



BRIC - NATIONAL INSTITUTE OF IMMUNOLOGY

Driving advanced research in immunology and allied sciences to promote human health

ANNUAL REPORT 2023-24



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MANDATE OF THE INSTITUTE

01

To undertake, aid, promote, guide and coordinate research of high caliber in basic and applied immunology

02

To carry out research for development of new vaccines and immunological reagents for communicable diseases

03

To develop immunological approaches for the regulation of male and female fertility

04

To interact with industry for the manufacture of vaccines and immunological reagents

05

To organize postgraduate courses, workshops, seminars, symposia and training programs of a specialized nature in the field of immunology, vaccine development and related areas



06

To organize training programs for technicians in immunological methods and related techniques

07

To establish affiliation with recognized universities and institutions of higher learning for the purpose of enabling research scholars to register for postgraduate degrees

08

To serve as a national reference center for immunology and to provide consultancy services to medical and veterinary institutions, public health agencies and industries in the country

09

To provide and promote effective linkages on a continuing basis between various scientific and research agencies/laboratories and other organizations working in the country in the field of immunology, vaccine development and related areas

10

To collaborate with foreign research institutions, laboratories and other international organizations in fields relevant to the objectives mentioned above



FOREWORD



The National Institute of Immunology (NII) is continuing its legacy of excellence in research and innovation since it was established almost four decades ago. The past year has been marked by significant strides in our understanding of complex biological processes, enabling us to move further in tackling some of the most challenging problems in biomedical sciences.

Immunology, an ever-evolving field, has underscored its pivotal role in biomedical research and public health. Groundbreaking discoveries through the years remind us of the potential that lies within the intricate network of our immune system. These advancements have catalyzed transformative approaches to disease prevention and treatment.

Since its establishment as a research institute in 1986, NII has been committed to driving advanced research in immunology and allied sciences to promote human health. Today, apart from immunology, our interdisciplinary research spans frontier areas in molecular & cell biology, chemical biology, and structural & computational biology.



After being recognized as an autonomous institute of DBT for nearly 38 years, in 2023-2024 NII embarked on a new journey with the establishment of the Biotechnology Research and Innovation Council (BRIC). BRIC has been envisioned as one autonomous body integrating all the institutes of DBT to foster multi-disciplinary research, build systemic collaborations, drive capacity building, and set a clear path for innovation and translation. In line with this vision, NII has undertaken major projects in the recent past that address global health concerns in various diseases like tuberculosis, malaria, cancer, metabolic disorders, and neurological diseases.

The Human Immunology Program is a flagship initiative aimed at population-based immuno-phenotyping to understand the baseline and pathogen-specific immune dynamics. This program will provide crucial knowledge for the development of new therapeutics and vaccines. NII is also the coordinator of the Indian TB Genome Sequencing Consortium (InTGS)—an initiative that uses genomics and machine-learning based data analytics for rapid identification of drug-resistant TB strains. This can potentially facilitate better strategies for control of TB. In collaboration with IBSD, NII has initiated a research program, which will evaluate the medicinal properties of plants from northeast India in mitigating metabolic dysregulations, inflammatory disorders, aging, and neurodegeneration.

Apart from these major initiatives, scientists and researchers at NII continued to make significant contributions to both basic and translational research throughout the year. Our world-class facilities empower our researchers to pursue research in frontier areas like genomics, proteomics, systems biology, and AI-ML applications in biomedical sciences. The accolades received by our researchers on both national and international platforms are a testament to the high caliber of work being conducted at NII. I highlight some of the important scientific achievements during the year here.

Infection and Immunity

Multiple groups at NII are involved in research that aims to enhance our understanding of the immune system and molecular basis of infectious diseases caused by bacteria, viruses, and parasites. Immunological memory of infections forms the basis for vaccinations; however, the rarity of the pathogen-specific memory T cells makes it difficult to study them. Now, rare human Cytomegalovirus (hCMV) antigen-specific memory T cells have been characterized in an unbiased manner using high throughput single-cell multi-omics at NII.

The study shows that the hCMV-specific memory T cells are highly heterogeneous and comprise of different flavors of long-term and effector memory T cells. The study can serve as a knowledge base for designing vaccines and therapeutic strategies to control hCMV infections.



Sepsis is an uncontrolled systemic immune response to infection, a prevalent condition in hospital settings, and a leading cause of mortality within intensive care units. One of the studies of NII elucidates the potential of Reconditioned Monocytes (RM) in regulating the dysregulated systemic immune response in sepsis and establishes RM as a promising therapeutic candidate for immune-inflammation modulation in sepsis. In earlier studies done at NII, *Mycobacterium indicus pranii* (MIP) has shown strong immunomodulatory activity in different animal and human tumor models and has been approved for the treatment of lung cancer patients as an adjunct therapy. MIP has shown TLR2/9 mediated activation of antigen-presenting cells/Th1 cells and their enhanced infiltration in mouse melanoma.

Researchers at NII have focused on understanding the mechanisms of the immunomodulatory activity of MIP and for the first time have shown that MIP immunotherapy involves type 1 interferon (IFN) signaling as one of the major signaling pathways to mediate the antitumor responses. Finally, continuing the work on COVID-19, one of the groups at NII have identified sitagliptin and linagliptin as inhibitors for viral cell entry by targeting interactions between viral receptor binding domain and host protein DPP4.

Cancer Biology

Research in cancer biology and development of novel therapeutic strategies is also a major focus area at NII with multiple groups working on it. Dysregulation of gene transcription leads to metabolic rewiring. This enables tumor cells to adapt their metabolic processes to meet increased energy demands and promote growth. Researchers at NII investigated the role of genome organizer SATB1 in transcriptional rewiring that promotes tumorigenesis. They showed that HDAC5 modulates the transcriptional activity of SATB1 to promote lung adenocarcinoma highlighting the pivotal role of the enzyme HDAC5 in tumorigenesis. Another group showed that an internal stretch of 32 amino acids in BLM interacts with RAD54, resulting in BLM-dependent enhancement of RAD54-mediated chromatin remodeling activity.

This enhances Homologous Recombination (HR) repair, leading to decrease in residual DNA damage thereby causing chemoresistance in cellular and preclinical colon cancer mice models. Further, the group established that targeting this BLM-RAD54 mediated chromatin remodeling by three FDA-approved small molecules can reverse chemoresistance in colon cancer with far-reaching possibilities in cancer treatment. In another study, the selective anti-cancer effect of the gut metabolite indoxyl sulfate on colon cancer cells was established paving the way for a novel regimen in the treatment of colorectal cancer. Treating colon cancer cells with indoxyl sulfate increased apoptosis and decreased cell proliferation and cell viability.



Tuberculosis

Tuberculosis has long been a significant health challenge for the nation, prompting NII to have multiple research groups that are dedicated to finding solutions through an interdisciplinary approach. In order to gain mechanistic insight into the secretion of virulence effectors of *Mtb*, a high-throughput secretome, phosphoproteome, and phospho-secretome analysis was reported by researchers of NII. This study established a new link between phosphorylation and secretion of virulence factors in the pathogen and revealed that bacterial virulence is modulated by phosphorylation of virulence factor CFP10.

In another study, structural snapshots of reverse catalysis by *Mtb* enolase (MtEno), an essential enzyme of the glycolytic and gluconeogenic pathways, broadened our current understanding of the functional and mechanistic aspects of MtEno catalysis. The structural information of MtEno in different catalytic states provides valuable clues for design of anti-TB inhibitors through a structure-guided drug discovery approach.

Malaria

Like tuberculosis, malaria is a persistent public health challenge, prompting research institutions to explore approaches to develop effective treatments and preventative strategies. Malaria research at NII takes a two-pronged approach, focusing on deepening the understanding of the disease's biology while advancing the development of vaccines and therapeutics. Researchers at NII discovered a novel pathway involving the protein kinase PfPK2 that is critical for the invasion of host cells by the malaria parasite.

This novel PfPK2 pathway could provide a promising target to develop effective anti-malaria interventions. One of the research groups of NII is working towards developing an improved malaria vaccine that can induce protection against infection in humans and minimize community transmission. The team has used human malaria parasite antigens expressed at the liver stage and mosquito stage as chimeric antigen for immunizations and efficacy studies. The preclinical studies with advanced chimeric antigen vaccine candidates have shown encouraging results and are being considered for translation into human study.



Neurodegenerative Diseases

The emerging role of gut microbiota and their metabolites in the modulation of the gut-brain axis has received much attention as a new hope for the treatment of hard-to-treat chronic neurodegenerative diseases like Alzheimer's disease. A study at NII now established the role of Triphala treatment in improving cognitive function, by modulating the APP pathway, reducing inflammation, and restoring the gut-brain axis by increasing the gut microbiota phyla of Bacteroides, Proteobacteria, Actinobacteria, etc., involved in maintaining the gut homeostasis.

Additionally, SG001, a potential disease-modifying therapeutic small molecule for the prevention and management of Alzheimer's disease, was developed and tested at NII. The compound was shown to modulate GSK-3 activity and improve cognition in animal models. A US patent has been obtained for the compound.

Metabolic Regulation and Aging

Nutrient-metabolic interactions and dysregulation of these networks can have long-term effects on health. In this context, one of the groups at NII is trying to understand the role of vitamin D, an essential micronutrient for homeostasis, in different aspects of metabolism at systemic and tissue levels. Recently, the group reported that in vitamin D receptor (VDR) knockout mice, a milk-fat enriched diet restores energy metabolism by circumventing the need for glycogen as energy resource. This study shows role of vitamin D in coordinating metabolism across organs, particularly influencing insulin production in the pancreas.

A multi-national, collaborative study involving multiple research groups at NII and other institutes in India and abroad showed the deficiency of taurine to be a driver of aging in animals. The group found taurine abundance decreases substantially with age in the bloodstream of mice, monkeys, and humans. Taurine supplementation increased health span and life span in mice and *Caenorhabditis elegans*. Evidence in humans, such as increase in taurine levels with exercise, suggests that taurine deficiency may be a driver of aging in humans as well. However, a randomized clinical trial would be necessary to determine if taurine supplementation improves health in humans. This study was published in Science. In another study using *C. elegans* it was shown that damage to somatic tissues in the body can influence the development of reproductive cells—particularly eggs. The study found that DNA damage signals from uterine tissue can stop egg cell formation through a key transcription factor FOXO, which is a highly conserved protein across different organisms.



Chemical and Structural Biology

Structural biology is vital to biomedical research as it reveals the three-dimensional structures of biological molecules, providing insights into their functions, interactions, and mechanisms. Researchers at NII find how GMP formation varies between two close homologs of human GTPase & reveal a new mechanism for GTP hydrolysis. The study published in *Biochemistry* could provide insight into how these two close homologs play crucial roles in host-mediated immunity through different mechanisms.

In another study, the same group studied the effect of the macromolecular crowding agents on the structure and function of human arginase-I, a therapeutically important enzyme. This study might be helpful for understanding how different enzymes work in a crowded/cellular environment. Another group at NII used solution NMR studies to characterize unique structural features of mitochondrial acyl carrier protein (ACP) from *Leishmania major*, which were distinct from structural features of the prokaryote/plastid type II ACP. Notably, this is the first in-depth study on the acyl intermediates of any mitochondrial ACP at the molecular level.

Science Outreach and Engagement

NII is committed to enhancing its societal engagement, recognizing that the impact of research goes beyond academic circles. Through initiatives like the Science Setu program, NII opens its labs to students and educators, fostering a hands-on learning environment. Over the past year, about forty students have received short-term training at NII labs. Moreover, NII has hosted around 265 students and teachers from eight schools and colleges across India, enabling them to visit the campus, interact with faculty and researchers, and utilize the advanced research facilities.

Furthermore, numerous scientists and scholars from NII have visited colleges in the Delhi NCR region and beyond to deliver talks, engage with students, and conduct practical workshops. The institute's Science Setu team also organized two open days during the year, welcoming approximately 320 students and teachers. NII also actively participated in significant national public outreach events, such as Global Bio India 2023, National Technology Day 2023 and the India International Science Festival 2023, further strengthening its connection with the community.



To build a robust research ecosystem, NII organizes seminars featuring esteemed national and international researchers. These events encourage knowledge sharing and collaboration between visiting experts, students, and faculty. Moreover, NII provides training programs for undergraduate and postgraduate students, focusing on scientific inquiry and offering practical experience with advanced biotechnological tools and techniques. Through these efforts, NII aims to cultivate the next generation of researchers and promote a culture of innovation in biomedical science.

Summarizing the extensive work of the scientists and researchers at NII in just a few pages is a daunting task. The institute's achievements stem from tackling a wide range of challenges, persistent efforts, collaborative research, and significant breakthroughs. I want to emphasize the vital role of collaboration in the interdisciplinary research conducted here. Science thrives as a collective human effort, and NII's growth is a testament to the outstanding contributions of its community, including administrative and technical staff, faculty, researchers, and graduate students. I extend our gratitude to the members of our Research Area Panel and Scientific Advisory for their valuable insights and guidance. Additionally, I thank the Department of Biotechnology and the Ministry of Science and Technology for their ongoing support throughout our journey.

This annual report outlines the institute's activities for the financial year 2023-24, along with a summary of key research outcomes from this period. I hope you find the information presented here both informative and enlightening.

Debasisa Mohanty
Director, NII
7th May 2024



RESEARCH

REPORTS

- 01.** IMMUNITY
AND INFECTION
- 02.** CHEMICAL BIOLOGY,
BIOCHEMISTRY AND
STRUCTURAL BIOLOGY
- 03.** GENETICS, CELL
SIGNALING AND
CANCER BIOLOGY

IMMUNITY AND INFECTION

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MICROBIAL INTERFACE BIOLOGY AND ASSOCIATED HOST IMMUNE RESPONSE

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Our research aims to decipher the molecular and cellular basis of B-cell responses to protein and polysaccharide antigens on *Streptococcus pneumoniae* (pneumococcus). It also investigates how pneumococcus causes disease and explores potential interventions. The focus is on strategies used by pneumococcus to evade the mammalian immune system and the host immune responses that can overcome these strategies. Objectives include characterizing B-cell responses, identifying virulence factors, understanding their interactions with the host immune system, and evaluating the vaccine potential of pneumococcal surface proteins. The study employs molecular, genetic, immunological, microbiological, and biochemical approaches using *in vitro* and *in vivo* models.

Microbial interface biology and associated host immune response

Our study investigates the development and maturation of anti-polysaccharide and anti-carrier protein antibody responses in mice immunized with the model glycoconjugate antigen PCP14-CRM197. Using hybridoma technology, monoclonal antibodies (mAbs) specific to PCP14 and CRM197 were generated from mice immunized with one and three doses of the vaccine. The antibodies were collected and analyzed from different time points to understand their molecular characteristics and evolutionary patterns.

Two sets of clonally related anti-PCP14 hybridomas were identified, each derived from a common ancestral B-cell. The first clone included three B-cells (B07B02, F03A11, and F04F09) with shared and unique mutations in their heavy and light chains, following a stepwise mutation process. These antibodies were of the IgM/ κ isotype. The second clone, initiated by a different B-cell, also belonged to the IgM/ κ isotype. A significant increase in mutational load was observed in the heavy chains of PCP14-specific hybridomas generated under a three-dose regimen compared to those generated after a single dose. This trend was similar for the light chains. However, no significant increase was noted in the mutational load of CRM197-specific hybridomas after booster shots.

The few IgG CRM197-specific hybridomas indicated a higher number of mutations compared to IgM hybridomas, but this difference was less pronounced in PCP14-specific antibodies. The study also found that the HCDR3 sequence ARWDY was identical in nearly half of the anti-PCP14 mAbs, despite variations in the gene segments used and junctional modifications. This sequence convergence was observed across all five mice used in the study, indicating strong antigen-driven selection. Additionally, many anti-PCP14 mAbs lacked DH gene-derived amino acids, highlighting their presence in the B-cell repertoire and their capability to bind the antigen effectively.

Functionally, anti-PCP14 mAbs demonstrated specific binding to PCP14 without cross-reacting with other pneumococcal polysaccharides or surface components. Flow cytometry confirmed their binding to the surface of *S. pneumoniae* serotype 14. Furthermore, six out of seven tested anti-PCP14 mAbs promoted bacterial killing in a blood bactericidal assay, showing their potential effectiveness in providing immunity against *S. pneumoniae* serotype 14. This comprehensive analysis of the antibody responses to PCP14-CRM197 provides insights into the molecular evolution and functional properties of anti-polysaccharide antibodies, revealing significant antigen-driven selection and functional diversity among the generated antibodies.





Molecular Immunology Group



PLASMODIUM PROTEINS INVOLVED IN VIRULENCE AND HOST MODULATION:

HOST-PARASITE INTERACTIONS IN PLASMODIUM LIVER STAGES

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Plasmodium species introduce effector molecules into hepatocyte cytosol to manipulate host metabolic and/or signaling pathways for its own benefit. Those could prove good targets for drug development. The host processes affected by them could also be target for intervention. Basic theme is to identify, new parasite molecules that affect the host cellular processes, and possible intervention strategies. We use reverse genetics tool to characterize the parasite proteins with regard to its functions.

Malaria vaccine

We are working with human malaria parasite (*Pf*) antigens expressed at liver stage and mosquito stage and using them as chimeric antigen for immunizations and efficacy studies.

Generation of *Pf* -antigen in *Pb* transgenic parasites:

To challenge mice immunized with chimeric *Pf* antigens we need dual transgenic parasites. Therefore, we first made four transgenic parasites having single *Pf* antigen gene (*PfCSP*, *PfDnaJ*, *PfSLTRiP* and *Pfs48/45*). These parasites were then crossed to get three dual gene-replaced parasites.

Preclinical studies with advanced chimeric vaccine candidate CSP-Pro6C:

Mice immunizations with antigens along with adjuvant MPLA or alhydrogel were performed. The ELISA titer of serum (3rd bleed) against CSP-Pro6C indicated an average total IgG titer of 1440000 ± 127593 . Avidity analysis of antibodies indicated good avidity of antibodies in the presence of 1M GdHCl at a dilution range of 10000-100000 of serum in all the immunized groups. The immunized mice were challenged with *Pf* CSP-*Pb* sporozoites 7 days after the 3rd boost. Results show a reduction of parasite burden $\approx 92-95\%$ in the immunized group. The flow-cytometry analysis of the antigen-stimulated T cell indicated a rise in the IFN- γ and TNF- α producing T-cells.

Expression, purification, immunization and protective efficacy of *PfSLTRIP3,4-Pf-DNAJ-T* chimera and *PfCSP-Pf-DNAJ-T* chimera:

To assess the immunogenicity and protective efficacy of *PfSLTRIP3,4-Pf-DNAJ-T* mice were immunized using MPLA as an adjuvant. Immunized mice when challenged one month after last boost, with 3000 transgenic sporozoites, *PfSLTRiP3,4* and *PfDNAJ-T* groups showed a two-day delay in the prepatent period as compared to the naive mice. On the other hand, *PfSLTRiP-PfDNAJ-T* chimeric protein immunized mice did not develop the blood stage infection even up to 15 days of observation. This shows complete protection.



Similarly, mice were immunized with low-dose antigen (10 ug), PfCSP, Pf-DNAJ-T or PfCSP-Pf-DNAJ-T chimera, adjuvanted with 2% Alhydrogel and challenged with 2000 dual transgenic sporozoites. While CSP or DNAJ-T alone immunizations gave a 2-day delay in the prepatent period, PfCSP-Pf-DNAJ-T-chimera gave a 3-day delay in the prepatent period.

Characterization of malaria vaccine candidates Pf-SLTRIP and Pb DNAJ:

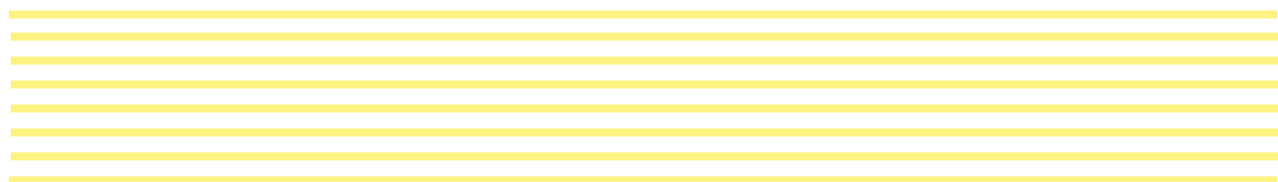
Earlier we showed that mouse parasite proteins Pb-SLTRIP and Pb-DNAJ full-length protein immunizations provide protection against infectious sporozoite challenge. Now we are working on the human malaria parasite protein PfSLTRiP, to identify the minimal protein fragment that can provide protection equivalent to full protein in PfSLTRiP.

Subfragments were expressed purified and used in immunizations. Immunized mice were challenged with sporozoites to assess the protection. For measuring the long-term protective efficacy immunized mice were challenged with 2000 sporozoites 10 months after the third boost. One day delay in PPP was observed even after 10 months post-immunization. This indicates Pb-DNAJ can induce long-term memory.

Publications

Original peer-reviewed articles

1. Anand R, Kashif M, Pandit A, Babu R, Singh AP* (2023) Reprogramming in *Candida albicans* gene expression network under butanol stress abrogates hyphal development. *Int J Mol Sci.* (MDPI): 24: 17227.
2. Singh AP*, Rathi B (2023) Editorial: Advances in anti-malarial drug discovery. *Front Drug Discov.* 3:1335842.
3. Erhunsea N, Kumari S, Anmol, Singh P, Omoregie ES, Singh AP, Sharma U, Sahal D (2023) *Annickia affinis* (Exell) Versteegh & Sosef methanol stem bark extract, potent fractions and isolated Berberine alkaloid inhibit the growth of both blood and liver stages of malaria parasites. *J Ethnopharmacol.* 319:117269
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PATENTS

I. Singh AP, Singh H, Kumar JD. A chaperone family protein-based malaria vaccine [Indian Patent No 508461; Granted on 08/02/2024]



Infectious Diseases Group



IMMUNE SIGNALING PATHWAYS IN HEALTH AND DISEASE

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Rajesh Gokhale (IISER-Pune)

Aneeshkumar G. (NII, New Delhi)

Sangeeta Bhaskar (NII, New Delhi)



In their anatomic niche, mammalian cells receive signals from a variety of stimuli that generate cross talks between signal-activated intracellular pathways. Combining biochemistry, genetics and computational modeling tools, I have been investigating the role of these cross-regulatory mechanisms in physiology and disease.

We are examining crosstalk between the NF- κ B pathways and those beyond NF- κ B signaling. We are mechanistically characterizing crosstalk mechanisms integrating cellular pathways within a network and exploring if such cross talks have functional relevance for intestinal inflammation and cancer and in anti-viral immunity. We hope our analyses will inform novel therapeutic approaches targeting cross-regulatory signaling mechanisms in human ailments.

A. Probing cell signaling pathways directing anti-viral immunity

Macrophages are critical for limiting viral multiplication in the periphery and restraining infection-inflicted pathologies in various anatomic niches. Macrophage-secreted inflammatory cytokines direct both cellular and humoral immune reactions against invading RNA viruses. However, excessive cytokine production by macrophages also leads to tissue destruction and inflammatory pathologies.

Viral sensing by macrophages activates canonical RelA/NF- κ B signaling, which mediates the expression of cytokines. However, it remains unclear how macrophage-intrinsic NF- κ B signaling impacts the viral pathogenesis. Here we focused on two important RNA viruses frequently associated with human epidemics in India, namely Chandipura (CHPV) and Chikungunya (CHPV) virus.

We perturbed the canonical RelA/NF- κ B signaling by inactivating the gene encoding I κ B α , which inhibits RelA-containing transcription factors, specifically in macrophages. We then challenged these *Nfkb1a* ^{Δ LysM} mice, which possessed heightened NF- κ B signaling in macrophages, and cells derived thereof, with CHPV and CHIKV.

Our studies revealed that heightened NF- κ B signaling in macrophages limits pathogenesis in mice infected with CHPV and CHIKV involving interferon-dependent and independent mechanisms.

B. Charting immune signaling in intestinal homeostasis and diseases

Dendritic cell (DC) deregulations have been implicated in the pathogenesis of inflammatory bowel disease. The non-canonical NF- κ B pathway, which activates the RelB:p52 transcription factor, controls DC differentiation. We examined whether DC-intrinsic non-canonical signaling also modulated intestinal inflammation. Our investigation revealed that ablating non-canonical NF- κ B signaling in DCs in *Relb* ^{Δ CD11c} or *Nfkb2* ^{Δ CD11c} mice blunts chemically-induced experimental colitis.



This diminished colitogenic sensitivity in our knockouts was accompanied by an increased frequency of regulatory T cells in the intestine, reduced inflammation, and an elevated level of luminal IgA, which promoted eubiosis. Our mechanistic investigation revealed an unexpected accumulation of β -catenin in noncanonical NF- κ B deficient DCs.

This correlated with the transcriptional upregulation of *Raldh2*, which imparted the retinoic acid gene signature and tolerogenic attributes in non-canonical NF- κ B-deficient DCs. Finally, analyzing single-cell RNA sequencing data, we also established the relevance of our newly identified DC network in human inflammatory bowel disease (IBD).

Therefore, our study identifies novel crosstalk between non-canonical NF- κ B-signaling and the β -catenin pathway in DCs at the mucosal interface that tunes intestinal homeostasis and inflammation. In a collaboration program, we are now investigating the medicinal properties of plants from northeast India in mitigating ailments associated with metabolic dysregulations, including leaky gut.

Publications

Original peer-reviewed articles

1. Roy G, Chakraborty A, Swami B, Pal L, Ahuja C, Basak S, Bhaskar S* (2023) Type 1 interferon-mediated signaling is indispensable for eliciting anti-tumor response by *Mycobacterium indicus pranii*. *Front. Immunol.* 14:1104711.
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Reviews

1. Mukherjee T, Kumar N, Chawla M, Philpott DJ, Basak S* (2024) The NF- κ B signaling system in the immunopathogenesis of inflammatory bowel disease. *Sci Signal.* 17: eadh1641.
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Systems Immunology Group



UNDERSTANDING THE ROLE OF INTERFERON REGULATORY FACTORS IN DENDRITIC CELL DEVELOPMENT AND INNATE IMMUNITY

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Ajay Kumar

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The dendritic cells (DCs) are collection of heterogeneous populations that are broadly categorized into plasmacytoid DCs (pDCs) and classical DCs (cDCs) represented by cDC1 ($CD8\alpha^+/CD103^+CD11b^-SIRP\alpha^-$) and cDC2 ($CD4^+/CD103^-CD11b^+SIRP\alpha^+$). Each DC subtypes are characterized by surface markers, gene expression patterns and unique functions.

Members of Interferon regulatory factors (IRFs) family play critical role in DC development and functions. Our laboratory focuses towards understanding the mechanisms of IRF directed diverse DC subtype development and defining the cross talk of IRFs with other transcription factors and signaling pathways. We have initiated study about the role of DCs in autoimmune disorders, microbial infection and cancer biology.

Understanding the role of interferon regulatory factors in dendritic cell development

IRF family members play a critical role in DC development and functions. Interferon regulatory factor 4 (*Irf4*) and Interferon regulatory factor 8 (*Irf8*) play pivotal role in generation of diverse DC subtypes. The development of $CD8\alpha^+$ cDC1 and pDC requires *Irf8*, whereas $CD4^+$ cDC2 subset is dependent on *Irf4*. In previous studies, we demonstrated that *Irf8* is the master regulator of cDC1 development and defined the functional significance of its interactions with *Batf3* and *Id2*, factors that are important in the process.

We focused on identifying the novel IRF interacting partners and evaluating the functional significance of these interactions. We have also initiated research towards identifying the mechanisms of DC development by IRF4 and IRF8. We had initiated efforts towards understanding the protein complexes formed by IRF8 by employing IRF8^{R294C} BxH2 mutant, which provides us with a unique opportunity as this natural mutation specifically impairs cDC1 development but not that of pDC subset suggesting a difference in the interactomes.

We expressed FLAG-IRF8^{WT/R294C}-HA in HEK293T cells and interacting partners were pulled down by immunoprecipitation using anti-FLAG magnetic beads. Interacting partner proteins were separated on SDS-PAGE followed by silver staining subsections of each lane were subjected to mass spectrometry to confirm the identity of the proteins.

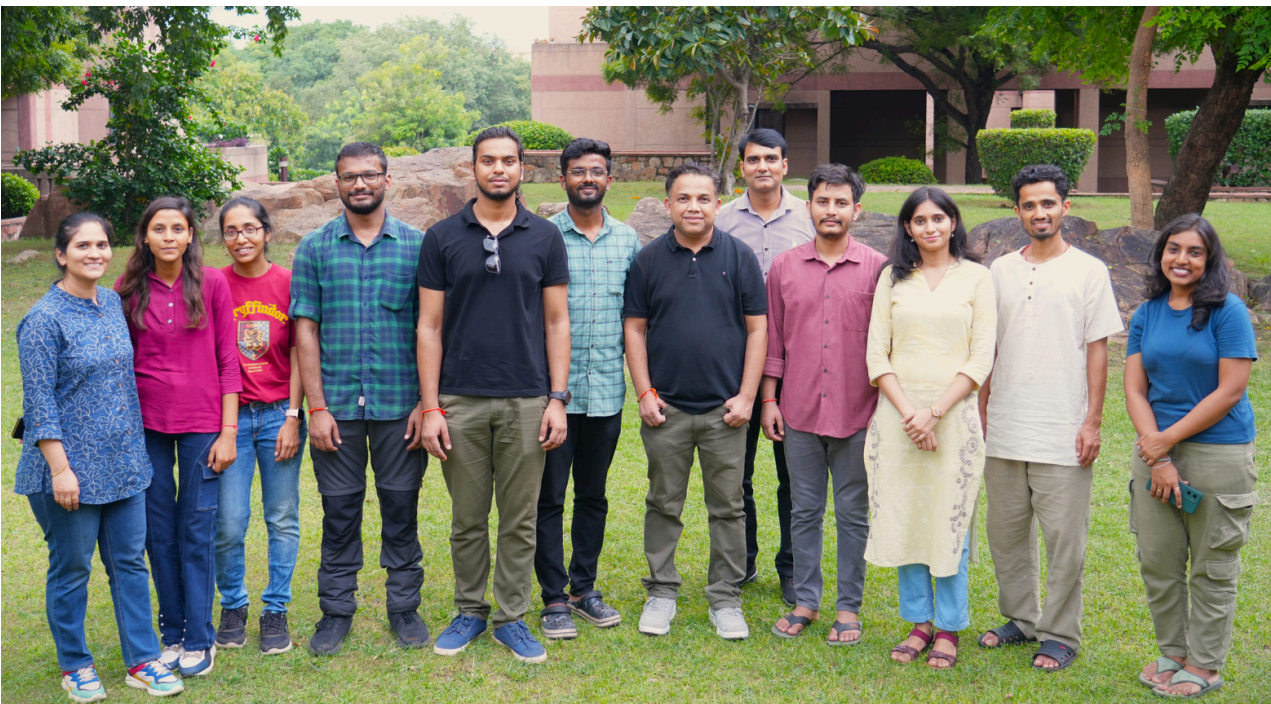
Among the various interacting partners, Nucleosome assembly protein 1 like 1 (NAP1L1) displayed distinct association with the native version of IRF8 but was defective in interaction with the BxH2 mutant. Hence, we further followed our study to understand the significance of this association. We confirmed the IRF8-NAP1L1 interaction by immunoprecipitation by co-transfection of Myc-tagged NAP1L1 and FLAG-tagged IRF8.

We also confirmed this interaction by yellow fluorescent protein (YFP) based Bi-molecular fluorescence complementation (Bi-FC) assay wherein YFP C-terminal half was expressed as fusion protein with IRF8^{WT} or IRF^{R294C} IRF association domain (IAD) dead mutant (IRF8^{WT}-YCC and IRF8^{R294C}-YCC respectively) and YFP N-terminal half was expressed as fusion protein with NAP1L1 (YNN-NAP1L1).

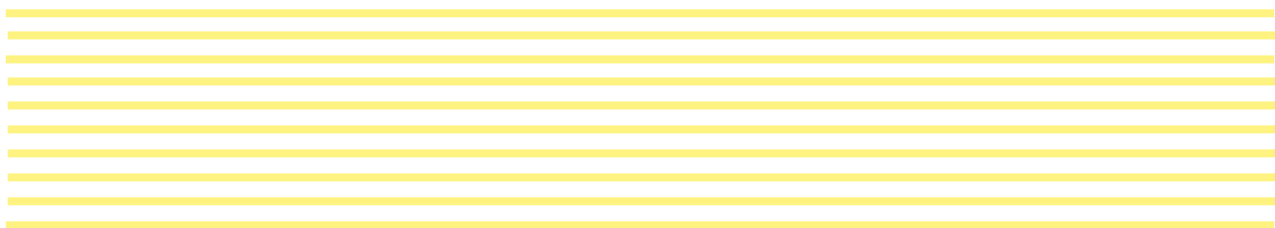


In our Bi-FC experiments YFP signals were efficiently detected in cells expressing IRF8^{WT}-YCC and YNN-NAP1L1 but not with the cells co-expressing IRF8^{R294C}-YCC and YNN-NAP1L1; validating data from our immunoprecipitation experiments. Similarly, by employing Bi-FC experiments; we examined the various regions of NAP1L1 for specificity of interaction with IRF8 and demonstrated that N-terminal region of NAP1L1 having alpha1 and alpha2 helices define interaction with IRF8. Evaluating the effect of the NAP1L1 and IRF8 interaction on various promoters, we identified that co-expression of these interacting partners selectively activated type I Interferon promoters *Ifna6* and *Ifnb* whereas it did not affect the induction of IL12p40 promoter and NF- κ B element containing promoter. Since NAP1L1-IRF8 co-expression selectively upregulated type I Interferon and as Type I Interferon plays a critical role in anti-viral responses; we examined the significance of IRF8-NAP1L1 interaction during viral infection by employing the New Castle Disease Virus (NDV) infection.

