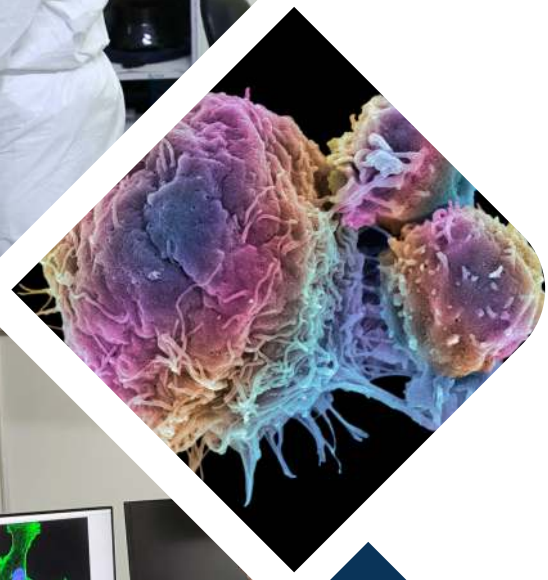
2022-2023

ANNUAL REPORT



राष्ट्रीय प्रतिरक्षाविज्ञान संस्थान

NATIONAL INSTITUTE OF IMMUNOLOGY

NATIONAL INSTITUTE OF IMMUNOLOGY

ANNUAL REPORT
2022-2023

CONTENTS

MANDATE OF THE INSTITUTE

- To undertake, aid, promote, guide and co-ordinate research of high calibre in basic and applied immunology
- To carry out research for development of new vaccines and immunological reagents for communicable diseases
- To develop immunological approaches for regulation of male and female fertility
- To interact with industry for manufacture of vaccines and immunological reagents
- To organise postgraduate courses, workshops, seminars, symposia and training programmes of a specialized nature in the field of immunology, vaccine development and related areas
- To organise training programmes for technicians in immunological methods and related techniques
- To establish affiliation with recognised universities and institutions of higher learning for the purpose of enabling research scholars to register for postgraduate degrees
- To serve as a national reference centre for immunology and to provide consultancy services to medical and veterinary institutions, public health agencies and industries in the country
- To provide and promote effective linkages on a continuing basis between various scientific and research agencies/laboratories and other organisations working in the country in the field of immunology, vaccine development and related areas
- To collaborate with foreign research institutions, laboratories and other international organisations in fields relevant to the objectives mentioned above

FOREWORD

The immune system is one of the most complex parts of the human body. The immensely intricate network of cells and molecules meant to protect us leaves us with questions still unanswered. Over the years, the centrality of research in immunology to biomedical studies and public health has been underscored. Crucial contributions from this field ranging from elucidating fundamental properties of blood to enabling the treatment and prevention of diseases such as cancer and COVID-19 have led to extraordinary medical advances.

Since its inception, the National Institute of Immunology has been at the forefront of unravelling the intricacies of this immune system for human health and wellbeing. In the past four decades, there has been significant progress in our ongoing efforts to develop new lines of research at NII. Today, researchers at NII are trying to address interdisciplinary research questions in areas of biological sciences spanning from immunology, infectious and chronic disease biology, molecular and cellular biology, chemical biology, and structural biology to computational biology.

We at NII have access to scientific and technical facilities of international standards, which has made cutting-edge research in emerging areas like genomics, proteomics, systems biology, and computational biology possible. In the past year, research carried out at NII has given rise to innovations that find applications from vaccine development to immunotherapeutics to the treatment of cancers, neurodegenerative disorders, and infectious diseases. The research excellence of NII is reflected in the national and international acclaim won by our scientists and students for their contributions to the field of immunology. I highlight below some of the important scientific achievements during the year.

