activation at flagellar promoters in *Pseudomonas aeruginosa*' at the Meeting on Molecular Biology held at CDFD Hyderabad from July 10-12, 2019.
4. Delivered an invited talk titled 'Functional complexes of prokaryotic transcription modulator: Structures and mechanism' at the International symposium on Multidisciplinary research at the European Synchrotron Radiation Facility: An opportunity for Indian Science held at RCB on June 14, 2019.
5. Co-organized the 'Open Day' at RCB under the banner of India International Science Fair on October 16, 2019.
6. Co-organized 'National Science Day', an outreach activity at the Regional Centre for Biotechnology on February 28, 2020.

Dr. Vengadesan Krishnan

1. Delivered an invited talk titled 'Visualization of pilus architecture from probiotic, *Lactobacillus rhamnosus* GG' at the '12th Asia-Pacific Microscopy Conference (APMC-2020)' organized by Electron Microscope Society of India at Hyderabad International Convention Centre (HICC), Hyderabad, during February 3-7, 2020.
2. Attended, chaired a session, and evaluated the posters at, 'International Conference on Drug Discovery – 2020' organized by BITS-Hyderabad at BITS-Hyderabad campus during February 29– March 2, 2020.

3. Involved in coordinating 'RCB open day: An outreach program on the occasion of National Science Day 2020', demonstrated work and 3D visualization of biomolecules and acted as a judge for sketching competition on February 28, 2020.
4. Involved as a peer-reviewer and panel member in 'Workshop on Science Communication and Careers', organized by RCB and IndiaAlliance DBT welcome at RCB during January 21-22, 2020.
5. Attended, 'Indo-Italian Elettra Beamline User Meeting and Outreach Program', held at AIIMS, New Delhi during November 11-12, 2019.
6. Attended 'National seminar on Enhancing the role of the Library with New Tools for Teaching and Learning' organized by NBRC at NBRC campus, Manesar on August 23, 2019.
7. Attended 'Library Summit 2019 on Libraries Enabling Tomorrows Discoveries with Yesterday's Content', organized by American Chemical Society at New Delhi on August 9, 2019.
8. Attended, 'Steering cum Negotiation Committee meeting of DeLCON' held at DBT, New Delhi on December 13, 2019.

Dr. Prem S Kaushal

1. Delivered an invited talk titled 'Cryo-electron microscopy (cryo-EM) studies of the ribonucleoprotein complexes: group II intron and ribosomes' at the 'IIT Roorkee' organized by IIT Roorkee, on April 19, 2019.
2. Delivered an invited talk titled 'Cryo-electron microscopy (cryo-EM) the fast emerging technique in modern biology' at the 'University of Jammu' organized by School of Biotechnology, University of Jammu, on May 13, 2019.
3. Delivered an invited talk titled 'The Cryo- EM structure of group II intron' at the '12th Asia Pacific Microscopy Conference, HICC Hyderabad' organized by Electron Microscopy Society of India from February 3 -7, 2020.

Prof. Prasenjit Guchhait

1. Delivered an invited talk titled 'Genetic adaptation of gain-of-function of prolyl hydroxylase-2 protects Tibetan highlanders from hypoxia-triggered inflammation' at the International Conference on Current Perspectives of Biochemistry in Health and Diseases, Banaras Hindu University, Varanasi, January 2020.
2. Delivered an invited talk titled 'Gain-of-function prolyl hydroxylase-2 (PHD2) D4E; C127S haplotype protects Tibetan from hypoxia-triggered inflammation at high altitude' at the National Conference on TRendys in Biochemistry, MS University, Baroda, January 2020.

Dr. Tushar K Maiti

1. Delivered an invited talk titled 'Proteomic signature in human saliva and vaginal fluid with progression of pregnancy' at the 'SINP School and Symposium on Advances in Biomedical Mass Spectrometry (SSABMS 2019)' organized by Saha Institute of Nuclear Physics, Kolkata from November 11-15, 2019.
2. Delivered an invited talk titled 'Proteomics studies on human pregnancy and pregnancy related complication: Quest for biomarker discovery' at the School of Biological Sciences, Indian Association for the Cultivation of Science, Kolkata on November 14, 2019.
3. Delivered an invited talk titled 'Proteomics studies on human pregnancy and pregnancy related complication like Preterm Birth in GARBH-Ini Cohort' at the 11th Annual Meeting of Proteomics Society, India and International Conference on Proteomics for System Integrated Bio-Omics, One Health and Food Safety" by ICAR- National Dairy Research Institute, Karnal, during December 2-4, 2019.

Dr. Sam J Mathew

1. Delivered an invited talk titled 'Myosins in development and disease' at the 'National Centre for Biological Sciences (NCBS), Bangalore on March 4, 2020.

2. Delivered an invited talk titled 'Signals that regulate skeletal muscle structure and function' at the '3rd BIO Group meeting' organized by the Indian Institute of Technology (IIT), Kanpur, from July 26-27, 2019.
3. Participated as an invited mentor at the orientation workshop for India Alliance Media Fellows, at SpringerNature, New Delhi, on April 3, 2019.
4. Invited participant at the U.S. Department of Health & Human Services (HHS) Office of Global Affairs (OGA) and The Wellcome Trust/DBT India Alliance organized meeting on "Fostering International Cooperation – Enabling Mobility, Research, and Capacity Building: A Listening Session", at the CSIR Institute of Genomics and Integrative Biology (IGIB), New Delhi, on September 26, 2019.

Dr. Geetanjali Chawla

1. Attended and presented poster in the Wellcome-DBT India Alliance Annual Fellows meet organized by Wellcome-DBT India Alliance, Bangalore, June 13-15, 2019.
2. Invited to serve as a judge in the poster competition for senior Ph. D students organized by Translational Health Science and Technology Institute (THSTI) on the occasion of THSTI foundation day at THSTI on July 15, 2019.
3. Delivered an invited talk titled 'Extending healthy lifespan with dietary restriction and non-coding RNAs' at the Cultural Innovation Centre, Delhi University organized by, Delhi University, August 28, 2019.
4. Attended and presented poster showcasing the research and academic programs of Regional Centre for Biotechnology at the 5th India International Science Festival (IISF) organized by the Ministry of Science and Technology, Ministry of Earth Sciences in association with Vijnana Bharati at Science city, Kolkata, November 6-8, 2019.
5. Attended and presented poster showcasing the research and academic programs of Regional Centre for Biotechnology at the Global Bio-India 2019 organized by DBT, at Aerocity, Delhi, November 21-23, 2019.
6. Delivered an invited talk titled 'Promoting healthy aging with dietary interventions and non-coding RNAs 'at the Miranda House organized by Zoological Society, Miranda House, Delhi University January 27, 2020.
7. Delivered an invited talk titled '*Drosophila miR-125* regulates DR dependent enhancement of lifespan *via* regulation of *chinmo* 'at the Buck Institute for Research on Aging, Novato, CA organized by Prof. Pankaj Kapahi, Buck institute, March 3, 2020.

Dr. Pinky Kain

1. Delivered an invited talk titled 'How circadian clocks influence tau mediated neurodegeneration' at the 'Society for Neurochemistry India' organized by Dr. Suhel Parvez, Jamia Hamdard, New Delhi, India, October 10-12, 2019.
2. Scientific outreach at Gyanostav, Sonepat, Haryana, February 14-15, 2020.
3. Science outreach program (for people 65+ years of age) - Understanding the link between sleep, circadian clocks and Alzheimer's disease. Buck Institute of Aging, Novato, CA, USA, July 11, 2019.
4. Science outreach program (for high school students) - Understanding taste and its modulation using Drosophila as a model system. Buck Institute of Aging, Novato, CA, USA July 19, 2019.
5. Science outreach program (for people 65+ years of age) - Understanding the link between sleep and circadian clocks in Alzheimer's disease. Buck Institute of Aging, Novato, CA, USA, July 25, 2019.
6. Science outreach program at Wonder nook preschool, Novato, July 29, 2019.

7. Visiting Scientist at BUCK institute of Aging, Novato, California, USA, August 2018 - August 2019.
8. Online student mentoring at Freedom Employability Academy (FEA), India, since 2018.

Prof. Sudhanshu Vrati

1. Chaired a session in the 10th Ramalingaswami Conclave, organized by National Brain Research Centre (NBRC), April 28 - May 1, 2019.
2. Chaired the panel discussion on 'Emerging Trends in Life Sciences Research' at the Regional Young Investigators' meeting at NIPGR, New Delhi on August 6, 2019.
3. Delivered an invited talk entitled "Development of a rotavirus vaccine: The India Story" organized by the Academic Staff College, JNU, New Delhi, on August 26 2019.
4. Presentation on the programs of Regional Centre for Biotechnology in Stakeholder Steering Committee meeting on Human and Institutional capacity building for Bio-economy at UNESCO Headquarters, Paris, France, on September 26, 2019.
5. Presentation on the programs of Regional Centre for Biotechnology in the UNESCO Regional Strategic Coordination Meeting "Science to Enable and Empower Asia Pacific for SDGs II" organized at UNESCO Office, Jakarta, Indonesia during September 16-19, 2019.
6. Delivered an invited lecture on 'Development of a rotavirus vaccine: The India Story' at the 60th Annual Conference of 'Association of Microbiologists of India (AMI-2019)' organized by Central University of Haryana on November 16, 2019.
7. Participated in the panel discussion on Innovative methods for basic science education at the 12th Meeting of International Basic Science Program organized by UNESCO, Paris during November 27-28, 2019.
8. Participated in the Annual Session of Guha Research Conference, Jaisalmer, Rajasthan during December 6-10, 2019.
9. Delivered a keynote lecture at the International Conference on 'Advancement of Biotechnology in Healthcare, Bioproducts and Environmental Research' organized by Gandhi Institute of Engineering and Technology, Odisha during December 13-14, 2019.