We observed that the NIH3T3 cell line co-expressing IRF8 and NAP1L1 upon NDV infection induced higher levels of type I IFN as well as interferon-stimulated genes (ISGs) than cells expressing only IRF8 or NAP1L1. Further we also noticed a significant drop in NDV transcript levels suggesting that IRF8-NAP1L1 interaction upregulated the type I Interferon arm of innate immunity enhancing the host anti-viral responses.



Innate Immunity Group



T-CELL IMMUNITY TO VIRUS INFECTION AND VACCINATION

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Vaccines are the most cost-effective preventive measure against infectious diseases. Our group aims to understand the development of long-term protective immunity by bridging fundamental and translational immunology.

We focus on how Tfh cells drive T-cell and B-cell collaboration to establish protective immunity. Using advanced human immunology techniques and cohorts of virus infections and vaccinations, we seek to identify T-cell determinants of long-lasting protective humoral immunity. Our goal is to leverage this knowledge for the rational design and development of potent vaccines.

Biology of Tfh cells in long-lasting protective immunity

Tfh cells in long-term sustained immunity in vaccination and infection

Here, we are investigating Tfh cells in longitudinal cohorts of JEV infection and vaccination (SA14142 JE vaccine), focusing on the durability of protective immunity. In a detailed immunological analysis of the cohort (N=87), 66% of seronegative participants seroconverted in response to the vaccine, with 38% of seroconverters achieving seroprotection (FRNT₅₀>10).

Seroconverters exhibited modest cellular and humoral immunity with a declined neutralizing antibodies below seroprotection levels by the second year. Interestingly, suboptimal T-B collaboration was marked in non-seroconverters or poor responders to vaccine. This data underscores the critical role of Tfh cells in orchestrating a potent humoral response to the JE vaccine.

Our study provides the evidence for effectiveness and durability of protective traits in single-dose SA14-14-2 immunization in adult population. Considering ~18% non-seroconverters and poor durability of immune mediators of protection, it'll be important to revisit the immunization policies in JE endemic regions.

Biology of Tfh cells in COVID-19 infection and vaccination

We are attempting to leverage upon the “hybrid immunity” model in COVID-19 to understand the Tfh-specific immune imprinting in context of broadly protective immunity.

To this, we examined the SARS-CoV-2 specific immune memory in individuals recovered from asymptomatic and symptomatic COVID-19 after up to 10 months post-diagnosis (Figure 1).



A robust immune memory was observed in both symptomatic and asymptomatic groups for up to 10 months. A decline in antibody and T-cell responses was observed against multiple variants. Vaccination greatly enhanced the protective immune mediators against VoCs from both the groups. However, magnitude of T cells and Tfh cells was not increased significantly after vaccination in either of the groups. It seems the vaccination or so called “hybrid immunity” might be contributing to the enrichment of specific clonotypes or subsets that are devising the breadth of reactivity against the variants.

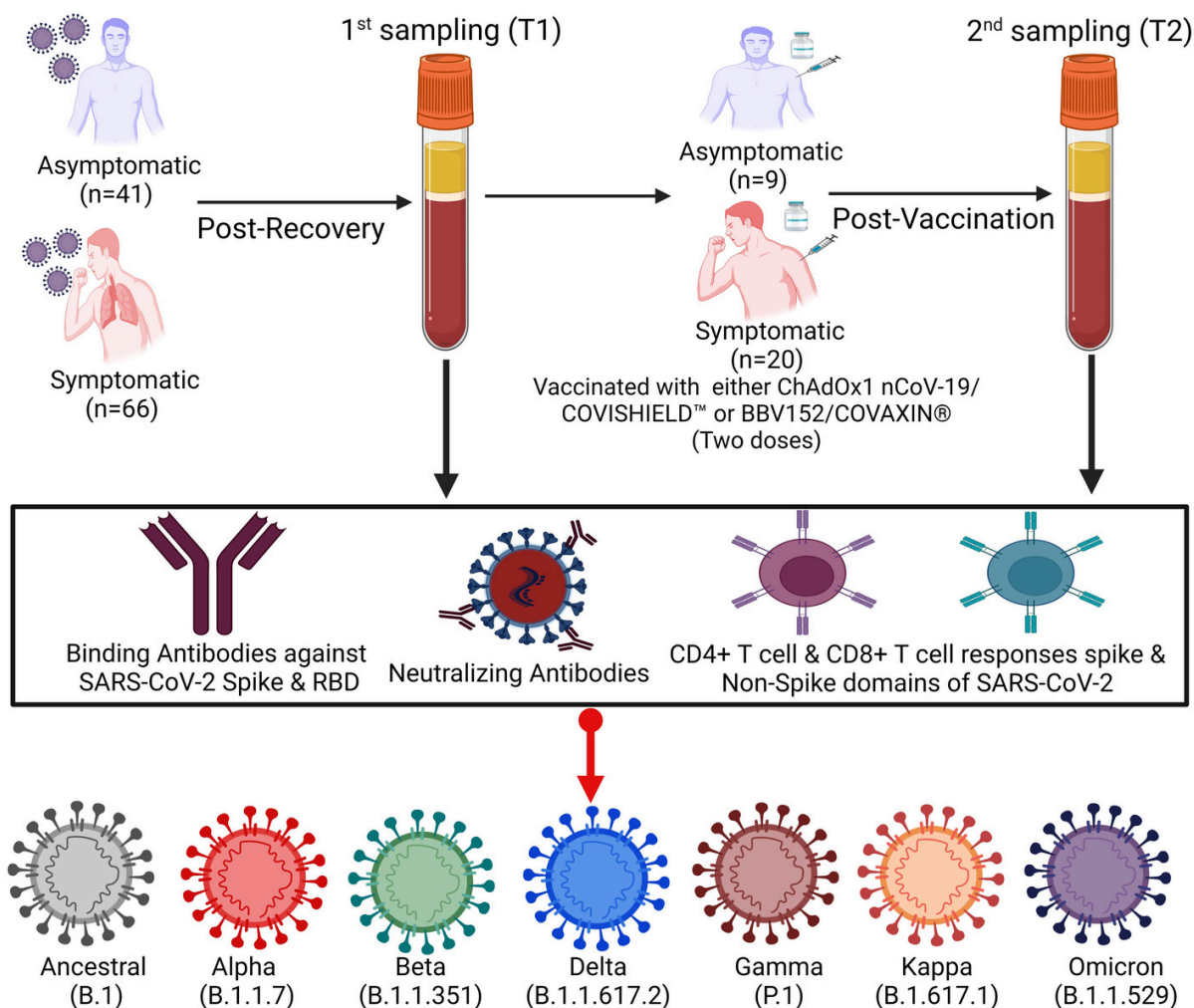


Figure 1: Study design to analyze immune memory in various COVID-19 infection outcomes and immune imprinting in the context of "hybrid immunity".

Function of Tfh cells in humoral immunity establishment to dengue virus

Dengue serves as an insightful model for studying Tfh cells and T-B collaboration in humoral responses to viruses. Our research addresses two main questions: the role of Tfh cells in antibody responses (both pathological and potentially neutralizing) and the mechanistic axis of T-B collaboration during humoral immunity development.



We studied a cohort of adult dengue patients with varying disease severities, identifying a dominant DENV-specific PD1-expressing peripheral CD4⁺ T-cell subset. This subset strongly correlates with plasmablasts and antibodies, secretes B-cell helper molecules, promotes plasmablast differentiation via IL21 signalling, and accumulates aberrantly in severe dengue cases. Transcriptomic and clonotypic analyses at single-cell resolution further established that the IL21⁺ subset is distinct from Tfh and cytotoxic cells within the PD1-expressing cell pool.

Our study offers crucial insights into T-cell-dependent regulation of humoral responses in dengue, identifying the IL21⁺ helper T-cell subset as a dominant determinant (Study preprint).

Human Immune Monitoring and T-cell Immunoassay Platform

As part of our translational efforts, we have established the "Human Immune Monitoring and T-cell Assay" platform, which is used for advanced immunological human trials of vaccines (Figure 2). The platform was instrumental in conducting phase 3 immuno-bridging trial of the intranasal COVID-19 vaccine "iNCOVACC", leading to its approval as the world's first intranasal COVID vaccine by the Indian regulators. Recently, this platform was employed for in-depth immunogenicity analyses of a COVID-19 subunit vaccine.

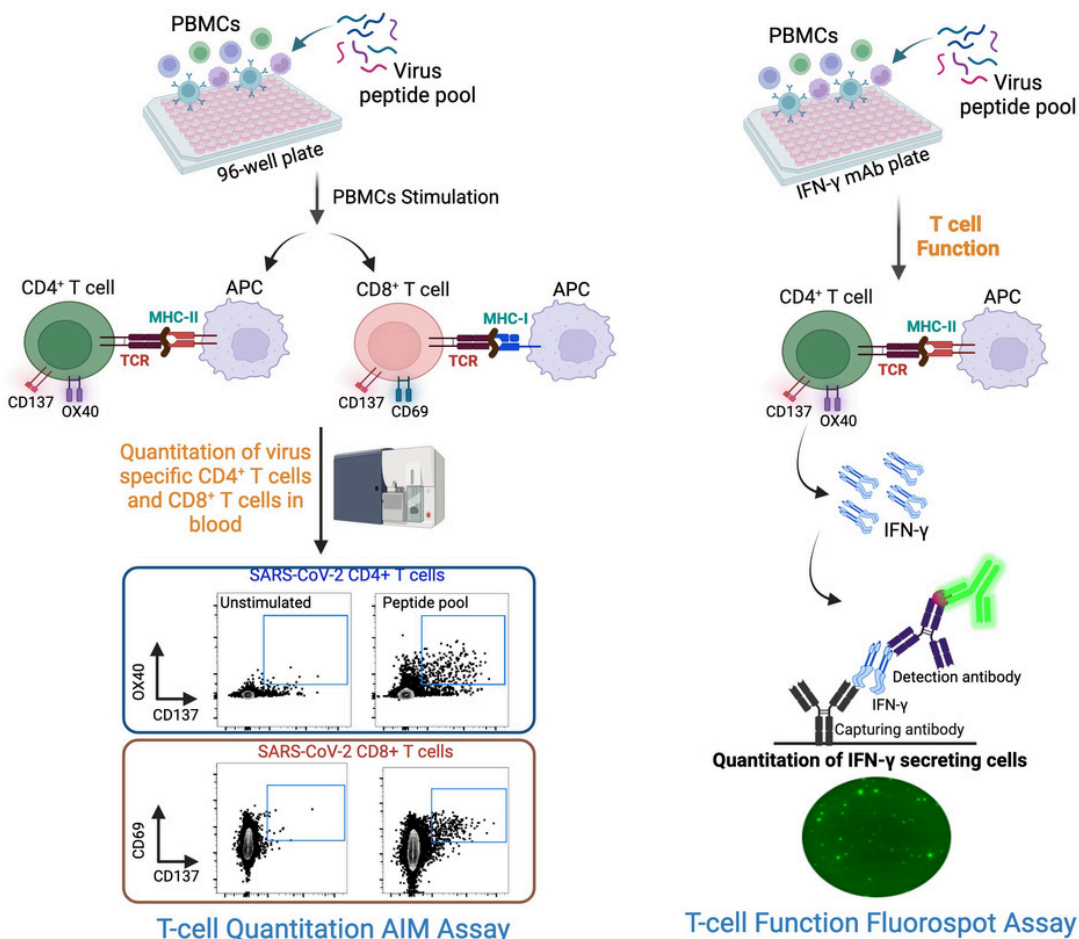


Figure 2: The Human Immune Monitoring and T-cell Assay platform offers advanced human immunology techniques for clinical trials of vaccines, biotherapeutics, and antivirals. The image depicts the assay for the quantitation of virus-specific T cells and their function in human blood.



Additionally, we have developed a novel T-cell assay that helps identify promising vaccine candidates by evaluating their potential to induce optimal T-cell-dependent humoral immunity (Figure 3; STAR Protocol, 2024).

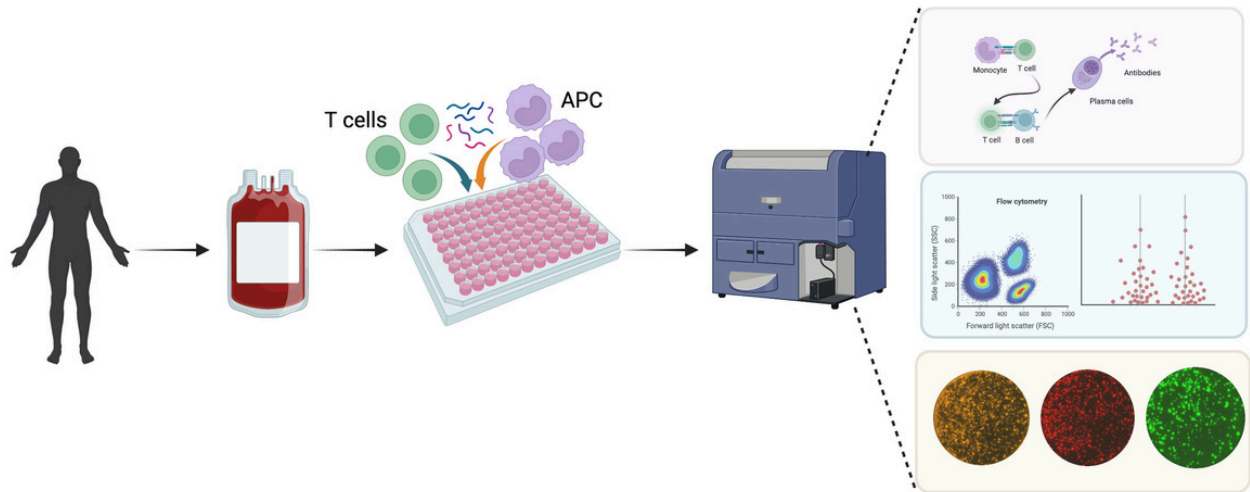
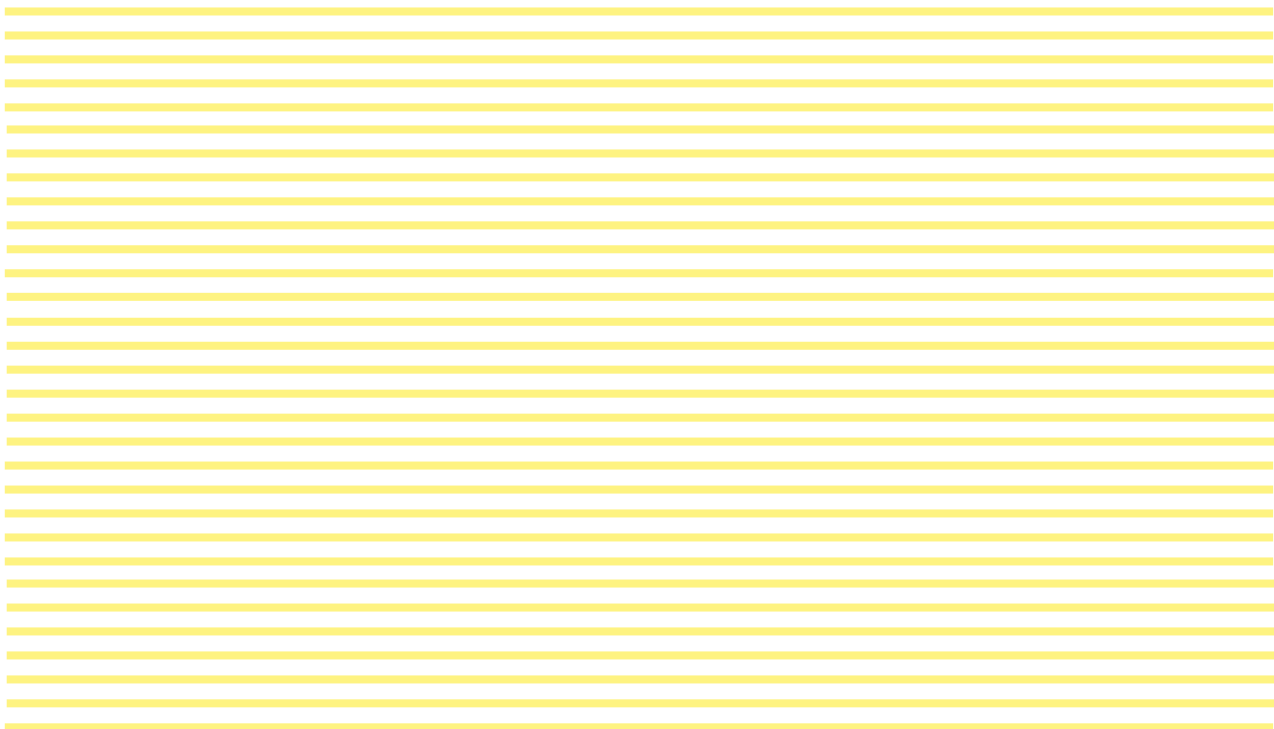


Figure 3: The image depicts a novel T-cell function assay designed to evaluate a vaccine's potential to induce T-cell-dependent humoral immunity. This assay, which can be performed using blood cells, has been demonstrated to assess vaccines against SARS-CoV-2, Japanese encephalitis virus, Dengue virus, Cytomegalovirus, and Mycobacterium tuberculosis.



PATENTS

1. Nimesh Gupta and Shilpa Sachan. Method for assessing follicular T helper cells specific immune response, peptide pools and application thereof. (Filed on 16/08/2023)



Vaccine Immunology Group

IMMUNE RESPONSE TO INFECTIONS IN HUMANS

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Research in our lab focuses on understanding the development of an immune response to human infections by studying the regulation of global gene expression patterns uniquely associated with a pathogen, immune cell type and/or disease stage using multi-omics and immunological tools. Two of the programs in the lab currently are—(i) understanding how the T cell memory is formed during the primary infection and maintained over the years to defend the subsequent secondary infection from the same pathogen, and (ii) understanding the immune response to sepsis in neonates by analyzing the dynamic change in immune cell proportions and the associated gene expression patterns.

A. Systems biology approaches to understand the biology of human CD4+ helper T cells with cytotoxic potential (CD4-CTLs) in viral infections

1A. Bulk multi-omics analysis of CD4 memory subsets:

To understand the developmental lineage connection and gene expression as well as regulation patterns of various memory subsets in comparison to CD4-CTLs, we have simultaneously performed ATAC-Seq, RNA-seq and TCR-Seq on various CD4 T cell memory compartments along with CD8-effectors. The preliminary analysis of these multiomics data sets showed that the CD4- T_{EMRA} (CD4-CTLs) and CD8- T_{EMRA} (CD8-CTLs) show enrichment for a similar set of genes and cluster together. We also observed a set of genes that were uniquely enriched in T_{CM} and T_{EM} and another set in T_{SCM} and T_{EMRA}^P and T_{EMRA}^E . The TCR data also shows relatively higher clonal sharing between T_{SCM} and CD4-CTL compartments compared to Naïve and T_{CM} . Through ATAC-seq analysis, we have identified expressed versus poised genes.

1B. Single-cell multi-omics analysis:

To identify both poised and expressed genes from the same cells, we have adopted 10X genomics' multiome where both RNA-Seq and ATAC-seq can be performed in the same cell. We have completed these assays on CD4-Naïve, T_{CM} , T_{EM} , CD4- T_{EMRA} from 8 donors using 10X genomics platform (over 35000 single-cells analyzed). The preliminary analysis has identified a small subset of cells majorly from the naïve compartment that shows upregulation of several genes identified through the bulk omics experiments (1A) shared between T_{SCM} and CD4-CTL subsets and the TFs identified are stem cell related. Further, the effector-specific TFs such as Eomes, TBX21 contain binding motif for these TFs.

1C. Differentiation of naïve CD4 T cells to CD4-CTLs in vitro:

We have developed an *in vitro* system to differentiate naïve CD4 T cells to CD4-CTL fate under T_H1 , T_H2 , or neutral polarizing conditions. The single-cell multiomics data from Day 10 and Day 20 shows a gradual increase in the expression of CTL genes as well as the number of cells differentiating to CTLs, indicating these are potential CD4-CTL precursor or pre-effector-like cells.

1D. Determine the phenotype and functional properties of virus-specific CD4-CTLs:

We have completed the analysis of over 35000 antigen-specific T cells for DENV, CMV and Influenza.



B. Understanding the dynamic changes in gene expression patterns of immune cell types associated with neonatal sepsis

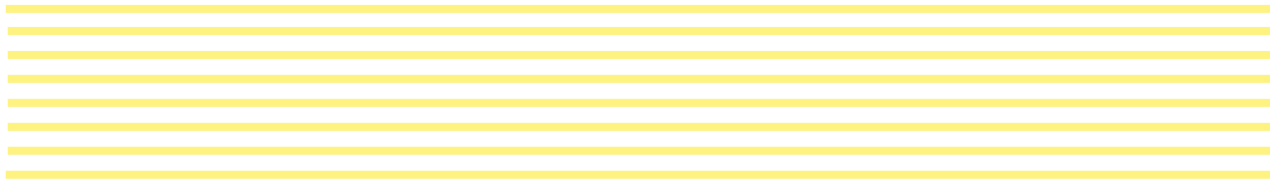
The main focus of this project was to analyze the immune response to sepsis by examining the dynamic change in immune cell proportion at pre-sepsis (at the time of suspicion), during-sepsis, and post-recovery from sepsis. The preliminary analysis so far indicated the following.

1. Single-cell multiomics analysis of ~1lakh cells from 60 donors across disease spectrum and controls indicates variation in quality and quantity of immune cells, based on donor/pathogen (pathogen-specific features), disease-stage specific, during the infectious phase the T cells clonally expand.
2. We observed a positive correlation between FACS and single-cell omics data sets
3. Both FACS and single-cell omics data suggested dynamic changes in immune cell proportions during the course of the disease

Publications

Original peer-reviewed articles

1. Kar R, Chattopadhyay S, Sharma A, Sharma K, Sinha S, Arimbasseri GA*, Patil VS*. (2024) Single-cell transcriptomic and T cell antigen receptor analysis of human cytomegalovirus (hCMV)-specific memory T cells reveals effectors and pre-effectors of CD8+ - and CD4+ -cytotoxic T cells. *Immunology*. doi: 10.1111/imm.13783.
2. Yadav P, Rana K, Nardini V, Khan A, Pani T, Kar A, Jain D, Chakraborty R, Singh R, Jha SK, Mehta D, Sharma H, Sharma RD, Deo SVS, Sengupta S, Patil VS, Faccioli LH, Dasgupta U, Bajaj A (2024) Engineered nanomicelles inhibit the tumour progression via abrogating the prostaglandin-mediated immunosuppression. *J Control Release*.368:548-565.
3. Kar A, Jain D, Kumar S, Rajput K, Pal S, Rana K, Kar K, Jha SK, Medatwal N, Yavvari PS, Pandey N, Mehta D, Sharma H, Bhattacharya D, Pradhan MK, Datta Sharma R, Srivastava A, Agarwal U, Mukhopadhyay A, Sengupta S, Patil VS, Bajaj A, Dasgupta U (2023) A localized hydrogel-mediated chemotherapy causes immunogenic cell death via activation of ceramide-mediated unfolded protein response. *Sci Adv*. 9: eadf2746
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Immuno-Genomics Group



SYNERGISTIC IMPACT OF MICROBIAL ECOLOGY, METABOLOMICS, AND MITOPHAGY ON IMMUNE DYNAMICS IN AN INFECTIOUS DISEASE PARADIGM

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As an independent investigator, my research aims to develop translational strategies to combat major chronic diseases in humans. The primary objective is to balance tolerance and immunity to prevent inflammation. I explore the potentiality of gut microbiome and nutritional therapies as interventions.

My research also delves into the dynamics of metabolism, brain function, placenta, T-cells paradigm, and mitophagy. I seek to understand how these factors interact to maintain maternal-child health and prevent disease. By integrating these diverse yet interconnected areas, my goal is to identify novel therapeutic approaches that can effectively mitigate chronic diseases and improve overall health outcomes.

Synergistic impact of microbial ecology, metabolomics, and mitophagy on immune dynamics in an infectious disease paradigm

β -catenin signaling in immune-metabolism landscape

Our research investigates β -catenin's role in *Toxoplasma gondii* infection and how its inhibition mitigates infection by promoting an anti-inflammatory environment. We examined the metabolic changes, focusing on enhancing oxidative phosphorylation and the pentose phosphate pathway, and their effects on immune tolerance. Additionally, we explore gut microbiota alterations and the role of compromised mitophagy and mitochondrial trafficking in supporting parasite growth. By promoting mitochondrial fitness, we aim to suppress inflammation, marked by increased IL-10 and TGF- β , and a transition of T-cells to Th2, Treg, and ThPD1 subsets, developing comprehensive therapeutic strategies.

Targeting DPP4 to mitigate SARS-CoV-2 infection: Gliptins' efficacy revealed

Our research demonstrated that the SARS-CoV-2 spike protein's receptor binding domain (RBD) interacts with human DPP4, aiding virus entry alongside ACE2. We identified that RBD forms hydrogen bonds and hydrophobic interactions with DPP4's α/β -hydrolase domain.

Using inhibitors like sitagliptin and linagliptin, we prevented RBD from binding both DPP4 and ACE2, thereby inhibiting viral entry and replication. These inhibitors effectively mitigate the growth of various SARS-CoV-2 variants, including alpha, beta, delta, and kappa, proposing a novel strategy to combat COVID-19. (Figure-1)



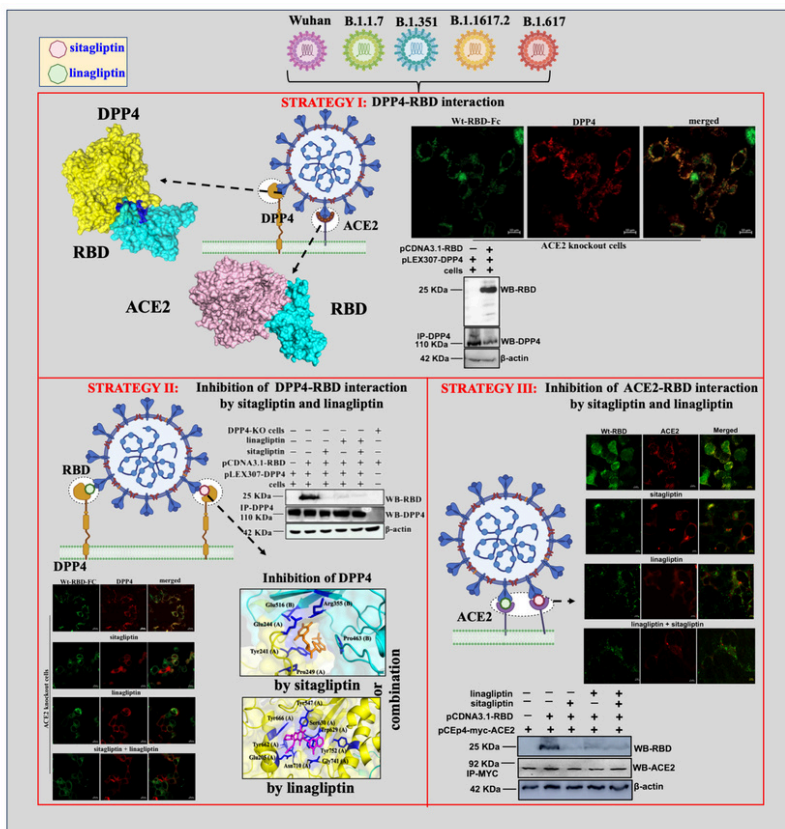


Figure 1: Pleotropic efficacy of sitagliptin, and linagliptin to impede pan-variants of SARS-CoV-2 infections. Strategy I: Establishing RBD of pan-variants of SARS-CoV-2 can interact with DPP4 in addition to ACE2 for the viral entry. Strategy II: Sitagliptin, and linagliptin, alone or in combination can suppress the growth of SARS-CoV-2 variants including most common VOCs like original SARS-CoV-2, alpha, beta, delta and kappa clade by impeding the DPP4 and RBD interaction. Strategy III: Both sitagliptin and linagliptin exhibit pleotropic effects as a result of gliptins' capacity to target ACE2-RBD interaction.

Immunoinformatics and reverse vaccine technology

Our strategy employs reverse vaccinology to combat *Helicobacter pylori* infections. We aim to identify T-cell epitopes that bind multiple HLAs, select TLR ligands to enhance antigenicity and validate a chimeric nano/micro-particle for oral delivery to elicit gut-localized immune responses.

This approach mimics pathogen components using PAMPs and protein antigens, facilitating IL-12-driven Th1 differentiation essential for protective immunity. Advantages include expelling *H. pylori*, generating memory responses, and avoiding drug resistance. Our research develops a multi-epitope vaccine targeting the Monkeypox virus by mapping highly immunogenic epitopes from structural glycoproteins.

The vaccine formulation includes adjuvants and linkers for enhanced stability and immunogenicity. Molecular dynamics simulations predict strong interactions with immune receptors, supporting robust memory immune responses and protective immunity *in silico*.



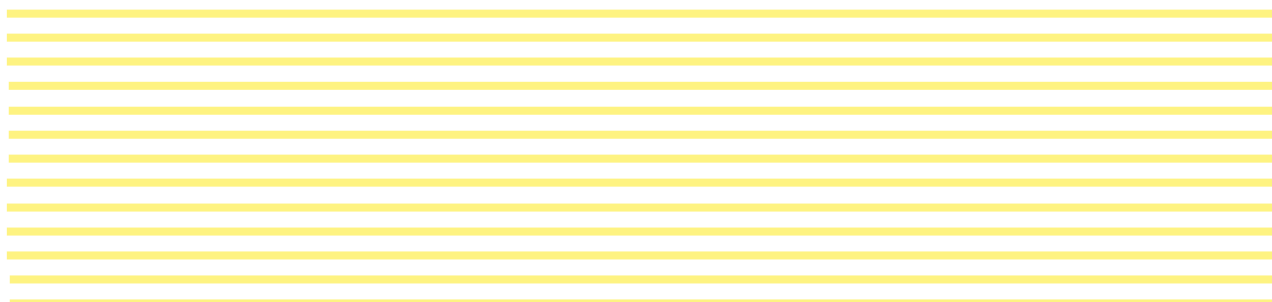
Immune modulation in circadian rhythm

Our research focuses on understanding the link between *Toxoplasma gondii* infection and circadian disorders through the microbiome and BMAL1-CLOCK signaling. We investigate BMAL1-CLOCK activation and its role in homeostasis and inflammation. We aim to dissect microbiota's role in tryptophan catabolism and its impact on circadian rhythms, exploring how microbiota shapes T-cell differentiation and inflammation. Using humanized mice and single-cell sequencing, we study microbiota-tryptophan imbalances and T-cell responses. Our goal is to develop intervention strategies, including nutritional approaches and genetically modified bacteria, to restore circadian behavior and reduce brain inflammation, potentially leading to identifying therapeutic solutions.

Publications

Original peer-reviewed articles

1. Ahuja R*, Kaur A, Kumari G, Kumar A, Kumar S, Roy A. K, Majumdar T* (2023) Enhanced expression and solubility of main protease (Mpro) of SARS-CoV-2 from E. coli. *Protein Expr Purif.* 211:106337.
2. Nag S, Mandal S, Mukherjee O, Majumdar T, Mukhopadhyay S, Kundu R (2024) Vildagliptin inhibits high fat and fetuin-A mediated DPP-4 expression, intracellular lipid accumulation and improves insulin secretory defects in pancreatic beta cells. *Biochim Biophys Acta Mol Basis Dis.* 1870: 167047.
3. Mukhuty A, Mandal S, Fouzder C, Das S, Chattopadhyay D, Majumdar T, Kundu R (2024) Nrf2 inhibition regulates intracellular lipid accumulation in mouse insulinoma cells and improves insulin secretory function. *Mol Cell Endocrinol.* 581:112112.
4. Mani S, Kaur A, Jakhar K, Kumari G, Sonar S, Kumar A, Das S, Kumar S, Kumar V, Kundu R, Pandey AK, Singh UP, Majumdar T* (2023) Targeting DPP4-RBD interactions by sitagliptin and linagliptin delivers a potential host-directed therapy against pan-SARS-CoV-2 infections. *Int J Biol Macromol.* 245:125444.
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Centre for Excellence in Vaccine Development



UNDERSTANDING THE SOURCES AND MEDIATORS OF META-INFLAMMATION IN METABOLIC SYNDROMES

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Metabolic homeostasis is at the core of non-communicable and communicable diseases. Though the role of energy flow underneath physiological and pathological conditions is discussed, the details of molecular events leading to metabolic deregulation and thereby amplifying pathology are largely superficial. Metabolic homeostasis is a result of an integrated network of multiorgan communication.

Areas of particular interest are how metabolic mediators oversee the functioning of multi-organ systems, what are specific cellular molecular events, and the translational potential of this metabolite in treating path ailments. Our group is particularly focused on detailed illustrations of these aspects in the context of energy-rich diet-associated metabolic disorders.

We have specifically invested our efforts in unravelling the metabolic collaboration with the host immune system in combating enteric infections. To explore the role of metabolic mediators in colon inflammation and breach of the gut epithelial barrier, we selected *Salmonella enterica* serovar Typhimurium (STM) as one of the enteropathogens that trigger these processes.