Through the COVID-19 pandemic, NII has been at the forefront of India's response to infectious diseases. The contributions of NII span from screening and genomic surveillance to vaccine research. A multicentric collaborative study, anchored at NII, provided the first evidence of the traits of immune memory generated in response to Covaxin (BBV152). The "Human Immune Monitoring and T-cell Immunoassay Platform" of NII was instrumental in the study of the effectiveness of Bharat Biotech's Intranasal COVID-19 vaccine "iNCOVACC". Further, efforts were made to design a nanoparticle vaccine with a multivalent display of the receptor binding domain (RBD) of SARS-CoV-2. Small animal studies established the potential of this formulation to be developed as a subunit vaccine against COVID-19. In a multi-institutional study, NII scientists were involved in the development of an extremely potent monoclonal antibody named P4A2 that could neutralize all the circulating variants of concern of SARS-CoV-2 with high efficiency, including Omicron. In another study, kinase-like activity

of the NiRAN domain was discovered and a drug repurposing approach was used to identify a number of widely used kinase inhibitors that could be developed as anti-viral agents for SARS-CoV-2. These and various other projects driven by researchers at NII continue to contribute to the knowledge required for the development of vaccines (RBD-based nanoparticles), neutralizing antibodies (P4A2 mAb), and therapeutics (anti-SARS-CoV-2 drug target) against COVID-19.

Apart from COVID-19, multiple groups at NII are involved in research that aims to enhance the understanding of the immune system and its processes as well as other infectious diseases caused by bacteria, viruses, and parasites. *Salmonella enterica* serovar Typhi (*S. Typhi*) shares a high degree of homology with a closely related serovar, *S. Typhimurium.* Yet, unlike *S. Typhimurium*, *S. Typhi* does not establish infection in mice. Research from NII indicates that the early onset and sustained presence of antibacterial activities distinguish the response of mice to *S. Typhi* from that of *S. Typhimurium*. Studies to improve mechanistic insight on human chorionic gonadotropin's (hCG) role in systemic autoimmunity revealed that hCG is a disease-promoting co-stimulant that in combination with specific apoptotic bodies enhances the intensity of multiple lupus-associated events. Tumor-targeted delivery of *Mycobacterium indicus pranii (MIP*) adjuvant encapsulated chitosan nanoparticles has demonstrated potential anti-cancer activity in the tumor microenvironment. Ongoing studies on MIP also establish that MIP therapy suppresses the systemic dissemination of tumor cells in the B16F10 murine model of melanoma. The results of this study have significant implications for the application of MIP in cancer treatment. In another study, the group found resting-state B cells to have higher protein synthesis levels than T cells *in vitro* and *in vivo* by maintaining an intermediate level of active mTORC1 pathway. Exploring the role of vitamin D in controlling cellular infections by the Chandipura virus, it was revealed that vitamin D instructs the homeostatic state of antiviral pathways like those regulating NF-κB and IFN regulatory factors, leading to cellular resilience to subsequent viral infections. Immune signaling homeostasis appears to connect micronutrients to antiviral immunity at the cellular level, and this finding may have a bearing on shaping public health policy during an outbreak. Research in the area of computational biology at NII has led to the development of a machine-learning-based computational method for the identification and annotation of small open reading frames in bacterial genomes. In silico drug design studies have resulted in the identification of allosteric inhibitors for PfCDPK1, an essential drug target against malaria. Inhibitors of the DNA polymerase of the monkeypox virus have also been identified at NII using a virtual screening approach.

Understanding how enzymes and receptors work is critical to our understanding of host-mediated immunity as well as disease biology. Studies on enzymes of the lipoic acid biosynthesis pathways resulted in the identification of a new substrate analog. This information might have implications for the treatment of patients with human mitochondrial fatty acid synthesis-related disorders. Studies at NII also revealed a mechanistic basis for the difference in GMP formation between two close homologues of human GTPases. This study could provide insight into how these two close homologs play crucial roles in host-mediated immunity through different mechanisms. Important contributions have been made towards a mechanistic understanding of neurological disorders like Alzheimer's Disease and Parkinson's Disease. AdipoRon an orally active adiponectin receptor agonist with therapeutic activity in

metabolic diseases was shown to ameliorate Alzheimer 's-like pathologies and associated cognitive impairment in mice.