Dr. Chittur V Srikanth

1. Participated as a panellist at, 'Fostering International Research Cooperation' organised by IA DBT Wellcome Trust at IGIB, Delhi on September 26, 2019.
2. Delivered a lecture on 'The unexpected joys of travelling the tricky terrains in biotechnology research' at Acharya Narendra Dev College Delhi University as a part of Trends in Life Sciences & Biotechnology: Innovative Paradigms, held on September 25, 2019.
3. Delivered a lecture on 'Tale of SUMO wrestling in gut inflammation: much learned, much to learn' at Amity University, on March 5, 2020.
4. Delivered a lecture on 'A SUMO tug-of-war at the epithelial-immune cell interface mediate intestinal homeostasis' at IISC Bengaluru, as a part of international symposium ICAL 2020, held on January 17, 2020.
5. Delivered a lecture on 'Epithelial SUMO-deSUMO proteome balance modulates vesicular transport to safeguard overall gut homeostasis' at NCCS Pune, as a part of minisymposia GUT on Jan 5, 2020.

Dr. Manjula Kalia

1. Delivered an invited talk titled 'Role of Cellular Stress Responses in the Pathogenesis of Japanese Encephalitis Virus' at the 'NCR Biotech Cluster Seminar Series on Virus-Host Interaction: From Basic Biology to Translational Research' organized by National Brain Research Center, Manesar, February 26, 2020.

2. Delivered an invited talk titled 'Impact of autophagy on Japanese encephalitis replication and pathogenesis' at the 'International Conference on Autophagy and Lysosomes 2020' organized by Indian Institute of Science, Bangalore, January 16-18, 2020.
3. Delivered an invited talk titled 'Applications of Super-Resolution Microscopy' at the 'Winter School for Advanced Techniques in Nano Science and Technology (A special program for young minds from Scheduled tribes)' organized by Institute of Nano Science and Technology, Mohali, December 2-7, 2019.
4. Delivered an invited talk at the 'Olympus FV confocal user meet' organized by Olympus Medical Systems India Private Limited, The Medicity Complex, Gurgaon, November 18-19, 2019.
5. Delivered an invited talk titled 'Membrane trafficking networks exploited by the Japanese encephalitis virus' at the 'Molecular Motors, Transport and Trafficking meeting' organized by National Brain Research Centre, Manesar, October 18-20, 2019.
6. Participant in the 'International Summit on Women in STEM: Visualizing the Future: New Skylines', organized by Department of Biotechnology, January 23-24, 2020.

Dr. Arup Banerjee

1. Delivered an invited talk titled 'Host Transcriptional Response to Dengue Virus Infection: Novel Insights into Mechanisms of Disease Progression' at the SINCLAIRS BAYVIEW PORT BLAIR, Andaman Islands organized by IISER, Kolkata, Dec 3-9, 2019.

Dr. Avinash Bajaj

1. Delivered an invited talk at Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore, India on February 19, 2020.
2. Delivered an invited talk at St John's Research Institute, St John's National Academy of Health Sciences, Bangalore, India on February 18, 2020.
3. Delivered an invited talk at conference on 'Emerging Trends in Translation Oncology' held at All India Institute of Medical Sciences, New Delhi, India on February 14, 2020.
4. Delivered an invited talk at Indian International conference on Biomaterial-based Therapeutic Engineering and Regenerative Medicine held at IIT Kanpur from November 28, 2019 to December 1, 2019.
5. Delivered an invited talk at NANOBIOTECK-2019 held at New Delhi from November 20-23, 2019.
6. Delivered an invited talk at the 2nd 'Lipids in the forefront: a lot more to discover' meeting held at Amity University Haryana, from December 12-13, 2019.
7. Delivered an invited talk at the 88th Annual Meeting of the Society and a conference on 'Advances at the Interface of Biology and Chemistry' (SBCI-2019) held at BARC Mumbai from October 31 - November 3, 2019.
8. Delivered an invited talk at Nano India 2019 held at Mahatma Gandhi University, Kottayam, Kerala, during April 26-27, 2019.

Dr. Sivaram V S Mylavarapu

1. Delivered an invited talk titled 'Endocytic-Exocytic Crosstalk in Cytokinesis' at the International Conference on Autophagy and Lysosomes (ICAL2020) held at the Indian Institute of Science, Bengaluru, on January 18, 2020.
2. Delivered an invited talk titled 'Collaboration between Endocytic and Exocytic Machineries during Cytokinesis' at the Microtubules, Motors, Transport and Trafficking (M2T2) conference 2019, held at the National Brain Research Centre (NBRC), Manesar, on October 20, 2019.
3. Delivered an invited talk at the INSPIRE Internship Science Camp for students of class XI and XII, organized by the DST, Ministry of Science and Technology, Government of India at HI-TECH Institute of Engineering and Technology, Ghaziabad, on August 1, 2019.

4. Delivered an invited talk titled 'Decoding molecular mechanisms of cell division and intercellular communication' at the Refresher Course in Life Sciences (SRC) on the theme 'Advancements in Life Sciences Leading to Improvements in Agriculture, Environment and Human Health' for University and College teachers organized by The Centre for Professional Development in Higher Education (CPDHE), UGC-HRDC, University of Delhi, on July 2, 2019.
5. Actively participated with the entire research group in the educational and research outreach activities of RCB as part of the RCB Open Day (November 2019) and RCB Open Day (February 2020).

Dr. Rajender K Motiani

1. Delivered an invited talk titled 'Orai3: Oncochannel with therapeutic potential' at the 'Emerging Trends in Translational Oncology' organized by AIIMS, New Delhi, February 14, 2020.
2. Delivered an invited talk titled 'Intriguing role of STIM1 in pigment cell biology' at 'EMBO| India Symposium on Calcium Signaling', organized by National Centre for Biological Sciences (NCBS), Bangalore January 29, 2020.
3. Delivered an invited talk titled 'Calcium signaling in human diseases: Opportunities for CRISPR editing' at 'Indo-US GETin workshop on CRISPR Editing in Mammalian Cells and Embryos' organized by Central Institute for Research on Buffaloes", Hissar on November 8, 2019.
4. Delivered an invited talk at titled 'Calcium channel Orai3: Identification, regulation and contribution to breast cancer progression' at 'National Symposium on Ion Channels' organized by Department of Biophysics, Delhi University, New Delhi, India September 28, 2019.

Dr. Prasad Abnave

1. Co-organized the 'Science Communication and Careers Workshop' in collaboration with the Wellcome Trust/DBT India Alliance at Regional Centre for Biotechnology, Faridabad during January 21-22, 2020.

Dr. Anil Thakur

1. Attended 'Global Bio-India 2019' at Aerocity, New Delhi, from November 21-23, 2019.

Dr. Ambadas Rode

1. Delivered an invited talk at 10th RNA Group Meet on "Targeting and Tuning Conformational Equilibria in RNAs: A Promising Approach for Biomedical Applications" at Rajiv Gandhi Centre for Biotechnology, Kovalam, Trivandrum, during May 2-4, 2019.
2. Presented a Poster at 10th India-Japan S&T Seminar; International Conference on Emerging Advancement in Science and Technology (IC-EAST): Divya Ojha, Ambadas B. Rode 'Rationally Reengineering Biological Systems Using Chemistry Based Approaches for Biotechnology and Biomedical Applications' at Manekshaw Auditorium, New Delhi, during September 5-6, 2019.
3. Participated in EMBO Symposium on 'Engineering meets Evolution-Designing Biological Systems' at IIT Madras, Chennai, during January 29-February 1, 2020.

Dr. Saikat Bhattacharjee

1. Delivered an invited talk titled 'Lipid interfaces in assembly of immunity and perception of a pathogen effector: Molecular insights into defense signaling' at the '2nd International Symposium on Lipids in the Forefront: A lot more to discover' organized by Amity University, Manesar, from December 12-13, 2019.

Dr. Divya Chandran

1. Delivered an invited talk titled 'Effectoromics-based identification of molecular targets for powdery mildew disease control' at the 'National Seminar on 'Present Day Biology: Impact of Research at Molecular and Cellular Level' organized by St. Xavier's College, Ahmedabad, January 3-4, 2020.
2. Delivered an invited talk titled 'Effectoromics-based identification of molecular targets for powdery mildew disease control' at the 'National Seminar on NGS: Myth or Miracle' organized by Pondicherry University, Pondicherry, December 12-13, 2019.
3. Attended the 'International Summit on Women in STEM– "Visualizing the Future: New Skylines' organized by Department of Biotechnology, New Delhi, January 23-24, 2020.
4. Attended the 'Roundtable on India-UK Crop Sciences Fellowships' organized by National Institute of Plant Genome Research, New Delhi, January 20-21, 2020.
5. Attended the 'Women Scientist and Entrepreneur Conclave' at the India International Science Conference, Kolkata, November 5-8, 2019.
6. Co-organized the 'Regional-Young Investigators' Meeting' held at the National Institute of Plant Genome Research, New Delhi, from August 6-7, 2019.
7. Participated in 'RCB Open Day' as part of the science outreach program for undergraduate students from Delhi NCR colleges, February 28, 2020.
8. Showcased RCB's research, training and education-related activities at the Mega Science, Technology & Industry Expo, India International Science Festival, Kolkata, November 5-8, 2019.
9. Participated in 'RCB Open Day' as part of the science outreach program for undergraduate students from Delhi NCR colleges, October 16, 2019.

Dr. Ramu S. Vemanna

1. Attended the 'Regional-Young Investigators' Meeting' held at the National Institute of Plant Genome Research, New Delhi, August 6-7, 2019.
2. Attended 'Global Bio-India 2019' held at Aerocity, New Delhi, November 21-23, 2019.
3. Co-organized the 'International conference on Calcium Signaling' held at RCB from January 31-February 1, 2020.