The *in vivo* murine model of colitis has been established by gavaging mice with multiple doses of logarithmic STM culture, ranging from 10^3 to 10^8 CFU, and monitoring their body weight change, survival post-STM infection, spleen weight measurement, and colon length reduction. We observed that the dose of 10^6 CFU and above was lethal for mice while the doses below 10^6 CFU were not enough to induce observable disease phenotype.

In another cohort of mice, we orally gavaged live STM (10^8 CFU) and heat-killed (HK) STM (10^8 CFU) and observed that the group infected with HK STM did not show any disease phenotype. There was no body weight decrease, splenomegaly, or colon length reduction in the mice infected with HK STM as opposed to a mice cohort infected with live STM bacteria.

Our data suggest that a live bacterium is indispensable for triggering host responses to pathogenic stimuli. Further, to dissect the interplay between HFD-mediated metabolic disturbances and STM infection-associated metabolic responses, we compared STM infection in chow-fed mice and HFD-fed mice.

Chow-fed mice and 2 weeks of HFD-fed mice cohorts were divided into 2 groups. The control cohort was administered with PBS and another half cohort was infected with STM via oral gavage. Mice were monitored for gut inflammation and STM pathogenesis. We observed that STM-induced pathogenesis was weak in HFD-fed mice with a slower decrease in the percentage of body weight.

However, a shortening of the colon in both infected groups fed on either a chow diet or HFD was insignificant. A marked difference in splenomegaly was observed in infected HFD-fed mice as compared to chow-fed-infected mice.



This suggests a strong host-mediated immune cells' response to STM infection in HFD-fed mice. This host immune response in HFD diet-fed mice could have curtailed STM pathogenesis leading to resistance to a decrease in body weight. Assessment of the metabolic hubs of the body viz. liver, and VAT highlighted striking differences between chow and HFD-fed mice post-STM infection.

Overall, this affects the survivability of mice post-STM infection. HFD-fed mice resisted additional 2 days as compared to chow-fed mice before succumbing to STM infection. This provides evidence for metabolic recalibration during infectious stimuli and corroborates our hypothesis that both host immune and metabolic effectors are working together to combat STM-mediated inflammation resolution. The experiments related to identifying metabolic mediators of robust host immune response and possible collaboration are underway.



Immuno-Inflammation Group



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ENZYMES REGULATION AND ITS IMPORTANCE IN BIOLOGY

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*Our research aims to understand the molecular mechanism of different classes of GTPases induced by immunomodulatory cytokine interferon- γ and to evaluate mechanistic similarities and differences with other GTPases within the same or different classes. The study has been currently focused on human guanylate-binding proteins. The study also focused on enzymes implicated in *H. pylori*'s polyamine production pathway. The mechanism, together with structural data, may provide insight into their role in biological functions and aid in developing a new strategy to design inhibitors against the gastric pathogen.*

Effect of the sequence variation in hGBP2 G-cap on GTPase activity

To check whether the sequence variation in the G-cap between hGBP2 and hGBP1 is responsible for reduced GMP formation in hGBP2, we individually mutated three residues of the hGBP2 G-cap to their corresponding residues in the hGBP1 G-cap. We also replaced the entire G-cap of hGBP2 with that of hGBP1. The data suggest that individual mutations or the G-cap replacement marginally increased GMP formation, which is still significantly lower than hGBP1.

Glu155 of *H. pylori* arginase also interacts with Lys57 and is essential for catalytic function

To explore whether Glu155 may also interact with other residue(s), we analyzed the 1.2 μ s simulated structures of *H. pylori* Mn²⁺- or Co²⁺-arginases. In both structures, Glu155 makes contact with Ser152. Analysis reveals that Glu155 makes additional contact with Lys57. This suggests that the Glu155-Lys57 contact may play a role in catalytic function. We prepared a Lys57Ala mutant and performed its kinetic assay.

Interestingly, its catalytic efficiency decreased 16-fold than that of the wild-type. We also prepared a double mutant, Lys57Ala/Ser152Ala. As expected, this mutant did not exhibit detectable activity, suggesting that the Lys57-Glu155-Ser152 interactions play a crucial role in catalytic function.

The interactions involving Lys57-Glu155-Ser152 are extremely crucial to catalysis

We performed the metal-binding assays to determine whether the decrease in the catalytic function of the above mutants was not due to the defect in the formation of a bimetallic center. Similar to wild-type, these mutants can bridge two metal ions. We also determined their substrate binding affinity. The above mutations do not affect the substrate binding. Thus, the loss of catalytic activity is caused by the defect in catalysis.



Lys57-Glu155-Ser152 interactions mediate the positioning of the insertion motif

To explore whether the interactions of Glu155 with Lys57 and Ser152 play a role in the positioning of the motif, we performed fluorescence anisotropy decay kinetic measurements for the wild-type and mutant holoproteins. In the absence of the Lys57 or Ser152 interaction with Glu155, the rigidity of the tryptophan side chain in either of these two mutants is reduced compared to the wild-type. This implies that the Glu155 interactions with both Lys57 and Ser152 play a role in the conformational rigidity of the Trp159 side chain and thus in the positioning of the insertion motif.

Structure-based virtual screening, molecular docking, and identification of small molecule inhibitor

Our study indicates that the insertion motif is critical to function through the interaction of its residue, Glu155 with both Lys57 and Ser152. Therefore, by targeting the motif and its surrounding region, we performed molecular docking-based virtual screening with the simulated structure of the *H. pylori* holoenzyme. Five molecules were shortlisted. Only compound C3 has an inhibitory effect on enzyme activity. We also determined the IC_{50} value for C3, which was nearly $129 \pm 15 \mu M$, suggesting that this compound has a moderate affinity towards the *H. pylori* enzyme. Interestingly, this molecule marginally affected the activity of human arginase, indicating that C3 has specificity towards inhibiting the *H. pylori* enzyme activity rather than the host counterpart.

Publications

Original peer-reviewed articles

1. Rashmi D, Gupta S, Kausar T, Sau AK* (2024) Helical domain of hGBP3 cannot stimulate the second phosphate cleavage of GTP. *J Biol Chem.* 300:105696.
2. Sadarangani V, Kalia A, Kausar T, Murarka P, Sau AK* (2023) Effect of the macromolecular crowding agents on the structure and function of human arginase-I, a therapeutically important enzyme. *J Phys Chem B.* 127:8749-8761.
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Reviews

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Protein Engineering Group



MOLECULAR MODELLING OF PROTEINS AND PROTEIN- LIGAND COMPLEXES

USING KNOWLEDGE-BASED APPROACHES AND ALL ATOM SIMULATIONS

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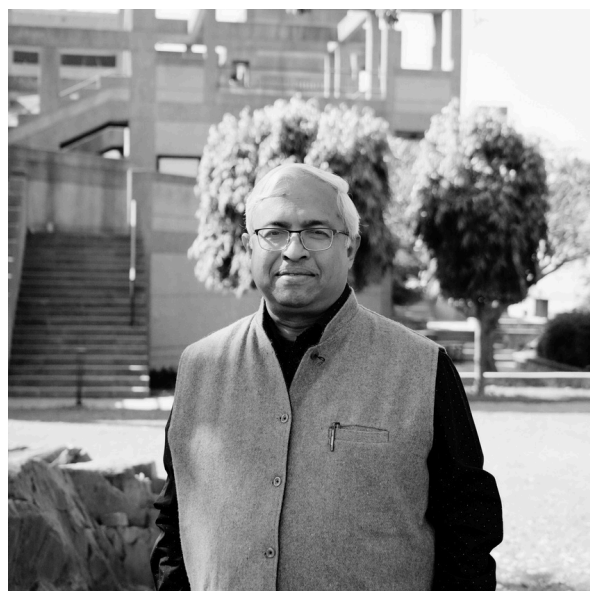
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The main theme of the research projects is to develop novel computational approaches for prediction of biomolecular structures, interactions and substrate specificity, and use them to analyse various genomes for identifying novel biosynthetic pathways, protein-protein interaction networks, and deciphering structural basis of various disease associated mutations.

The objectives of the major ongoing projects are **(A)** Structure-based analysis of oncogenic mutations in EGFR kinase and development of small molecule inhibitors for targeting mutant kinases, **(B)** Identification of novel resistance-associated mutations in *Mycobacterium tuberculosis* and analysis of the structural basis of drug resistance, and **(C)** Machine learning approach to predict the recognition specificities of TCR-pMHCs

Structure-based analysis of oncogenic mutations in EGFR kinase and development of small molecule inhibitors for targeting mutant kinases

Our earlier work highlighted how binding of allosteric inhibitors to the mutant kinases can potentially shift the population of conformers from active to inactive state. Now, we have developed a ML-based regression model for prediction of the quantitative binding affinity by utilizing structural features of receptor-ligand interactions available in PDBbind dataset for model training (Figure 1).

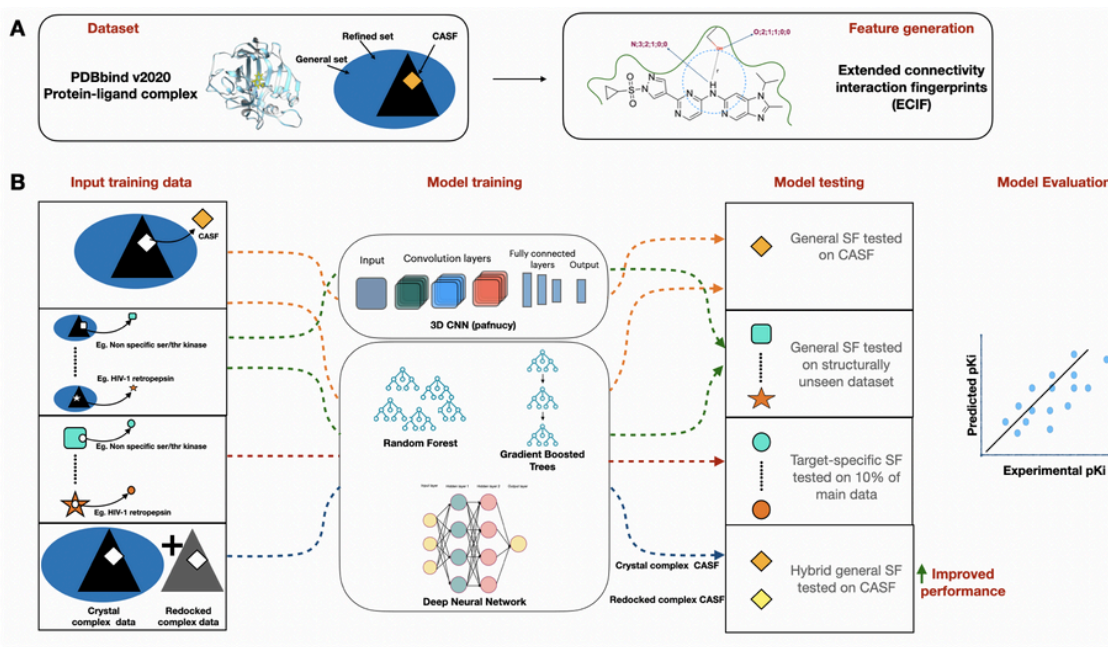


Figure 1. Overview and workflow of the ML-SF development and analysis. (A) PDBbind v2020 was used to train various ML models. The protein-ligand complex information was encoded into a feature vector with the help of extended connectivity interaction fingerprints (ECIF). (B) Different ML scoring functions were developed to analyse the effect of training data on the ML model's performance



In order to analyse the performance of ML scoring function (MLSF) on structurally unseen dataset, we developed ten different ML models removing the crystal complexes of a particular enzyme class one at a time. The PCC of ten models decreased, ranging from 0.41 to 0.76. Alternatively, developing target-specific scoring functions where the ML model was trained and tested on a specific enzyme class showed improved performance in the range of 0.60 to 0.88.

One of the interesting observations from our analysis was that while models trained on crystal structures of protein-ligand complexes showed poor performance on docked complexes, the performance of the ML-based scoring functions on the redocked CASF dataset improved significantly when the crystal structures in the training set were supplemented with redocked protein-ligand complexes. The final ML scoring function developed shows a better performance compared to conventional scoring functions and several other MLSFs.

Identification of novel resistance-associated mutations in *Mycobacterium tuberculosis* and analysis of the structural basis of drug resistance

Our AI/ML-based method for prediction of genotypic drug resistance (DR) for *Mycobacterium tuberculosis* had identified several DR associated mutations in new genes or new mutations in known resistance genes. Structural modelling of DR associated mutant proteins were carried out to understand mechanism of drug resistance. AI/ML methods predicted 10 completely new mutations in resistance genes (*katG*, *pncA*, *gidB* and *rpoB*), among them 4 were studied.

Using crystal structures taken from PDB (PDB ID: 2CCA, 3PII, 7EFE and 5UHG) and mapping the frameshifted part of these proteins showed that *katG* p.G124fs mutation affects the substrate access channel, important for substrate and heme interaction. Similarly, p.V131fs in *pncA* disrupts the Cys138-Asp8-Lys96 catalytic triad needed for pyrazinamide activation. R118fs mutation in *gidB* may disrupt SAM binding, impacting methyltransferase activity required for methylation of 16S rRNA, thus leading to streptomycin resistance.

The *rpoB* protein, a crucial RNA polymerase subunit involved in DNA transcription, is targeted by Rifampicin. Binding pocket analysis of wild type *rpoB* (target for Rifampicin) and *rpoB* p.F433dup mutant revealed that the insertion of an additional phenylalanine residue at position 433 resulted in a bulge within the binding pocket, which can potentially hinder the binding of rifampicin.

Machine learning approach to predict the recognition specificities of TCR-pMHCs

Understanding TCR-pMHC recognition is important for TCR engineering, vaccine development, and other immunotherapies. We developed peptide-specific (individual model for each epitope) and pan-specific (single model for all epitopes) ML models for prediction of recognition specificities of TCR-pMHCs. The peptide-specific models were developed for 53 different epitopes while the pan-specific model was developed with two different approaches, namely, Random split (random splitting of train and test data) and Strict split (Training data: Epitope contains ≥ 5 TCRs and Test data: Epitope contains ≤ 5 TCRs).



The AUC-ROC (0.86) and PR-AUC (0.89) of the random split model with BLOSUM62 feature and Random Forest algorithm showed significant predictive power. Additionally, we noted that the classical features performed better than the large language model-based features. The strict split model had ROC-AUC and PR-AUC values of 0.85 and 0.82, respectively. The strict split model, in which the test datasets were completely unseen during training, showed that the generalized model could predict the novel peptide-TCR pairs.



Bioinformatics Group



CHEMICAL GLYCOBIOLOGY

GLYCOFORM MODULATION, CARBOHYDRATE-BASED DRUG DESIGN, AND GLYCOMICS

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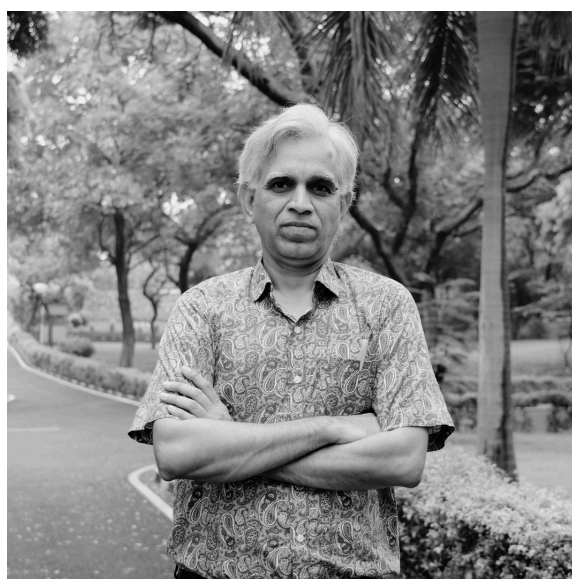
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Living systems depend on four fundamental building blocks, viz., nucleic acids, amino acids, fatty acids, and monosaccharides. Glycans are biosynthesized, on proteins and lipids, using a variety of monosaccharides and display immense complexity and diversity due to stereochemistry, linkage isomerism, and extensive branching. Biosynthesis of glycoconjugates is governed by non-template driven processes and is affected by fluctuations in the availability of metabolic intermediates. In this regard, we strive to apply chemical biological methodologies for the development of small molecule probes and inhibitors for the manipulation of glycosylation in living systems with a goal to unravel their structure and biological functions.

A. Tools for the modulation of glycans

ManNAc analogues enhance sialyl Lewis-X (sLeX/CD15s) levels and cell adhesion

Extravasation of leukocytes, for both immune surveillance and inflammatory response, is governed by the interaction of E-selectin with the sLeX/CD15s (NeuAc α 2 \rightarrow 3Gal β 1 \rightarrow 4(Fuc α 1 \rightarrow 3)GlcNAc-R) (**Fig 1**). Loss of sLeX is associated with poor homing efficiency of hematopoietic stem cells and leukocyte adhesion deficiency disorders. We reasoned that ManNAc analogues carrying cycloalkyl moieties on their *N*-acyl side chain would result in the expression of NeuAc analogues with *N*-cycloalkyl moieties, which in turn could alter their interactions with sialoglycan binding proteins (SBP).

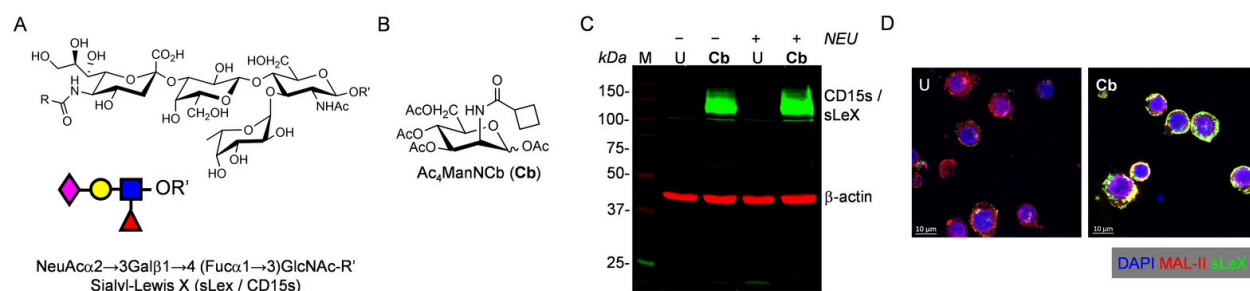


Figure 1. Enhancement of sialyl-Lewis X (sLeX / CD15s) levels in HL-60 cells through MGE. (A) Structure and SNFG nomenclature of sLeX, a tetrasaccharide, expressed on glycoproteins and glycolipids. (B) Structure of the ManNAc analogue, Ac₄ManNCb (**Cb**). (C) Cells were incubated with **Cb** (50 μ M, 72 h), along with untreated (U) control, subjected to *Vibrio cholerae* neuraminidase (NEU) treatment, lysed, and probed by duplex western blotting using anti-sLeX (CSLEX1; green) and anti- β -actin (red) antibodies. sLeX modified by **Cb** were found to be resistant to cleavage by NEU. (D) Confocal microscopy images of cells treated with **Cb**, along with control (U), fixed, permeabilized, and stained with anti-sLeX (CSLEX1) antibody (green), *Maackia amurensis* lectin-II (MAL-II) (red), and DAPI (blue); scale bar 10 μ m. Treatment with **Cb** induced higher levels of sLeX. Pink diamond, *N*-acetyl-D-neuraminic acid; yellow circle, D-galactose; blue square, *N*-acetyl-D-glucosamine; red triangle, L-fucose; SNFG, symbol nomenclature for glycans; MGE, metabolic glycan engineering.



Earlier results showed that the peracetyl *N*-cyclobutyl-D-mannosamine (Ac₄ManNCb, **Cb**) enhanced the sLeX/CD15s levels in HL-60 (human acute myeloid leukemia) cells by four-fold, while the wild-type peracetyl ManNAc (Ac₄ManNAc, **Ac**) did not show any effect; the straight-chain alkyl control analogue peracetyl *N*-pentanoyl-D-mannosamine (Ac₄ManNPent, **Pe**) showed a moderate increase of two-fold. HL-60 cells incubated with either vehicle or **Cb** (50 μM, 72 h) and subjected to treatment with *Vibrio cholerae* neuraminidase revealed that the **Cb**-treated samples were resistant to hydrolysis of modified sialic acids. This suggested that **Cb** could be used at a low concentration to achieve the desired modulation of cell adhesion.

Inhibition of O-glycosylation suppresses melanogenesis and melanoma tumor growth

PMEL17/gp100 is a glycoprotein essential for the structural integrity of melanosomes and predicted to possess 64-sites for O-glycans. Incubation of B16F10 (mouse melanoma) cells with Ac₅GalNTGC (**Tg**) (0-200 μM, 48 – 72 h), an efficient pharmacological inhibitor of O-glycosylation, resulted in a dose-dependent decrease in the melanin content compared to the controls. Evaluation of glycoforms of gp100 showed the abrogation of HMB-45 epitopes upon **Tg** treatment. Our results suggest that an appropriate O-glycosylation of gp100 is essential for normal pigmentation and that disruptions in the MTOG could result in pathological conditions.

B. Metabolic engineering of glycoconjugates in mycobacteria

A panel of analogues of 2AzGlc was evaluated for metabolic incorporation in *Mycobacterium smegmatis* for structure-activity relationships. Incubation of *M. smegmatis* with 2AzGlc, bioorthogonal labeling using DBCO-Cy5, followed by infection of RAW264.7 mouse macrophage cells showed the applicability of labeled *M. smegmatis* for imaging in an *in vitro* intracellular infection model.



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2. Sampathkumar SG, Parashar S, Tasneem A and Rautela J. Hexosamine compounds and methods thereof [US Patent Application Number: 18/248,503; Filed on 10/04/2023; WO Application Number: PCT/IN2022/050551; WIPO Publication Number: WO/2022/264171]



Chemical Glycobiology Group

STRUCTURAL STUDIES ON PROTEINS, DYNAMICS AND LIGAND INTERACTIONS USING NMR

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Fatty acids play an important role in cell metabolism, membrane biogenesis, and generation of signaling molecules. Though the overall biosynthetic machinery is similar in most microorganisms, subtle structural and functional differences exist at the molecular level that can be exploited for inhibitor design, specifically against a particular organism.

Thus, the broad theme of our research focuses on studying the biochemical properties, structure, dynamics, and ligand interactions of proteins involved in fatty acid metabolism and its associated pathways, viz. lipoic acid synthesis, biotin metabolism etc. of microorganisms in comparison with their human host.

Structure and function of proteins/enzymes involved in mitochondrial fatty acid synthesis

Fatty acid synthesis machinery has been broadly classified into Type I & Type II based on structural organization. All the components/enzymes of the type I pathway exist as domains of a large, multidomain, multifunctional, megasynthase complex. The pathway has been well characterized in mammals, and a few microorganisms like *Mycobacterium tuberculosis*, *Saccharomyces cerevisiae*, and *Candida albicans*.

The type II pathway is found mostly in prokaryotes e.g. *Escherichia coli*, *Bacillus subtilis*, *M. tuberculosis*, etc. In this pathway, the catalytic enzymes exist as monofunctional entities, and the growing acyl cargo remains well protected in the acyl carrier protein (ACP) core. Akin to prokaryotes, a few organelles like mitochondria and plastids also harbor a type II fatty acid synthesis pathway (FAS). Plastid FAS is functionally similar to prokaryotes, while the mitochondrial pathway remains to be characterized.

Mitochondrial ACP (mtACP) also known as NDUFAB1 (NADH dehydrogenase (ubiquinone) 1 beta subcomplex), is a nuclear-encoded protein, expressed with an N-terminal mitochondrial targeting sequence. Unlike prokaryote/plastid ACPs that primarily synthesize fatty acids, mitochondrial ACP are versatile, participating in several regulatory processes of the mitochondria in addition to fatty acid synthesis. Octanoyl-ACP, a product of this pathway is utilized for lipoic acid synthesis, while the longer products are involved in the assembly of mitochondrial complexes.

Cryo-EM structures of mitochondrial complexes show mtACPs as structural components, coordinating the assembly of several large multiprotein complexes of the mitochondria, viz. respiratory complex I, II & III, Fe-S cluster biogenesis machinery, and mitochondrial ribosome assembly. Deletion/knockout of mtACP results in a drastic decrease in these complexes. Given the multifaceted nature of mtACP, we have carried out extensive studies on *Leishmania major* ACP (*LmACP*) and its acyl-intermediates.

Sequence comparison of *LmACP* with bacterial, plastid, and mitochondrial ACP from different sources suggests that, unlike type II ACP, mitochondrial ACP displays high sequence conservation. To further understand how the differences in the sequence of mitochondrial ACP with the canonical type II ACP manifest in their function, *LmACP* acyl-intermediates were biochemically characterized using NMR.



Notably, the amide chemical shift changes upon acylation were extremely small in C_8 -*LmACP* (Dd C_8 -dholo) compared to C_8 -*EcACP* (Dd C_8 -dholo). Notably, in the $^1H^{15}N$ HSQC spectra of C_8 -*LmACP* (Dd C_8 -dholo), overall changes were extremely small, and approx. 3/4th of the peaks did not display a change in chemical shift upon acylation. In contrast, most of the peaks in the *EcACP* spectra displayed large chemical shift perturbations compared to their holo-form. Also, the backbone structure of *LmACP* displayed major differences with other type II ACPs, especially in helix I and loop I in the crystal structure. Using a mutagenesis approach, we observed that Leu 34 is crucial for the overall fold of *LmACP*.

The CastP server disclosed a relatively smaller hydrophobic cavity of *LmACP* compared to other type II ACPs. This small-sized cavity, combined with the small chemical shift perturbations observed in the C_8 - or C_{12} -*LmACP* intermediates suggests only a marginal expansion of the cavity in the intermediates. C_8 -chain hydrolysis of octanoyl-*LmACP* was also relatively faster compared to other type II ACPs, suggesting lower C_8 -chain stability. All these studies highlight major structural and functional differences between mitochondrial and prokaryote type II ACPs.

Publications

Original peer-reviewed articles

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Nuclear Magnetic Resonance-2 Group



THERAPEUTIC INTERVENTIONS IN CHRONIC DISEASES

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My multi-disciplinary research group is adopting an integrated approach to drug discovery that combines medicinal chemistry, basic biology, and biochemistry principles for an efficient drug design process. Interests of the group lie in identifying underlying principles in disease pathogenesis to discover new targets, designing molecular intervention strategies, and confirming the biological/therapeutic activities of the designed compounds/formulation. The small molecule/peptide regulators contribute to both drug development and understanding of biological systems in the human body.

Prion diseases (PrDs) are incurable, rapid and only infectious neurodegenerative disorders. PrDs are highly transmissible across the species, hence also known as transmissible spongiform encephalopathy (TSE). The main causative agent of PrDs is “Prions”, which leads to the trans-conformational conversion of the cellular form of PrP (PrP^C) to infectious scrapie form (PrP^{Sc}) by well-established protein-only hypothesis.

Cellular PrP is a highly glycosylated protein that undergoes folding and is post-translationally modified in the endoplasmic reticulum (ER). Manifestation of PrP^{Sc} via sporadically, genetically, or acquired form interrupts normal protein folding of PrP^C in ER and leads to the generation of unfolded, misfolded PrP and eventually formation of PrP^{Sc}. Chronic accumulation of prion-like misfolded proteins in the ER lumen perturbs ER homeostasis and generates ER stress.

Earlier studies on clinical human brain samples as well as on prion animal and cellular models have shown elevated ER stress owing to severe accumulation of unfolded PrP^C and PrP^{Sc}. These observations suggest a direct link between prion disease and ER stress. Accumulated PrP^{Sc}-induced ER stress causes chronic UPR activation, which is one of the fundamental steps in prion disease progression.

However, the role of various ER-resident proteins in prion-induced ER stress is elusive. This study demonstrated that ARL6IP5 is compensatory upregulated in response to chronically activated UPR in the cellular prion disease model (RML-ScN2a). Furthermore, overexpression of ARL6IP5 overcomes ER stress by lowering the expression of chronically activated UPR pathway proteins. We discovered that ARL6IP5 induces ER-phagy to reduce the PrP^{Sc} burden by releasing ER stress (fig 1A-C).

Conversely, the knockdown of ARL6IP5 leads to inefficient autophagic flux and elevated PrP^{Sc} burden (fig 1A-C). Our study also uncovered that ARL6IP5-induced ER-phagy depends on Ca²⁺-mediated AMPK activation and can induce 3MA-inhibited autophagic flux. The detailed mechanistic study revealed that ARL6IP5-induced ER-phagy involves interaction with soluble ER-phagy receptor CALCOCO1 and lysosomal marker LAMP1, leading to degradation in lysosomes. Here, we delineate the role of ARL6IP5 as a novel ER stress regulator and ER-phagy inducer that can effectively reduce the misfolded PrP^{Sc} burden (fig 1D-G). We reported that ARL6IP5 regulates ER stress homeostasis and eliminates prion aggregates by inducing ER-phagy. In a cellular model of prion disease, knocking down ARL6IP5 enhanced PrP^{Sc} accumulation, but upregulating the protein lowered PrP^{Sc} burden and improved prion-infected cell morphology.



ARL6IP5 undergoes phase separation to mediate ER-autolysosome/lysosomes interaction. The soluble ER-phagy receptor, CALCOCO1 degrades ARL6IP5-enriched PrP^{Sc}-containing ER sites in lysosomes. This is the first report indicating ARL6IP5 acts as an ER-phagy inducer to reduce prion burden by suppressing the chronically activated UPR. Our research opens up a new avenue of selective autophagy in prion disease and represents a potential therapeutic target.

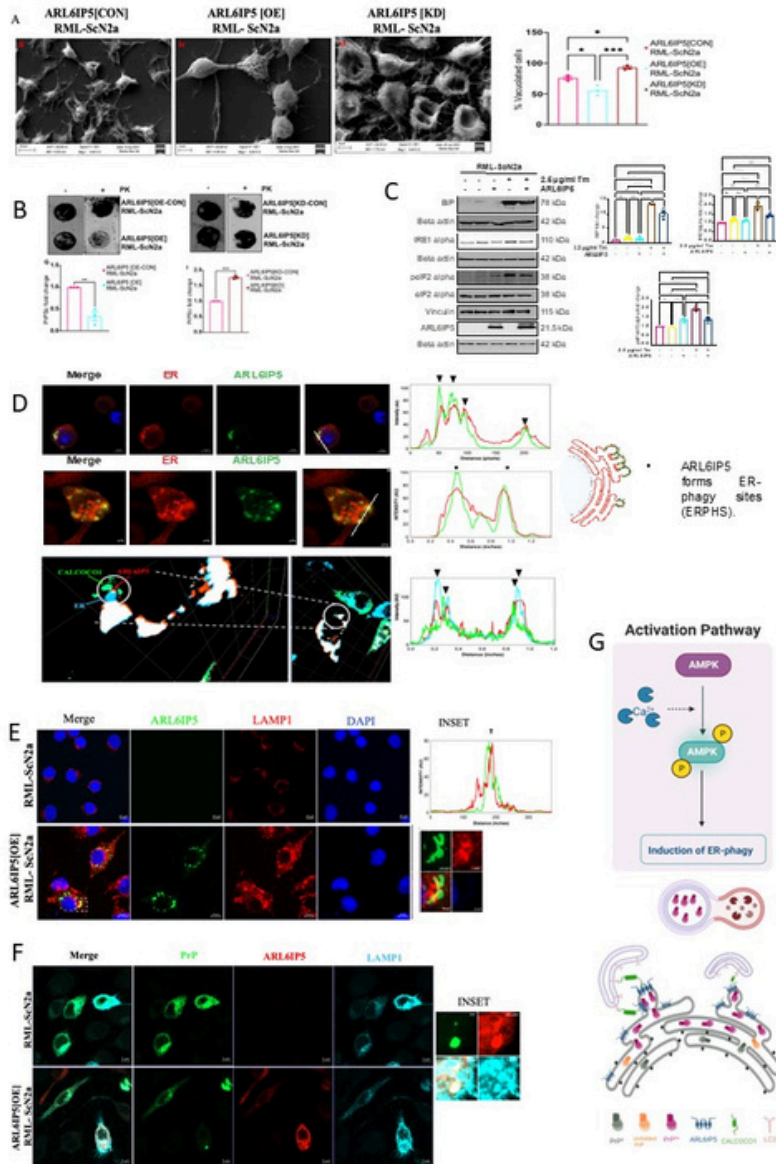


Figure 1: A novel ER stress regulator ARL6IP5 induces ER-phagy to ameliorate the prion burden.

(A) Representative SEM images were obtained after ARL6IP5[OE] and ARL6IP5[KD] in RML-ScN2a cells, with magnifications of 6KX, scale bars 4 μm, with quantification of vacuolated cells per condition. ~300 cells from three independent experiments were analyzed.

(B) Cell blots of PrP^{Sc} on ARL6IP5[OE] and ARL6IP5[KD] in RML-ScN2a cells compared to control along with quantification of relative PK resistant PrP^{Sc} level of the cell blot.



(C) Immunoblots showing effect of ARL6IP5[OE] on Tm-induced ER stress in RML-ScN2a, probed for BiP, IRE1alpha, pelf2alpha, eIF2alpha, and ARL6IP5 with loading controls beta-actin and vinculin with densitometric analysis of the immunoblots in the right.

(D) ARL6IP5 initiates ER-phagy in RML-ScN2a cells. Representative confocal images showing mCherry-ER and GFP-ARL6IP5-mediated ERPHS formation in RML-ScN2a cells. Scale bars: 5 μm, ~10 cells from three independent experiments were analyzed.