Research undertaken at NII has also made important contributions in the areas of genetics, cell signaling, and cancer biology. A collaborative study involving NII, CCMB, and IISc showed that the depletion of the primary sigma factor σA of *Mycobacterium tuberculosis (Mtb)* results in a severe survival defect *in vitro*, *ex vivo*, and *in vivo* in a murine infection model. This study provides insights into how *Mtb* modulates its genetic machinery to survive under hostile host conditions. Another study identified that EmbR, a transcription factor, plays important roles in modulating cellular morphology, antibiotic resistance, and survival of *Mtb* in the host.

Of late, there has been an upsurge in interest in phosphoinositides (PIP) signaling in apicomplexan parasites such as *Toxoplasma* and *Plasmodium* spp. as they have been implicated in several critical processes. Researchers at NII reported a VPS15-like kinase that regulates apicoplast biogenesis and autophagy by promoting PI3P generation in *Toxoplasma gondii*.

Therapeutic methods to modulate skin pigmentation have important implications for skin cancer prevention and treating cutaneous hyperpigmentary conditions. A multicentric study identified the transient yet critical role of SREBF1-mediated fatty acid metabolism during the melanogenic phase. This study suggests that inhibitors of fatty acid metabolism may be effective in resolving hyper pigmentary conditions.

Studies were taken up to test the effects of rifampicin during hyperglycemia in *C. elegans* and a mouse model of obesity-induced type 2 diabetes. The observed protective effects of rifampicin and its analog in both the models and the increase in life span in *C. elegans* indicate the potential to reposition these drugs to treat hyperglycemia-related complications in patients.

Researchers at NII showed in both patients with retinitis pigmentosa (RP) and a mouse model of the disease that the immunological consequences of RP contribute to the progression of retinal degeneration. Although the eye is an immune-privileged organ, RP alters the ocular immune privilege mechanisms and creates an auto-reactive immune environment that accelerates retinal degeneration.

The generation of gut microbiota-derived trimethylamine N-oxide (TMAO) from the metabolism of dietary L-carnitine and choline is associated with adverse effects in humans, particularly inflammatory effects in colon cells. A rapid, highly sensitive, and economical molecularly imprinted polymer-based electrochemical sensor was developed at NII in collaboration with JNU (New Delhi) to detect TMAO in clinical samples.

NII recognizes that developing research ecosystems that produce high-quality research requires capacity-building activities. We have been inviting leading national and international researchers to NII for seminars to promote understanding of the frontiers of biomedical research. Such visits allow student and faculty interactions with visiting researchers leading to resource and knowledge sharing, including the possibilities of future collaborations. Additionally, NII offers training to both undergraduate and postgraduate science students through various programs. The goal of this training is to enhance their

scientific research skills by teaching them the process of scientific inquiry and providing hands-on experience in advanced tools and techniques used in biotechnology and other multidisciplinary fields.

The pandemic resulted in a 'halt' in NII's efforts to actively engage with society on matters of health, science, and technology. However, in the past year, we have been able to broaden our engagement with society through talks, demonstrations, open days, and interactions. Under the Science Setu program, NII welcomed students and teachers from schools and undergraduate colleges into its campus and labs while the scientists of NII visited schools and colleges for interactions and talks. Last year NII hosted two open days that saw the participation of approximately 200 students and teachers. I take this opportunity to thank the faculty and students of NII for their efforts geared to foster scientific temper and interest in science and technology among the youth. NII would continue to work to make scientists accessible as role models to make science more appealing to students as well as bridge the gap between science and society.

I reiterate that science is a human, collaborative endeavor. The growth of NII has only been possible because of the exceptional work of its community–the administrative and technical staff, faculty, researchers, and graduate students. The fact that the smallest breakthrough in immunology can have profound effects worldwide–demonstrated by the COVID-19 vaccine development–underscores the importance of our work at NII. We thank the members of our Research Area Panel and Scientific Advisory for their appraisals, critiques, and counsel that steers our work here. Lastly, we thank the Department of Biotechnology and the Ministry of Science and Technology for their support all along the journey.

This annual report provides information about the institute and the activities it undertook in 2022-2023. I hope you find the information herein both useful and insightful.