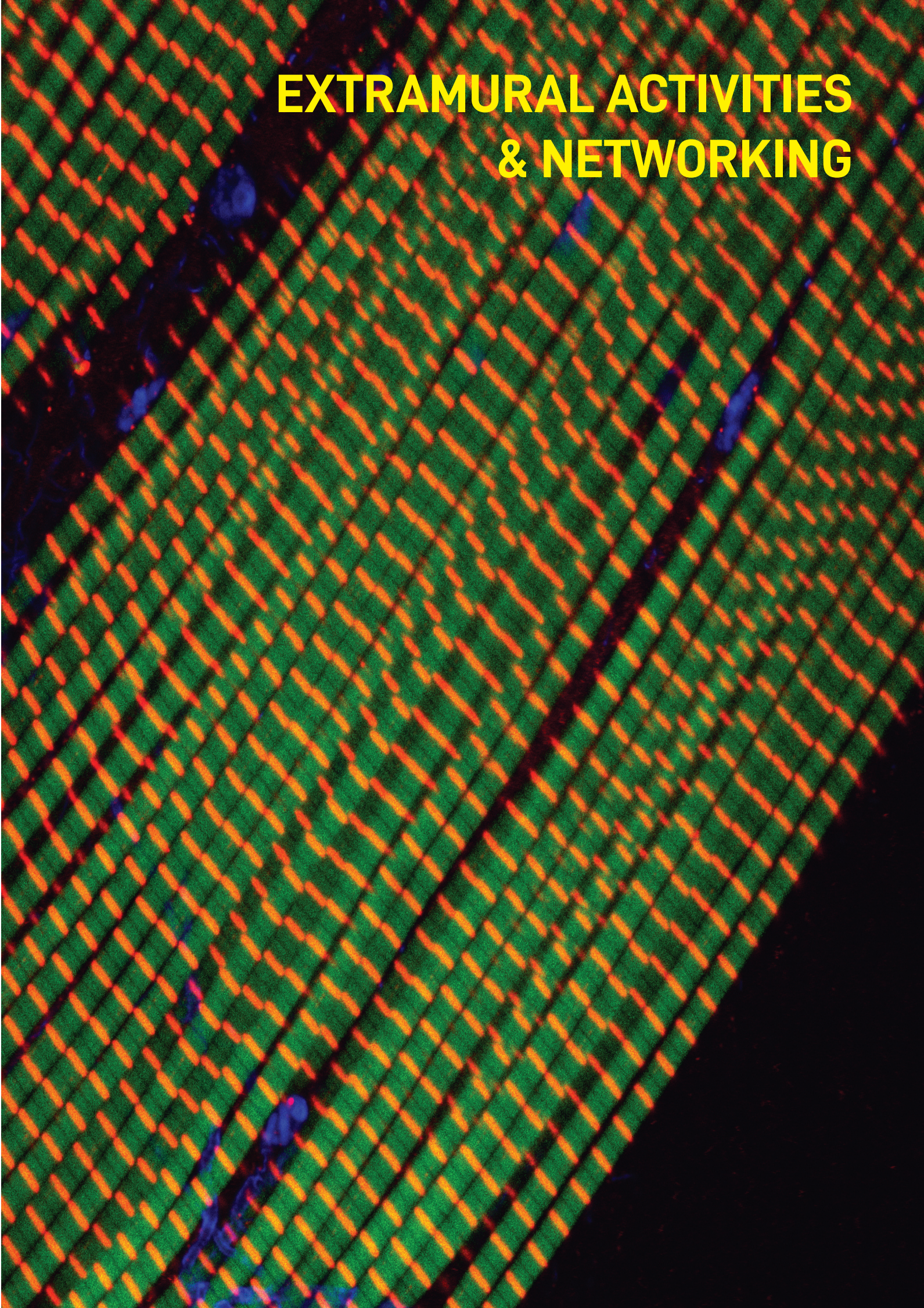
Dr. Prashant Pawar

1. Attended the 'Regional-Young Investigators' Meeting' held at the National Institute of Plant Genome Research, New Delhi, August 6-7, 2019.
2. Poster presented at 'National Conference of Plant Physiology' organized by Kerala Agricultural University, Thrissur, Kerala, December 19-21, 2019.
3. Co-coordinator of 'Workshop of Scientific Communication & Careers in Science' organized by RCB in collaboration with DBT/Wellcome India Alliance, January 21-22, 2020

Dr. Nidhi Adlakha

1. Delivered an invited talk titled "Protein production using bioreactor" at the RCB-ATPC, RCB, Faridabad, July 2-3, 2019.

EXTRAMURAL ACTIVITIES & NETWORKING



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-proprietary 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. This program has provided tremendous support to the Indian structural biologists and has benefited a large number of young research students.

Since the start of this arrangement, the program has enabled about 75 Indian researchers to travel to ESRF and collect, X-ray diffraction, small angle X-ray scattering or Cryo-Electron microscopy data at the ESRF. The users are from 25 different institutes/universities present all over India. Researchers from the following research establishments have visited ESRF: 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, National Centre for Cell Sciences (Pune), Indian Institute of Science Education & Research-Thiruvananthapuram, Central Drug Research Institute (Lucknow), Saha Institute of Nuclear Physics (Kolkata), National Institute of Mental Health & Neurosciences (Bangalore), 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, National Institute of Science Education & Research (Bhubaneswar), Translational Health Sciences & Technology Institute (Faridabad), National Chemical Laboratory (Pune), and Indian Institute of Technology-Kharagpur. The access to ESRF has helped Indian scientists to obtain data that will aid formulation of innovative solutions to problems faced by the nation in public health, agriculture and environmental issues. All these users were trained on-site by beamline scientists at ESRF and personnel associated with the project in cutting-edge methods at this state-of-the-art facility. To date, about 80 publications have been published in different international peer-reviewed journals. The productivity builds on the 210 publications that appeared during 2009-2016 based on the earlier agreement between ESRF and India. The corresponding studies have enabled identification of novel intervention points in different pathogens that can be the target of novel drugs.

Academic Program with GSK SmithKline

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

Collaborators of Faculty Members

RCB Principal Investigator	Collaborators
Prof. Deepak T Nair	Prof. D. N. Rao (IISc, Bangalore), Prof Sudhanshu Vrati, Dr. Deepti Jain, Dr. K Vengadesan (RCB), Dr. Debasisa Mohanty (NII, New Delhi), Mr. Sudhir Chandra (National Informatics Institute), Dr. Dinesh Gupta, Dr. Dinakar M. Salunke, (ICGEB, New Delhi), Prof. Ajit Kembhavi (Inter-University Centre for Astronomy & Astrophysics, Pune)
Dr. Deepti Jain	Prof Sudhanshu Vrati, Prof. Deepak T Nair, Dr. Divya Chandran (RCB), Dr. Gopaljee Jha (NIPGR, New Delhi)
Dr. Vengadesan Krishnan	Dr. Airi Palva (University of Helsinki, Finland), Dr. Priti Saxena (SAU, New Delhi)
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), 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, Dr. Tushar K Maiti (RCB)
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. Sam J Mathew	Dr. Gabrielle Kardon (University of Utah, USA), Dr. Dimple Notani (NCBS, Bengaluru), Dr. Palanimurugan Rangasamy (CSIR-CCMB, Hyderabad)
Dr. Geetanjali Chawla	Dr. Monika Garg (NABI, Mohali, Punjab), Prof. Pankaj Kapahi (Buck Institute, CA, USA)
Dr. Pinky Kain	Prof. Pankaj Kapahi (Buck institute of Aging, Novato, USA), Prof. Teiichi Tanimura (Nagoya University, Nagoya, Japan), Prof. Axel Brockmann (NCBS-TIFR, Bangalore), Prof. S.V. Eswaran (TERI, New Delhi), Prof. Suhel Parvez (Jamia Hamdard, New Delhi)
Prof. Sudhanshu Vrati	Dr. Rajesh Kumar, Dr. Milan Surjit (THSTI), Dr. Renu Wadhwa (AIST, Japan), Dr. Anirban Basu (NBRC, Manesar), Dr. Arup Banerjee (RCB)
Dr. Chittur Srikanth	Dr. Vineet Ahuja, Dr. Pramod Garg, Dr. Saurabh Kedia, Dr. Sujoy Paul, Dr. Prasenjit Das (Gastroenterology, AIIMS, Delhi), Dr. Girish Ratnaparkhi (IISER, Pune)
Dr. Manjula Kalia	Dr. Sudhanshu Vrati (RCB), Dr. Sankar Bhattacharyya, Dr. Dinesh Mahajan, Dr. Shailendra Asthana (THSTI), Dr. Nimesh Gupta (NII, New Delhi), Dr. Rashmi Kumar (KGMU, Lucknow)
Dr. Arup Banerjee	Dr. Sujata Mohanty (AIIMS, New Delhi), Dr. Anirban Basu (NBRC, Manesar), Dr. Prafullakumar B. Tailor, (NII, New Delhi)
Dr. Avinash Bajaj	Dr. Sagar Sengupta, Dr. Vinay Nandicoori and Dr. Arnab Mukhopadhyay (NII, New Delhi), Dr. Ujjaini Dasgupta and Dr. Rajendra Prasad (Amity University Haryana), Dr. Aasheesh Srivastava (IISER Bhopal), Dr. Prasenjit Das and Dr. Vineet Ahuja (AIIMS, New Delhi), Dr. C. V. Srikanth (RCB)