Airyscan images showing ARL6IP5 (green) enriched ER sites (red) in RML-ScN2a cells. Imaged under live-cell conditions. Scale bars: 2 μm, ~10 cells from three independent experiments were analyzed. Line scans are intensity profiles of ARL6IP5 (green) and ER (red) from the drawn line. The arrowhead indicates colocalization. Cartoon showing ARL6IP5 (green) enriched sites of ER (red) forming ERPHS.

The representation shown was created with BioRender.com. lower (row 3) Interaction with CALCOCO1 is required for ARL6IP5-induced ER-phagy. Representative confocal images under live cell imaging conditions of RML-ScN2a cells co-transfected with GFP-CALCOCO1, mCherry-ARL6IP5 and pm-turquoise2-ER showing direct interaction between GFP-CALCOCO1 and mCherry-ARL6IP5 enriched turquoise-ER.

Scale bars: 5 μm. ~10 cells from three independent experiments were analyzed. Images are single slices from z-stacks. Line scans are intensity profiles of ARL6IP5 (red), CALCOCO1 (green), and ER (turquoise) from the drawn line. Arrowheads indicate the point of interaction. Three-dimensional rendering image created using ZEN software 3D imaging module.

(E) Co-immunofluorescence staining of GFP-ARL6IP5, lysosomes (LAMP1, red), and DAPI (blue) in RML-ScN2a cells. Scale bars: 10 μm. ~15 cells from three independent experiments were analyzed. Images are single slices from z-stacks. (I) Line scans are intensity profiles of ARL6IP5 (green) and LAMP1 (red) from the drawn line. The arrowhead indicates colocalization.

(F) . (L) Representative confocal images showing control RML-ScN2a cells expressing full-length GFP-PrP, pm-turquoise2-LAMP1 and RML-ScN2a cells co-expressing mCherry-ARL6IP5 with full-length GFP-PrP, pm-turquoise2-LAMP1. Scale bars: 5 μm. ~25 cells from three independent experiments were analyzed. Images are single slices from z-stacks. The inset shows localization of PrP in LAMP1 positive puncta.

(G) ARL6IP5 promotes ER-phagy through Ca²⁺/AMPK pathway. Schematic illustration of ARL6IP5-mediated degradation of prion burden by ER-phagy.

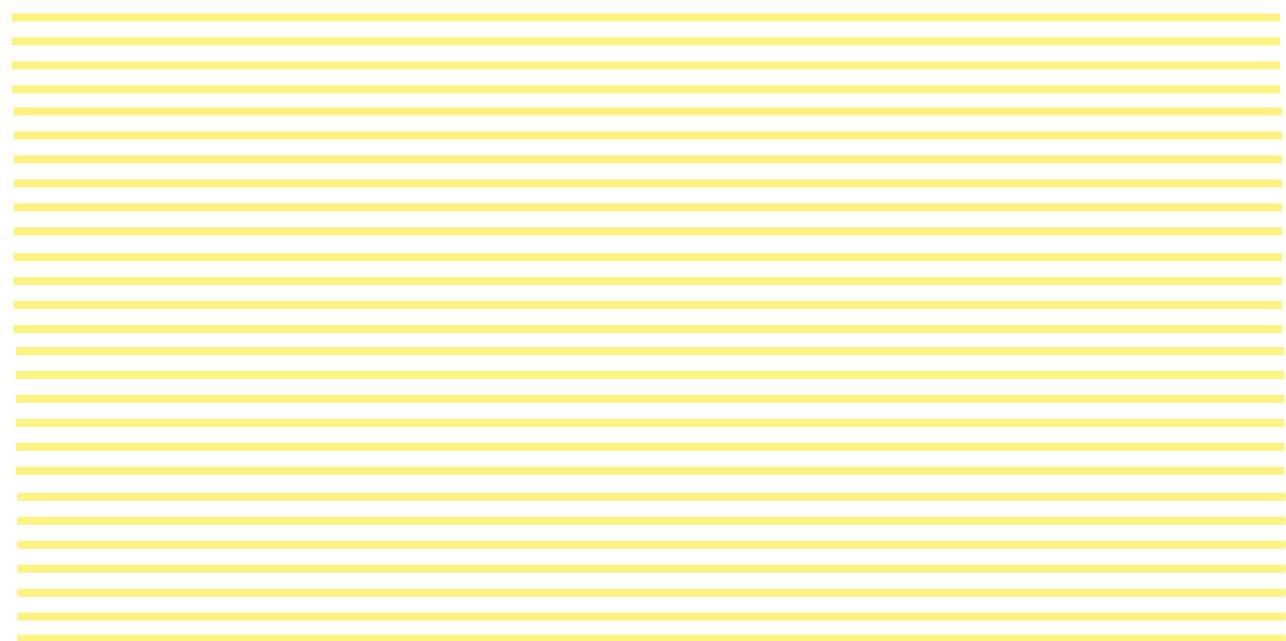
Publications

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1. Arora N, Hazra J, Roy S, Bhati G, Gupta S, Yogendran K, Chaudhuri A, Sagar A, Rakshit S* (2024) Emergence of slip-ideal-slip behavior in tip-links serve as force filters of sound in hearing. Nat Commun. 15:1595.
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Molecular Science Group



STRUCTURAL AND DYNAMIC STUDIES OF ANTIGEN-ANTIBODY AND HOST- PATHOGEN INTERACTIONS

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The theme of our laboratory is to understand the role of structure, allostery, and dynamics in the antigen-antibody/host-pathogen interactions using the combination of NMR spectroscopy, X-ray crystallography, and molecular dynamic simulations along with other biophysical and biochemical techniques. We are also pursuing the structural, functional, and dynamic studies on viral proteins (using dengue virus and SARS-CoV-2) and their interacting host proteins (such as calmodulin, phosphatases, and kinases) to elucidate the molecular basis for such interactions.

A. Structural/Dynamic studies on antigen-antibody interactions

In this project, the molecular basis for the antigen-antibody interactions using the glycoprotein E DIII domain of dengue viral protein as a model system will be elucidated to identify the similarities/differences among the four DENV serotypes. The key questions are:

- (i) Can solution NMR spectroscopy be used as a fast and reliable method for the characterization of epitopes in DENV serotypes, that are inaccessible by other methods?
- (ii) Does the E protein of DENV serotypes switch between different conformations, one of which is selected by the antibodies (conformational selection) or do the antigens adopt different conformations upon binding to antibodies to enhance their binding (induced fit)?
- (iii) What is the role of highly flexible regions of the DIII domain in the glycoprotein E of DENV serotypes, and how do they influence the dynamics of antigen-antibody interactions?
- (iv) Is it possible to develop small synthetic binding proteins to mimic the function of full-length neutralizing antibodies?
- (v) Is it possible to identify small molecule inhibitors that inhibit the DIII domain of all DENV serotypes by in-silico drug screening?

B. Molecular basis for host-pathogen interactions

In this project, we propose to study the interactions between viral and human proteins that play a crucial role in viral infection using DENV and SARS-Cov-2 proteins as model systems. The key questions are:

- (i) What is the molecular basis for the substrate specificity of protein phosphatase 1 in mediating the phosphoregulation of SARS-CoV-2 viral transcription?
- (ii) What is the role of phosphorylation in the interaction of the N protein of SARS-CoV-2 with RNA, and how it aids in the distinction between viral and non-viral RNA?
- (iii) What is the role of phosphorylation in the structure, allostery, and dynamics in the RNA binding domain of SARS-CoV-2 N protein with RNA?



Publications

Original peer-reviewed articles

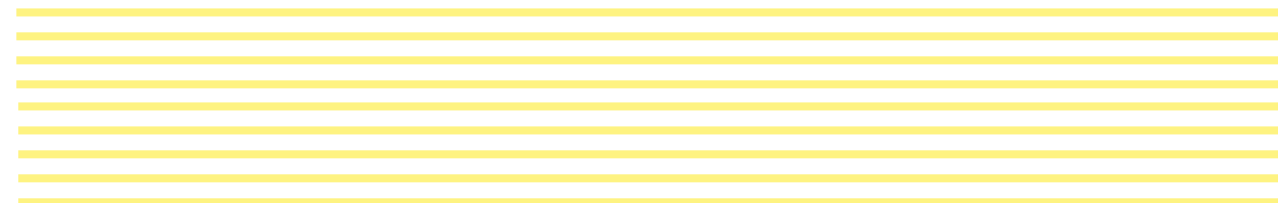
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Integrative Structural Biology Group



DESIGNING NEW ANTI-TB MOLECULES THROUGH STRUCTURAL AND COMPUTATIONAL BIOLOGY APPROACH

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My laboratory majorly aims at deriving mechanistic understandings of the function of metabolic pathways enzymes of *Mycobacterium tuberculosis* (*Mtb*), the organism that causes human tuberculosis (TB). Furthermore, we intend to develop novel anti-TB small molecules by integrating structural, biochemical, computational biology, and *in vivo* studies to address the drug resistance crisis effectively. In this regard, we primarily focus on studies pertaining to enzymes of *Mtb* histidine biosynthesis. Briefly, *Mtb* biosynthesizes Histidine *de novo* from 5-phosphoribosyl-1-pyrophosphate employing 10 enzymes through 10 distinct steps. The essentiality of this pathway for *Mtb* to mount a sustained TB infection in mouse models combined with its absence in humans makes this pathway an important anti-TB drug target.

Designing new anti-TB molecules employing structural and computational biology approach

Every living organism needs amino acids to make proteins critical for various cellular processes. However, different organisms fulfil their amino acids requirements by various means. For example, humans do not make nine amino acids *de novo*, therefore they rely on external sources such as dietary source for these amino acids; whereas *Mtb* possesses *de novo* pathways to biosynthesize all amino acids. A vast amount of mechanistic and genetic studies in the past several years on *Mtb* amino acids biosynthesis pathways particularly on Histidine (His), Arginine, Methionine and Tryptophan underline the criticality/essentiality of these amino acids for bacterial growth and therefore for mounting a sustained TB infection.

Notably, using genetics and immunological studies, we have shown that *Mtb* fulfils its His requirement mainly through its *de novo* biosynthesis pathway. IGPD (imidazole glycerol phosphate dehydratase), an enzyme that catalyzes the sixth step of the His pathway, has been an important anti-herb, anti-bacterial and anti-fungal drug target. A vast number of efforts particularly in the area of developing potent herbicides targeting IGPD has led to the discovery of an ample number of small molecules. Our earlier studies and reports from other groups suggest that triazole and imidazole derivative compounds have better prospects of inhibiting the function of IGPD. The 3D experimental structure of this enzyme from *Mtb* has been elucidated by our group and from other organisms by others.

The results from our recent high-resolution crystal structure show that the functional unit of the enzyme forms a multi-subunits complex by forming a 24-meric assembly with 24 identical active sites. By utilizing this structural information to identify enzyme-specific small molecule inhibitors, we constructed a library comprising of triazole-scaffold compounds and calculated the binding affinity of each of these compounds with IGPD. The binding scores together with their absorption, distribution, metabolism, and excretion properties suggested that these molecules possess anti-bacterial potential. A few of these molecules were synthesized commercially and their binding affinity and specificity were evaluated by determining high-resolution crystal structures and carrying out biochemical studies. Further, their *in vitro* and *in vivo* efficacies were investigated. The results from these studies show that a number of these molecules exhibited anti-bacterial activity and a significant lowering of the bacterial burden in both lungs and spleen relative to the untreated animals was observed. Our studies demonstrated that disrupting the function of Histidine biosynthesis promises new prospects in curtailing *Mtb* infection.



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Original peer-reviewed articles

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Structural and Functional Biology Group



DESIGN AND SYNTHESIS OF SMALL MOLECULES TO ACT AS NON-KINASE INHIBITORS IN CANCER CELLS

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Our laboratory is a drug designing laboratory and dedicated for designing of several serine proteases inhibitors especially HGFA, hepsin, and matriptase. In detail the overexpression of the growth factor hepatocyte growth factor (HGF) by mesenchymal cells contributes to the development of cancer and resistance to treatment. The cysteine proteases HGFA, hepsin, and matriptase are responsible for converting Pro-HGF to HGF. Our laboratory will use X-ray, computational and chemical tools to design peptide-based inhibitor libraries and understand how they interact with enzyme-binding pockets. Our project will involve the production of recombinant HGFA and binding assays. Further, we will explore biochemical assay to understand the proteolysis process of pro-HGF to HGF in the presence or absence of promising peptide inhibitors. We will perform X-ray crystallography of promising candidates for understanding binding patterns in the catalytic pocket. Further, functional assays like phosphorylation measurement in cancer cells would be performed in a dose-dependent manner to identify promising therapeutic candidates and develop structure-activity relationship of designed molecules. Finally, the promising candidates will be selected for animal studies.

Objectives

1. Design of inhibitor libraries using computational and chemical tools to explore their interaction within enzyme binding pockets.
2. Solution phase synthesis of designed inhibitors as in substrate-based, peptide-based inhibitors.
3. Expression and purification of HGFA serine protease domains and Km determination using substrate.
4. Binding assay and Biochemical assay to identify promising candidates with subsequent use of X-ray crystallography for understanding binding pattern in catalytic pocket.
5. Functional assay: c-MET phosphorylation measurement using breast cancer cell lines treated with HGFA-processed pro-HGF followed by selection of promising candidates for dose-dependent studies. Further, selection of promising candidates for animal studies.

Publications

Review

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Drug Design Group



COMPUTATIONAL APPROACHES FOR ANTIGEN DISCOVERY AND VACCINE DESIGN

Principal Investigator

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Our lab is interested in understanding the immune system through computational means, leveraging data-driven approaches. Our main interest lies in investigating how immune effector molecules such as T-cell receptors and antibody interact and recognize antigens. To this end, we aim to develop computational tools for predicting epitopes and assessing their immunogenicity.

We will use these tools in our broad research program which encompasses the development of computational frameworks for the identification of neoepitopes in various cancers using omics data and predicting their immunogenicity. These neoepitopes are crucial for designing cancer-specific vaccines. We are also developing computational pipelines for analyzing high-throughput omics data from cancer patients, utilizing publicly available datasets.



We have established computational pipelines for the processing of Next-Generation Sequencing (NGS) data and are developing AI/ML-based computational methods to predict the TCR specificity of antigenic peptides. These tools will make use of experimentally determined peptide-MHC-TCR interaction data, which include x-ray structures of MHC complexes with peptide and TCR, and TCR-seq data.

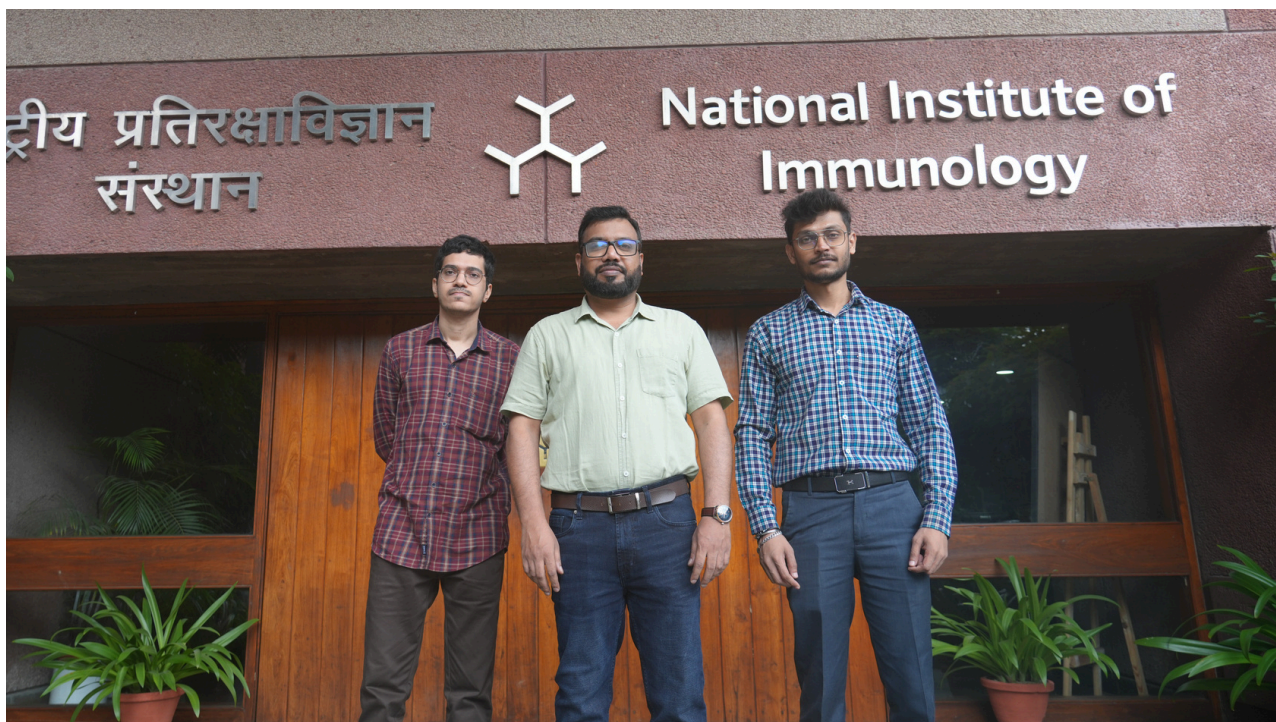
This is crucial for the accurate detection of neoantigens and their potential use in cancer immunotherapy. The tools developed will enhance the efficacy of immunotherapies and contribute to precision medicine in oncology. In this regards the lab will undertake the following tasks:

- (i) Develop a framework to store and analyses multi-omics data from cancer patients.
- (ii) Create computational tools for neoantigen detection in cancer patients.
- (iii) Establish a prioritization pipeline for neoantigen selection to be used as vaccine candidates.
- (iv) Develop a comprehensive neoantigen database.
- (v) Develop computational tools for related other immunotherapies such as CAR-T cell therapy

Over the past year, our lab has made progress in developing computational tools for antigen prediction. We have improved our computational tools for epitope prediction, MODPROPEP, which can predict epitopes for any allele using a library of structural templates. Approximately 300 structures of MHC-peptide complexes have been standardized and added to the template library of the software. We have also collected a large number of neoantigens from various public databases for training and benchmarking of the tool's predictive accuracy. This will aid in accurate neoantigen prediction crucial for personalized cancer vaccines. We plan to integrate advanced AI/ML techniques to enhance our predictive methodology further.

We are setting up computational pipelines for analyzing high throughput NGS sequencing data including RNA-seq, ChIP-seq, and single-cell RNA-seq data. These pipelines are fully automated and produce interactive output. This infrastructure is integral to our ability to store, analyze, and visualize diverse datasets.





Immuno-Informatics Group



GENETICS, CELL SIGNALING AND CANCER BIOLOGY

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DETERMINING THE SIGNALING AND REPAIR PATHWAYS THAT ARE ALTERED DURING GENOMIC INSTABILITY IN THE NUCLEUS AND MITOCHONDRIA

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In our research program, we study genomic instability in both nucleus and mitochondria. Multiple proteins which cause genomic instability either positively or negatively are studied. For example, we study the functions of caretaker tumor suppressors like BLM and RECQL4. Germline mutations in BLM and RECQL4 helicases result in two autosomal-recessive disorders with pronounced cancer predisposition, Bloom syndrome (BS) and Rothmund-Thomson syndrome (RTS), respectively. Both these helicases are intimately involved in many processes involving DNA metabolism and thus are ideal candidates to investigate the signaling and repair pathways that are altered during genomic instability and subsequently neoplastic transformation.

RAD54 and BLM helicase are known to play pivotal roles during homologous recombination (HR) repair ensuring the maintenance of genome integrity. We now show that an internal stretch of 32 amino acids in BLM was essential for its interaction with RAD54. Biochemically, we demonstrate that this interaction enhanced the functioning of RAD54 as a chromatin remodeler.

Functionally, in colon cancer cells this interaction caused an increase in the levels of active RAD51 and RAD54, enhanced HR, leading to decreased residual DNA damage in the cells. The phenomena were demonstrated to contribute to chemoresistance to three frontline drugs used currently for colon cancer therapy, namely cisplatin, camptothecin and oxaliplatin thereby driving enhanced tumorigenesis in cellular and preclinical colon cancer mice models.

Abrogation of this interaction using siRNA against either BLM or RAD54 led to a reversal in the growth of resistant colon cancer tumors. Using BLM ChIP-sequencing data BLM was found to be recruited to promoters of five key multidrug resistance (MDR) genes. Using one of these MDR genes, MRP2 as the prototype, increased BLM/RAD54 co-recruitment was observed in camptothecin-resistant colon cancer cells, which led to BLM-dependent enhancement of RAD54 chromatin remodeling on the reconstituted MRP2 promoter.

Having established a linkage between BLM-RAD54 interaction and therapy resistance, we screened the Prestwick small molecule library to revert camptothecin and oxaliplatin-induced chemoresistance. This led to the discovery of three FDA/EMA-approved candidates, which could disrupt BLM-RAD54 interaction *in vitro* and *in vivo* in a nanomolar concentration range. These small molecules bind to RAD54 and thereby abrogate the BLM-RAD54-dependent chromatin remodeling on G5E4 and MRP2 arrays.

Further, we provide evidence that each of these compounds reduced HR repair efficiency in resistant lines, diminished the anchorage-independent growth and abrogated the proliferation of tumors generated using camptothecin and oxaliplatin-resistant colon cancer cells in preclinical mouse models in BLM, RAD54 and MRP2 dependent manner. Thus, the three identified small molecules are viable candidates for adjunct therapy in colon cancer treatment.



Publications

Original peer-reviewed articles

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Signal Transduction II Group



EPIGENETIC REGULATION OF THE EUKARYOTIC GENOME:

ROLE OF CTCF AND ENHANCERS IN ORGANIZING CHROMATIN

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Chromatin structure and organization influence interactions between cis acting regulatory elements and trans-acting factors in the nucleus. The dynamism of these interactions and the regulatory mechanisms underlying them are important to understanding the intriguing complexity of gene regulation during mammalian development and effector functions. There is growing recognition that beyond the malfunctioning of proteins and lncRNA due to mutations, aberrations in chromatin organization lead to developmental disorders as well as metabolic diseases.

Chromatin organization and its dynamics during development are also critically important for VDJ recombination of antigen receptor loci and that leads to generation of vast and diverse Immunoglobulin and T cell receptor repertoire. We are investigating the nature of chromatin organization and its dynamics during lymphocyte development for regulation of transcription and VDJ recombination at the murine TCRb locus.

A. Role of CTCF in chromatin organization

Appropriate interactions between enhancers, promoters, insulators, transcription factors and chromatin remodeling factors are necessary for the regulation of nuclear processes. There is only a limited understanding of the mechanisms by which these *cis* and *trans* factors interact especially when the *cis*-regulatory elements are located at long distances from each other separated by several kilobases of intervening DNA.

In this context, CTCF, a DNA-binding protein having 12 Zn fingers, is particularly relevant. It has thousands of binding sites in mammalian genomes. CTCF, along with cohesion, is crucial for the establishment of chromatin loops that bring *cis*-regulatory elements in spatial proximity or, alternatively, insulate them from each other. Murine TCRb has 21 CTCF binding sites.

In previous years, we have investigated the role of CTCF-based chromatin organization in the regulation of TCRb locus by ChIP-qPCR and Chromosome Conformation Capture analysis (3C-qPCR). We hypothesized that CBS interspersed amongst V segments act as punctuating marks during the process of chromatin extrusion for defining dynamic chromatin loops that facilitate VDJ recombination at the TCRb locus.

Consistent with this, V segments located in the vicinity of CBS, are used more frequently than other V segments for VDJ recombination. Analysis of CRISPR/Cas9-based mouse mutants in which CBS have been deleted confirms their crucial importance for defining the usage of V segments. The data suggest that the CBS act as punctuating marks during chromatin extrusion and hence generate an ensemble of chromatin loops that support VDJ recombination.

Further, the orientation of CBS appears to be important for organizing chromatin to support VDJ recombination as has been shown for establishing domains that regulate transcription. Our observations demonstrate that CTCF binding in an orientation-dependent manner is critical for appropriate chromatin loop organization and consequent usage of V segments for VDJ recombination.



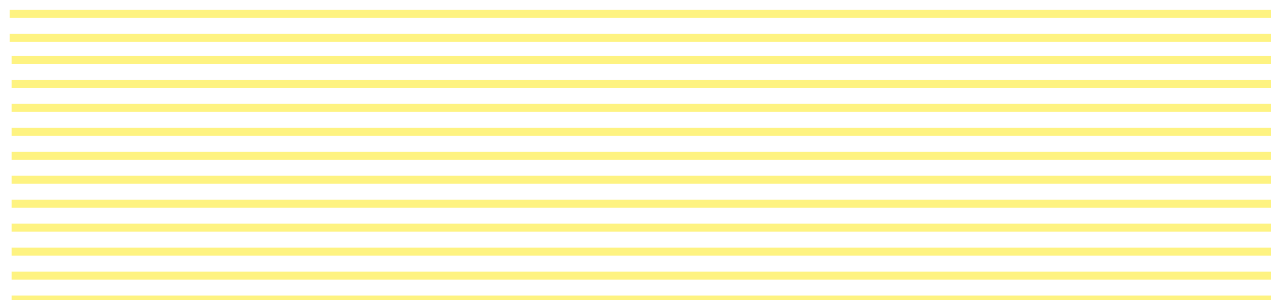
B. Mechanisms underlying enhancer activity

Significant changes in intranuclear positions during differentiation have been reported for several genes. Despite substantial enhancement in our understanding, aided by a combination of genomic, biochemical and microscopic technologies, the principles and mechanisms underlying nuclear organization and its link to gene regulation remain enigmatic. Our analysis revealed a novel role of activated enhancer Eb in locating the TCRb locus out of the chromosome territory (CT) in thymocytes.

Our observations have interesting implications for understanding mechanisms underlying enhancer-dependent activation of genes and set the stage for more elaborate investigations within the framework of the ANC-INC model of nuclear organization. Our observations also hint towards the relevance of repositioning away from CT for regulation of VDJ recombination – an aspect worthy of being examined at other antigen receptor loci.



Epigenetics Research Group



ROLE OF CELL SIGNALING IN EUKARYOTIC DEVELOPMENT

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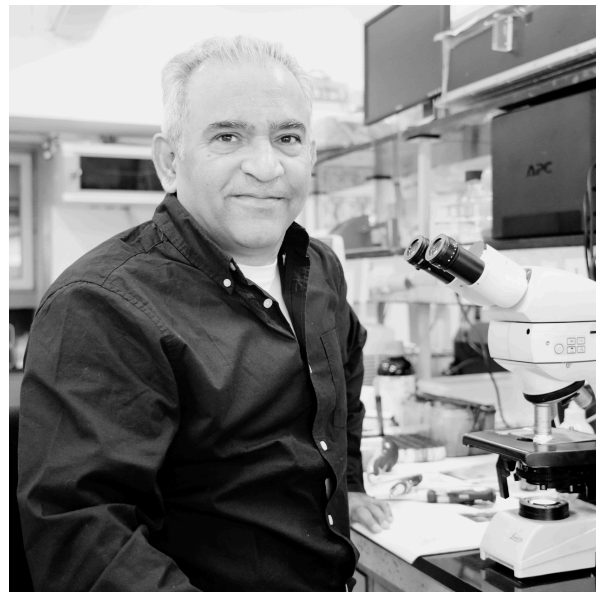
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It is well known that extracellular signals control biological responses in most eukaryotic cells by regulating specific intracellular signaling and trafficking cascades. We are interested in signaling and trafficking events in two diverse cell types: 1) Apicomplexan parasites like *Plasmodium falciparum* and *Toxoplasma gondii* and 2) mammalian neurons. A brief account of some of our recent studies in the above-mentioned areas is provided:

I. Dissection of intracellular signaling and trafficking cascades that operate in *Plasmodium falciparum* and *Toxoplasma gondii*

We are investigating the role of reversible phosphorylation in parasite division mediated by protein kinases (PKs) and phosphatases (PPs). We recently reported a novel pathway involving protein kinase PfPK2 (Rawat et al., Plos Pathogens 2023), which as mentioned in previous reports, is critical for host erythrocyte invasion by *P. falciparum*. More recently, we have been investigating phosphosignaling networks involved in the division of parasites. In this context, we have elucidated the role of protein phosphatase PfPPM2 and a protein kinase PfArk2 in parasite division and differentiation. Here are brief highlights of these studies:

A. Dissection of the role of PfArk2 in parasite division

PfArk2 is an essential protein kinase (Zhang, Wang et al. 2018) but its role in the parasite life cycle remains unclear. Since PfArk2 is refractory to gene disruption in *Plasmodium falciparum*, a conditional knockdown strategy was used to generate a parasite transgenic line of PfArk2 using rapamycin (RAP)-inducible dimerizable Cre (DiCre) recombinase-based approach.

Ultra Expansion Microscopy (UEXM) revealed that PfArk2 may be present at centrosome-like organelles called Centriolar Plaques (CPs) or MTOC before their duplication and subsequently it localizes to the spindle microtubules. PfArk2 depletion severely impaired parasite growth and it was striking to note that PfArk2-depleted parasites had abnormally enlarged nuclear size, and these "bulky" nuclei remained unsegregated.

As a result, the number of properly segregated merozoites was greatly reduced. Collectively, these and other studies suggested that PfArk2 may regulate the formation of mitotic spindles, which are critical for nuclear segregation and successful cytokinesis. In order to understand the mechanisms via which PfArk2 regulates parasite division, comparative phosphoproteomics was performed to identify its parasitic targets.

Several targets which have been implicated in cell division and nuclear functions emerged as possible targets of PfArk2, which included proteins implicated in kinetochore-related functions like Nuf2 and centromeric histone CenH3/CSE4. When PfArk2 was depleted, it resulted in a major loss of PfCenH3 foci in most parasites, which suggested that the centromere-kinetochore axis may be disrupted and/or may impair the function of PfCenH3.

These observations were interesting as they explained the loss of spindle formation mentioned above as mitotic spindles associate with the kinetochore complex and CenH3 plays an important role in the stabilization of the complex, which may be critical for spindle attachment and/or stabilization.



B. Elucidating the role of PfPPM2 in parasite development

In our quest to understand how protein phosphatase PfPPM2 regulates the development of malaria parasite, we had reported phosphoproteomic studies which revealed aberrant phosphorylation of several proteins involved in chromatin remodeling including HP1, Histone H3 and its variant H3.3. PfHP1 maintains the heterochromatin and is known to play a role in *var* gene silencing, parasite sexual conversion and also asexual development of the parasite.

We had reported that S33 present in the chromodomain (CD) of PfHP1 was found to be hyperphosphorylated upon PfPPM2 depletion. We have investigated the role of PfPPM2-mediated dephosphorylation of HP1. Upon depletion of PfPPM2, a significant reduction in sexual conversion was observed.

The transcription factor Ap2-g is a master regulator of sexual commitment, which is kept under a repressed state by HP1 and H3K9me3 and its expression is critical for the conversion of asexual forms to sexual gametocytes. PfPPM2 depletion caused a dramatic increase in both HP1 as well as H3K9me3 occupancy at the Ap2-g locus, which explained the reduced expression of Ap2-g in PfPPM2-depleted parasites and their decreased sexual conversion rates.

Strikingly, overexpression of phospho-deficient S33A mutant of HP1 caused the conversion of the majority of parasites to gametocytes. These data strongly indicated that dephosphorylation of HP1 at S33 by PfPPM2-mimicked by the S33A mutant is critical for the conversion of the parasite to sexual forms.

Collectively, these and other studies shed light on a novel mechanism involved in parasite differentiation to gametocytes, which involves the activation of PfPPM2 that results in the dephosphorylation of HP1. As a result, HP1's association with H3K9me3 is disrupted favoring euchromatin formation, which facilitates the expression of Ap2-g and other genes related to gametocyte formation and development.

II. Molecular mechanisms that regulate Cell Cycle Related Neuronal Apoptosis (CRNA)

We have identified miRNAs that are deregulated in neurons from the transgenic Alzheimer's Disease mouse model APP/PS1 (TgAD). Several of these may target cell cycle-related genes in response to A β_{42} in Alzheimer's Disease (AD) and are of interest to us as we are trying to understand mechanisms that contribute to aberrant activation of the neuronal cell cycle in AD and contribute to CRNA. miR-16-5-p overexpression using lentivirus in TgAD mouse brain prevented some AD-like learning and memory defects exhibited by these mice.

Detailed investigations revealed that the repression in miR-449a and miR-16-5p contributes to aberrant cell cycle re-entry and neuronal apoptosis. Further studies revealed that the deregulation of these miRNAs in TgAD neurons is epigenetically regulated.

Histone H3K27me3 was involved in the repression of these miRNA and inhibition of histone methyl transferase EZH2 restored their expression. The analysis of the promoter of these miRNAs revealed the sites for H3K27me3 occupancy, which was found to be significantly enriched in TgAD neurons.



Publications

Original peer-reviewed articles

1. Rawat RR, Gupta A, Antil N, Bhatnagar S, Singh M, Rawat A, Keshava Prasad TS, Sharma P* (2023) Protein kinase PfPK2 mediated signalling is critical for host erythrocyte invasion by malaria parasite. PLoS Pathog.19: e1011770.