Dr. Debasisa Mohanty
Director, NII

Date: 22nd August 2023

RESEARCH REPORTS

IMMUNITY & INFECTION

Study of immunotherapeutic potential of *Mycobacterium indicus pranii* (MIP) and the underlying mechanisms in animal models of tumor

Sangeeta Bhaskar

Principal Investigator	**Sangeeta Bhaskar**
Co-Investigator	Pramod K. Upadhyay
Ph.D. Students	Anush Chakraborty Gargi Roy Bharati Swami

Generation of antitumor immunity is difficult in the tumor-bearing host because of various negative regulatory mechanisms which can be overcome by activation of innate and Th1 immune response. MIP induces Th1 response which is also important for antitumor activity. Hence, we had started this study to evaluate the immunotherapeutic activity of MIP in mouse model of tumor. Both direct and indirect effect of MIP on cancer cells is being studied. Also, role of MIP on metastasis and angiogenesis in murine melanoma model and underlying mechanisms were studied.

A. Mechanism of MIP mediated tumor reduction: Direct and Indirect effect of MIP on cancer cells

Earlier studies from our lab on very aggressive and poorly immunogenic melanoma (B16F10) tumor model provide evidence of immunotherapeutic potential of MIP for cancer. MIP therapy altered the immunosuppressive tumor milieu to immunologically active one. Apart from the role of MIP in activation of immune response against tumor, direct effect of MIP on cancer cells was evaluated. Cancer cells treated with MIP in *in vitro* showed decreased survival and proliferation along with cell cycle arrest at G1/G0 phase. MIP significantly decreased ROS levels in cancer cells. Along with ROS there is decrease in autophagy levels after MIP treatment. Autophagy maintains expression of cancer progression markers like CD44. Studies done in our lab showed MIP treatment reduces CD44 expression on cancer cell surface. Similarly, other cancer progression markers like CTLA-4 and PD-L1 showed reduced expression upon MIP treatment. The decrease corresponds to the decrease in autophagy levels in these cells, confirmed by chloroquine treatment. Further, *in vivo* studies showed that MIP treated tumor sections showed accumulation of LC3 as compared to control, hence confirming the role of MIP in autophagy modulation. These findings suggest that MIP mediated autophagy modulation is one of the mechanisms involved in tumor reduction in MIP treated animals.

B. Mechanism of MIP mediated tumor reduction: Role of tumor infilterating B cells

Previous studies from our group have shown role of Th1 type response in MIP mediated tumor reduction in animal models but role of B cells was not known. When percentage of major lymphocytes population in the tumor draining lymph nodes of MIP treated / control mice was analysed, B cells number showed highest increase. To see if MIP has any role in B cell proliferation, B cell proliferation status inside the TDLNs and TME was analysed. Interestingly, $Ki67^{+}$ $B220^{+}$ B cells were significantly higher in MIP treated group as compared to control. Other possible reason for increased B cell percentage could be higher recruitment of B cells at the tumor site. For this, we performed a recruitment assay in which CFSE

labeled B cells from naïve mice were adoptively transferred to the tumor bearing mice. We found that the percentage of B cell infiltration was higher in MIP treated tumor bearing mice as compared to the control. These results suggest that MIP leads to higher proliferation as well as infiltration of B cells in tumor microenvironment. Further, these B cells exhibited higher expression of co-stimulatory molecules CD40, CD80 and CD86 in MIP treated group as compared to control. Interestingly, there was significant decrease in the immunosuppressive B_{reg} ($B220^{+}$ IL-10^{+}) percentage in MIP treated group. Expression of B and T lymphocyte attenuator (BTLA) on B cells which plays regulatory function was also found to be decreased in dLNs of MIP treated mice. Apart from this, there was conversion of follicular B cells ($CD23^{+}$) to marginal zone B cells ($CD21^{+}$/$CD35^{+}$) in TME. Over all this study suggests that B cells play an important role in MIP mediated anti-tumor response but further studies are needed.

Publications

Original peer-reviewed articles

1. Chakraborty A, Roy G, Swami B, & Bhaskar S* (2023). Tumor targeted delivery of mycobacterial adjuvant encapsulated chitosan nanoparticles showed potential anti-cancer activity and immune cell activation in tumor microenvironment. **Int. Immunopharmacol.** 114:109463.