Dr. Sivaram V S Mylavarapu	Dr. Mahak Sharma (IISER Mohali), Dr. Jayanta Bhattacharya (THSTI), Dr. Divya Chandran (RCB), Dr. Sourav Banerjee (NBRC, Manesar), Dr. Anjana Saxena (CUNY, New York), Dr. Megha Kumar (CSIR-CCMB, Hyderabad)
Dr. Rajender Motiani	Dr. Rajesh S Gokhale (NII, New Delhi), Dr. Sridhar Sivasubbu (CSIR-IGIB, New Delhi)
Dr. Anil Thakur	Dr. Alan G. Hinnebusch (NIH, USA), Dr. Kinshuk Raj Srivastava (RCB)
Dr. Ambadas B Rode	Prof. Naoki Sugimoto (FIBER, Konan University), Prof. Sheshnath Bhosale (Goa University), Dr. Deepak Salunke (Panjab University), Dr. Asthana (THSTI), Dr. Sunil Tekale (Dr BAMU University, Aurangabad)
Dr. Saikat Bhattacharjee	Dr. Nimisha Sharma (GGSIPU, Delhi), Dr. Gabriel Schaaf (Univ. of Bonn, Germany), Dr. Ricardo FH Giehl (Leibniz-Institute of Plant Genetics & Crop Plant Research, IPK, Germany), Dr. HA van den Burg (Univ. of Amsterdam, Amsterdam), Dr. K. Vengadesan, Dr. Divya Chandran, Dr. Ramu Vemanna (RCB)
Dr. Divya Chandran	Dr. Mary Wildermuth (University of California Berkeley, USA), Dr. Igor Grigoriev (Joint Genome Institute, USA), Dr. Shri Ram Yadav (IIT, Roorkee), Dr. Atul Goel (CDRI, Lucknow), Dr. Yashwant Kumar (THSTI), Dr. Bonamali Pal (Thapar Institute of Engineering and Technology, Patiala), Dr. Senjuti Sinharoy, Dr. Senthil K Muthappa (NIPGR, New Delhi), Dr. Deepti Jain, Dr. Saikat Bhattacharjee, Dr. Sivaram Mylavarapu (RCB), 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. Maneesh Bhandari (Forest Research institute, Dehradun), Dr. Avinash Bajaj (RCB)
Dr. Prashant Mohan Pawar	Dr. Ramesh Sonti, Dr. Gopaljee Jha (NIPGR, New Delhi), Dr. Ewa J Mellerowicz (Umea, Sweden)
Dr. Nidhi Adlakha	Dr. Shams Yazdani (ICGEB, New Delhi), Dr. Tarun Sharma (THSTI), Prof. Rakesh Bhatnagar (BHU)
Dr. Kinshuk Raj Srivastava	Dr. Manoj Tripathi (IIT Ropar), Prof. David Sherman (University of Michigan, Ann Arbor)

Extramural funding

S. No.	Investigator	Project title	Funding Agency	Grant Amount (Rs.)	Duration
1.	Prof. Deepak T Nair	The role of DNA polymerase IV in ROS mediated lethality: Structure & Mechanism (as part of National Bioscience Award, 2014)	Department of Biotechnology	15 lakh	2016-2020
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	2017-2020
3.	Prof. Deepak T Nair	"Does variation occur in the dinB gene during stress adaptation?"	Department of Biotechnology	58.86 lakh	2018-2021
4.	Prof. Deepak T Nair	Molecular Interactions critical for DNA Mismatch Repair	Science & Engineering Research Board	Total grant: 59.62 lakh Grant for RCB: 24.91 lakh	2017-2020
5.	Prof. Deepak T Nair	Access to Macromolecular Crystallography Beamlines, France	Department of Biotechnology	1749.41 lakhs	2017-2020
6.	Prof. Deepak T Nair	Data-Driven Initiatives in Astronomy and Biology, National Knowledge Network	National Knowledge Network	Total grant: 300 lakhs Grant for RCB: 150 lakhs	2016-2020
7.	Dr. Deepti Jain	Insights into the signal transduction mechanism of GraXSR regulon required for antibiotic resistance in *Staphyloccocus aureus*	Science & Engineering Research Board	43.82240 lakh	2019-2022
8.	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 lakh	2018-2021
9.	Dr. Deepti Jain	Establishing the mechanism of action of Bg_9562, the broad spectrum antifungal protein	NCR BioCluster Grant	20 lakh	2019-2021

10.	Dr. Deepti Jain	Mechanism of FleR mediated transcription initiation in *Pseudomonas aeruginosa*	Ignite LifeScience Foundation (First awardee)	10000	2019
11.	Dr Vengadesan Krishnan	Structural studies on pilus proteins from Lactobacillus ruminis	Department of Biotechnology	44.5 lakh	2018-21
12.	Dr Vengadesan Krishnan	Investigating Functional Role of Polyketide Modifying Enzymes in Mycobacterial Biology	Science & Engineering Research Board	*Total grant:* 46.7 lakh *Grant for RCB:* 8.1 lakh	2019-22
13.	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
14.	Dr. Prem S Kaushal	Understanding the translation strategies adopted by *M. tuberculosis* during dormancy	Science & Engineering Research Board	46.33 lakh	2019-21
15.	Prof. Prasenjit Guchhait	Mechanism of rapid propagation of dengue virus during infection	Department of Biotechnology	100.1 lakh	2018-21
16.	Prof. Prasenjit Guchhait	Identification of small molecule inhibitors of PF4 and CXCR3 to prevent Dengue and JEV infection in host	Department of Science and Technology	57.0778 lakh	2019-22
17.	Prof. Prasenjit Guchhait	Role of platelet activation in the development of systemic inflammations in patients with type-2 diabetes.	Department of Biotechnology	71.5885 lakh	2019-22
18.	Prof. Prasenjit Guchhait	Investigating the mechanism of two anti-platelet drugs, RTX-101 and RTX 301	RythRx Therapeutics, LLC, Ann Arbor, USA	7.6 lakh	2018-20
19.	Dr. Tushar Kanti Maiti	Inter-institutional programme for Maternal, Neonatal and Infant Sciences: a translational approach to studying PTB	Department of Biotechnology	Total grant: 4885 lakh Grant for RCB: 613 lakh	2013-20
20.	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

21.	Dr. Sam J Mathew	The role of developmental myosin heavy chains in skeletal muscle development, regeneration, homeostasis and disease	India Alliance DBT Wellcome Trust Intermediate Fellowship	352 lakh	2014-20
22.	Dr. Sam J Mathew	The Role of MET-CBL signaling in Rhabdomyosarcoma	Department of Biotechnology	24 lakh	2015-19
23.	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
24.	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	2018-21
25.	Dr. Geetanjali Chawla	Post-transcriptional regulators of aging and dietary restriction	India Alliance DBT Wellcome Trust Intermediate Fellowship	359 lakh	2018-22
26.	Dr. Pinky Kain	Understanding taste and its modulation using *Drosophila melanogaster*	India Alliance DBT Wellcome Trust Intermediate fellowship	350 lakh	2016-21
27.	Prof. Sudhanshu Vrati	Development of small molecule antivirals against Chikungunya and Japanese encephalitis virus	Department of Biotechnology	4.807 crores	2020-23
28.	Prof. Sudhanshu Vrati	Setting up of the Indian Biological Data Centre Phase-I	Department of Biotechnology	75.78 crores	2020-22
29.	Prof. Sudhanshu Vrati	DBT-AIST International Center for Translational and Environmental Research (DAICENTER)	Department of Biotechnology	144.90 lakh	2018-21
30.	Dr Kachan Bhardwaj (Mentor, Prof. Sudhanshu Vrati)	Metagenome Sequence Analysis of the Distal Gut Virome in Healthy Indian Adults	Department of Biotechnology	58.21 lakh	2017-20
31.	Prof. Sudhanshu Vrati	DBT-HRD Project & Management Unit at RCB, Faridabad	Department of Biotechnology	414.72 lakh	2020-21
32.	Dr. CV Srikanth & Dr. Girish Ratnaparkhi (IISER-Pune)	From the gut SUMO cycles its way into gastrointestinal disorders	MHRD-STARS grant	93.34 lakh	2020-23

33.	Dr. Manjula Kalia	Interactions between Japanese Encephalitis virus and host autophagy pathway: Implications for pathogenesis	Science and Engineering Research Board	58.40 lakh	2016-19
34.	Dr. Manjula Kalia	Pharmacological Modulation of Autophagy as a Potential Therapeutic for Japanese encephalitis	Department of Biotechnology	81.20 lakh	2019-22
35.	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
36.	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
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	Engineering of membrane targeting molecular probes for diagnosis of mycobacterial infections	Science and Engineering Research Board	50.446 lakh	2019-2022
40.	Dr. Avinash Bajaj	Spatiotemporal targeting of multiple pathway using engineered polymer gatekeepers in porous nanomaterials for cancer combination therapy	Science and Engineering Research Board	60.8 lakh	2018-21
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	Development of biocompatible surfaces for ESKAPE pathogens	Department of Biotechnology	41.3 lakh	2017-20
43.	Dr. Avinash Bajaj	Molecular engineering of low molecular weight injectable hydrogels with sustained drug release for cancer therapy	Department of Biotechnology	42.6 lakh	2016-19

44.	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
45.	Dr. Sivaram V S Mylavarapu	Delineating the molecular determinants required for the intercellular transmission of HIV1 through tunnelling nanotubes	Indian Council of Medical Research (ICMR)	38 lakhs	Awarded 2020
46.	Dr. Sivaram V S Mylavarapu	Prolyl Isomerization of Dynein Light Intermediate Chain Subunits as a Regulatory Driver in Mitosis	Science & Engineering Research Board	22 lakhs	2018-21
47.	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 lakhs	2014-20
48.	Dr. Rajender Motiani	Demystifying the mystery of STIM1 augmentation: Understanding molecular mechanisms controlling expression of STIM1, a novel regulator of melanoma progression and skin pigmentation	Science and Engineering Research Board	31 lakhs	2019-21
49.	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
50.	Dr. Ambadas B Rode	Rationally targeting & tuning riboswitch mediated gene regulation for therapeutic and synthetic biology application	Department of Biotechnology	88 lakh	2018-23
51.	Dr. Ambadas B Rode	Design and synthesis of small molecules to target nucleic acids structures for therapeutic applications: Targeting riboswitches for antibacterial therapy	Science and Engineering Research Board	19.324 lakh	2019-2021