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Eukaryotic Gene Expression Group



UNDERSTANDING MOLECULAR PERTURBATIONS INTRINSIC TO TUMORIGENESIS

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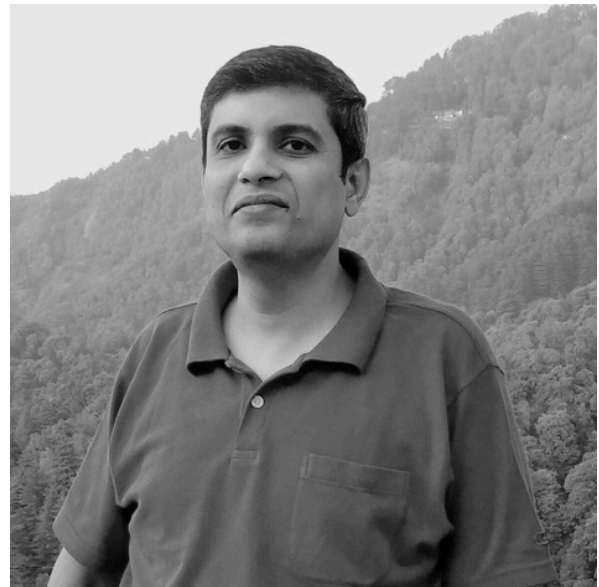
Shabnam

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The focus of the lab is to understand the molecular mechanisms underlying tumorigenesis. Here, we report the work carried out on two proteins viz. HDAC5 and PKM2 which determine malignant phenotype. Altered expression of HDAC5 has been linked to tumorigenesis. Limited non-histone substrate repertoire of HDAC5 restricts the understanding of its role as transcriptional regulator. PKM2 is a glycolytic enzyme with non-glycolytic nuclear oncogenic functions. It has been reported to translocate into the nucleus and function as transcriptional co-activator or as protein kinase. Thus, potential role of PKM2 in the dynamic integration between metabolic reprogramming and alterations in gene expression patterns during tumorigenesis is an area of notable interest.

A. Understanding the role of HDAC5 in transcriptional dysregulation during malignant transformation

HDAC5 has been reported to be upregulated across different cancer types. Hence, exploring its substrate repertoire can enhance our understanding of its role in tumorigenesis. To understand the molecular axis and determine the precise role of HDAC5, we performed an acetylome screen following HDAC5 depletion. Our analysis revealed increased acetylation of various proteins, prominent amongst which was PARP1. Poly (ADP-ribose) polymerase 1 (PARP1), is amongst the first signaling protein being recruited to both single-stranded breaks (SSBs) and double-stranded breaks (DSBs).

In addition to its role as a DNA damage responder, PARP1 acts as a potent modulator of transcription. The dynamic regulation of its DNA repair and transactivation functions is poorly understood. At the outset, we determined whether PARP1 is a bona fide HDAC5 substrate. We demonstrated that HDAC5 determines PARP1 acetylation at Lys498 and Lys521 sites. We next investigated the effect of PARP1 deacetylation on DNA damage response.

Our results suggest that HDAC5 modulated acetylation status determines PARP1-mediated DNA damage response. Previous studies suggest that genotoxic stress results in DNA damage-induced PARP1 auto-PARylation which is determined by its acetylation status. HDAC5-mediated deacetylation at the Lys498 site regulates PARP1 DNA damage response and facilitates efficient recruitment of DNA repair factors at damaged sites thereby promoting cell survival. Thus, our study establishes a preeminent role for acetylation status in determining PARP1 functions.

B. Investigating the role of PKM2 in tumorigenesis

Most cancer cells express high levels of PKM2 as it augments aerobic glycolysis and provides a discerning advantage for tumor growth. Thus, PKM2 is reported to be upregulated in multiple cancer types. However, the molecular details of mechanisms by which PKM2 harmonizes high energy demands with high anabolic activities to support tumorigenesis are yet unclear. In contrast to the established role of PKM2 in glycolysis, PKM2 has been reported to localize to the nucleus where it functions as a protein kinase or coactivator. To gain mechanistic insights into the oncogenic functions of PKM2, we used a biochemical approach to identify novel interactors of PKM2. Among the novel interactors, Matrin 3 was of particular interest.



Matrin 3 is an RNA-binding protein which plays an important role in transcription, RNA splicing and turnover. We have now established that PKM2 binds to and phosphorylates Matrin 3 at a threonine residue. We sought to unravel the specific Matrin 3 site that undergoes PKM2-dependent phosphorylation. Our results indicate that PKM2 interacts with and phosphorylates Matrin 3 at the conserved Threonine 239 residue upon EGF treatment. As phosphorylation is one of the important post-translational modifications, regulating protein stability, we investigated the role of PKM2-mediated phosphorylation in the context of Matrin 3 stability.

Our results indicated that Matrin 3 phosphorylation and Matrin 3 total protein levels were induced upon mitogenic stimulation in the presence of PKM2. Downregulation of PKM2 is associated with reduced invasive/migration potential and tumor suppression, as well as recurrence-free survival of patients. Matrin 3 expression has been reported to be upregulated in neuroblastomas which correlates with poor survival of patients. Thus, we plan to investigate the role of Matrin 3 in determining PKM2 oncogenic functions.

Publications

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Molecular Oncology Group



ELUCIDATING THE MOLECULAR MECHANISMS OF AGING AND INNATE IMMUNITY USING CAENORHABDITIS ELEGANS AS A MODEL SYSTEM

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We investigate signaling events that trigger changes in gene expression during aging. Our research is uncovering molecular mechanisms of dietary restriction. Specifically, we explore the interplay of kinases, transcription factors, and co-regulators downstream of the nutrient-sensing pathways that regulate longevity, metabolism, stress response, and pathogen resistance. Additionally, we examine how micronutrients influence life history traits, and how animals have evolved regulatory mechanisms to counteract them. We are also interested in investigating how organisms detect damage in somatic cells and regulate germline development and reproductive aging, focusing on the role of nutrient-sensing pathways. Furthermore, we are exploring phytochemicals to treat complications associated with metabolic disorders and aging.

1. Regulation of longevity and reproductive aging by the Insulin/IGF-1-like signaling (IIS) pathway

CYCLIND/CYD-1 depletion in IIS receptor mutant *daf-2* worms led to vulval defects (protruded vulva or vulvaless). Interestingly, *daf-16;daf-2* worms did not exhibit such vulval defects (DAF-16 is the FOXO transcription factor negatively regulated by IIS). Removal of *cyd-1* in *daf-2* (where FOXO/DAF-16 is activated) resulted in distorted vulval muscle structure. Activated DAF-16 plays a crucial role in causing vulval impairments following *cyd-1* knockdown (KD) in *daf-2*. AJM-1::GFP (adherens junction marker) mis-localized and its expression was diminished upon *cyd-1* depletion in *daf-2* (but not in *daf-16;daf-2*). Abnormal or absent expression of VPC (vulval precursor cell) markers (*cdh-3::gfp*) suggested incomplete or aberrant vulval cell divisions, that were restored in *daf-16;daf-2*. Transcriptomics analysis revealed significant downregulation of genes related to cell cycle, cell fate, oogenesis, and reproduction in *daf-2;cyd-1* RNAi worms (but not in WT). Together, we showed that the knockdown of *cyd-1* elicited a DAF-16-dependent somatic gonadal abnormalities, impacting oogenesis.

2. Studying inter-tissue cross-talk that regulates aging in response to different vitamin B12 content of diet

We investigated the role of serotonergic signaling in the kinase-dead *flr-4* mutant [*flr-4(-)*] phenotypes using a *tph-1* (*tryptophan hydroxylase*) mutant. In *flr-4(-);tph-1(-);Pcyp-35B1::gfp* worms, CyTP reporter expression was suppressed, while the increased lifespan of *flr-4(-)* was fully suppressed in *flr-4(-);tph-1(-)*. To confirm the role of 5-HT, we supplemented it to *flr-4(-);tph-1(-);Pcyp-35B1::gfp* worms, where GFP expression was initially suppressed due to lack of serotonergic signaling; remarkably, GFP expression was restored. Further investigations revealed that the 5-HT receptor MOD-1 acted downstream of *flr-4*, significantly impacting CyTP gene expression, osmotic tolerance, and longevity. We found that serotonergic neurotransmission via the Methionine cycle (Met-C)-p38-MAPK cascade functioned downstream of *flr-4*, as 5-HT supplementation restored GFP expression and osmotic tolerance in *flr-4(-);metr-1(-)* worms. We found that Met-C exclusively in the ADF serotonergic neurons enhanced CyTP gene expression and stress tolerance. Interestingly, the glycoprotein hormone/neuropeptide FLR-2, downstream of 5-HT signaling, connected signals from MOD-1-expressing interneurons to the intestine. *Flr-2* mutation suppressed GFP expression, osmotic stress tolerance, and lifespan in *flr-4(-)* worms, emphasizing FLR-2's role in this intricate network.



3. Deciphering the role of TORC2 in development and aging

In *C. elegans*, bacteria serve dual roles as dietary components as well as the microbiome. We explored interspecies crosstalk by studying the bacterial One-C cycle's impact on host physiology. *E. coli* One-C mutants (*metE*, *metF*, and *metH*) had no effect on stress tolerance of wild-type worms. However, the increased osmotic stress tolerance in the TORC2 regulatory subunit mutant *rict-1* worms [*rict-1(-)*] was suppressed. Methionine supplementation to these mutant bacteria (worms are unable to synthesize this essential amino acid and depend on bacteria) restored osmotic stress tolerance, while S-adenosyl methionine (SAM) did not.

Next, we investigated the role of the mitochondrial vitamin B12-dependent enzyme methyl malonyl CoA mutase (*mmcm-1*) in *rict-1(-)*. Knockdown of *mmcm-1* decreased osmotic stress tolerance, showing reliance on the canonical vitamin B12 pathway. Interestingly, acyl-CoA dehydrogenase (*acdh-1*) was not involved, suggesting independence from the shunt pathway. Knockdown of other transsulfuration pathway enzymes (*cbs-1*, *pcca-1*, or *mce-1*) also reduced *rict-1(-)* osmotic stress tolerance.

Publications

Original peer-reviewed articles

1. Sarkar GC, Rautela U, Goyal G, Datta S, Anand N, Singh A, Singh P, Chamoli M, Mukhopadhyay A* (2023) DNA damage signals from somatic uterine tissue arrest oogenesis through activated DAF-16. *Development* 150: dev201472. <https://doi.org/10.21203/rs.3.rs-1119544/v1>
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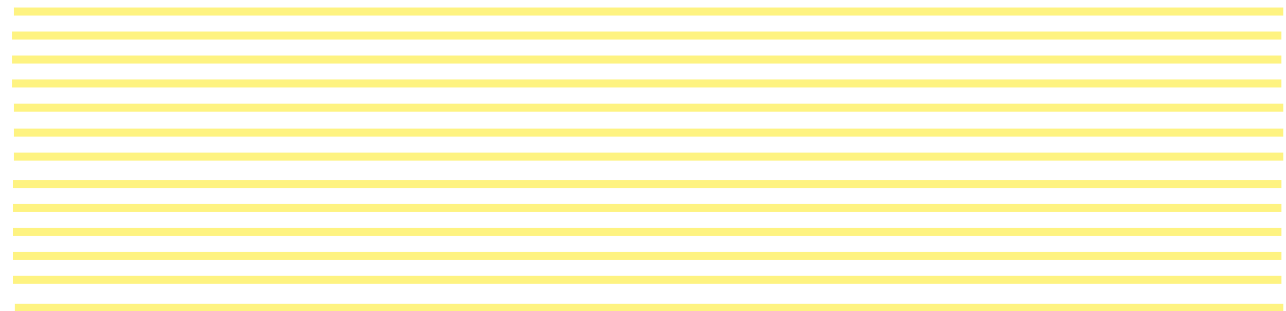
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[*Corresponding author]

Book Chapter

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Molecular Aging Group



ROLE OF METABOLISM-MEDIATED GENE REGULATION IN DEVELOPMENT AND DISEASE

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INSACOG consortium
TIFR-ARUMDA
Wastewater Surveillance Consortium
(DST-SERB)



Malnutrition is a major healthcare problem that affects the entire human population as either undernutrition or overnutrition. Both conditions pose significant risks for cardiovascular and metabolic disorders. In India, the National Survey of Family Health (NFHS) identified that adolescents are increasingly showing signs of both undernutrition (stunting) and overnutrition (obesity).

This double burden of malnutrition has been shown to be a risk factor for later-life metabolic disorders. We focus on different forms of malnutrition to understand the mechanisms of long-term defects. Our research will help to develop nutritional strategies (precision nutrition) to prevent the onset of metabolic disorders.

Weaning-associated dietary changes modulate gut health.

Early childhood is a vulnerable time in terms of mammalian nutrition. This stage is characterized by rapid growth and maturation of the body, and an imbalance in nutrition during this period can have a long-term impact on the individual's metabolic and cardiovascular health. Weaning is a process where the young offspring starts taking solid food apart from the mother's milk. The gradual shift from milk to completely solid food is also associated with changes in the macronutrient composition of the diet, as milk has higher levels of fat, and solid food has carbohydrates as the predominant carbon source.

The fat-carbohydrate ratio has been well known to affect gut health. We asked how the gut health will be affected by a prolonged milk-like diet in mice. To address this, we weaned the mice directly to a milk-based diet. We found that, compared to the control mice, which were weaned onto a regular chow diet (RCD), the mice weaned onto a milk-based diet (MBD) showed better protection when subjected to gut inflammation using Dextran Sodium Sulfate (DSS). We performed single-cell RNAseq analysis of these mice to reveal that a continued milk-based diet increased gut barrier function in these mice and reduced pathologic inflammation.

These changes were associated with alteration of the gut microbiota: MBD led to a battery of well-known gut-protective bacteria to increase in the colon. Indeed, the MBD feeding correlated with higher expression of various gut barrier-protective mRNAs and pathways. Taken together, we show that the prolonged milk-like diet is protective against gut inflammation, probably through maintaining good microbial flora.

Vitamin D deficiency leads to muscle regeneration defects.

We have previously shown that mice lacking VDR exhibit severe muscle atrophy. However, the molecular mechanisms by which vitamin D affects muscle regeneration are unknown. Now, we have established a diet model to study vitamin D deficiency in adults. To address this, the TA muscles of these mice were injured using BaCl₂. The expression levels of VDR (both mRNA and protein levels) were found to be temporally regulated during muscle injury and regeneration. From almost undetectable levels in the uninjured muscles, the expression peaks on 2-3 days post-injury followed by a decline in the levels by day 6.



This indicates that vitamin D signaling may play a role in the early phase of muscle regeneration. To test this, we subjected 7-week-old mice to a vitamin D deficiency diet (VDD) and subjected them to injury. We observed that the VDD diet led to decreased muscle cross-sectional area after injury, indicating a defect in regeneration. We will be analyzing the cellular and molecular pathways in muscle injury that are regulated by vitamin D.

Publications

Original peer-reviewed articles

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Molecular Genetics Group



TOWARDS UNDERSTANDING THE ROLE OF GUT MICROBIOTA AND THEIR METABOLITES IN THE CAUSATION AND TREATMENT OF COLORECTAL CANCER

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We are working on understanding the events leading to the development of colorectal cancer (CRC) through microbial metabolites which may provide novel insight into pathology and potentially lead to new therapeutic modalities. We are also engaged in investigating the anticancer role of gut microbiota-derived metabolites for developing therapeutic interventions for colorectal cancer. The development of an aptamer/MIP-based sensor/biosensor for the detection of gut bacteria and their metabolites is another research area in our laboratory.

A. Gut metabolite 4 Ethylphenyl Sulfate (4EPS) has selective deleterious and anticancer effect on colon cancer cells

4-ethylphenol (4EP) is well known for its implication in chronic kidney diseases but it is least studied for its role in cancer progression and treatment. Till now, there is no study on the effect of 4EPS on gut adenocarcinoma cells. The present study deals with the cytotoxic effect of 4-ethylphenyl sulfate on human epithelial adenocarcinoma cell lines i.e., HCT-116 as well as normal colon cells i.e., CCD 841 cells. Cells were treated with different concentrations of 4-EPS from 0.25mM to 10mM for three incubation periods i.e., 24hrs, 48hrs and 72hrs. After treatment of 24hrs, 48hrs and 72hrs, decreases in cell proliferation efficiency were observed, and these were most effective at 5mM and 10mM 4EPS concentration.

All tested subjects showed a significant decrease in cell viability, and cellular ATP content in time and dose-dependent manner, and a 10mM concentration of 4EPS at 72hrs proved to be most cytotoxic to cells. After being exposed to a concentration of 10 mM 4EPS, the viability of HCT-116 cells was seen to be 55%, 24%, and 7% after 24, 48, and 72 hours, respectively. Conversely, the normal cell line CCD 841 cells exhibited no toxicity when treated with 4EPS for 24 and 48 hr. But for 72 hr, at a dose of 5 and 10mM of EPS showed slight toxicity to normal cell lines. Based on the results of different assays, it can be reckoned that 4EPS has some implications in colorectal cancer and probably also with other types of cancer.

B. Culture-based bacterial profiling of colorectal cancer biopsies from Indian patients

The present work deals with the isolation and identification of bacteria from 10 colorectal cancer biopsy samples. Different media such as Brain heart infusion (BHI), Anaerobic Basal Agar (ABA), and Trypticase soy agar (TSA) and culture conditions have been manipulated to maximize the tapping of bacteria residing in biopsy samples. The predominant bacterial families identified were *Enterobacteriaceae*, *Enterococcaceae*, and *Streptococcaceae* across all samples. In tumor samples, *Enterobacteriaceae* and *Enterococcaceae* were most abundant, while in adjacent healthy tissue, *Enterobacteriaceae*, *Enterococcaceae*, and *Streptococcaceae* were prevalent. Interestingly, there were significant differences in bacterial profiles between individuals and between tumor and healthy tissue. Tumor tissue exhibited greater bacterial diversity than healthy tissue. Specifically, tumor tissues contained bacteria from the genera *Enterococcus*, *Escherichia*, *Klebsiella*, *Shigella*, and *Citrobacter*. Notably, *Streptococcus* was not found in tumor tissues. On the other hand, healthy tissues had bacteria from *Escherichia*, *Shigella*, *Enterobacter*, and *Streptococcus* genera, with *Klebsiella* being absent.



Publications

Original peer-reviewed articles

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Gene Regulation Group



NANOTECHNOLOGY-BASED IMMUNOTHERAPEUTIC PLATFORM FOR CANCER

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Our lab focuses on formulating a nanotechnology-based immunotherapeutic platform for inhibiting tumor growth. The sub-optimal expansion of antigen-specific T-cells and compromised presentation of tumour-associated antigens (TAA) by tumor cells or professional antigen-presenting cells (APCs) are the major challenges in cancer immunotherapy. We formulate nanoscale artificial antigen-presenting cells (a-APCs) that display peptide-major histocompatibility complex-I (p-MHC-I) and co-stimulatory molecules to expand antigen-specific T-cells in a valency (#p-MHC per nanoparticle) dependent manner for inhibiting tumor growth.

We also introduce nano-delivery platforms to enhance the TAA presentation by professional APCs. Additionally, we reprogram the tumor cells to present the TAA in the context of MHC-I to further strengthen the effectiveness of our approach.

Nanoscale a-APCs to inhibit the tumor growth:

Expansion of antigen-specific T-cells *in-vivo* in the presence of a tumor is one of the major hurdles in building effective immunotherapy. To address these challenges, we formulated a-APCs on polyethylene glycol-coated iron-oxide nanoparticles coupled with avidin for conjugating different valencies of tumor-specific p-MHC and co-stimulatory molecules. We evaluated these a-APCs in the Ova-B16F10 (expressing ovalbumin as tumor surrogate antigen) murine model, and we found that a-APCs with higher valencies of p-MHCs could effectively inhibit tumor growth, but not the a-APC-with the lower valencies, despite the dose of p-MHC remains same.

Next, we investigated whether this inhibition of tumor growth is associated with the expansion of antigen-specific CD8⁺ T-cells and identified that the higher valency a-APC significantly expanded antigen-specific CD8⁺ T-cells and also showed better infiltration in the tumor microenvironment (TME). Also, we observed that infiltrated antigen-specific CD8⁺ T-cells fall into the effector/effector memory (CD44⁺CD62L⁻) and central memory (CD44⁺CD62L⁺) subset with a comparable percentage. In the survival study, we found that higher valency a-APCs could offer better protection than lower valency a-APCs. Overall, our study revealed the optimum designing of a-APCs suitable for inducing anti-tumor T-cell responses to restrict tumor growth.

Reprogramming of tumor cells using chaperone inhibitor to present tumor-associated antigen:

Artificial APC induced CD8⁺ T-cell mediated anti-tumor immune responses further can be enhanced by the elevated presentation of TAA in the context of MHC-I. Inspiringly, we found that the Ova-B16F10 cells induced ~3-4-folds (IFN- γ) higher activation of cognate CD8⁺ T-cells and showed elevated expression of H-2K^b and co-stimulatory molecule (CD80) when treated with chaperone inhibitors. Collectively, data suggest that a low dose of chaperone inhibitor could increase the presentation of tumor-antigen on the MHC-I and subsequently activate the cognate T-cells.



Tumor-antigen-loaded mesoporous silica particles induce MHC-I mediated antigen presentation to promote CD8+ T-cell activation:

To complement the therapeutic potential of a-APC mediated expansion of CD8+ T-cells, we further design mesoporous silica particles with high (MSN-HI-amine), intermediate (MSN-IM-amine), and low (MSN-LO-amine) amount of surface amine to control the delivery of TAA to professional APCs. We found that *in-vitro* bone marrow-derived dendritic cells (BMDC) treated with ovalbumin-loaded MSN-HI-amine elicited significantly higher activation of Ova₍₂₅₇₋₂₆₄₎-K^b restricted CD8+ T cells in comparison to BMDC treated with MSN-IM-amine, and MSN-LO-amine. Next, we immunized mice with Ova-MSN-HI-amine and found that the immunized cohort showed significant inhibition of tumor growth and enhanced survival as compared to the control. We will further investigate to understand the details of the mechanistic events of this anti-tumor immunity.

Formulation of p-MHC-based tetramer for identifying antigen-specific T-cells:

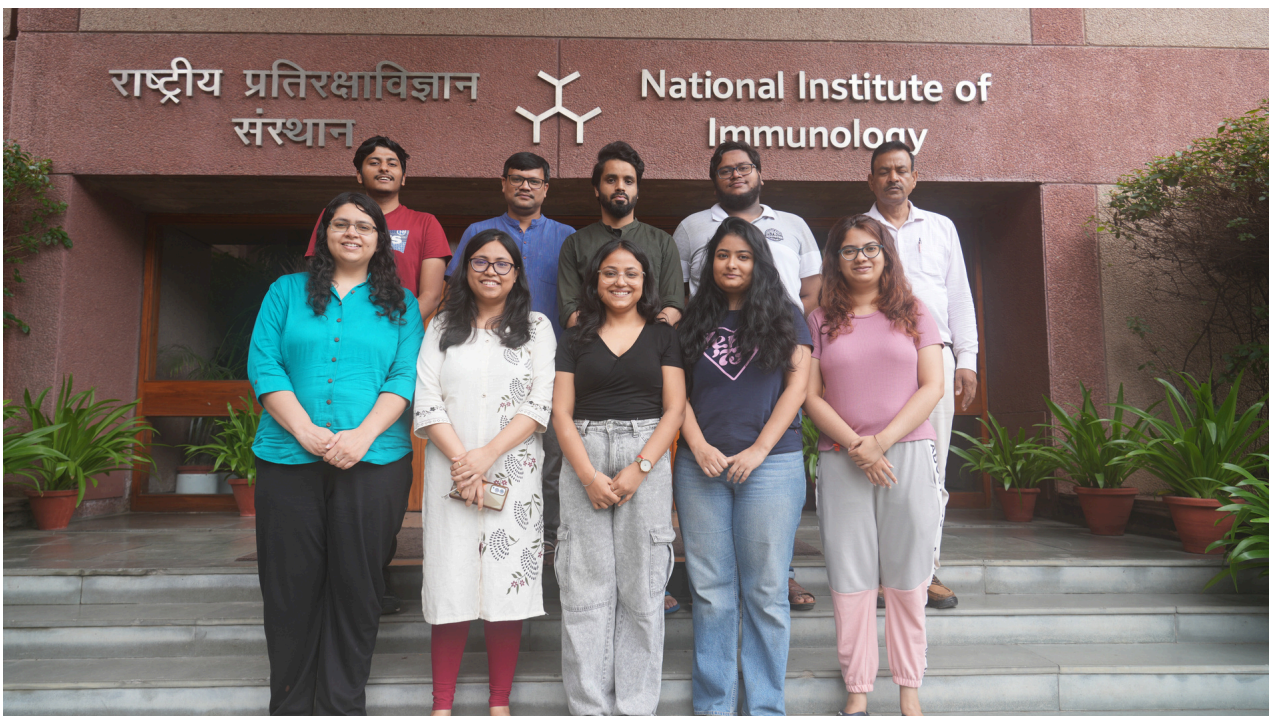
We have successfully established the facility for producing murine peptide-major histocompatibility (p-MHC) tetramer for identifying antigen-specific T-cells. We have produced different types of class-I p-MHCs (such as Ova₍₂₅₇₋₂₆₄₎-K^b, mTRP2₍₁₈₀₋₁₈₈₎-K^b and Influenza-NS2₍₁₁₄₋₁₂₁₎-K^b), capable of detecting disease relevant CD8+ T-cells. This facility can produce p-MHC based on customized peptides.

Publications

Original peer-reviewed articles

1. Deb S, Azharuddin M, Ramström S, Ghosh K, Singha S, Romu T, Patra HK (2023) Self-Reporting Theranostic: Nano Tool for Arterial Thrombosis. *Bioengineering (Basel)*. 10:1020.





Nano-biotechnology Group



CANCER EPIGENOMICS AND GENOMIC INSTABILITY IN IMMUNOTHERAPY

Principal Investigator

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Collaborators

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Histones are not only the packaging material of eukaryotic DNA but also control the dynamic nature of chromatin which acts as the signalling platform to regulate gene expression in cancer cells and immune cells. Our research program is to understand how epigenetic mechanisms contribute to cancer pathogenesis, genomic instability, and cancer immunotherapy. Using cellular and molecular biology approaches with genomics, we will identify mechanisms of histone mutations in glioblastoma and breast cancer. Furthermore, we propose to enhance the antitumor potential of Chimeric Antigen Receptor (CAR) T cells by manipulating chromatin modifiers. We aim to develop cellular and chemotherapeutics in cancer management.

In the year 2023-2024, we have set up a Cancer Epigenomics Laboratory (CEL). We are setting up a programme, which will investigate the role of chromatin in cancer and genomic instability. Additionally, we are working on the molecular biology of Chimeric Antigen Receptor (CAR) design for cancer immunotherapy.

A. Study of onco-histone and cancer-associated histone mutants

Next-generation sequencing of cancer cells has identified somatic recurrent mutations in all the histones (H3, H4, H2A, H2B and H1) with various frequencies in various tumour types. It is critical to decipher the oncogenic potential of histone mutations to discover any chemotherapeutics for cancer management. Importantly, well-characterized H3K27M (Lysine to Methionine), H3G34R/V (Glycine to Arginine or valine), and H3K36M (Lysine to Methionine) mutations are termed as onco-histone mutants because of their wide role from the defect in cellular differentiation, transcriptional dysregulation, perturbed epigenomic profiles to genomic instability. New mutations in histone H3 such as H3E73K/Q (Glutamic acid to lysine or Glutamine), H3E105K/Q (Glutamic acid to lysine or Glutamine), H3E97K (Glutamic acid to lysine) mutations are also identified in pan-cancer.

We are in the process to develop CRISPR Cas9 technology to introduce histone mutations in various cell types to dissect their contributory role on promoting tumorigenic phenotypes and unravelling the underlying molecular mechanism. We have engineered mutations within plasmids and transfected these constructs into mammalian cellular models. Subsequent investigations will evaluate the expressions of mutant histone H3.3 and its incorporation into nucleosomes. We have successfully introduced the H3 E73K mutation in fission yeast (genetically tractable model organism) to understand the functional implications of the histone mutation on cellular processes and chromatin dynamics.

B. Manipulating the epigenome of Chimeric Antigen Receptor (CAR) T cells to enhance its efficacy in solid tumours

Chimeric antigen receptor (CAR) T cells therapy has been successful in hematological malignancy but its role in solid tumour treatment needs active research. We are working to develop a detailed and robust pipeline for generating CAR-T cells against solid tumors.



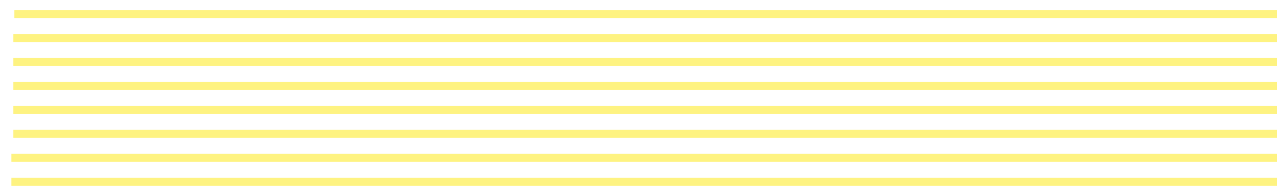
Through the verification, linearization, and recombination processes, we are generating a recombinant CAR vector with the anti-GD2 scFv sequence integrated in place of the anti-CD19 scFv sequence. The expected outcome is a verified recombinant CAR vector, confirmed by sequencing to ensure the absence of unwanted mutations or additional sequences at the junctions of anti-GD2 gene. Additionally, the purified Cas9 protein, validated by SDS-PAGE and western blot analysis, will further facilitate targeted genome editing to enhance CAR-T cell effectiveness.

C. Identifying novel genetic interaction of erasers/ readers genes with DDR pathway genes.

To investigate the role of Histone demethylases in the DNA damage response (DDR) pathway, we aim to investigate “genetic interactions between” histone demethylases (*epe1*) with DNA mismatch repair, mutL homologous gene (*pms1*). Camptothecin (CPT) cause DNA damage through replicative stress whereas Zeocin causes DNA damage through double-strand break. So, mechanisms of DNA lesion generation are different due to these drugs. *epe1Δ* and *pms1Δ* show differences in their growth profile on CPT and Zeocin. Therefore, we may speculate the crucial role of chromatin context in DNA damage.



Cancer Epigenetics Group



ANNEXURE 1

PUBLICATIONS

AND PATENTS

Original peer-reviewed articles

1. Ahmad M, Jha B, Bose S, Tiwari S, Dwivedy A, Kar D, Pal R, Mariadasse R, Parish T, Jeyakanthan J, Vinothkumar KR*, Biswal BK* (2023) Structural snapshots of *Mycobacterium tuberculosis* enolase reveal dual mode of 2PG binding and its implication in enzyme catalysis. IUCrJ. 10:738-753.

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Reviews

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Book Chapters

1. Nair T, Verma S and Mukhopadhyay A* (2023) Diet-gene interactions that regulate longevity and diseases. In: *Evidence-based functional foods for prevention of age-related diseases* (Eds. Surajit Pathak, Antara Banerjee, Asim K. Duttaroy, Springer, Singapore.) pp 37-59
[*Corresponding author]

Patents

1. Sampathkumar SG, Parashar S, Tasneem, A and Rautela J. Hexosamine compounds and methods thereof [US Patent Application Number: 18/248,503; Filed on 10/04/2023]

2. Nishu Dalal, Anil Kumar. Methods and compositions for treating colorectal cancer with indoxyl sulphate [US Patent Application Number: 18/539,826; Filed on 14/12/2023]

3. Vijayan V, Siddique IA, Gupta S. Carboxylated osteocalcin for treatment of amyloidosis or diseases associated with abnormal protein folding [Indian Patent Number: 478376; Granted on 07/12/2023]

4. Gupta S, Ahmed I, Nilakhe A, Upadhyay P. Novel compound modulating GSK-3 activity [US Patent Number: 11820764; Granted on 21/11/2023]



5. Panda AK, Prasad A. A method for efficient entrapment of water-soluble antibiotics in polymer scaffold to be used for wound dressing [Indian Patent Number: 468323; Granted on 10/11/2023]
6. Singh AP, Singh H, Kumar JD. A chaperone family protein-based malaria vaccine [Indian Patent Number: 508461; Granted on 08/02/2024]
7. Sultan F, Kochar M, Bhosale RS, Natarajan VT, Gokhale RS. Compositions having application against hyper-pigmentation [Indian Patent Number: 495136; Granted on 05/01/2024]
8. Solanki P, Lakshmi GBVS, Kumar A. A novel detection method for Trimethyl N-Oxide. [Indian Patent Number: 509887; Granted on 12/02/2024]
9. Polachira SK, Nair R, Jayalekha R, Gupta SK, Mishra NN and Agarwal A. Herbal microbicide formulation for preventing HIV [Indian Patent Number: 524274; Granted on 13/03/2024]
10. Sampathkumar S-G, Parashar S, Tasneem A, Rautela J. Hexosamine compounds and methods thereof [Indian Patent Number: 529123; Granted on 19/03/2024]



AWARDS, DISTINCTIONS AND FELLOWSHIPS

1. Dr Arnab Mukhopadhyay was elected fellow of the Indian Academy of Sciences Bengaluru (IASc), 2024.
2. Dr Arnab Mukhopadhyay received the prestigious Jagadish Chandra Bose National Fellowship, 2023.
3. Dr Sagar Sengupta was conferred the GK Manna Memorial Award Lecture 2023 by the All India Congress of Genetics and Genomics for work on Cancer Genomics and the Lalji Singh Memorial Award Lecture by the Society for Mitochondrial Research & Medicine for work in Cancer Biology.
4. Dr Sagar Sengupta received the prestigious Jagadish Chandra Bose National Fellowship for his work in the field of Biological Sciences and Cancer Biology.
5. Dr Sarika Gupta was selected for the award of the prestigious Tata Innovation Fellowship 2023-24.
6. Naveen Kumar received the James Carlyle Top Live Presenter Award at the 9th Science and Society Conference of the Beyond Sciences Initiative.
7. Arnab Kumar Sahoo and Antara Mondal jointly secured the first prize and Khushboo Chaudhary bagged the second prize in the poster presentation category at Nano-Bio Interface 2024 held at the School of Biotechnology, JNU, 18-19 February 2024.
8. Anirban Molla bagged the Best Poster Award at the 46th Annual Meeting of the Indian Biophysical Society held at TIFR Hyderabad and the University of Hyderabad, 15-17 March 2024.
9. Umanshi Rautela received the best poster prize at the Indian Society of Developmental Biologists Biennial Meet 2024 held at the Bangalore Life Science Cluster, 21-24 February 2024.
10. Witty Tyagi was selected as a winner of the 'Saransh: Thesis Presentation Competition 2023' of INYAS INSA.