2. Chakraborty A, Roy G, Fatima F, Swami B, & Bhaskar S* (2023). *Mycobacterium indicus pranii* therapy suppresses systemic dissemination of tumor cells in B16F10 murine model of melanoma. **Biomed. Pharmacother.** 160:114307.

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

[* Corresponding author]

Disorders of proliferation: Analysis of novel pathways and targets

Rahul Pal

Principal Investigator	**Rahul Pal**
Project Associate	Ruchi Sachdeva
Ph.D. Student	Moumita Sarkar
Collaborators	Usha Agrawal (NIP, New Delhi) Uma Kumar (AIIMS, New Delhi) Ravi Datta Sharma (Amity University, Gurugram) Ilpo Huhtaniemi (Imperial College, London)

Characterization of lupus-associated immune responses

Apoptotic bodies contain autoantigens and are believed to contribute to a break in self-tolerance. Previous work in our lab has investigated the characteristics of early humoral responses to dying cells, and the roles they might play in the progression of systemic autoimmune disease (**J Immunol.** 175:7669-7677, 2005; **Cell Death and Differ.** 13:1715-1726, 2006; **Eur J Immunol.** 38:3561-3574, 2008; **Lupus** 25:684-698, 2016; **Clin Exp Immunol.** 187:353-368, 2017).

Pregnancy can be associated with disease "flares", the reasons for which remain obscure. Previous studies in our lab potentially link human chorionic gonadotropin (hCG) with immunopathology in lupus (**Front Endocrinol.** doi:10.3389/fendo.2018.00742, 2018). It has been demonstrated that post-apoptotic events can be influenced by the nature of apoptosis-inducing stimuli. Whether autoantigenic constituents of apoptotic bodies vary with varying cellular insults, and whether such variations can be immunologically consequential in the context of lupus, was investigated. Apoptotic bodies elicited by different drugs demonstrated the differential presence of lupus-associated autoantigens, and immunization of tamoxifen-induced apoptotic bodies in lupus-prone mice generated higher humoral autoreactive responses than did immunization with cisplatin-induced apoptotic bodies. Incubation of lupus splenocytes with hCG along with tamoxifen-induced apoptotic bodies (but not cisplatin-induced apoptotic bodies) induced increases in the secretion of lupus-associated cytokines as well as autoantibodies; these events were associated with the heightened phosphorylation of several signaling intermediates. hCG can therefore act as is a potential disease-promoting co-stimulant in a lupus-milieu. A role for luteinizing hormone (LH) can now be envisaged, given that hCG and LH act via the same receptor; such a link would serve to further augment theories of lupus progression (**Front Immunol.** doi: 10.3389/fimmu.2022.1051779, 2022).

Delineation of the role of hCG in tumorigenesis

βhCG is associated with advanced-stage, poorly differentiated cancers, as well as with poor patient prognosis. Previous work in our lab has shed some light on a few pro-tumorigenic attributes of the hormone, including its ability to enhance tumor cell invasion and promote angiogenesis, while creating

an environment conducive to the generation of Treg cells (**BMC Cancer** doi:10.1186/s12885-015-1938-x., 2015; **Mol Carcinog.** 56:359-370, 2017; **Oncotarget** 9:34670-34680, 2018).

Menopause is associated with an increased risk of several cancers. Interestingly, post-menopausal women, even in the absence of tumors, can display high levels of hCG or βhCG. The current study was based the hypothesis that ovarian hormones can exert an ameliorating influence on the growth of βhCG-responsive tumor cells. Progesterone mediated the apoptosis of such cells, acting via non-nuclear receptors. The transgenic expression of βhCG in mice, particularly in the absence of the ovaries (a mimic of the post-menopausal state) constituted a potent pro-tumorigenic signal. Significantly, the administration of progesterone had significant anti-tumor effects. RNA-seq profiling identified molecular signatures associated with these processes. TCGA analysis revealed correlates between the expression of several newly-identified genes and poor prognosis in post-menopausal patients of lung adenocarcinoma, colon adenocarcinoma, and glioblastoma. Specifically in these women, the detection of intra-tumoral/extra-tumoral βhCG could serve as a useful prognostic indicator, and treatment with progesterone may prove beneficial (**iScience** doi: 10.1016/j.isci.2022.104527, 2022)