52.	Dr. Saikat Bhattacharjee	The identification and characterization of defense signaling pathways primed by Sea6 Energy products	Sea6 Energy Pvt. Ltd., Bengaluru	7.6 lakh	2019-2020
53.	Dr. Saikat Bhattacharjee	Investing a Key regulatory defense assembly and pathogen effector-induced perturbations duing innate immune signaling of plants	Department of Biotechnology	92 lakh	2018-2021
54.	Dr. Divya Chandran	Deriving gene regulatory networks mediating legume host-powdery mildew pathogen cross-talk during compatible and incompatible interactions	Department of Biotechnology	46.16 lakh	2016-2020
55.	Dr. Divya Chandran	Identification of novel regulators and nodes of response mediating powdery mildew sporulation on legumes	Science and Engineering Research Board	38.05 lakh	2017-2020
56.	Dr. Naini Burman (mentor Dr. Divya Chandran)	Functional characterization of HY5 homolog in rice	Department of Science and Technology (INSPIRE faculty)	35 lakh	2018-2023
57.	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	2019-2022
58.	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	2017-2022
59.	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	2017-2020
60.	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	2019-2021

61.	Dr. Nidhi Adlakha	Development of Paenibacillus polymyxa as a platform for the production of branched chain alcohols	Mission Innovation- IC4 grant	*Total grant:* 89.58 lakh *Grant for RCB:* 0 lakh	2019-2022
62.	Dr. Nidihi Adlakha	Department of Science & Technology		35 lakh	2015-2020
63.	Dr. Kinshuk Raj Srivastava	Biocatalytic combinatorial synthesis of cyclic dipeptides for diverse biological applications	Department of Biotechnology	42.5 lakh	2019-2024

RESEARCH & INNOVATION INFRASTRUCTURE

BSC BioNEST Bio-Incubator

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 start-up 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).

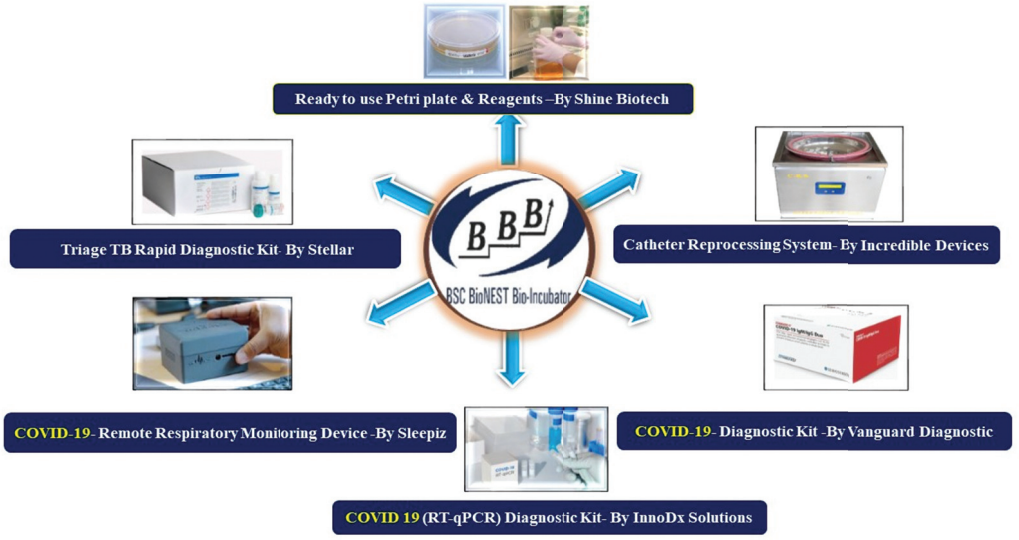
BBB is one of the largest Bio-incubator dedicated to support healthcare based start-ups in the NCR region. The facility is available to the start-ups at very affordable cost. It provides globally competitive and superior incubation facilities & infrastructure, spread across 35000 sq. ft. covered area 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 start-ups.

Incubatees have access to the Advanced Technology Platform Centre (ATPC), which is the state-of-the-art advanced instrumentation facility. In addition, start-ups 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 attracted 12 start-ups during the FY (2019-2020). Fifteen start-ups were benefitted from the facility during the reporting period and 07 of them are trying to find innovative solutions for COVID-19. Two incubatee companies (Shine Biotech Pvt. Ltd. and InnoDx Solutions Pvt. Ltd.) have also won the prizes for their idea on coronavirus detection. Two start-ups (Vanguard Diagnostic Pvt. Ltd. and InnoDx Solutions Pvt. Ltd.) have received approval from ICMR for COVID-19 diagnostic kit.

Incubatee companies at BBB

BBB has been successful in creating a vibrant entrepreneurial ecosystem in Delhi-NCR since its inception. Incubatees get all kind of critical services, which are required for young start-ups to move on the fast-track to success. The start-up ecosystem of the facility motivates young start-ups to solve the global issues related with biotechnology and healthcare. Some start-ups have also developed innovative product prototype and their work has been recognised by different public or private agencies.



Prototypes developed by Incubatee companies

BBB is actively promoting entrepreneurial aptitude among young innovators through its unique strategic programs & outreach activities such as **IDEA, EMPOWER, IDEATHON, LEARN** etc. It also regularly conducts workshops, seminars and facilitates the interaction between entrepreneurs. BBB has excellent pool of mentors who guide the young entrepreneur during their journey of entrepreneurship. BBB being a new age Bio-incubator has conducted 36 events in FY 2019-2020.

Programs & Outreach activities by BBB

Strategic Programs	*No*
IDEA (Talk on Bio-entrepreneurship)	*15*
EMPOWER (Worskshop)	*3*
FACE (Conference & Seminars)	*5*
Networking Events	*11*
IDEATHON (Innovation Challenge)	*1*
FDP (Faculty Development Program)	*1*

Events & Outreach Activities	*No*
Internal	*14*
External	*22*
Total	*36*

BBB Event Details

BBB is operated and managed by seasoned and skilled professionals with rich corporate experience. The team acts as a support system for all the start-ups at various stages of their development. Team aims to provide excellent incubation services to the incubatee companies and try to maintain supportive & exhilarating working environment within the facility.

BBB has created a niche in the area of Bio-Incubation in Delhi NCR. BBB invites all start-ups and innovators to come forward and experience the unique ecosystem of the facility.

Biosafety Support Unit

Biosafety Support unit (BSU) is an extramural research support unit established by Department of Biotechnology, Government of India as a part of the reforms to strengthen biosafety regulatory system. The Biosafety Support Unit is being managed by the Regional Centre for Biotechnology (RCB).

Major activities undertaken by BSU during the reporting period 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 also include 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.
- 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 Institutional Biosafety committees (IBSCs) and other stakeholders working in the area of biotech science regulation.
- Indian Biosafety Knowledge Portal has been made operational and serves as a communication platform for scientific community and other stakeholders 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 (172nd to 181st Meetings) during the year 2019-2020 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 drafted and submitted 15 RARMP documents for Agri-Biotechnology related applications. Bio-Pharma Group assessed 162 Import/ Export/ Transfer/ Receipt applications, 82 Product development related applications and 465 Research & Development information applications during the reporting period.

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.

a. The BSU assisted different working groups in preparing the following draft guidelines for consideration by the RCGM: 1. Guidelines on assessment of GE micro-organisms, 2. Guidelines on Stacked GM plants/ genes.

b. BSU has undertaken the task of updating the IBSC handbook as per the suggestions of the expert committee. After Handbook and E-learning modules are finalized, training for IBSC's should be taken up.

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

BSU assisted the Advisory Committee, the Apex committee and 3 sub-committees constituted for preparation of draft document on the regulatory framework and data requirement for Genome edited organisms/products. The Draft regulatory framework and Data requirement document was finalized by RCGM and recommended for public consultation. The draft guidelines were kept for public consultation for 30 days from 8th Jan 2020 to 23rd Feb 2020. BSU assisted RCGM-DBT in compilation of more than 90 comments received, which included National and international organization (like US and Canada Government, Bill & Melinda Gates Foundation, CropLife International, Alliance of Bioversity International, CIAT The Americas Hub, Canada Grains Council, International Seed Federation, and Brazilian Seed and Seedlings Association, Indian Council of Agriculture Research (ICAR), Council of Scientific & Industrial Research (CSIR), National Academy of Agricultural Sciences (NAAS), Seed industry representation, Civil society groups etc.) and individual submissions. Further, a stakeholder consultation meeting was held on 12th March 2020 on the public feedback. The document is to be finalized based on the feedback of the consultation process.

4. Simplified procedure for Import/Export and exchange of materials

With a view to have a relaxed regulatory approval process and empowered IBSC to accord related approvals, a revised notification on Simplified Procedures & Guidelines on Exchange, Import & Export of GE organisms & Products thereof for R&D purpose, BSU prepared the draft which has been issued by DBT on 17th January 2020.

5. Commissioning of Indian Biosafety Knowledge Portal (IBKP)

In line with Government of India's ease of doing business and digital India, an online web portal, IBKP, has been launched by the Department of Biotechnology. BSU Scientists facilitated RCGM secretariat for the development of IBKP. The portal has been fully functional with registration of Institutional biosafety committees and uploading of new applications being carried out through it.

6. 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 through IBKP portal. BSU is facilitating the RCGM in the monitoring of IBSCs.