11. Rimpay Arun and Aftab Mohammed received poster awards at the 92nd Annual Meeting of the Society of Biological Chemists held at IISc Bangalore, 18-20 December 2023

12. Satish Tiwari bagged the best poster award at the 50th National Seminar on Crystallography NSC50 held at CSIR-IMTECH, 22-23 November 2023.

13. Aishwarya Rajan received the best poster award and a citation at the 15th Annual Meeting of the Proteomics Society, International Conference on Integrated Proteomics: Applications in Food, Nutrition, & Health held at BRIC-NIPGR, 20-22 November 2023.

14. Sachin Kushwaha received the First Prize in Oral Presentation at the Golden Jubilee Conference of the Indian Immunology Society IMMUNOCON-50 held at AIIMS New Delhi, 5-8 October 2023.

15. Alvina Deka and Bhushan received abstract and poster awards at the American Association of Immunologist's conference "Immunology 2023" held at the Walter E. Washington Convention Center, Washington, 11-15 May 2023.



ANNEXURE 2

PHD DEGREES AWARDED TO NII SCHOLARS

S.no	PhD Scholar	Topic of Research	Guide
1.	Mr. Rahul Singh Rawat	Signalling pathways involved in the development of <i>Plasmodium</i> and <i>Toxoplasma</i>	Dr. R. P. Roy
2.	Ms. Charu	Chemical biology approaches for engineering of glycoconjugates in mycobacteria and applications in host-pathogen interactions	Dr. S. Gopalan Sampathkumar
3.	Ms. Rohini Tamang	Understanding the role of Cyclin F in tumorigenesis	Dr. Sanjeev Das
4.	Mr. Sumit Murmu	Structural and biochemical characterization of sortases	Dr. S. Gopalan Sampathkumar/ Dr. R. P. Roy
5.	Mr. Satish Tiwari	Targeting an essential metabolic pathway of <i>Mycobacterium tuberculosis</i> to design new anti-TB compounds	Dr. B. K. Biswal



6.	Mr. Asgar Ansari	CXCR5- T helper subset in humoral immunity establishment to dengue virus	Dr. Nimesh Gupta
7.	Ms. Kamble Kajal Gangaram	Delineating the role of ARL6IP5 in modulation of prion burden in the cellular model of Prion Disease	Dr. Sarika Gupta
8.	Mr. Manti Kumar Saha	Computational modeling of the pathogen- responsive signaling circuit	Dr. Soumen Basak
9.	Ms. Monika Mittal	Unraveling the molecular Basis for less GMP formation in hGBP2 and to elucidate its catalytic mechanism of GTP hydrolysis	Dr. Apurba K. Sau
10.	Ms. Ramya Venkataraman	Establishing and developing novel CAR-T cell strategies for cancer immunotherapy	Dr. Prafullakumar Tailor
11.	Ms. Sidra Khan	Delineating the signaling pathways in <i>Mycobacterium tuberculosis</i> and elucidating the mechanism of regulation	Dr. Vinay K. Nandicoori
12.	Ms. Sonika Bhatnagar	Understanding the molecular basis of biotinylation by Leishmania major Biotin Protein Ligase	Dr. Monica Sundd
13.	Ms. Anam Tasneem	Metabolic engineering of sialoglycans and profiling of glycosylation of β -human chorionic gonadotropin (β hCG) using hexosamine analogues	Dr. S. Gopalan Sampathkumar
14.	Mr. Aamir Khan	Understanding the mechanisms which cause mitochondrial dysfunction in cells lacking RECQL4, the protein mutated in Rothmund Thomson Syndrome	Dr. Sagar Sengupta/ Dr. Arnab Mukhopadhyay



SCIENTIFIC LECTURES

International Immunology Day

The 29th of April is celebrated as the International Day of Immunology worldwide to strengthen the public's awareness about immunology and its impact on individuals as well as public health and well-being. The day was celebrated at NII by hosting a public talk by Dr Amit Awasthi, Senior Professor, THSTI on 'T-cells in Health and Diseases'.

Apart from students and faculties of NII, several students/researchers from the Delhi-NCR region also participated in the event. The event was also streamed live on YouTube.



Faculty, staff, and research scholars of NII with Dr Amit Awasthi on International Day of Immunology



The 37th Foundation Day of NII

NII celebrated its 37th Foundation Day on 6 October 2023. The event featured the Foundation Day lecture entitled “Managing Non-Communicable Diseases: Harmonizing Technology with Task-Sharing”, which was delivered by Professor Nikhil Tandon, Head of Endocrinology and Metabolism, AIIMS New Delhi.

The event was attended by Prof GP Talwar, Founding Director NII; Dr Debasisa Mohanty, Director NII; Dr Alka Sharma, Scientist H, DBT; Dr Sanjay Mishra, Scientist H, DBT; other dignitaries from various research institutes and organisations; and the faculty, staff, and students of NII.

In addition to the lecture, a cultural night was also hosted to commemorate the occasion. The highlight of the 37th Foundation Day was the alumni meeting. It was a time for celebration with some reflection and reminiscence with the alumni of NII taking centre stage.



Prof Nikhil Tandon, Head of Endocrinology and Metabolism, AIIMS New Delhi



Felicitation of Prof Nikhil Tandon by Dr Debasisa Mohanty



Faculty, staff, scholars, and alumni of NII with Prof GP Talwar, Dr Dinakar Salunke, and Dr Debasisa Mohanty



PUBLIC LECTURES AT NII

Dr. Ashish K. Jha, Dean, Brown University School of Public Health, USA delivered a public lecture at NII on “From Crisis to Opportunity: The Transformative Power of Science, Innovation, and Partnerships in Global Public Health” on 13th November 2023. Dr. Ashish K. Jha is a global leader in pandemic preparedness and response who was appointed the White House COVID-19 Response Coordinator in March 2022. This talk was organized by NII in collaboration with the Department of Biotechnology and was attended by the science community of Delhi NCR.

Eric Joseph Rubin, MD, PhD, Professor of Medicine, Medicine-Brigham and Women's Hospital, Harvard Medical School delivered a public lecture on “ Safe but not too safe – Human challenge in TB” at NII on 29 September 2023. This was a well-attended lecture which was followed by a lively discussion on the advances and challenges in TB research. Prof Rubin interacted with researchers and students working on TB at this event.

Prof Anil K Gupta, the founder of the Honey Bee Network, SRISTI, GIAN, and the National Innovation Foundation-India, was on NII campus on 30 May 2023 for a public talk titled “Can healthy people, ecosystems, and grassroots innovations/knowledge systems teach us something new?” This was a great opportunity for students, researchers, and innovators to interact with Prof Gupta and better understand the nuts and bolts of the innovation, entrepreneurship, and intellectual property ecosystem.





Prof Ashish K. Jha (right) with Dr Rajesh Gokhale, Secretary DBT (left) and Dr Debasisa Mohanty, Director NII (centre)



Prof Anil K Gupta, the founder of the Honey Bee Network, SRISTI, GIAN, and the National Innovation Foundation-India



IMPORTANT SCIENTIFIC VISITS AND DISCUSSIONS

On 18 March 2024, Prof. Peter Jay Hotez, Dean of the National School of Tropical Medicine and Co-Director of the Texas Children's Hospital Center for Vaccine Development, and Prof. Maria Elena Bottazzi, Senior Associate Dean of the National School of Tropical Medicine and Co-Director of the Texas Children's Hospital Center for Vaccine Development, Baylor College of Medicine, visited NII to discuss research interests and explore potential collaborations in the fields of immunology research and vaccine development.



*Prof. Peter Jay Hotez and Prof. Maria Elena Bottazzi
with the faculty and research scholars of NII*



To promote collaboration between India and France in the field of infectious diseases and strengthen future disease preparedness, experts from the Department of Biotechnology including faculty from NII participated in the Indo-French Workshop on Infectious Diseases at the Centre National de la Recherche Scientifique (CNRS France), 5-7 February 2024.

On January 18, 2024, Dr. Giry Claire, General Director for Research & Innovation at the French Ministry of Research and Higher Education, led a French delegation to visit NII. During the visit, they had the opportunity to observe NII's advanced research infrastructure and engage in discussions with the Director and faculty members of NII.



Dr. Giry Claire, General Director for Research & Innovation at the French Ministry of Research and Higher Education with a French delegation at NII



On 4 November 2023, Prof Anna Philpott, Head of the School of Biological Sciences, University of Cambridge visited NII with Dr Vibhuti J Patel, Senior Associate Director International (South East Asia and Australia), University of Cambridge. They had an insightful exploration of scientific synergies and collaborative opportunities with the Director and faculty of NII.



Prof Anna Philpott visiting the Central Instrumentation Facility of NII with Dr Debasisa Mohanty

A group of scientists from the Institute of Bioresources & Sustainable Development (IBSD) and NII attended a Research Collaborative Meeting at Shillong on 1 November 2023 for “Translational Research on Medicinal Plants” of the Northeast region. India is, unfortunately, emerging as a global hub for diseases linked to dysregulated metabolism. Under this collaboration, both institutes envision harnessing the potential of traditional knowledge in addressing the burden of such diseases. Researchers of NII and IBSD will evaluate the medicinal properties of plants from northeast India in mitigating ailments associated with metabolic dysregulations. While the study has only been initiated, this collaborative program represents an important step in aligning some of NII’s efforts in validating traditional Indian medicines in standard laboratory settings.

Prof Janko Ž. Nikolich, Co-Director, Arizona Center on Aging, The University of Arizona visited NII on 10 October 2023 and delivered a talk on “Age-related dysfunction of immune responses against emerging and reemerging infections”. During this visit, Prof Nikolich had discussions with Dr Debabsisa Mohanty, Director NII and other faculty members leading to the signing of an MoU with the Arizona Board of Regents, University of Arizona on behalf of its 'Health Sciences Aegis Consortium for a Pandemic Free Future' to enhance biomedical research for human health & well-being through collaboration.



*Prof Janko Ž. Nikolich, Co-Director, Arizona Center on Aging
with Dr Debabsisa Mohanty, Director, NII*



FAREWELL TO

PHD STUDENTS

As the graduate students of the 2018 batch crossed the Rubicon, NII bid them a fond farewell. The farewell function for PhD students with Dr Debasisa Mohanty, Director NII and the staff scientists of NII was marked by the planting of tree and a special dinner for the outgoing students.



The PhD batch of 2018 with Director, Faculty and Senior Manager of NII



SCIENCE FESTIVALS AND EXPOSITIONS

NII Open Day: India International Science Festival 2023 Outreach

The National Institute of Immunology conducted an open day on 11 January 2024 on the theme of “India’s Vaccine Self-Reliance”. The open day was used as a platform to showcase the India International Science Festival 2023 and encourage the students as well as public at large to visit and participate in the festival.

The open-day program consisted of public talks, poster sessions, lab demos, sophisticated research facility visits, discussions, quizzes and games. Dr Shekhar Mande, Former DG of CSIR and National President of VIBHA delivered an online talk on “History of Biomedical Sciences in India” and interacted with the attending students.

Dr Nimesh Gupta, Faculty of NII, unpacked the science behind vaccines while illustrating the success story of India’s vaccine self-reliance. During the day, one of the main events was a poster session showcasing the projects and research of NII researchers. The topics covered a wide range, including immunology, infectious and chronic disease biology, molecular and cellular biology, chemical biology, structural biology, and computational biology.

Other events included visits to NII research facilities, games, and quizzes. The open day featured a special science exhibition and a demonstration by the National Science Museum, New Delhi. The open day saw the participation of over 150 students and teachers from schools and colleges of Delhi NCR.





*Glimpses from the IISF
Outreach Open Day of NII*



India International Science Festival 2023

The 9th edition of the India International Science Festival (IISF) 2023 was held at Faridabad, Haryana from January 17th-20th, 2024 at the campus of Translational Health Science and Technology Institute (THSTI) and Regional Centre for Biotechnology (RCB) of Department of Biotechnology in Faridabad. The theme of this edition of the festival was 'Science and Technology Public Outreach in Amrit Kaal'.

NII took part in this mega science festival, providing a platform to inspire the public, including students, educators, scientists, researchers, industry professionals, entrepreneurs, and science communicators. Many labs of NII showcased their work using posters. Some of the labs had also set up live demos.

The staff and students of NII also conducted games and quizzes for the visitors at the festival; these immunology-theme-based games and quizzes were used to talk to the public about important concepts in immunology and vaccinology.



Glimpses from NII's stall at the India International Science Festival



National Science Day 2024

The 28th of February, celebrated as the National Science Day to commemorate the discovery of the Raman Effect, is a day of honour for all associated with the scientific enterprise — an enterprise that contributes to the progress of knowledge and understanding.

Understanding and mitigating global environmental change, achieving innovations for improving public health, and creating technological solutions to widespread societal challenges—science drives it all. So, it would not be wrong to say Science is for Everyone.

In that spirit, the family of NII celebrated this day by hosting an open day on campus. In line with the theme for National Science Day 2024, "Indigenous Technology for Viksit Bharat", Prof. Anurag S Rathore, Institute Chair Professor from the Department of Chemical Engineering at the Indian Institute of Technology-Delhi, gave a public talk on "Opportunities for Contributing to Achieve a \$600 Billion Indian Bioeconomy by 2030".

Scholars from the National Institute of Immunology presented their work through posters and a series of flash talks. Approximately 100 undergraduate students from Delhi University attended these events and took part in science quizzes and games specially designed for them.



Prof. Anurag S Rathore, Institute Chair Professor from the Department of Chemical Engineering at the Indian Institute of Technology-Delhi



Global Bio India 2023

BIRAC's Global Bio India 2023 was a unique business networking platform for India's biotech R&D innovation and bio-manufacturing ecosystem and international stakeholders. The 3-day exhibition (4-6 December 2023) brought together researchers, innovators, entrepreneurs, policymakers, next-gen researchers, and science enthusiasts on one platform. Faculty, scholars and staff of NII participated in this exhibition with enthusiasm. The poster presentation topics ranged from vaccines and drug development to applications of artificial intelligence and machine learning in biology. In addition, there were immunology-based games and hands-on activities for the visiting students.



Glimpses from NII's participation in the Global Bio India 2023 exhibition

National Technology Week 2023

Every year, India celebrates May 11th as National Technology Day to commemorate the successful testing of nuclear weapons in Pokhran in the year 1998. In 2023, National Technology Week was held from May 11th to May 14th at Pragati Maidan, New Delhi. The theme for the year was 'School to Startup - Igniting Young Minds to Innovate'. The event was inaugurated by the Hon'ble Prime Minister Sh. Narendra Modi, who emphasized nurturing and providing platforms to young minds to inspire them to become future Technopreneurs. NII showcased its Science and Technology achievements, with interactions and potential collaborations with technopreneurs and researchers being the key highlights of the exhibition.



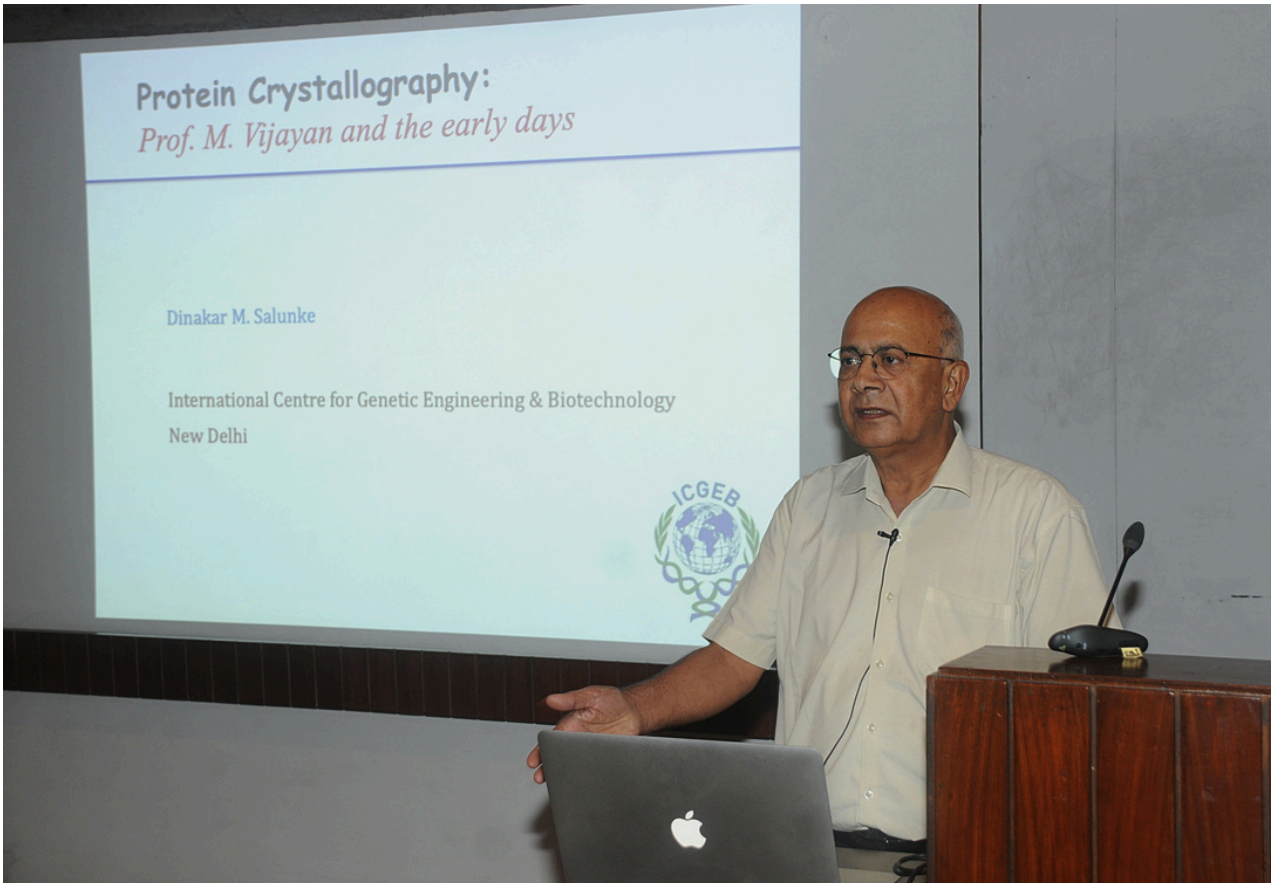
TRAINING AND WORKSHOPS

The Prof M. Vijayan School of Macromolecular X-Ray Crystallography

The National Institute of Immunology anchored "The Prof M. Vijayan School of Macromolecular X-Ray Crystallography" in September 2023. This school dedicated to Prof Vijayan, a stalwart in structural biology, is a five-day school designed to introduce young researchers to the principles and practice of the field.

The school comprised of lectures and hands-on demonstrations on various topics including crystal systems, asymmetric unit, symmetry (point groups and space groups), theory of X-ray diffraction by crystals, crystallization of proteins (principles of protein crystallization and crystallization techniques), X-ray data collection, and solving and analysing structures. The school was attended by over 50 young researchers from the Delhi NCR region.





Dr Dinakar Salunke delivering a lecture at the inauguration of the school



Participants of the school



Scientific Writing Workshop

From 27 January to 10 March 2024, a 14-session workshop was held on campus for NII PhD Scholars. The workshop, which used a hybrid format, aimed to enhance the scholars' writing skills in the field of science. It covered various topics such as scientific writing, reading and writing papers, formulating research questions, literature search, theories of communication, improving English language skills, as well as designing and presenting research proposals. The workshop was facilitated by KP Madhu, a Science Writing Consultant from Current Science.

Workshop on Computational Analyses of Transcriptomics

Data Systems biology and Big Data science are remarkably impacting our understanding of infectious diseases, metabolic disorders, and cancers. Rapidly moving fields such as genomics and proteomics with their technological innovations now generate large amounts of quantitative data at scales ranging from molecular to organismal level. However, quickly adopting computational tools for interrogating large-scale data, for example, transcriptomics data, continues to pose challenges for biologists. To this end, NII conducts an annual workshop on “Computational Analyses of Transcriptomics Data” on campus for its Ph.D. students and scholars.

This year, the workshop ran from 1 September 2023 to 28 October 2023 and catered to around fifteen NII researchers through sixteen two-and-a-half-hour sessions over eight weeks. Dr. Rintu Kutum, Faculty Fellow of Computer Science, at Ashoka University, led the workshop which was designed to be a combination of theoretical and hands-on sessions.



Participants of the Computational Analyses of Transcriptomics Data workshop with Dr Rintu Kutum and Dr Narendra Kumar



Training on Flow Cytometer Data Analysis and updates on High-Parameter Spectral Flow Cytometry

A one-day hands-on training session on Flow Cytometer Data Analysis and updates on High-Parameter Spectral Flow Cytometry was conducted for researchers from NII and other institutes in Delhi NCR on January 22, 2024. The workshop, led by trainers Dr. Mirco Corselli and Dr. Robert Baldera, was designed to be inclusive for researchers at all career stages.

Training for a National Diploma in Equine Husbandry, Medicine, and Surgery

The National Institute of Immunology (NII) recently hosted a contingent of Army officers from the Remount Veterinary Corps (RVC Centre Meerut) for their practical training as part of a national diploma program in equine husbandry, medicine, and surgery. During their visit, the officers had the opportunity to tour the Primate Research Facility, Small Animal Facility, Transmission Electron Microscopy, and Central Instrumentation Facility of the institute. This experience provided them with valuable insights into the care and management of small animals and primates, as well as exposure to state-of-the-art equipment and technologies used in research and diagnostics. Additionally, the officers engaged in various discussions and interactive sessions related to the subject, gaining valuable exposure to cutting-edge technologies that will equip them with the necessary skills and knowledge to apply these advancements in their future endeavors in animal health, breeding programs, and overall veterinary services within the Indian Army.



The contingent of Army officers from the Remount Veterinary Corps (RVC Centre Meerut) in the Central Instrumentation Facility of NII



Workshop on Enhancing Self Esteem and Nurturing Confidence

Amaha Health, a mental health organisation, conducted a workshop on campus for PhD Scholars where the complexities of addressing low self-esteem were discussed and techniques to transform self-perception were introduced.



Mahati Chandrasekhar, Senior Psychologist, Amaha Health, conducting a self-esteem workshop at NII



SCIENCE SETU

To foster scientific temper and interest in science and technology among the youth, NII conducts an array of programs that help people especially young students connect with new scientific advances. NII is committed to making scientists accessible as role models to make science more appealing to students as well as bridge the gap between science and society. Science Setu is one such program of the Department of Biotechnology that connects young students of schools and colleges and their teachers with cutting-edge research laboratories.

To better implement the Science Setu program, MoUs have been signed with several colleges of Delhi University. NII, under the Science Setu initiative, organizes various activities including one-day campus visits, short-term lab trainings, talks, and workshops. Over the past year, about forty students have received short-term training at NII labs. Moreover, NII has hosted around 265 students and teachers from eight schools and colleges across India, enabling them to visit the campus, interact with faculty and researchers, and utilize the advanced research facilities.

Furthermore, numerous scientists and scholars from NII have visited colleges in the Delhi NCR region to deliver talks, engage with students, and conduct practical workshops. The institute's Science Setu team also organized two open days during the year, welcoming approximately 320 students and teachers.





*Glimpses from Science Setu
Activities in the Institute*



ANNUAL GENERAL

MEETING

FIRST ANNUAL GENERAL MEETING OF THE BIOTECHNOLOGY RESEARCH AND INNOVATION COUNCIL (BRIC)

In a historic development, Dr Jitendra Singh, Hon'ble Minister of Science & Technology launched BRIC, the Biotechnology Research and Innovation Council, and chaired its Society's first Annual General Meeting at the National Institute of Immunology, New Delhi on 2 December 2023. BRIC is the apex autonomous society that will unify the 14 research institutions of the Department of Biotechnology to centralise governance, streamline synergies, and maximise impact of biotech research across India and worldwide.

Dr Jitendra Singh, at this meeting said that the new apex autonomous society will fulfil the Government of India's vision for a 'Atma Nirbhar Bharat' in areas like healthcare, food and energy needs by scaling biotech research and innovation. Dr Singh also launched the Citizen Centric "Zero Waste Life on Campus" or the "Shoonya Apashisht Jeevan" program of DBT on the occasion. Under this program each BRIC campus will serve as a testbed to address the global challenges of climate change, biodiversity loss, and pollution.





Glimpses from the first Annual General Meeting of BRIC



INVITED SEMINARS

S.no	Title	Speaker	Date
1.	Molecular Tango: Peptidergic signaling affects social behaviors in <i>C. elegans</i>	Dr. Jagan Srinivasan, Associate Professor, Worcester Polytechnic Institute (WPI), Worcester, MA, USA	26 May 2023
2.	Can healthy people, ecosystems, and grassroots innovations/knowledge systems teach us something new?	Prof Anil Kumar Gupta, Indian Institute of Management, Ahmedabad, India	30 May 2023
3.	DNA damage-induced metabolic reprogramming in aging	Dr Aditi U. Gurkar, Assistant Professor of Medicine, Aging Institute, University of Pittsburgh, USA	21 July 2023
4.	Microbiome: A new-age health descriptor for health and wellness	Dr. Sharmila Mande, Advisor, Life Sciences R&D, TCS Ayush Distinguished Scientific Chair, Ministry of Ayush, GOI	9 August 2023
5.	Design principles of cellular decision-making networks in cancer cell plasticity and T cell differentiation	Dr Mohit K. Jolly, Assistant Professor, IISc, India	11 August 2023



6.	Host-parasite metabolic interactions in Apicomplexa: it's all about lipids!	Dr. Cyrille Botté, Director ApicoLipid Team, Institute for Advanced Biosciences, CNRS, Université Grenoble Alpes, INSERM, Grenoble, France	23 August 2023
7.	Molecular regulation and assembly pathways of the human mitochondrial outer membrane channels	Dr. R. Mahalakshmi, Professor Department of Biological Sciences, IISER-Bhopal, India	25 August 2023
8.	Where will endangered species be in the future? A genetic perspective	Prof. Uma Ramakrishnan Professor NCBS, Bengaluru, India	22 September 2023
9.	Age-related dysfunction of immune responses against emerging and reemerging infections	Prof Janko Nikolich-Zugich, Department Head, Immunobiology Co-Director, Arizona Center on Aging University of Arizona Cancer Center, USA	10 October 2023
10.	Immune control of emerging flavivirus infection	Dr. Mehul Suthar, Associate Professor, Emory Vaccine Center, Department of Pediatrics, University Emory School of Medicine, USA	23 November 2023
11.	It's the small things that count	Dr. Shiladitya Sengupta, Associate Professor, Medicine Brigham and Women's Hospital and Harvard Medical School	15 December 2023



12.	A drug-like molecule engages nuclear hormone receptor DAF-12/FXR to regulate mitophagy & extend lifespan	Dr Manish Chamoli, Research Scientist, BuckInstitute for Research on Aging and Co-founder, Symbiont Bio	21 December 2023
13.	Enabling discoveries using macromolecular structure data	Dr. Sameer Velankar, Team Leader and Senior Scientist, EMBL-EBI, UK	8 January 2024
14.	Fine-tuning immunity: Nerve and Airway Associated Macrophages (NAMs) in respiratory health, infection, and inflammation resolution	Prof. Kamal M. Khanna, Associate Professor, Department of Microbiology, NYU Grossman School of Medicine, New York University	1 March 2024



GRADUATE STUDENT SEMINAR SERIES

S.no	Title	PhD Scholar	Laboratory	Date
1.	Understanding the role of zinc efflux and allocation in Mtb during host-pathogen interaction	Mohit Yadav	Immuno-Metabolism Lab	20 April 2023
2.	Understanding the mechanism of hyper ubiquitylation and aggregate formation in PEO patient mutants offer a potential clinical intervention	Aftab Mohammed	Signal Transduction II Lab	20 April 2023
3.	Effect of different high-fat containing diets on gut health	Chen Chongtham	Molecular Genetics Lab	27 April 2023
4.	Delineating the potential of pneumococcal biotin protein ligase as a drug target	Shivani Karalia	Nuclear Magnetic Resonance Lab	27 April 2023
5.	Interspecies interactions regulate longevity in Caenorhabditis elegans through neuron-gut signaling	Sabnam Sahin Rahman	Molecular Aging Lab	4 May 2023



6.	Understanding Kupyaphore turnover during Mtb pathophysiology	Rashmi Bhosale	Immuno-Metabolism Lab	4 May 2023
7.	Machine learning-based approach for predicting antibiotic resistance and identification of novel antibiotics resistance-associated mutations in Mycobacterium tuberculosis	Ankita Pal	Bio-informatics Centre	18 May 2023
8.	Ubiquitin-mediated recruitment of RMI1 upon replication stress	Rimpy Arun	Signal Transduction II lab	18 May 2023
9.	Analyzing mutation-induced conformational changes in EGFR kinase and the development of small molecule drugs using Machine-learning based methods	Sapna Pal	Bioinformatics Centre	25 May 2023
10.	Elucidating the underlying basis for structural stability of human arginase-I: a therapeutically important enzyme	Anjali Kalia	Protein Engineering lab	25 May 2023
11.	Multi-omics approaches to understand the biology of human CD4+ cytotoxic T lymphocytes	Raunak Kar	Immunogenomics Lab	1 June 2023
12.	Nano-scale artificial antigen-presenting cells for anti-tumor adoptive T cell therapy	Antara Mondal	Nano-biotechnology Lab	1 June 2023
13.	Exploring the NiRAN domain of the RNA-dependent RNA polymerase as a novel therapeutic target against SARS-CoV-2 and its variants	Deepsikha Kar	Structural and Functional Biology Lab	15 June 2023
14.	Cysteine/Cystine transporter is required for pneumococcal fitness and virulence	Shabnam	Molecular Immunology Lab	15 June 2023



15.	Delineating the mechanism of protection conferred by a potential malaria vaccine candidate	Shreya Bhattacharya	Infectious Diseases Lab	22 June 2023
16.	Temporal regulation of PARP1-mediated DNA damage response and metabolic flux by HDAC5 determines tumorigenesis	Ankita Pal	Bio-informatics Centre	22 June 2023
17.	Effect of inhibition of O-glycosylation on tumor growth in a mouse melanoma model	Abhiraj R.	Lab of Chemical Glycobiology	6 July 2023
18.	Understanding the basic components of the Type VII secretion system of Mycobacterium tuberculosis: Progress so far	Soumya Banerjee	Structural and Functional Biology Lab	6 July 2023
19.	Dissecting the role of miRNA in Cell cycle Related Neuronal Apoptosis (CRNA)	Komal	Eukaryotic Gene Expression Lab	13 July 2023
20.	Understanding the role of nucleotide salvage pathway in pneumococcal biology and virulence	Ankita Yadav	Molecular Immunology Lab	13 July 2023
21.	Investigating the dendritic cell-intrinsic role of RelB-NF- κ B pathway in instructing gut immunity	Naveen Kumar	Systems Immunology Lab	20 July 2023
22.	Metabolic Profile of Follicular T Helper (Tfh) Cells	Someshwar Nath Jha	Vaccine Immunology Lab	20 July 2023



INVITED TALKS, LECTURES, AND WEBINARS

DELIVERED BY NII SCIENTISTS

S.no	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organisation	Date of Presentation
1.	Dr. Devinder Sehgal	Breaking Free from Neutrophil's Stranglehold: How a Nuclease Saved the Day for Streptococcus pneumoniae (online)	International Day of Immunology; Post Graduate Institute of Medical Sciences, Rohtak	20 April 2023
2.	Dr. Devinder Sehgal	Evidence for Antigen-Driven Selection, Convergent Evolution, and Clonal Expansion during Anti-Polysaccharide Antibody Response Elicited against Glycoconjugate Vaccine	The Molecular Immunology Forum Meeting 2023, Uttarakhand; Organized by the Molecular Immunology Forum	6 May 2023



3.	Dr. Devinder Sehgal	Priority Areas, Discovery and Monoclonal Antibody Selection: Gaps, Challenges and Solutions	First meeting of Sectoral Expert Committee on Biomanufacturing of Precision Biotherapeutics - Monoclonal Antibodies held at IIT Indore; Organized by Department of Biotechnology	11 August 2023
4.	Dr. Devinder Sehgal	Advances in the Understanding of B Cell Mediated Immune Response	Organized by Indian Immunology Society at AIIMS, New Delhi	5 October 2023
5.	Dr. Devinder Sehgal	Immunity to Streptococcus pneumoniae: Molecular Insights from Protective Monoclonal Antibodies	Golden Jubilee Annual Conference of the (IMMUNOCON 50) at AIIMS, New Delhi; Organized by Indian Immunology Society	5-8 October 2023
6.	Dr. Devinder Sehgal	The Fascinating World of Immune Escape (online)	28th Refresher Course in Life Sciences and Biotechnology at Jawaharlal Nehru University, New Delhi; Organized by UGC-MMTC	29 November 2023
7.	Dr. Devinder Sehgal	Germinal Centres: The Physiological Birthplace of Adaptive Immunity	Expert lecture for Master's students of Immunology at Nirma University, Ahmedabad	8-9 November 2023
8.	Dr. Devinder Sehgal	Recruitment of B Cells Expressing Heavy Chains Lacking DH Gene-Derived Amino Acids in the Immune Response against Streptococcus pneumoniae	International conference "Vistas in Life Sciences 2024" at Jawaharlal Nehru University, New Delhi; Organized by Jawaharlal Nehru University, New Delhi	21-24 January 2024