Publications

Original peer-reviewed articles

1. Sarkar M, Sharma H, Singh P, Ranu R, Sharma RD, Agrawal U, Pal R* (2022) Progesterone limits the tumor-promoting effects of the beta-subunit of human chorionic gonadotropin via non-nuclear receptors. **iScience.** doi: 10.1016/j.isci.2022.104527.

2. Sachdeva R, Pal R* (2022) A pregnancy hormone-cell death link promotes enhanced lupus-specific immunological effects. **Front Immunol.** doi: 10.3389/fimmu.2022.1051779.

3. Sarkar M, Singh P, Pal R* (2023) Workflow in transgenic mice for the study of specific cancers associated with the post-menopausal state. **STAR Protoc.** doi: 10.1016/j.xpro.2023.102242.

[*Corresponding author]

Review

1. Sachdeva R, Pal R* (2022) The influence of reproductive hormones on systemic lupus erythematosus. **Explor Immunol.** 2: 351-362.

[*Corresponding author]

Microbial interface biology and associated host immune response

Devinder Sehgal

Principal Investigator	**Devinder Sehgal**
Project Associate	Rashi Jain
Ph.D. Students	Ankita Yadav Hema Sori Jashobanta Behera Pratiksha Shome Sachin Kushwaha Shabnam
Collaborators	Ayub Qadri (Islamic University of Science and Technology, Kashmir) Dileep Vasudevan (ILS, Bhubaneswar) Nimesh Gupta (NII, New Delhi) Rajesh Kumar (IAV, Thiruvananthapuram) Tom Rothstein (Western Michigan University, USA) Santiswarup Singha (NII, New Delhi)

Molecular evolution and repertoire diversity of antibodies elicited during immune response to a model glycoconjugate vaccine

We are interested in understanding how the anti-polysaccharide and anti-carrier protein antibody responses evolves and matures in mice immunized with a model glycoconjugate vaccine pneumococcal capsular polysaccharide type 14 conjugated to Cross-Reactive Material 197 (PCP14-CRM197). PCP14 and CRM197 are traditionally considered T-cell independent type 2 and T-cell dependent antigen, respectively. In order to understand the molecular features of the anti-PCP14 antibody response, we generated PCP14- and CRM197-specific monoclonal antibodies (mAbs) using hybridoma technique from mice immunized with one- and three-doses of PCP14-CRM197. Anti-PCP14 and anti-CRM197 mAbs were generated on day 21 from a mouse that was given a single shot of PCP14-CRM197. Additional, anti-PCP14 mAbs were generated on day 14 and 28 following a single shot of the glycoconjugate. Anti-PCP14 and anti-CRM197 mAbs were generated on day 35 from the same mouse after giving three shots (on day 0, 14 and 28) of PCP14-CRM197.

We performed a comprehensive sequence analysis of the anti-PCP14 (n = 26) and anti-CRM197 (n = 22) mAbs generated from mice immunized with the PCP14-CRM197. Our analysis resulted in some unexpected findings regarding antibody response generated against glycoconjugate antigens. Increased mutational load and higher class-switching was observed in the polysaccharide-specific antibodies in mice that were immunized with the glycoconjugate vaccine indicating that the polysaccharide-specific antibodies acquired molecular features of anti-protein-like (T-cell dependent) antibody response upon conjugation with a carrier protein. Our findings also indicate that the conjugation of the polysaccharide with a carrier protein interferes with the development of carrier protein-specific antibody responses.