7. Standards and specifications for Establishment of Biosafety Containment Level 3 and 4 Facilities & Standard Operating Procedures (SOPs)

A need was felt to define the standards and specifications 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 is extending help in the preparation of document on standards/ specifications for certification and auditing of BSL-3 & 4 facilities.

8. Establishment of Notified Field Trial Sites (NFTS)

BSU prepared draft scheme on NFTS based on recommendations of committee chaired by Prof. B. S. Dhillon and was circulated to ICAR and MoEF&CC. The scheme on NFTS will be implemented jointly by DBT and ICAR.

II. Other activities

a) BSU has extended support to the Sub-Committees constituted for formulating Biosafety guidelines on (a) conduct and monitoring Confined Research Trials (CRTs) on genetically engineered (GE) Mosquitoes and (b) GE silk worm. BSU also prepared (a) Response to the concordance between biological items (Parasites; item 2C) in Special Chemicals, Organisms, Materials, Equipment and Technologies (SCOMET) list and international conventions/ agreements, (b) Comments on origin of parasites in the SCOMET List, (c) Inputs on proposed intervention points on items at UN BWC Meeting of Experts 2019.

b) As per the RCGM requirement, BSU staff participated in various monitoring committees such as Central Compliance Committee (CCC) which ensures compliance during confined field trials/ facility evaluation etc.

c) Supported RCGM/GEAC for drafting affidavits/ replies for various Supreme Court cases and parliamentary questions.

III. Training and Capacity Building:

a) Two BSU scientists attended the Eighth Training Workshop for the Institutional Biosafety Officers and scientists of ICAR as a Trainer at National Institute for Plant Biotechnology, New Delhi on September 20, 2019.

b) Three BSU scientists attended Global Bio- India, during November 21-23, 2019

c) BSU scientist presented on India Acts, Rules and Guidelines related to Biosafety matters and Indian Biosafety Knowledge Portal (IBKP) during the two-day Orientation Session on 10 October, 2019 for members of the newly constituted RCGM committee. BSU staff presented posters on "Towards

developing a sustainable and science based regulation on genome editing in India", during 15th ISBR Symposium, Spain, April 2019.

d) BSU scientist attended "CRISPR/Cas mediated genome editing: applications, tools and experimental design", during May 2019 at Delhi University.

Advanced Technology Platform Centre

Advanced Technology Platform Centre (ATPC) is a Department of Biotechnology (DBT), Government of India-funded platform that provides a medium for innovative researchers to turn their scientific ideas into reality. The primary goal of the Advanced Technology Platform Centre 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 project 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 have availed our services. We regularly provide support and help scientists in analyzing samples from IIT Kanpur, IIT Roorkee, Jamia Hamdard and AIIMS Delhi, THSTI, NIPGER, ICGEB and other institutes. BioLayer Interferometry instrument runs at 85-90% of its working capacity in terms of usage hours. We have processed 70-80 samples on the FPLC system in this fiscal year. In

line with our commitment towards capacity building, we have organized two hands-on workshops in last financial year. One focused on learning basic principles and procedures in 'Protein Production & Purification strategies' while the second workshop aimed to train the scientists in the field of interaction kinetics using Surface Plasmon Resonance (SPR), BioLayer Interferometry (BLI) and MicroScale Thermophoresis (MST).

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:

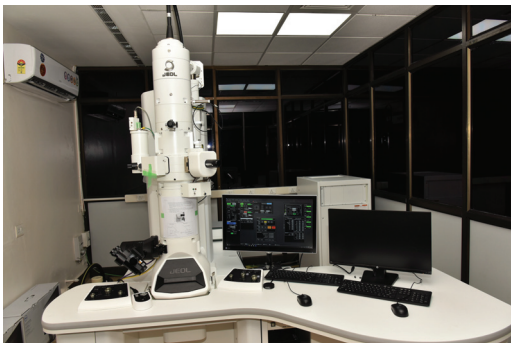
- Identification and quantitation (labelled, TMT /iTRAQ/SILAC/label free) and intact mass analysis of proteins by high resolution liquid chromatography ESI Q TOF (SCIEX 5600 Plus Triple–TOF) system and a high throughput SCIEX 5800 Plus matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (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, amongst others. More than 1000 samples from 113 different 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 (TEM, 120kV JEM-1400 Flash)
- Field Emission Scanning Electron Microscope (FESEM, Apreo Volume Scope)

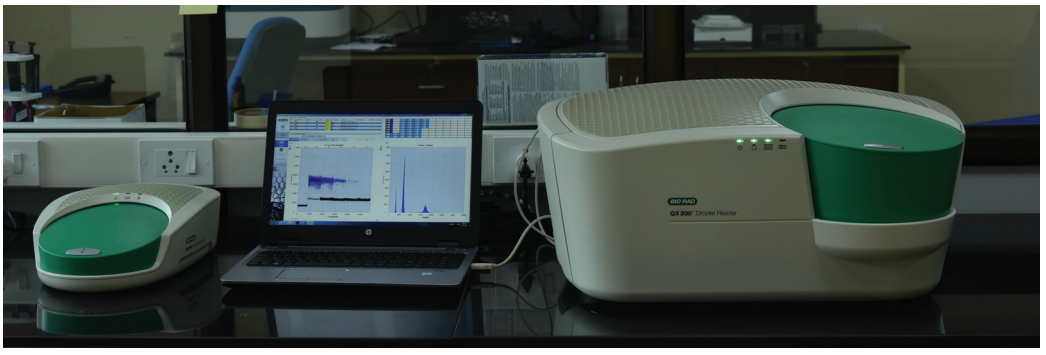


The JEM-2200FS is a field emission electron microscope with a 200 kV field emission gun (FEG), piezo-controlled goniometer, holders for cryo-observation, and tomography, in-column energy filter (Omega filter), and Gatan direct detection camera (K2 summit). This instrument is capable of high-resolution 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 including institutes of NCR Biotech cluster, JNU, and CSIR-IMTECH. The electron microscopy facility has analyzed 180 samples to date. 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. Genomics Facility has carried out 2266 DNA sequencing reactions using AB3500 Genetic Analyzer during this financial year and the beneficiary institutes include Translational Health Science and Technology Institute, National Brain Research Centre, National Institute for Plant Biotechnology, New Delhi, National Institute of Cancer Prevention

and Research, Noida, UP, 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. Towards empowering student community with skill development, this facility conducted a workshop on 'DNA Sequencing Technology and Droplet Digital PCR' during August 7-8, 2019. Thus, this facility continues to aid Scientists in their research endeavors, productively.

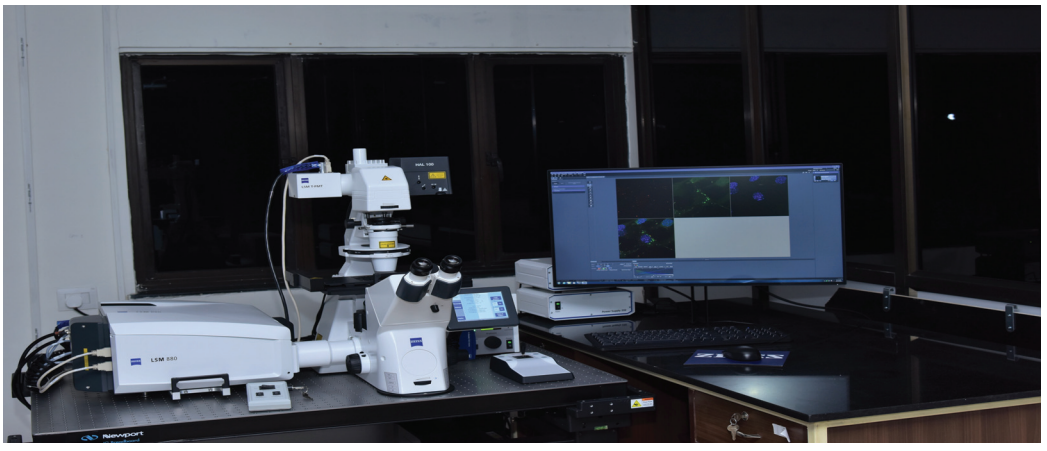
5. Optical Microscopy facility

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

Those who avail facilities are scientists and researchers from academics and industries, mainly from RCB and Clusters institutes. Apart from the bio-cluster, we have been providing support and help to scientist from IIT-Delhi. Industrial Researchers from Akamara Biomedicine Pvt. Ltd and Vyome Therapeutics pvt. Ltd have been regularly availing the facility for their research work.



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) and
- 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, that included 165 hours of usage for the Flow Cytometry Analyzer and a total of 82 hours of Cell Sorter usage during this financial period. Apart from RCB, the institutions that utilized our services include CSIR-Institute of Genomics and Integrative Biology, ICAR-National Bureau of Plant Genetic Resources, Jamia Hamdard Deemed University, 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. Trainings held include BD FACSVerse Training (8-9 July 2019; 30th Sept, 2019); BD Influx Cell Sorter Training (27-29 August, 2019); Training for Gallios Flow Cytometry Analyzer (Beckman Coulter) (5-6 September 2019). Thus, this facility continues to contribute to scientific advancement.

Manpower trained:

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

S.No.	Platform/ facility	Training/ Workshop	Date	No. of Participants
1.	Protein Production & Purification	Protein Production & Purification Workshop	July 2-4, 2019	15
2.	FACS Facility	FACS Verse Training	July 8-9, 2019	11
3.	Protein Production & Purification	Biomolecular Interaction study Technologies	November 5-8, 2019	11
4.	Optical Imaging	Basic course on high content imaging	November 25 -27, 2019	15

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

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, Turnitin, Endnote x6/x8/x9, and Corel Draw Graphics Suite x6 for preparing manuscripts, various reports and presentations. Quick heal Seqrite end point security total edition 7.4 has been implemented as protection from viruses, adware, spyware etc. Biometric Attendance System has also been enabled for the staff, to register attendance by simply presenting his/her biometric (fingerprint). In addition, online resources are available for scholars for research, case studies and for preparation of their projects.