9.	Dr. Devinder Sehgal	The Amazing World of Antibodies: Immunology and Therapeutic Applications	CME-based course on Immunology under the auspices of the Indian Immunology Society; Organized by Nirma University, Ahmedabad	22-23 February 2024
10.	Dr. Devinder Sehgal	Unravelling the Molecular Attributes of Protection-Confering Antibodies	Indo-French Workshop on Infectious Diseases held at the CNRS headquarters in Paris, France; Organized by CNRS France	5-6 February 2024
11.	Dr. Anil Kumar	Inflammatory and Deleterious Role of Gut Microbiota-Derived Trimethylamine on Colon Cells	International Conference on Cancer Biology at Indian Institute of Technology, Chennai	14 September 2023
12.	Dr. Anil Kumar	Towards Developing MIP-based Sensor for Quantifying Gut Microbiota Derived Metabolites	In a brainstorming session entitled "Emerging Trends in Nanobiotechnology " at DUVASU, Mathura	15 December 2023
13.	Dr. Anil Kumar	Emerging Implication of Gut Microbiota and Metabolites in Cancer Biology	JNU-ECS student chapter on "Oral Hygiene in Human Health and Diseases" under the Electrochemical Society (ECS), JNU, New Delhi	16 December 2023
14.	Dr. Anil Kumar	Gut Metabolite Indoxyl Sulfate has Selective Deleterious and Anticancer Effect on Colon Cancer Cells	International Conference on Traditional Medicine & Phytopharmaceuticals, CSIR-IIIM, Jammu	17 February 2024
15.	Dr. Anil Kumar	Towards Developing MIP-Based Sensor for Quantifying Gut Microbiota Derived Metabolites	One-day symposium on "Biomedical Devices", JNU, New Delhi	19 March 2024



16.	Dr. Apurba Kumar Sau	Mechanistic Understanding of how Macromolecular Crowders affect the Structure and Function of a Therapeutically Important Enzyme	Biophysical Society Network; Organized by IIT Delhi	15 September 2023
17.	Dr. Apurba Kumar Sau	How Structure-Function Studies of Metabolic Enzymes in Pathogens can be Employed for Therapeutics?	Institute of Home Economics, New Delhi (Science Setu talk)	2 November 2023
18.	Dr. Apurba Kumar Sau	Arginine Metabolism in Helicobacter pylori: An Opportunity for the Development of Inhibitors for this Bacterium	Center for Biomedical Engineering, IIT Delhi	29 November-1 December 2023
19.	Dr. Apurba Kumar Sau	Polyamine Biosynthetic Pathways in Helicobacter pylori: An Important Target for the Development of Inhibitors for this Bacterium	International Conference (Deshbandhu College, University of Delhi, Kalkaji)	6-8 December 2023
20.	Dr. Apurba Kumar Sau	How Structure-Function Studies of Metabolic Enzymes in Pathogens can be Employed for Therapeutics?	Department of Biotechnology, Jaypee Institute of Information Technology, Noida	31 January-2 February 2024
21.	Dr. Apurba Kumar Sau	A New Mechanism to Elucidate The Difference in Second Phosphate Cleavage of GTP between Two Human GBP Homologs	Indian Biophysical Society Meeting at TIFR Hyderabad	17 March 2024
22.	Dr. Veena S. Patil	Understanding Human Immunology in the Genomics Era	Rhetor 4.0, Annual symposium, IISER Thiruvananthapuram, Kerala	25-27 August 2023



23.	Dr. Veena S. Patil	Unravelling the Heterogeneity in Human T Cell Memory at Single-Cell Resolution	Workshop on Flow Cytometry Cell Sorting using CytoFLEXSRT at Special Centre for Molecular Medicine, JNU, New Delhi	2-3 November 2023
24.	Dr. Veena S. Patil	Single-Cell Transcriptomic and T Cell Antigen Receptor Repertoire Analysis of Viral Antigen-Specific Memory T Cells in Humans	Human Cell Atlas (HCA), Asia 2023, Kolkata	27-28 November 2023
25.	Dr. Veena S. Patil	Single-Cell Transcriptomic Analysis of Viral Antigen-Specific Memory T Cells in Humans	92nd Annual Meet of The Society of Biological Chemists (SBC 2023) at BITS, Goa	18-20 December 2023
26.	Dr. Veena S. Patil	Visualization of Complex Multi-Dimensional Data using FlowJo to Understand Human Immunology	National Flowcytometry workshop at RCB, Faridabad	8-9 January 2024
27.	Dr. Veena S. Patil	Human CD4+ T Cell Memory Subsets in Infectious Diseases: Lessons from Multi-omics Analysis	Indo-French Workshop on Infectious Diseases, CNRS, Paris, France	5-6 February 2024
28.	Dr. Pushkar Sharma	Dissection of Phospho-Signaling Networks involved in the Development of Malaria Parasite	Invited Talk, Pasteur Institute, Paris	June 2023
29.	Dr. Pushkar Sharma	Phosphosignaling Networks in Apicomplexan Parasites	15th Annual Proteomics Society of India Meeting, NIPGR, India	November 2023



30.	Dr. Pushkar Sharma	Signaling Pathways in Apicomplexan Parasites	Indo-French Workshop on Infectious Diseases, CNRS, Paris, France	February 2024
31.	Dr. Pushkar Sharma	Novel Insights into Signaling Pathways in Malaria Parasite	The Proteomics in Biotechnology and Biomedical Sciences Symposium-2024, THSTI-Faridabad	March 2024
32.	Dr. Nimesh Gupta	T cell Immunity to COVID-19 vaccine	14th Asian Federation of Biotechnology Regional Symposium, Faridabad	27 April 2023
33.	Dr. Nimesh Gupta	T cell Response to Virus and Vaccines	Molecular Immunology Forum, Jim Corbett, Nainital	5 May 2023
34.	Dr. Nimesh Gupta	Vaccine immunology	CME Programme on Fundamentals and Advances in Immunology, Department of Biotechnology & Bioinformatics, NEHU, Shillong	6 May 2023
35.	Dr. Nimesh Gupta	How to Apply Immunology for Rational Design of Human Vaccines	National Workshop on Advances in Bioprocess Technologies on the theme "Vaccines & Biotherapeutics", IMTECH, Chandigarh	30 June 2023
36.	Dr. Nimesh Gupta	Harnessing the Potential of Flow Cytometry : A Journey into COVID-19 Vaccine Development	Workshop on Multicolor Flow Cytometry & Single Cell Sorting, ICGEB, New Delhi	25 July 2023
37.	Dr. Nimesh Gupta	Delving Deeper: Exploring T-cell Dynamics in Viral Infection at Single-Cell Resolution	National Hands-on workshop on 10X single cell genomics, ILS, Bhubaneshwar, Odisha	31 August 2023



38.	Dr. Nimesh Gupta	Distinct Features of a Peripheral T helper Subset that Majorly Drives the B cell Response in Dengue	Keystone Symposia on "T and B cell Collaboration in Germinal Centres and Beyond; Whistler, Canada	2 October 2023
39.	Dr. Nimesh Gupta	Session Chair: Dengue Vaccine Development	Golden Jubilee Conference of the Indian Immunological Society: IMMUNOCON-50	7 October 2023
40.	Dr. Nimesh Gupta	Session Chair: Immunology and Autoimmunity	7th International Conference on Translational Research, Innovation in Translational Research: Transforming Tomorrow, AIIMS, New Delhi	16 October 2023
41.	Dr. Nimesh Gupta	Accelerating Next-Generation Vaccine Development Through Translational Immunology	Biopharma Summit on Emerging Technologies in Biopharmaceuticals and a Roadmap for Translational Research, IIT Bombay, Mumbai	24 November 2023
42.	Dr. Nimesh Gupta	Human T cell Assay Platform	35th JWG Meeting of the Indo-U.S. Vaccine Action Program, New Delhi	27 November 2023
43.	Dr. Nimesh Gupta	Japanese Encephalitis in India: Current Status and Future Prospects	Symposium on Japanese encephalitis, Institute Pasteur Foundation, Tokyo, Japan	2 December 2023
44.	Dr. Nimesh Gupta	New Vaccine Technology Platforms	Animal Health Conclave, Ministry of Animal Husbandry, New Delhi	18 December 2023
45.	Dr. Nimesh Gupta	Biology of Tfh cells and T-B Collaboration in Virus Infection and Vaccination	Indo-French workshop on Infectious Diseases, CNRS, Paris, France	6 February 2024



46.	Dr. Nimesh Gupta	T cell-B cell Collaboration in Dengue Virus Infection	Global Immunology Summit, THSTI, Faridabad	16 February 2024
47.	Dr. Nimesh Gupta	Roadmap for Viksit Bharat	Biotechnology Industry Research Assistance Council, New Delhi, India	20 March 2024
48.	Dr. Sarika Gupta	Interdisciplinary R&D and Skill Development	One week One Lab, NPL, New Delhi	24 April 2023
49.	Dr. Sarika Gupta	Biosafety and Bioethics: How far we can go?	Public lecture on biosafety and bioethics, ITM, Gwalior	3 May 2023
50.	Dr. Sarika Gupta	Developing Therapeutic Interventions for Chronic Diseases: Role of Animal Models	World Animal Day, ILBS, New Delhi	4 October 2023
51.	Dr. Agam Prasad Singh	HEA (hydroxy ethyl amine) based Potent and Safe Antimalarials	ICBTM 3.0, International symposium, Udaipur, Rajasthan	8-10 March 2024
52.	Dr. Sanjeev Das	Exploring the Cross-talk between Metabolism and Epigenetics in Cancer	92nd Annual Meeting of Society of Biological Chemists, 2023- BITS, Goa	December 2023
53.	Dr. Sanjeev Das	Deciphering the Cross-talk between Metabolism and Epigenetics in Cancer	International Conference on Molecular Signaling- University of Hyderabad	January 2024
54.	Dr. Sagar Sengupta	Trying to Reach the Bed from the Bench: the Gap Remains	Department of Biochemistry, University of Calcutta, India	18 April 2023



55.	Dr. Sagar Sengupta	MITOL-dependent Ubiquitylation Negatively Regulates the entry of Proteins involved in Mitochondrial Replication	Dr. Lalji Singh Memorial Award Lecture, 9th Annual Conference of the Society for Mitochondrial Research & Medicine, Centre for DNA Fingerprinting and Diagnostics (CDFD), Hyderabad	22 June 2023
56.	Dr. Sagar Sengupta	Disruption of Chromatin Remodeling leads to Chemosensitivity and Possibility of Adjunct Therapy in Colon Cancer	4th Indian Cancer Genome Atlas (ICGA), IISER-Pune, Pune, India	6 October 2023
57.	Dr. Sagar Sengupta	Translational Research Possibilities for Mitochondrial Disorders	7th International Conference on Translational Research, AIIMS-New Delhi, New Delhi	16 October 2023
58.	Dr. Sagar Sengupta	Remodeling of the Epigenome: Link to Chemosensitivity and Adjunct Therapy in Colon Cancer	Saha Institute of Nuclear Physics, Kolkata	29 November 2023
59.	Dr. Sagar Sengupta	Disruption of Chromatin Remodelling Leads to Chemosensitivity, which can help in Colon Cancer Adjunct Therapy	43rd Annual Convention of the Indian Association for Cancer Research (IACR), IISER Pune, Pune	19 January 2024
60.	Dr. Sagar Sengupta	Translational Research Possibilities for Mitochondrial Disorders	"Biology Beyond Boundaries" Mitochondrial Insights, Computational Breakthroughs, and Clinical Transformations", Savitribai Phule Pune University (SPPU), Pune	29 January 2024



61.	Dr. Sagar Sengupta	Small Molecules Reverting Chemoresistance are Viable Candidates for Adjunct Therapy in Colon Cancer	EMBO satellite meeting on Evolution and diversity of the DNA damage response, IISER Pune, Pune	17 February 2024
62.	Dr. Tanmay Majumdar	Repurposing of Gliptins as a Pleiotropic Therapeutic Strategy to Mitigate pan-SARS-CoV-2 Infections	International Conference on "Integrative Chemical Science for Health and Environment (ICHE-2023). Indian Association of Solid State Chemistry & Allied Scientist in collaboration with Augusta University, USA at Deshbandhu College, University of Delhi, Kalkaji, New Delhi	6-9 October 2023
63.	Dr. Tanmay Majumdar	Repurposing of itagliptin and Linagliptin as a Pleiotropic Therapeutic Strategy to combat pan-SARS-CoV-2 Infections.	5th Edition Biopharma Conclave (Vaccines), Mumbai	11-12 October 2023
64.	Dr. Tanmay Majumdar	Repurposing of Sitagliptin and Linagliptin as a Therapeutic Strategy to Abrogate pan-SARS-CoV-2 Infections	VIROCON & Annual Meeting of Indian Virology Society (India), Trichi, India	1-3 December 2023
65.	Dr. Soumen Basak	Investigating the Role of Non-canonical NF-kappaB Signaling in Gut Inflammation	Departmental Seminar, AIIMS New Delhi	28 July 2023
66.	Dr. Soumen Basak	Investigating the Immunoregulatory Role of Cell Signaling Crosstalks: a Tale of the Non-canonical NF-kappaB Pathway	Global Immunotalks (online lecture series) Online, International Seminar	25 August 2023



67.	Dr. Soumen Basak	Regulating the Genome Landscape during Inflammation: Learning from the NF-kB System	Immuno-India 2023 course on Epigenetic Regulation of the Immune Response RGCB, Kerala	1-5 October 2023
68.	Dr. Soumen Basak	An App to Listen to Conversation Within Immune Cells	Guest Lecture, Science Setu Student Outreach Sri Venkateswara College, Delhi	18 October 2023
69.	Dr. Soumen Basak	Investigating the Immunoregulatory Role of Cell Signaling Crosstalks: A Tale of the Non-canonical NF-kappaB Pathway	Guest Lecture Shiv Nadar University	19 October 2023
70.	Dr. Soumen Basak	Investigating the Immunoregulatory Role of Cell Signaling Crosstalks: A Tale of the Non-canonical NF-kappaB Pathway	Conference/Indo-French Bilateral Initiatives, CNRS, Paris, France	5-6 February 2024
71.	Dr. Soumen Basak	Investigating the Immunoregulatory Role of Cell Signaling Crosstalks: A Tale of the Non-canonical NF-kappaB Pathway	Global Immunology Summit, THSTI-Faridabad	14-15 February 2024
72.	Dr. Soumen Basak	Viruses and Vitamin D: An Intricate Interplay	Guest Lecture, Science Setu, Student Outreach PSGR Krishnammal College for Women, Coimbatore	29 February 2024
73.	Dr. Soumen Basak	Non-canonical NF-kB Signaling promotes Intestinal Inflammation by Restraining the Tolerogenic β -catenin-Raldh2 axis in Dendritic Cells	Departmental Seminar, NCBS-Bangalore	13 March 2024



74.	Dr. Soumen Basak	Investigating the Role of the Non-canonical NF- κ B Pathway in Intestinal Inflammation	National Conference on Advances on Biomedical Sciences Central University of Rajasthan	20-21 March 2024
75.	Dr. G. Senthil Kumar	Protein Structure and Function	SERB Karyashala Workshop, Panjab University, Chandigarh	9-15 October 2023
76.	Dr. G. Senthil Kumar	Dynamic Studies of Antigen-antibody Interactions of Dengue Virus	NMRS Conference, CBMR, Lucknow	2-5 February 2024
77.	Dr. G. Senthil Kumar	Protein Structure and Function	National Science Day Lecture, Jamia Millia Islamia University, New Delhi	28 February 2024
78.	Dr. Arnab Mukhopadhyay	Interspecies Interactions that Regulate Longevity: The Story of a Worm and its Diet	ACTREC, Navi Mumbai	18 December 2023
79.	Dr. Arnab Mukhopadhyay	Interactions of a Nutrient-sensing Pathway with Cell Cycle Proteins in Regulation of Reproductive Aging	Indian Institute of Science, Bengaluru	14 January 2024
80.	Dr. Arnab Mukhopadhyay	Interspecies Interactions Regulate Longevity in <i>Caenorhabditis elegans</i>	IISER Bhopal	10 January 2024
81.	Dr. Arnab Mukhopadhyay	Interspecies Interactions Regulate Longevity in <i>Caenorhabditis elegans</i>	IISER Trivandrum	3 February 2024



82.	Dr. Arnab Mukhopadhyay	Inter-tissue Crosstalk that Eegulates Progeny Fitness on Somatic DNA Damage	inSTEM, Bengaluru	22 February 2024
83.	Dr. Arnab Mukhopadhyay	<i>Caenorhabditis elegans</i> as a Model System to Study Toxicology	Jamia Hamdard, New Delhi	2 March 2024
84.	Dr. Arnab Mukhopadhyay	How to Use <i>C. elegans</i> for Behavioural Studies and Neurobiology	Amity University, Noida	22 March 2024
85.	Dr. Devram Sampat Ghorpade	Evaluating Medicinal Plants from Northeast India in Mitigating Ailments Associated with Metabolic Dysregulations	IBSD, Shillong	2 December 2023
86.	Dr. Devram Sampat Ghorpade	Learning about Pathophysiology by Virtue of Multi-organo-kine Circuits	CNRS Paris, France	5 February 2024
87.	Dr. G. Aneeshkumar Arimbasseri	Impact of Nutrition on Metabolism and Immunity	Indo-French Workshop On Infectious Diseases, CNRS Paris, France	5 February 2024
88.	Dr. G. Aneeshkumar Arimbasseri	Effect of Nutritional Transitions on Intestinal Barrier Function	Annual meeting of TIFR-ARUDA, TIFR Hyderabad	1 March 2024
89.	Dr. Debasisa Mohanty	Computational Microscope to Digital Twins: How exascale computing is going to drive major advances in biology & medicine?	CDAC, Pune	20 July 2023



90.	Dr. Debasisa Mohanty	Computational Microscope to Digital Twins: How exascale computing is going to drive major advances in biology & medicine?	IUAC, New Delhi	24 July 2023
91.	Dr. Debasisa Mohanty	In silico genome mining for identification of novel small ORFs and biosynthetic enzymes: Applications to bacterial genomes & human microbiome	BRIC-NIBMG, Kalyani, West Bengal	5 September 2023
92.	Dr. Debasisa Mohanty	Role of Open and FAIR Data Ecosystems in AI/ML driven innovation in Bioscience and Biotechnology	International Conference on "Open and FAIR Data Ecosystem: Principles, Policies and Platforms", IIC, New Delhi	12 September 2023
93.	Dr. Debasisa Mohanty	AI for propelling/scaling biotech research approaches promoting biomanufacturing.	Discussion meeting on Bio-AI organized by DBT at IIT, Guwahati	15 September 2023
94.	Dr. Debasisa Mohanty	Molecular Simulations to Digital Twins: How scientific computing is driving major advances in biology & medicine?	Deen Dayal Upadhyay College, DU	20 September 2023
95.	Dr. Debasisa Mohanty	Evaluation of AI/ML based methods for prediction of novel folds, oligomeric complexes of proteins and binding affinity of protein-ligand complexes	India Biological Data Center, RCB, Faridabad	8 March 2024



96.	Dr. Debasisa Mohanty	Role of data driven research and machine learning in modern biology	School of Life Sciences, JNU, New Delhi	11 March 2024
97.	Dr. Debasisa Mohanty	In silico identification of novel small ORFs and prediction of their post-translational modifications in bacterial genomes & human microbiome	THSTI, NCR Bio-Cluster, Faridabad	18 March 2024
98.	Dr. Srinivasa-Gopalan Sampathkumar	Chemical Tools for the Modulation of Interaction of sialyl-Lewis X (sLeX / CD15s) with E-selectin (CD62E)	Department of Organic Chemistry, Indian Institute of Science (IISc), Bangalore.	23 June 2023
99.	Dr. Srinivasa-Gopalan Sampathkumar	Glycoproteomic Profiling of CD43 Provides Insights on the role of O-glycans in Immune Synapse Formation	15th Annual Meeting of Proteomics Society, India (PSI) & International Conference on Integrated Proteomics: Applications in Food, Nutrition, and Health, New Delhi	20-23 November 2023
100.	Dr. Srinivasa-Gopalan Sampathkumar	Chemical Tools for Unravelling the Structure and Function of Glycoconjugates in Living Systems	National Organic Symposium Trust (NOST), XXIII Organic Chemistry Conference, Bhubaneswar, India	29 February – 03 March 2024
101.	Dr. Bichitra Kumar Biswal	Intensifying the Impact of Structural Biology in Drug Discovery	IIT Delhi	2 August 2023



102.	Dr. Bichitra Kumar Biswal	Developing Novel Anti-TB Small Molecules through Structural Biology Approach	SASTRA University, Thanjavur	8 October 2023
103.	Dr. Bichitra Kumar Biswal	Developing New Anti-TB Small Molecules through Target-based Approach	Gautam Buddha University, Greater Noida	11 October 2023
104.	Dr. Bichitra Kumar Biswal	Developing New Anti-TB Small Molecules Targeting Histidine Biosynthesis	IMTECH, Chandigarh	23 November 2023
105.	Dr. Prafullakumar Tailor	Understanding the Role of Interferon Regulatory Factors in Dendritic Cell Development and Innate Immunity	International, CNRS headquarters, Paris, France at Indo-French workshop on infectious diseases	5 February 2024
106.	Dr. Prafullakumar Tailor	Understanding the Significance of DNA methylation in plasmacytoid Dendritic Cell (pDC) Biology	Global Immunology Summit at THSTI, Faridabad	16 February 2024
107.	Dr. Santiswarup Singha	Nano-scale Artificial Antigen-Presenting Cells to Reprogram Anti-tumor Immune Responses	CNRS headquarters, Paris, France (Indo-French Workshop on Infectious Diseases)	5-6 February 2024
108.	Dr. Santiswarup Singha	Nanomaterials for Immunotherapy: Peptide-MHC-based Nanomedicine for Autoimmune Diseases	Jawaharlal Nehru University, New Delhi, India (Workshop on "Exploring the Nanoscale: Synthesis, Characterization, and Interaction of nanomaterials with Cells")	16-17 February 2024



109	Dr. Santiswarup Singha	Nano-scale Artificial Antigen-Presenting Cells to Expand Tumor-specific CD8+ T-cells for Inhibiting Tumor Growth	Jawaharlal Nehru University, New Delhi, India (National Conference on Nano-Bio Interface-2024 (NBI-2024))	18-19 February 2024
110.	Dr. Chhuttan Lal Meena	Design and Synthesis of Small Molecules to Act as Non-Kinase Inhibitors in Cancer Cells	Bhaskar Acharya Collage, New Delhi	12 November 2023
111.	Dr. Narendra Kumar	Drug Discovery Tools and Introduction to Multi-omics Technologies	Deen Dayal Upadhyay College, University of Delhi	2 November 2023



RESEARCH

INFRASTRUCTURE

Central Instrumentation Facility and Other Equipment

The Central Instrumentation Facility (CIF) houses several high-end, state-of-the-art instruments available to researchers from within and outside of NII. Major analytical instruments of CIF are cross flow filtration system (ÄKTAflux 6), fast performance liquid chromatography (ÄKTA Avant 150, NGC Chromatography System BIO-RAD), Bio-Layer Interferometry (BLI, Octet R8 Operations) multiplex immunoassay system (Bio-plex 200, BIO-RAD), chemiluminescence imaging system (Azure 600), realtime PCR (Quant Studio-6 Pro, Thermo Fisher Scientific), anaerobic workstation (Whitley A20, Don Whitley Instruments), zetasizer nano (Malvern Instruments), Typhoon laser scanner (GE Healthcare), different centrifuges, and a lyophilizer.

The Centralized Mass Spectrometer Facility (CMSF) of NII provides support and services for protein identification and characterization. Core activities of this facility include the identification of proteins and determination of posttranslational modification using state-of-art mass spectrometry. The major equipment at this facility is Thermo TSQ Altis Plus Triple Quadrupole MS, Orbitrap Exploris 240 MS and Gas chromatography-Mass Spectrometer (GC-MS).

Other advanced analytical facilities that aid multidisciplinary research at NII include Transmission electron microscopy (Tecnai TECNAI G2 20 TWIN), Scanning electron microscopy (Carl Zeiss EVO Ls10), confocal microscopy (Zeiss LSM 9 8 0 Meta System), NMR spectrometer (Bruker Avance III 700 MHz), Circular Dichroism (CD) Spectrometer, a dual-wavelength X-ray generator for X-ray crystallography, various flow cytometers including analyzers and cell sorters, micro computed tomography (Quantum GX2 microCT, Perkin- Elmer), Nano String Platform (nCounter Digital Analyzer 5s), small animal imaging system with X-ray (Lago X, Spectral Instruments Imaging), 10x Chromium Single Cell Platform (Chromium ix GCG-SR-1), SEAHORSE (XFe24 Metabolic Analyser), Min Ion Nanopore Sequencer, and Next Generation Sequencing (NextSeq2000).



Small Animal Facility

The Small Animal Facility of the Institute ensures humane care and breeding of experimental animals used in approved research. The facility caters defined strains of mice and rats to the scientific community of the institute. At present, the small animal facility houses 116 mouse strains, four rat strains, and one stock of rabbits.

The breeding of all defined strains is maintained in a three-tier system: i. the Foundation Stock (FS), ii. Pedigreed Expansion Stock (PES), and iii. Production Stock (PS). Genetically modified mouse strains are bred either by homozygous mutant (-/-) x homozygous mutant (-/-), heterozygous mutant (-/+) x homozygous mutant (-/-), or heterozygous mutant (-/+) x heterozygous mutant (-/+).

Defined breeding protocols and careful management and husbandry procedures are followed to safeguard the purity of each strain. To maintain the genetic purity of inbred mice, inbred strains are periodically replaced with new breeders to minimize genetic drift and inbreeding depression. Also, genetic monitoring is performed for inbred mice of foundation, expansion and production stock with the help of a few microsatellite markers to ensure their genetic purity. The mutant mice are periodically genotyped to maintain the breeding program.

The health monitoring program includes a regular screening of pathogens using sentinels through culture, biochemical analyses, PCR, and ELISA. Additionally, periodic FACS analyses are done on immunodeficient mice to check for leakiness, if any.

Standard quality control protocols are implemented in the facility to avert transmission of infection between cages. These include careful handling of animals, supply of irradiated feed to breeding colonies, automated washing procedures, use of sterilized corn cob bedding, autoclaved cages, and acidification of water.

The breeding and experimental colonies are maintained in a barrier system with individually ventilated cages of international standards. Necessary actions are taken by the veterinarian based on clinical signs and necropsy/autopsy of the infected/diseased animals. A preventive and recommended schedule of medication is strictly followed to prevent the infection/s.

Primate Research Centre

The National Institute of Immunology has a facility for studies on non-human primates—the Primate Research Centre (PRC). Macaques are bred and maintained in the PRC for the generation of in-house animals of known ages for approved basic, pre-clinical, and toxicological research using non-human primates. Group mating is done, under the breeding program, for the production of healthy animals.

This helps in providing animals of known age and parentage. The facility has large open pens, which are used for group mating under semi-natural conditions where food and water are provided *ad libitum*. Infants are weaned at the age of six to twelve months (depending on season and weight of infants) after which they are transferred to open enclosures/semi-natural housing for overall growth and better development of bones, muscles and coordination.



Monkeys are housed in independent cages at around pubertal age. To prevent cross-cage contamination or infection strict hygienic procedures are adopted in routine practice. Daily observations of animals are done, and sick animals are isolated and treated properly after necessary investigations. The primates are fed with standardized pellet feed as per the recommendation.

In addition to this, bread, soaked Bengal gram, vegetables and/or fruits are also given daily. Regular supplementations with vitamins and calcium in bread are given. The staff at PRC undergo preventative health check-up. Any surgeries, injuries and medication/treatment on non-human primates are performed by a registered veterinarian.

Technical expertise required for surgery, immunization, bleeding, and biopsy is provided by experienced staff at PRC. A research laboratory is situated in the centre to provide basic services like the primary processing of biological samples to various investigators.

At the PRC, clearance of the research proposals by the Committee for Control and Supervision of Experiments on Animals (CCSEA) after primary clearance from the Institutional Animal Ethics Committee is necessary for performing research on primates.

The macaques at this centre are useful in research related to infectious diseases, reproduction, endocrinology, immunology, and contraception. The staff at the PRC make sure that all the procedures involved in animal handling are pain-free with minimum stress to the animal. Experimental animals are supplemented with special feed, whenever needed. A constant effort is made to keep the animals in a comfortable zone and stress-free environment as per the available guidelines.

There are seventeen open enclosures with swings and shelters, some of these are used for the rotation of monkeys and some for rehabilitation and or socializing. Attempts are made to keep most of the macaques in groups at open enclosures depending on climatic conditions.



SERVICE UNITS

Establishment, Personnel and General Administration Services

The division continues to provide key support for optimally utilizing and integrating human and administrative resources aimed at realizing the vision of the Institute. During the reporting period, administrative support was provided in formulating policies and ensuring their effective implementation.

Other key areas included handling of all service matters and recruitments, coordinating career development initiatives, and operational support for foreign visits of scientists for training, conferences, or bilateral exchange.

The division also carries out functions related to staff welfare and the dispensation of post-retirement benefits. Submission of periodic reports to the ministry and preparing responses to parliament questions also fall under the purview of this division. To bolster capabilities and enhance productivity, the Institute periodically sponsors administrative and technical staff for training at recognized training institutes.

The Institutes' 'Right to Information (RTI)' Cell files quarterly report on the RTI portal. The Institute also has an effective grievance redressal mechanism to deal with the public as well as staff grievance petitions, ensuring quick redressal.

Financial and Accounting Services

The division has been responsible for the preparation of the annual budget and annual financial statements; management and utilization of funds; implementation of PFMS, GEM, etc.; settlement and disbursement of all payments; getting accounts audited by DST internal auditors and statutory and CAG auditors; sending reports, SoE, and UC to funding agencies; recovery and remittance of TDS, GST, etc.; filing an institutional income tax return and preparing compliance report; preparing income tax assessment, obtaining required exemptions from the Income Tax Department; maintaining bank accounts; management of CPF and Gratuity Fund; and remittance of subscriptions of NPS.



Stores and Purchase Department

The Stores and Purchase Department of NII deals with the procurement of chemicals, consumables, glassware, plasticware equipment, and other items that are used in research laboratories of the Institute. Various purchase committees evaluate all critical aspects of purchase before an order is placed. Such purchase committees comprise three or more scientific staff, the Finance and Accounts Officer and the Stores and Purchase Officer.

Occasionally, external experts with special domain knowledge are also invited to serve on these committees. The department monitors all aspects of purchase till the payment is made. Close rapport with the order departments of the Institute is maintained to mitigate any bottlenecks that may arise.

Engineering, Maintenance and Instrumentation Services

The Engineering Department of the Institute has been entrusted with all the engineering activities involving maintenance, services, and capital works. The department ensures continuous upgradation of systems to enable the use of the latest technologies. Major activities undertaken during the reporting year are as follows:

- Replacement of the cooling coil of the Air Handling Units (AHUs)
- Re-carpeting and repairing of internal roads at the NII campus
- Upgradation of various laboratories of NII
- Supply, installation, testing, and commissioning of a 2*400 sq mm LT cable for and renovation of the electrical/civil infrastructure of the Primate Research Centre
- Restoration and upgradation of staff quarters and laboratories in the NII campus as well as the staff quarters in Dwarka
- Upgradation of the main building's raw water and soft water pumping system
- Repairing of the chilled water header line of the Central Air Conditioning System
- Replacement of window/split AC units at various locations of NII
- Waterproofing of the terrace of the main building of NII
- Repairing of the Sewage Treatment Plant aeration grids and other allied work
- Miscellaneous works in the PRC Building at NII
- Creation of international-standard badminton courts at NII



The department is currently working on the following projects:

- Construction of staff quarters at Sector-5 Dwarka through the Central Public Works Division
- Upgradation of the BSL-3 facilities at the Institute
- Establishing new ABSL-2 and BSL-3 laboratories/facilities
- Upgradation of various laboratories at NII
- Replacement of the cooling coils of AHUs at various locations at NII
- Renovation of the Heating, Ventilation and Air Conditioning system of the old SAF at NII
- Renovation of the swimming pool at NII
- Replacement of lifts at NII
- Setting up of the BRIC office at NSIC complex Okhla through NBCC
- Creation of space over the terrace of the main building and upgradation of the Data center at NII through NBCC
- Renovation of the guest rooms in RSH at NII

Library and Documentation Services

The Library and Documentation Department plays a crucial role as a support unit, acting as both an Information Repository and a Dissemination Centre. Its main goal is to provide information services to the institute's scientific, administrative, and technical staff, and researchers, using a mix of archival and modern digital resources.

The library holds an extensive collection of books and journals, many of which are available online for the institute's scientific staff and students. As a member of the DeLCON consortium under the Department of Biotechnology, the library oversees the subscription process for journals, e-book databases, and handles the payment of journal publication fees. The department has also automated all housekeeping tasks and maintains a searchable Web-Online Public Access Catalogue (Web-OPAC).

The library is actively engaged in the compilation, design, and printing of the institute's Parliamentary and Scientific Annual Reports in both Hindi and English. It also produces monthly pictorial research publications and bibliometric reports. Additionally, the department assists in collecting, compiling, editing, designing, and printing various institutional reports, including the RAP-SAC report, workshop reports, and documentation for the Scientific Industrial Research Organization registration.

Information about e-journal and e-book subscriptions, new acquisitions, and the publications list is regularly updated on the NII website. The library also maintains a searchable Institutional Digital Repository (IDR) containing full-text articles published by NII since 2008. The department conducts induction programs for new members and organizes workshops on topics such as plagiarism detection software and Scopus usage.

Moreover, the library manages all binding and photocopying work for the institute and maintains a collection of Hindi books and magazines, including those on administrative practices, to promote the Hindi language. In the past year, fifteen new books have been added to the library's collection.



Academic and Training Services

The activities of the Academic and Training Department can be categorized under three major groups: student affairs, in-house training, and training at other institutions. The department has been involved in Ph.D. admissions, pre-Ph.D. registration courses, scheduling of doctoral committee meetings and academic committee meetings, and the disbursement of fellowships of scholars.

The Institute takes in scientists who have been awarded independent fellowships from the following organisations who then work with different principal investigators: Indian Institute of Science Bangalore (DBT-RA), ICMR (SRF/RA), DST-SERB (NPDF), DST-Inspire Faculty, DST (WOS), CSIR (SRA/RA), DHR-Young Scientist, and Ramalingaswami Re-entry Fellowship.

The department also coordinates the training programs of the Institute such as short-term training of the fellows sponsored by the Indian Academy of Science, Bengaluru, six-month project work towards completion of master's degree for students of different Universities/Institutions, and short-term training of undergraduate students of different colleges under the Science Setu programme. The department has also been involved in arranging the participation of scientific, technical, and administrative officials of the Institute in various training courses.

Vigilance Cell

The Institute has a Vigilance Cell headed by a scientist nominated as a part-time Chief Vigilance Officer (CVO) by the Central Vigilance Commission (CVC). The CVO and the support staff perform activities related to vigilance as adjunct duties to their primary responsibilities.

The Cell follows instructions issued by the CVC from time to time to ensure effective implementation of measures aimed at strengthening vigilance and anti-corruption activities. Emphasis is laid on preventive vigilance, which when properly conceived and executed, can aid in reducing improper conduct at the Institute.

NII has been reviewing existing procedures to identify corruption-prone areas, making policies more transparent to avoid ambiguity, and streamlining procedures to achieve a working environment free of corruption. Staff employed in areas prone to corruption are periodically reassigned duties.

Sizeable purchases of chemicals, consumables, and instruments are handled through various purchase committees of the Institute; thus, eliminating the possibility of collusions detrimental to quality and price of purchases. Periodically, the institutional committees are reconstituted. The Cell has been rendering periodical reports to the administration and CVC.





The institute observes Vigilance Awareness Week (30 October to 5 November 2023)



Computer Centre

The Computer Centre has been providing all information technology-related support to the Institute. The major functions are managing switches, Wi-Fi controllers, Access Points in a 1000-node LAN, System administration of multiple LINUX-based E-mail and Web servers, backup services for mail/web servers, managing UTM devices for network security, and integrating internet bandwidth from multiple ISPs.

The staff of the Centre facilitates day-to-day troubleshooting, maintenance, and anti-virus support of about 850 PCs and other peripheral devices. In addition, the Centre also maintains and updates the institution's website, provides specialized services like management of HPC clusters, and manages floating licenses for access to Bioinformatics softwares over LAN.

It also provides support for the development of in-house software for PayRoll, an online complaint logging system, and the online creation of email IDs. The Centre also helps organize and conduct virtual meetings and lectures. The Centre has enabled the adoption of E-office, transforming NII into a paperless environment for file movement.



SUMMARY OF

NOTABLE ACTIVITIES

Academic Courses, Training Programmes and Interaction with Other Academic Institutes

The Institute imparts long-term residential training leading to a Ph.D. degree awarded by the Jawaharlal Nehru University, New Delhi. Among a large number of applicants from across the country, every year 30-35 scholars are admitted to this programme through a national-level examination followed by interviews. The Institute conducts two sessions annually for the intake of PhD candidates: winter and monsoon sessions.

The Ph.D. programme of the Institute was launched in the academic year 1986-87. In the year 2023-24, Monsoon Session 23 Students and in Winter Session 14 students were admitted by the Institute. So far 556 students have been awarded their Ph.D degrees including 15 who obtained the degree in academic year 2023-24. Many others are at various stages of their research work for the award of their degree.

In addition, the Institute hosts undergraduate, postgraduate, and school students for short-term training and projects.

Publications

Seventy-eight research papers were published this year. Of these publications, sixty-seven were published in journals as peer-reviewed research papers and the remaining eleven as reviews/proceedings. Details of these papers are available in Annexure-I



Patents

The Institute has a policy of protecting intellectual property rights of inventions made within its laboratories. Early research leads are evaluated for commercial viability and patentability. The Institute files applications first in India and when necessary, at patent offices in other countries. During the year under report, the Institute has filed ten patent applications, while eight patents were granted. Details of these patents are available in Annexure-I

Lectures/Talks Delivered and Papers Presented on Invitation

During 2023-2024, scientists of the Institute continued to deliver lectures including keynote/inaugural addresses, participate in panel discussions, conduct workshops, and present their work at various institutions, conferences, symposia, workshops, and training programmes in India and abroad.

Lectures/Seminars by Visiting Scientists/Guest Investigators

The Institute continued to host scientists from all over the world. On such visits, the visiting scientists interact with the faculty and students of NII and deliver a seminar in their field of study. During 2023-2024, thirty-six seminars were organized on the campus, which included graduate students' and invited seminars. These seminars were attended not only by the scholars and scientists of the Institute but also by investigators from other neighbouring institutions.

Anti-Terrorism Day

Anti-Terrorism Day was observed on 21st May 2023. On this day, the anti-terrorism/violence pledge was taken which stated, "We the people of India having abiding faith in our country's tradition of non-violence and tolerance, hereby solemnly affirm to oppose with our strength and all forms of terrorism and violence. We pledge to uphold and promote peace, social harmony and social understanding among all fellow human beings and fight the forces of disruption threatening human lives and values".



Sadbhawna Diwas

Sadbhavana Diwas is observed on 20th August 2023 to commemorate the birth anniversary of former Prime Minister Late Sh. Rajiv Gandhi. Sadbhawana Diwas is observed to promote peace, national integration, and the strengthening of the concept of Unity in Diversity. On the occasion of Sadbhavana Diwas, the staff took the following pledge: "I take this solemn pledge that I will work for the emotional oneness and harmony of all the people of India regardless of caste, region, religion or language. I further pledge that I shall resolve all differences among us through dialogue and constitutional means without resorting to violence."

Rashtriya Ekta Diwas (National Unity Day)

Rashtriya Ekta Diwas is observed on 31st October 2023 in commemoration of the 148th birth anniversary of the great leader, Late Sri Sardar Vallabhbhai Patel. On the occasion of Rashtriya Ekta Diwas, the staff took the following pledge: "I solemnly pledge that I dedicate myself to preserve the unity, integrity, and security of the nation and also strive hard to spread this message among my fellow countrymen. I take this pledge in the spirit of unification of my country which was made possible by the vision and actions of Sardar Vallabhbhai Patel. I also solemnly resolve to make my own contribution to ensure internal security of my country".





Glimpses of the Run for Unity on National Unity Day at NII



Independence Day

Independence Day was celebrated on 15th August 2023 in the Institute. The event was marked by a message from Dr. Debasisa Mohanty, Director NII followed by the singing of the National Anthem by the students and children of the staff of the Institute.



Glimpses of the Independence Day celebrations at NII



Samvidhan Diwas

Samvidhan Divas is celebrated on 26th November to commemorate the adoption of the Constitution of India. On 26th November 1949, the Constituent Assembly of India adopted the Constitution of India, which came into effect on 26th January 1950.

On the occasion of Sadbhavana Diwas, the staff took the following pledge: "WE, THE PEOPLE OF INDIA, having solemnly resolved to constitute India into a SOVEREIGN SOCIALIST SECULAR DEMOCRATIC REPUBLIC and to secure to all its citizens: JUSTICE, social, economic and political; LIBERTY of thought, expression, belief, faith and worship; EQUALITY of status and of opportunity; and to promote among them all FRATERNITY assuring the dignity of the individual and the unity and integrity of the Nation; We do hereby give to ourselves this Constitution".

International Women's Day

International Women's Day celebrates the social, economic, cultural, and political achievements of women. On this day, the institute celebrated the pivotal role of women in shaping its journey in the Indian research ecosystem. Several activities were planned to ensure that the women of the institute had a fun and memorable experience. In addition, a session on health awareness was also conducted by Dr Deepika Chauhan, Head of Department, Radiation Oncology, Venkateshwar Hospital, Dwarka.





International Women's Day celebrations at NII

International Yoga Day

Yoga keeps our body healthy and enhances the wellness of our minds. We celebrated the 9th International Day of Yoga on campus on 21 June 2023 to emphasize embracing yoga for a healthy lifestyle for everyone. On this occasion, a yoga session was organised with Mr. Nilesh Mourya from the Morarji Desai Institute of Yoga, Ministry of Ayush, Government of India.



A Yoga session in progress at NII



Representation of Scheduled Castes, Scheduled Tribes, Other Backward Classes, and Economically Weaker Sections

While making appointments, the Institute complies with reservation guidelines as per the directives of the Government of India to ensure representation of Scheduled Castes, Scheduled Tribes, Other Backward Classes and the Economically Weaker Sections.

Representation of Persons with Benchmark Disabilities

The Institute follows reservation guidelines for persons with benchmark disabilities as per Government of India directives to ensure appropriate representation.

Implementation of Official Language Policy

The Official Language Policy of the Government of India is followed in letter and spirit:

- To promote Hindi as an Official Language, a Hindi Pakhwara (Hindi Fortnight) was celebrated with great zeal in the institute from 18 September 2023 to 03 October 2023. During this period, various Hindi competitions such as Hindi Sulekh (Hindi writing), Hindi Srutlekh (Hindi Dictation), Hindi Samaanyagyaan (Hindi General Knowledge), Hindi Vayavhaarik (Hindi noting and drafting) and Hindi Aashubhashan (Pick and Speak) competitions were organized. Many faculty, staff and students participated in these competitions. Prizes were distributed on the last day of Hindi Pakhwada.
- The Institute organized quarterly Hindi workshops/lectures for employees during the year to enable its staff to use Hindi in official work with ease and confidence.
- An incentive scheme was implemented at NII to encourage scientific and technical staff members to write articles and research papers in Hindi on scientific and technical subjects.

The institute has published the 5th edition of its in-house magazine, "JAIVPRATIRAKSHA DARPAN," in Hindi. The process for publishing the 6th edition of the magazine has started and it will be published soon.





A Hindi workshop conducted for the staff of NII

RTI ANNUAL RETURN

INFORMATION SYSTEM

REPORT ON RECEIPT AND MONTHLY DISPOSAL OF RTI CASES APRIL 2023 - MARCH 2024

Sl. No.	Year	Month	Opening Balance	Receipt	Disposed	Closing Balance
1	2023	April	476	2	2	478
2	2023	May	478	1	0	479
3	2023	June	479	1	0	480
4	2023	July	480	3	1	483
5	2023	August	483	2	0	485
6	2023	Sept	485	4	3	489
7	2023	Oct	489	5	3	494
8	2023	Nov	497	3	1	497
9	2023	Dec	497	6	2	503
10	2024	Jan	503	2	1	505
11	2024	Feb	505	3	2	508
12	2024	March	508	5	3	513
	Total			37		

Total RTI cases received as on 31st March 2024 = 37



RTI ANNUAL RETURN INFORMATION SYSTEM (2023-2024)

ANNUAL RETURN FORM

Ministry /Department /Organization: Department of Biotechnology
(National Institute of Immunology), New Delhi-110067

Year 2023-24 (up to March 2024)

	Opening balance As on 1-04-2023	Received during the Year 2023-2024 (including cases transferred to other Public Authority)	No. of cases transferred to other Public Authority	Decisions where request/ appeals rejected	Decision where requests/ appeals accepted
Request	0	37		0	37
First Appeal	0				



No. of cases where disciplinary action taken against any Officer	NIL
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No. of CAPIOs designated	No. of CPIOs designated	No. of AAs designated
0	1	1

No. of times various provisions were invoked while rejecting requests

Relevant Sections of RTI Act 2005

Sections 8(1)										Sections			
a	b	c	d	e	f	g	h	i	j				Others
									8				

Amount Charges Collected (in Rs)

Registration Fee Amount	Additional Fee & Any other charges	Penalties Amount
60	-	-

Last date of Uploading the Pro-active Disclosures on the website of PA	http://www.nii.res.in/others/right-information
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Name of the person who is entering/updating data	P Nagarajan
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COMMITTEES OF THE INSTITUTE

GOVERNING BODY

Dr. Rajesh S. Gokhale

Chairperson
Secretary
Department of Biotechnology
Ministry of Science & Technology
Government of India
New Delhi

Sh. Vishvajit Sahay

Additional Secretary & Financial Adviser
Department of Biotechnology
Ministry of Science & Technology
Government of India
New Delhi

Sh. Chaitanya Murti

Joint Secretary (Admin)
Department of Biotechnology
Ministry of Science & Technology
Government of India
New Delhi

Dr. Suchita Ninawe

Adviser/Scientist-'G'
Department of Biotechnology
Ministry of Science & Technology
Government of India
New Delhi



Prof. Soniya Nityanand

Director, RMLIMS, Lucknow and
Professor, Department of Hematology
Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGI)
Lucknow

Dr. Anurag Agrawal

Dean, Ashoka University Haryana and
Former Director, CSIR-Institute of Genomics and Integrative Biology (CSIR-IGIB)
New Delhi

Dr. Manoj Kumar Bhat

DBT Distinguished Scientist and
Former Director, National Centre for Cell Science (NCCS)
Pune

Dr. (Prof.) Minakshi Bhardwaj

Former Director & MS, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS)
and Dr. Ram Manohar Lohia Hospital
New Delhi

Dr. Rajesh Ghangal

Nodal Officer of NII in DBT and
Scientist- 'D', Department of Biotechnology
Ministry of Science & Technology
Government of India, New Delhi

Dr. Debasisa Mohanty

Director
National Institute of Immunology
New Delhi

Dr. Pushkar Sharma

Staff Scientist-VII
National Institute of Immunology
New Delhi

Dr. D. K. Vashist

Senior Manager
National Institute of Immunology
New Delhi

SCIENTIFIC ADVISORY COMMITTEE

Dr. R. V. Hosur

Chairperson
Department of Chemical Sciences,
Tata Institute of Fundamental Research
1-Homi Bhabha Road, Colaba
Mumbai



Prof. Amita Aggarwal

Head of Department of Clinical Immunology and Rheumatology
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow

Prof. Shubhada V. Chiplunkar

Former Director
Advance Centre for Treatment, Research & Education in Cancer (ACTREC)
Tata Memorial Centre
Navi Mumbai

Dr. Sudhir Gupta

Professor of Medicine,
Pathology & Laboratory Medicine and
Microbiology & Molecular Genetics
Chief, Division of Basic & Clinical Immunology
University of California, Irvine, USA

Prof. Trinad Chakraborty

Professor of Medical Microbiology and
Director, Institute for Medical Microbiology
Justus-Liebig-University Faculty of Medicine
Giessen, Germany

Prof. Soniya Nityanand

Head Department of Haematology
Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGI), Lucknow

Dr. Anurag Agarwal

Dean, Trivedi School of BioSciences, Ashoka University, Haryana
Former Director, CSIR-Institute of Genomics and Integrative Biology (CSIR-IGIB)
New Delhi

Dr. Minakshi Bharadwaj

Professor of Pathology
Dr. Ram Manohar Lohia Hospital (RML) Hospital and
Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS)
New Delhi

Dr. Manoj Kumar Bhat

DBT Distinguished Scientist and
Former Director, National Centre for Cell Science (NCCS)
Pune

Dr. Anamika Gambhir

Member (Ex-Officio)
Scientist- 'G'
Department of Biotechnology
Government of India, New Delhi

Dr. Debasisa Mohanty

Director
National Institute of Immunology, New Delhi



RESEARCH AREA PANELS (RAP)

Dr. Rajan Sankaranarayanan

Outstanding Scientist, Structural Biology Laboratory
CSIR-Centre for Cellular and Molecular Biology (CCMB), Hyderabad

Dr. Souvik Maiti

Director, CSIR- Institute of Genomics and Integrative Biology
Mathura Road, New Delhi

Prof. R. Sankararamakrishnan

Professor
Department of Biological Sciences & Bioengineering (BSBE)
Indian Institute of Technology, Kanpur

Dr. Dinakar M. Salunke

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International Centre for Genetic Engineering and Biotechnology
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New Delhi

Dr. Sharmila A Bapat

Director (Additional Charge)
National Centre for Cell Science (NCCS)
NCCS Complex, Pune University Campus, Pune

Prof. V. Nagaraja

Honorary Professor
Department of Microbiology and Cell Biology
Indian Institute of Science (IISc)
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Senior Principal Scientist (Functional Genomics)
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Dr. Lolitika Mandal

Associate Professor, Biological Sciences
Indian Institute of Science Education and Research (IISER)
Mohali, Punjab

Dr. Sathees C. Raghavan

Professor
Department of Biochemistry
Indian Institute of Science (IISc)
Bengaluru, Karnataka



Prof. Apurva Sarin

CEO, DBT/Wellcome Trust India Alliance
Hyderabad

Prof. Yogendra Singh

Professor
Department of Zoology
University of Delhi, New Delhi

Dr. Mohan Wani

Scientist 'G'
National Centre for Cell Science Complex
Savitribai Phule Pune University Campus
Pune

Dr. Pawan Malhotra

Group Leader, Malaria Biology
International Centre for Genetic Engineering and Biotechnology
Aruna Asaf Ali Marg
New Delhi

Dr. Neel Sarovar Bhavesh

Group-Leader
International Centre for Genetic Engineering and Biotechnology
New Delhi

Prof. Ullas Kolthur-Seetharam

Director
Centre for DNA Fingerprinting and Diagnostics
Hyderabad



FINANCE COMMITTEE

Sh. Vishvajit Sahay

Chairperson
Additional Secretary & Financial Adviser
Department of Biotechnology
Ministry of Science & Technology
New Delhi

Dr. Suchita Ninawe

Scientist-G
Department of Biotechnology
Ministry of Science & Technology
New Delhi

Dr. Subhra Chakraborty

Director
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Aruna Asaf Ali Marg,
New Delhi

Dr. Monica Singhania

Professor
Faculty of Management Studies,
University of Delhi
New Delhi

Sh. Sanjay Gupta

Former President
Institute of Cost Accounts of India,
New Delhi

Dr. Debasisa Mohanty

Director
National Institute of Immunology
New Delhi

Dr. D.K Vashist

Senior Manager
National Institute of Immunology
New Delhi

Sh. Pradeep Chawla

Member Secretary
Finance & Accounts Officer
National Institute of Immunology
New Delhi



BUILDING COMMITTEE

Shri Ashwani Nagar

Chairperson
Retired Principal General Manager and
Head of Civil Engineering Division of
Department of Telecom

Director, NII

Member (Ex-Officio)
Ex-Officio Director
National Institute of Immunology
New Delhi

Director, NIPGR

Member (Ex-Officio)
Ex-Officio Director
NIPGR
New Delhi

Executive Director, RCB

Member (Ex-Officio)
Ex-Officio Executive Director
Regional Centre for Biotechnology
Faridabad

Dr. Dinakar Salunke

Member,
Ex-Director, ICGEB
New Delhi

Dr. Agam P. Singh

Member
Staff Scientist-VI
National Institute of Immunology
New Delhi

Shri M. K. Gupta

Member
Ex-Engineer (Civil)
IUAC
New Delhi

Senior Manager

Member Secretary (Ex-Officio)
Ex-Officio Senior Manager,
National Institute of Immunology
New Delhi



ACADEMIC COMMITTEE

Dr. Debasisa Mohanty

Chairperson
Director,
National Institute of Immunology
New Delhi

Prof. Shantanu Chowdhury

Member
Chief Scientist (Functional Genomics)

Prof. Pradeep Kumar Burma

Member
University of Delhi
New Delhi

Prof. Anand Ranganathan

Member
Jawaharlal Nehru Univeristy
New Delhi

Prof. Satish Chandra Garkoti

Special Invitee
Rescor-I, Jawaharlal Nehru University
New Delhi

Dr. Madhulika Srivastava

Academic/Students Affairs
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Arnab Mukhopadhyay

Member
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Nimesh Gupta

Member
Staff Scientist
National Institute of Immunology
New Delhi



INSTITUTIONAL ANIMAL ETHICS COMMITTEE

Dr. Devinder Sehgal

Chairperson
Biological Scientist
National Institute of Immunology
New Delhi

Dr. P Nagarajan

Member Secretary
Scientist, Incharge of Animal House Facility
National Institute of Immunology
New Delhi

Dr. Pravin Kumar Atul

CCSEA Main Nominee
National Institute of Malaria Research
New Delhi

Dr. Krushnarvind Babalbhai Patel

CCSEA Link Nominee
Institute of Liver and Biliary Sciences
New Delhi

Dr. Suresh Kumar Dwarikadheesh

CCSEA Nominated Member
National Institute of Biologicals
Noida

Dr. Kakali Purkayashtha

CCSEA Nominated Member
All India Institute of Medical Sciences
New Delhi

Dr. Soumen Basak

Staff Scientist
National Institute of Immunology
New Delhi

Dr. Nimesh Gupta

Staff Scientist
National Institute of Immunology
New Delhi

Dr. Surender Singh

Veterinarian
National Institute of Immunology
New Delhi



INSTITUTIONAL BIO-SAFETY COMMITTEE

Dr. Arnab Mukhopadhyay

Chairman
National Institute of Immunology
New Delhi

Dr. Soumen Basak

Member Secretary
National Institute of Immunology
New Delhi

Prof. Krishnamurthy Natarajan

DBT Nominee
Jawaharlal Nehru University
New Delhi

Dr. Mohammed Faruq

Bio-safety Officer
Institute of Genomics & Integrative Biology
New Delhi

Dr. Dhiraj Kumar

External Expert
International Centre for Genetics and Engineering Biotechnology
New Delhi

Dr. Sarika Gupta

Internal Member
National Institute of Immunology
New Delhi

Dr. Prafullakumar B Tailor

Internal Member
National Institute of Immunology
New Delhi

Dr. Devram Ghorpade

Internal Member
National Institute of Immunology
New Delhi



INSTITUTIONAL HUMAN ETHICS COMMITTEE

Prof. Subrata Sinha

Chairman
All India Institute of Medical Sciences
New Delhi

Dr. Sandeep Mathur

Vice-Chairperson
Member, Basic Medical Scientist
All India Institute of Medical Sciences
New Delhi

Dr. Arnab Mukhopadhyay

Member Secretary
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Shinjini Bhatnagar

Member, Clinician
Translational Health
Science & Technology Institute
Faridabad

Maj. Gen B. S. Dhillon (VSM)

Member, Social Scientist
201 Rose Apartments
Gurugram

Dr. Goutam Bhattacharya

Member, Legal Expert
K & S Partners
Intellectual Property Attorneys
Gurugram

Dr. Nimesh Gupta

Member, Basic Medical Scientist
Staff Scientist
National Institute of Immunology
New Delhi

Sh. Sudhir Patwal

Member, Layperson
National Institute of Plant Genome
Research
New Delhi

Dr. Rahul Pal

Member
Ex- Emeritus Scientist
National Institute of Immunology
New Delhi



STAFF OF THE INSTITUTE

As on 31.03.2024

SCIENTIFIC STAFF

Core and Infrastructure Scientists

Dr. Debasisa Mohanty, Director
Dr. Pushkar Sharma, Staff Scientist-VII
Dr. Madhulika Srivastava, Staff Scientist-VII
Dr. Vinay K. Nandicoori, Staff Scientist-VII (On Deputation)
Dr. Sagar Sengupta, Staff Scientist-VII (On Deputation)
Dr. Devinder Sehgal, Staff Scientist-VII
Dr. Apurba K. Sau, Staff Scientist-VII
Dr. Monica Sundd, Staff Scientist-VII
Dr. Sanjeev Das, Staff Scientist-VII
Dr. Arnab Mukhopadhyay, Staff Scientist-VI
Dr. S. Gopalan Sampathkumar, Staff Scientist-VI
Dr. Bichitra K. Biswal, Staff Scientist-VI
Dr. Prafullakumar B. Tailor, Staff Scientist-VI
Dr. Soumen Basak, Staff Scientist-VI
Dr. Agam P. Singh, Staff Scientist-VI
Dr. Sarika Gupta, Staff Scientist-VI
Dr. Vidya Raghunathan, Staff Scientist-V (*Superannuated on 30.09.2023*)
Dr. Nimesh Gupta, Staff Scientist-V
Dr. Aneeshkumar A.G., Staff Scientist-V
Dr. Veena S. Patil, Staff Scientist-V
Dr. P. Nagarajan, Staff Scientist-IV
Dr. Devram Ghorpade, Staff Scientist-IV
Dr. Santiswarup Singha, Staff Scientist-IV
Dr. Anil Kumar, Staff Scientist-IV
Dr. Tanmay Majumdar, Staff Scientist-IV
Dr. Senthil Kumar, Staff Scientist-IV
Dr. Chhuttan Lal Meena, Staff Scientist-IV
Dr. Rajesh Kumar Yadav, Staff Scientist-IV
Dr. Narendra Kumar, Staff Scientist-IV
Dr. Ankita Varshney, Staff Scientist-III



Other Scientific Staff

SCIENTIST (PROJECT)

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Ms. Aakriti Jha
Ms. Pooja Mishra
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Ms. Atheena Menon G.
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Sh. Hemant Kumar

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Ms. Antara Mondal

Ms. Chandrima Bharadwaj

Mr. Chen Chongtham

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Ms. Anjali Kalia

Ms. Komal

Mr. Mohit Yadav

Mr. Naveen Kumar

Ms. Rashmi Sanjay Bhosale

Mr. Raunak Kar

Ms. Rimpay Arun

Ms. Sabnam Sahin Rahman

Ms. Sapna Pal

Ms. Shabnam

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Mr. Someshwar Nath Jha

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Ms. Witty Tyagi

Ms. Ankita Yadav

Mr. Ajay Kumar

Mr. Anirban Molla

Ms. Annu Nagar

Mr. Arnab Kumar Sahoo

Ms. Khushboo Chaudhary

Ms. Kirti Sharma

Ms. Niti Shokeen

Mr. Md Azad

Ms. Pratiksha Shome

Ms. Savita

Ms. Shaikh Zikra Arkam

Ms. Simran Aittan

Ms. Simran Motwani

Ms. Summaiya Khan

Ms. Suvechchha Pandit

Ms. Swati Kumari

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Ms. Ankita Paraste

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Ms. Chayanika Gogoi

Mr. Faisal Jamal

Ms. Geetika Kumari Ramesh Chandra

Mr. Jashobanta Behera

Ms. Jasleen Kaur

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Ms. Pratiti Bakshi

Ms. Rakhi

Ms. Shweta Mahapatra

Ms. Sonanjali Aneja

Ms. Tavleen Kaur

Mr. Varun Kumar

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Ms. Aishwarya Rajan



Mr. Amit Kumar
Ms. Arundhati Karmakar
Mr. Bhanu Pratap Singh
Mr. Debodyuti Sadhukhan
Ms. Dorle Archana Mukund
Mr. Jawahar P
Ms. Khushboo
Ms. Meenakshi
Mr. Mohd Irfan
Ms. Mohini
Mr. Rahul Yadav
Mr. Ratulananda Bhadury
Ms. Shalini Kumari
Ms. Shivangi Vaish
Ms. Shreya Sinha
Ms. Shubhi Khare
Mr. Sk Asif Ali
Ms. Sumnil
Ms. Swapnava Basu
Ms. Vaidehee
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Mr. Ashish Kumar Mishra
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Ms. Sanchi Arora
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Ms. Yojana Narendra Vaidya
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Ms. Sangita Dey
Ms. Sazida
Ms. Zainab Khatun
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TECHNICAL STAFF

SENIOR TECHNICAL OFFICERS

Ms. Sweety Batra (*Superannuated on 30.09.2023*)
Ms. Rekha Rani (*Superannuated on 30.09.2023*)
Ms. Sushma Nagpal
Dr. Neerja Wadhwa
Dr. Archana Ranjan
Ms. Neetu Kunj
Sh. Ranbir Singh (*Superannuated on 31.03.2024*)
Sh. Md Aslam
Sh. Ashok Kumar (*Superannuated on 31.07.2023*)
Sh. Ram Bodh (*Superannuated on 31.03.2024*)
Sh. Rajit Ram
Sh. Kevlanand
Sh. Inderjit Singh
Sh. Chanderdeep Roy
Sh. Sunder Singh Bisht
Sh. Dhramvir Singh
Sh. Roshan Lal
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Sh. Manoj Kumar
Sh. Kumod Kumar
Sh. Deshraj
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Sh. Sooraj Prakash
Sh. R.K. Bharadwaj
Sh. R.K. Sharma
Sh. Yogesh Kr. Tripathi
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Primate Research Centre

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Sh. Ram Dev Yadav

Sh. Ram Surat

Sh. Subhash Chand III

Sh. Krishen



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Sh. Darwan Singh

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JUNIOR ASSISTANT II

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Sh. Mahender Singh

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Sh. Nand Lal Malakar
Sh. Jawahar Singh
Sh. Chatter Singh
Sh. Ram Chander
Sh. Ajay Kumar
Sh. Rakesh Kumar II
Sh. Rajeev Kumar
Ms. Usha
Sh. Himanshu

Finance & Accounts

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Sh. Pradeep Chawla (*Superannuated on 31.12.2023*)

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Sh. Naveen Negi



Stores and Purchase

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Patent Cell

Dr. Anil Kumar

SECTION OFFICER

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Public Relations

PUBLIC RELATION OFFICER

Dr. Banya Kar (*Short Term Contract Basis*)



SIX MONTH PROJECT TRAINEES 2023-2024

S.No	Name	Lab-In-Charge	D.O.J
1	Somesh Kumar Jha	Dr. Arnab Mukhopadhyay	03.04.2023
2	Prakhar Varshney	Dr. Nimesh Gupta	22-05-2023
3	Minhaaz Suhail	Dr. Arnab Mukhopadhyay	01-05-2023
4	Shristy Kothiwala	Dr. Veena S. Patil	16-05-2023
5	Mainak Sarkar	Dr. Devinder Sehgal	16-05-2023
6	Mm Prajwal Roopanath	Dr. Nimesh Gupta	15-05-2023
7	Akanksha Pattanaik	Dr. Debasisa Mohanty	29.05.2023
8	Barri Yaswitha	Dr. P Nagarajan	01-05-2023
9	Minhaaz Suhail	Dr. Arnab Mukhopadhyay	01-05-2023
10	Bhagat Khevna	Dr. Devram Ghorpade	17-05-2023
11	Sheral Vimal Bhardoliya	Dr. Santiswarup Singha	17-05-2023
12	Nishant Parida	Dr. Prafullakumar B. Tailor	03.07.2023
13	Vertika Rai	Dr. Ankita Varshney	05.07.2023
14	Anjali	Dr. Ankita Varshney	07.07.2023
15	Kashish Mittal	Dr. Sarika Gupta	07.07.2023
16	Sachin	Dr. Tanmay Majumdar	17.07.2023
17	Shubhangi Sharma	Dr. Agam P. Singh	17.07.2023
18	Sohini Mukhopadhyay	Dr. Sarika Gupta	20.07.2023
19	Himanshi	Dr. CL Meena	04.10.2023
20	Smriti Raina	Dr. Arnab Mukhopadhyay	11.12.2023
21	Vaani Bhardwaj	Dr. Veena S. Patil	11.12.2023
22	Esha Garg	Dr. Rajesh Kumar Yadav	19.12.2023
23	Shahana V	Dr. Devinder Sehgal	01.01.2024
24	Divyanshi Sahu	Dr. Nimesh Gupta	01.01.2024
25	Riddhi Pandey	Dr. C. L. Meena	01.01.2024
26	Ashwani Singh	Dr. Sarika Gupta	01.01.2024
27	Ankita Ravindra	Dr. Sarika Gupta	01.01.2024
28	Devansh Fulara	Dr. Devram Ghorpade	01.01.2024
29	Shefali Dahiya	Dr. Rajesh Kumar Yadav	02.01.2024
30	D. Oviya	Dr. Arnab Mukhopadhyay	03.01.2024



31	Ishu Sharma	Dr. CL Meena	05.01.2024
32	Jahnvi Hora	Dr. Narendra Kumar	15.01.2024
33	Amina Ali	Dr. Bichitra Kumar Biswal	15.01.2024
34	Sauvika Kumari	Dr. Tanmay Majumdar	16.01.2024
35	Kajal Keshri	Dr. Tanmay Majumdar	16.01.2024
36	Harsha Verma	Dr. Anil Kumar	22.01.2024
37	Vinit Chauhan	Dr. Agam P. Singh	22.01.2024
38	Gunjan Lunthi	Dr. Rajesh K. Yadav	23.01.2024
39	Srishti Aggarwal	Dr. Apurba K Sau	01.01.2024
40	Shreya Srivastava	Dr. Ankita Varshney	01.01.2024
41	Manvi Aswani	Dr. Tanmay Majumdar	01.02.2024






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