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 internet connection is distributed to users and facilities through RCB's network infrastructure, which 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 95+ wireless access points. Wi-Fi access is provided to internal users by media access control (MAC) address authentication and to visitors by separate guest accounts. 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.

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.

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.

Office Automation

RCB is moving towards adapting a paperless work environment in which the use of paper is eliminated or greatly reduced. This is done by converting documents and other papers into digital form and development of various online applications (services or facilities) through the intranet portal named eRCB. All the faculty and students have access to this customised online software package being used for administrative applications. The major modules in eRCB are online leave management, user management, vehicle booking, vendor management, HR, visitor management, bill claim portal, purchase workflow etc. In continuation of paperless work environment using office automation, ERP System has been implemented to certain modules which is likely to expand 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, which can also be accessed outside the institute. The major (among others) are:

- Implemented GeM for all kind of purchases at RCB
- 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
- Vendor Registration portal etc.

Office of Connectivity

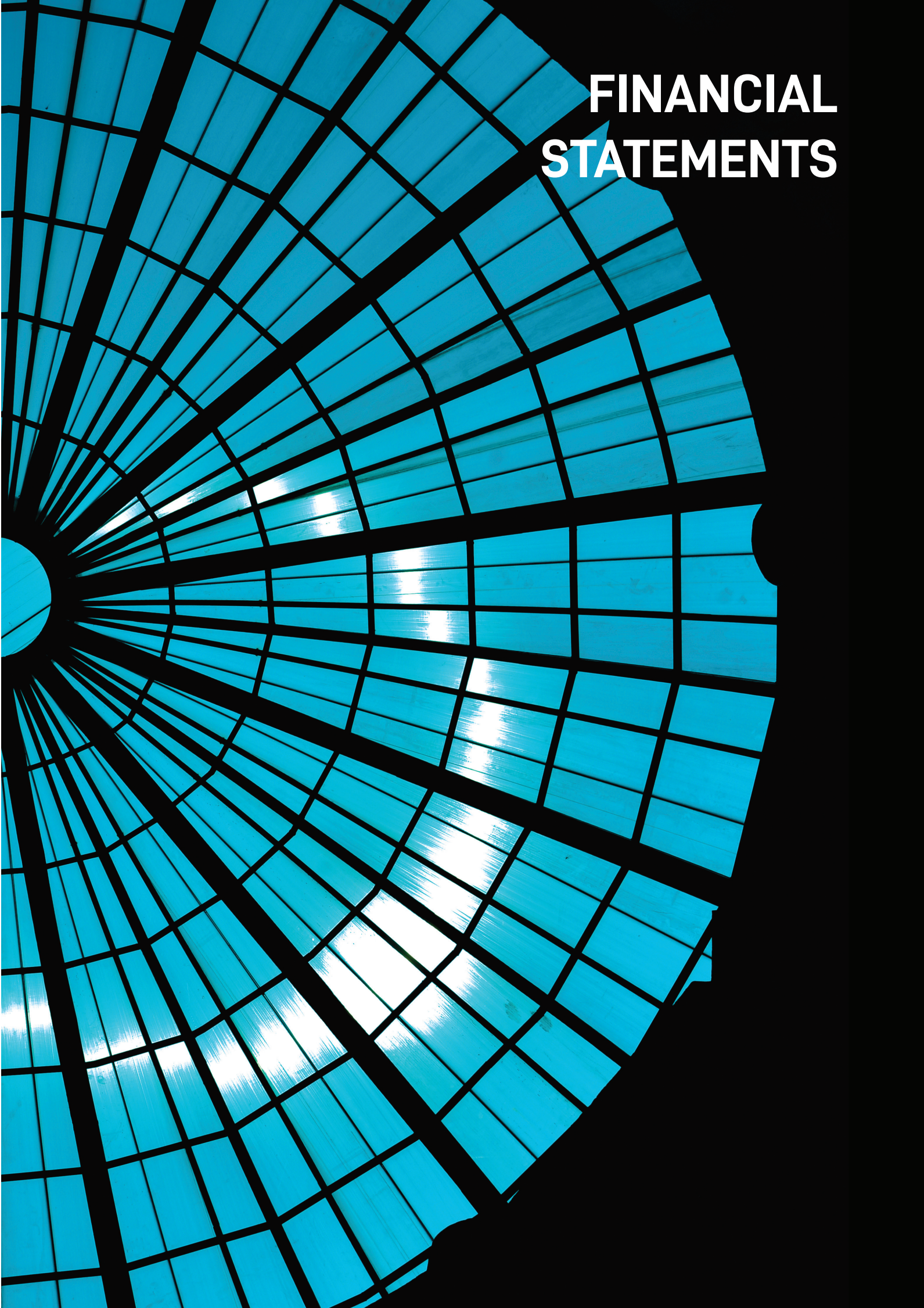
Office of Connectivity has been conceptualized as the cluster office for the NCR Bio-cluster and is envisaged under the project entitled "Establishment of the NCR Biotech Science Cluster". It is primarily responsible to establish a governance structure for the management and utilization of common facilities. Office of Connectivity 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. The cluster office has the mandate for integrating the partner institutions 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 2019-20, an interim Office of Connectivity has been set up and recruitments on key positions have been completed to oversee the implementation of Phase-II construction works of the NCR Biotech Science Cluster. This office is also acting as a hub for integration of the future infrastructural requirements of the partner institutions. In the very first year of establishment, this office has been able to achieve the following milestones:

1) Phase-II Construction works of the NCR Bio-cluster including the following common facilities is near completion:
   a) Office of Connectivity Building
   b) Biosafety Level-3 Facility
   c) Vertical Extension of Hostel Building
2) Mechanisms and procedures for pooling of funds and for the construction of buildings have been established.
3) Master plan for Zone-II of the NCR Bio-cluster has been prepared in coordination with the partner institutions and it has been approved by the Building Committee.
4) Capitalization of Phase-I Buildings of the NCR Bio-cluster has been completed in coordination with the partner institutions.
5) Final settlement of accounts for Phase-I Extension works of NCR Bio-cluster has been completed.
6) Cluster seminar series has been formalized and has served as a medium to develop operational connectivity between the partner institutions of the cluster.

7) Effective liaison with the local authorities has resulted in timely statutory approvals, removal of encroachments from the cluster land and also for the relocation of animal carcass disposal point that was a potential health hazard.

Architectural Scheme of Office of Connectivity



FINANCIAL STATEMENTS

REGIONAL CENTRE FOR BIOTECHNOLOGY,FARIDABAD
BALANCE SHEET AS AT 31ST MARCH, 2020

Amount (in Rs.)

SOURCES OF FUNDS	SCHEDULE	31.03.2020	31.03.2019
CORPUS / CAPITAL FUND	1	650,749,409	576,503,654
DESIGNATED/EARMARKED/ENDOWMENT FUNDS	2	-	-
CURRENT LIABILITIES AND PROVISIONS	3	1,655,289,308	1,489,084,474
Total		2,306,038,717	2,065,588,128
APPLICATION OF FUNDS	SCHEDULE	31.03.2020	31.03.2019
FIXED ASSETS	4	1,412,742,927	1,246,051,277
TANGIBLE ASSESTS		535,882,655	555,355,443
INTANGIBLE ASSETS		1,681,272	1,177,569
CAPITAL WORK IN PROGRESS (BIOTECH SCIENCE CLUSTER)		875,179,000	689,518,265
INVESTMENTS FROM EARMARKED/ENDOWMENT FUNDS	5	-	-
LONG TERM		-	-
SHORT TERM		-	-
INVESTMENTS OTHERS	6	619,043,926	521,817,706
CURRENT ASSETS	7	66,008,642	71,668,053
LOANS, ADVANCES & DEPOSITS	8	208,243,222	226,051,092
Total		2,306,038,717	2,065,588,128
SIGNIFICANT ACCOUNTING POLICIES & NOTES ON ACCOUNT	23		
CONTINGENT LIABILITIES	24		

Schedules 1 to 24 form an integral parts of Accounts

(REETESH AGARWAL)
INTERNAL AUDITOR

(VIVEK AGARWAL)
FINANCE OFFICER

विवेक अग्रवाल, वित्त अधिकारी
Vivek Agarwal, Finance Officer
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

(DR. DEEPIKA BHASKAR)
REGISTRAR

डॉ. दीपिका भास्कर, कुलसचिव
Dr. Deepika Bhaskar, Registrar
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

(DR. SUDHANSHU VRATI)
EXECUTIVE DIRECTOR

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

REGIONAL CENTRE FOR BIOTECHNOLOGY

INCOME AND EXPENDITURE ACCOUNT FOR THE YEAR ENDED 31st MARCH, 2020

Amount (in Rs.)

INCOME	Schedule	31.03.2020	31.03.2019
Academic Receipts	9	5,347,602	2,809,111
Grants/Subsides	10	292,000,000	235,270,777
Income from Investments	11	-	-
Interest Earned	12	113,113	-
Other Income	13	13,111,414	9,763,057
Prior Period Income	14	-	1,996,929
Deferred Income-Fixed Assets	4	69,879,738	46,668,435
Total (A)		**380,451,867**	**296,508,309**
EXPENDITURE			
Staff Payments & Benefits (Establishment expenses)	15	96,636,571	67,872,066
Academic expenses	16	11,455,714	13,022,426
Administrative and General Expenses	17	139,859,963	109,137,054
Transportation expenses	18	2,375,677	3,768,556
Repairs & Maintenance	19	25,602,952	20,364,841
Finance costs	20	89,419	6,728
Depreciation	4	69,879,738	46,668,435
Other expenses	21	-	-
Prior Period Expenses	22	21,301,069	22,280,101
Total(B)		**367,201,103**	**283,120,208**
Balance being excess of Income Over Expenditure (A-B) Transfer to/ from Designated Fund		**13,250,764**	**13,388,101**
Building Fund		-	-
Others (Specify)		-	-
Balance being surplus/(Deficit) carried to capital Fund)		**13,250,764**	**13,388,101**
Significant accounting policies and Notes to Accounts	23		
Contingent Liabilities	24		

Schedules 1 to 24 form an integral parts of Accounts

(REETESH AGARWAL)
INTERNAL AUDITOR

(VIVEK AGARWAL)
FINANCE OFFICER

विवेक अग्रवाल, वित्त अधिकारी
Vivek Agarwal, Finance Officer
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

(DR. DEEPIKA BHASKAR)
REGISTRAR

डॉ. दीपिका भास्कर, कुलसचिव
Dr. Deepika Bhaskar, Registrar
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

(DR. SUDHANSHU VRATI)
EXECUTIVE DIRECTOR

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 23: Accounting Policies and Notes Forming Parts of the Balance Sheet and Income & Expenditure Account for the Year Ended at 31st March, 2020

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 2019-20 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. 7,01,24,781.37

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.

विवेक अग्रवाल, वित्त अधिकारी
Vivek Agarwal, Finance Officer
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

डॉ. दीपिका भास्कर, कुलसचिव
Dr. Deepika Bhaskar, Registrar
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

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

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. The Institute has received contribution of Rs. 4,652.95 Lakhs (including RCB) from various institutes for the under Phase II of the construction of campus at Faridabad. The consolidated details are as under:

Rs. In lakhs)

Sl.No	Constituent Partner	Opening Balance as on 1.4.2019	Received during 2019-20	Total receipts on 31.3.2020
1	THSTI	450.00	0.00	450.00
2.	RCB	369.00	81.00	450.00
3.	NCR – BSC Project	567.00	3161.00	3728.00
4.	Interest on investment of BSC funds	20.10	4.85	24.95
	Total	1406.10	3246.85	4652.95

13. Advance of Rs. 500 Lakhs transferred to THSTI for construction of NCR Biotech Science Cluster Phase III construction work of NCR BSC, which relates to the work of Hostel, Sports Centre and Utility Block (G Floor).

14. 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.

विवेक अग्रवाल, वित्त अधिकारी
Vivek Agarwal, Finance Officer
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

डॉ. दीपिका भास्कर, कुलसचिव
Dr. Deepika Bhaskar, Registrar
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, 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

15. Interest earned on saving bank account and fixed deposits during the financial year 2019-20 of Rs.125.98 Lakhs has allocated to the respective projects on pro-rata basis.

Schedule 24: Contingent Liabilities

1. Purchase orders for consumables worth Rs.1,29,90,064.00 ordered during 2019-20 are outstanding as on 31.3.2020 which have not been recognized in the books of accounts.

2. Purchase orders for Equipment worth Rs.2,35,95,146.00 ordered during 2019-20 are outstanding as on 31.3.2020 which have not been recognized in the books of accounts.

(Vivek Agarwal)
Finance Officer
विवेक अग्रवाल, वित्त अधिकारी
Vivek Agarwal, Finance Officer
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

(Dr. Deepika Bhaskar)
Registrar
डॉ. दीपिका भास्कर, कुलसचिव
Dr. Deepika Bhaskar, Registrar
क्षेत्रीय जैवप्रौद्योगिकी केन्द्र
Regional Centre for Biotechnology
फरीदाबाद, हरियाणा / Faridabad, Haryana

(Dr. Sudhanshu Vrati)
Executive Director
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

Place: Faridabad
Date: 22/06/2020

INSTITUTIONAL GOVERNANCE

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
- **Prof. Saumitra Das (Ex-officio Member)**
  Director
  National Institute of Biomedical Genomics
  Kalyani- 741 251, West Bengal
- **Executive Director (Ex-officio Member)**
  Translational Health Science & Technology Institute
  Faridabad - 121 001
- **Mr. Eric Falt (Ex-officio Member)**
  Director
  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)**
  Forme Professor & Head,
  Department of Pharmacology All India
  Institute of Medical Sciences New Delhi 110 029
- **Dr. Debashis Mitra (Member)**
  Director
  Centre for DNA Fingerprinting and Diagnostics
  Hyderabad 500 039
- **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
- **Sh. Chandra Prakash Goyal (Member, Ex-officio)**
  Joint Secretary (Administration)
  Department of Biotechnology
  Govt. of India, New Delhi 110 003
- **Mr. Eric Falt (Member, Ex-officio)**
  Director
  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 (Ex-officio Member)**
  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

- **Registrar (Member)**
  IIT-Delhi
  Delhi 110 016

- **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

Board of Studies (BOS)

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

- **Deans and Sub-Deans (Member, Ex-officio)**
  Regional Centre for Biotechnology
  Faridabad 121 001

- **Dr. Prasenjit Guchhait (Member)**
  Professor
  Regional Centre for Biotechnology
  Faridabad 121 001

- **Dr. Deepak T. Nair (Member)**
  Professor
  Regional Centre for Biotechnology
  Faridabad 121 001

- **Dr. C. V. Srikanth (Member)**
  Associate Professor
  Regional Centre for Biotechnology
  Faridabad 121 001

- **Dr. V. S. Bisaria (Member)**
  Former Professor, Dept. of Biochemical Engineering & Biotechnology
  Indian Institute of Technology-Delhi
  New Delhi 110 016

- **Dr. Rajiv Bhat (Member)**
  Professor, School of Biotechnology
  Jawaharlal Nehru University
  New Delhi 110067

- **Dr. Goutam Ghosh (Member)**
  Senior Vice President
  Panacea Biotech Limited
  New Delhi 110 044

- **Dr. Deepika Bhaskar (Permanent Invitee)**
  Registrar
  Regional Centre for Biotechnology
  Faridabad 121 001

Scientific Personnel

Faculty

Executive Director and Professor

Prof. Sudhanshu Vrati

Professor

Dr. Prasenjit Guchhait:

Dr. Deepak T. Nair

Associate Professor

Dr. Avinash Bajaj

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

Assistant Professor

Dr. Divya Chandran

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

Wellcome Trust-DBT IA Intermediate Fellowships

1. Dr. Pinky Kain Sharma
2. Dr. Geetanjali Chawla

Wellcome Trust -DBT IA Early Career Fellowship

1. Dr. Pushpa Kumari
2. Dr. Masum Saini

DST INSPIRE Faculty

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

Young Investigators

1. Dr. Siddhi Gupta
2. Dr. Shivendra Pratap
3. Dr. Yashika Walia Dhir
4. Dr. Raghavendra Aminedi

DBT Women BioCARe awardee

1. Dr. Kanchan Bhardwaj
2. Dr. Babitha Chandrashekhar

Ramalingaswami Fellowship

1. Dr. Kinshuk Srivastava
2. Dr. Ambadas B. Rode

Ramanujan Fellowship

1. Dr. Ramu S. Vemanna

SERB PDF

1. Dr. Bhargab Kalita
2. Dr. Vijay Kumar

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
Dr. Deepika Bhaskar

Finance Officer
Mr. Vivek Agarwal

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

Section Officers
Mr. Sanjeev Kumar Rana
Mr. Sudhir Kumar (On Deputation)

Management Assistants
Mr. Chakrawan Singh Chahar
Mr. Sumit Sharma
Mr. Vinod Kumar

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 Tiwari

Technical Assistants
Mr. Madhav Rao M.
Ms. Vishakha Chaudhary
Mr. Nagavara Prasad G.
Mr. Shaminder Singh
Mr. Dharmender Gupta

Consultant (Scientific & Technical)
Dr. Nirpendra Singh

Advanced Technology Platform Centre

Technology Managers
Dr. Raghavan Sampathkumar
Dr. Shailesh Bajpai

Application Scientists
Dr. Rashmi Kumariya
Dr. S. Chandru
Dr. Indu Barwal
Dr. Neha Sharma

Sr. Technical Officers
Ms. Shubhra Agarwal
Mr. Ankit Verma

Technical Officers
Mr. Ashish Kumar Pandey
Mr. Subodh Jain
Dr. Richa Mehra
Ms. Priyanka Bhardwaj
Mr. Ghanshyham Sharma
Ms. Meena Kapasiya
Ms. Neema Bisht
Mr. Manoj Soni

Mech/Electronics Engineer
Mr. Rajesh Kumar

Software Engineer
Mr. Mohit Kumar Vats

Executive Assistants
Mr. Praveen Kumar
Mr. Navin Kumar Yadav

BSC BioNEST Bio-incubator

Chief Operations Officer
Ms. Suman Gupta

Business Development Manager
Mr. Sudhanshu Shekhar

Intellectual Property Manager
Ms. Malvika Garg

Technical Assistant
Mr. Anshumouli Bhardwaj

Management Assistant
Ms. Natasha Thapa

Office of Connectivity

Chief Executive Officer
Dr. Feroz Khan Suri

Dy Manager (Civil)
Mr. Vijay Kumar Arora

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


GIONAL CENTRE FOR BIOTECHNOLOGY


क्षेत्रीय जैवप्रौद्योगिकी केंद्र
Regional Centre for Biotechnology
आरोहण: RCB OPEN DAY
An Outreach Program on National Science Day
अभिव्यक्ति
अभिभावना
अविष्कार
अनुसंधान

United Nations
Educational, Scientific and
Cultural Organization

क्षेत्रीय जैव प्रौद्योगिकी केन्द्र
Regional Centre
for Biotechnology

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