Our data supports the following working model. Upon immunization with PCP14-CRM197, PCP14-specific B cells from the pre-immune B cell repertoire are recruited to form germinal centers. In the germinal centers, proliferating PCP14-specific B cells accumulate mutations and undergo isotype class switch recombination in the dark zone. Dividing B cells compete for the antigen displayed by the follicular dendritic cells in the light zone to generate memory B cells and plasma cells. Upon re-exposure, antigen-experienced B cells and/ or memory B cells participate in a second round of germinal center reaction, accumulating further mutations and undergoing isotype class switching. On the contrary, during primary germinal center response, CRM197-specific B cells from the pre-immune B cell repertoire accumulate very few or no mutations and exhibit very little isotype class switching. In contrast to anti-PCP14 response, booster shots resulted in the recruitment of CRM197-specific B cells from the naive B cell compartment as suggested by no or low number of mutations. Additionally, the VH and VL gene segments used in the anti-CRM197 antibody induced during the primary response had very little overlap with the antibody pool elicited following the three-shot regimen with PCP14-CRM197. Booster shots induced isotype switching in the CRM197-specific B cells.

These observations have implications in designing glycoconjugate vaccines in general and glycoconjugate vaccines wherein both the polysaccharide and protein are from a homologous source.

Publications

Original peer-reviewed articles

1. Parray HA, Narayanan N, Garg S, Rizvi ZA, Shrivastava T, Kushwaha S, Singh J, Murugavelu P, Anantharaj A, Mehdi F, Raj N, Singh S, Dandotiya J, Lukose A, Jamwal D, Kumar S, Chiranjivi AK, Dhyani S, Mishra N, Kumar S, Jakhar K, Sonar S, Panchal AK, Tripathy MR, Chowdhury SR, Ahmed S, Samal S, Mani S, Bhattacharyya S, Das S, Sinha S, Luthra K, Batra G, Sehgal D, Medigeshi GR, Sharma C, Awasthi A, Garg PK, Nair DT and Kumar R. (2022) A broadly neutralizing monoclonal antibody overcomes the mutational landscape of emerging SARS-CoV-2 variants of concern. **PLoS Pathog.** doi: 10.1371/journal.ppat.1010994.

2. Ahuja R, Shelly A, Meena J, Singh M, Sehgal D and Panda AK (2022) Enhanced immunogenicity of recombinant pneumococcal protein delivered using thermostable polymer particles. **Mater Today Commun.** 32: 103894.

Plasmodium proteins involved in virulence and host modulation: Host-Parasite interactions in *Plasmodium* liver stages

Agam Prasad Singh

Principal Investigator	**Agam Prasad Singh**
Project Associate	Rajesh Anand
Project Fellows	Shams Tabrej Charu Garg Arushi Goel
Ph.D. Students	Pooja Shreya Bhattacharya Sumaiya Khan Zikra S. Arkam Neha Gupta
Collaborators	Brijesh Rathi (Delhi University, Delhi) Poonam (Delhi University, Delhi) Shailja Singh (JNU, New Delhi) Praveen K Verma (JNU, New Delhi) Kailash C Pandey (NIMR-ICMR, New Delhi) Ashis Das (BITS-Pilani, Pilani) Susheel K Singh (RMRC, Bhuvneshwar) Prakasha Kempaiah (Mayo Clinic Florida, USA) Dinkar Sahal (ICGEB, New Delhi) Pawan Malhotra (ICGEB, New Delhi)

Basic theme is to identify, new parasite molecules that affect the host cellular processes, and possible intervention strategies. Plasmodium species introduce effector molecules into hepatocyte cytosol to manipulate host pathways for its own benefit. Those could prove good targets for drug / vaccine development.

Malaria Vaccine

RTS,S-AS01 a malaria subunit vaccine, has limited efficacy of only 30-40%. According to WHO, malaria vaccines should have at least 75% efficacy. To address the issue we are working with human malaria (Pf) antigens, expressed at liver and mosquito stages, as chimeric antigen to find out an effective vaccine formulation. We are investigating the immunogenicity and protective efficacy of the *P. falciparum* recombinant chimeric malaria antigens (rCMAs) consisting of full-length CSP together with DnaJ-protein (another pre-erythrocytic antigen) or PfsPro.6C (consisting of subdomains from Pfs230 & Pfs48/45, both leading transmission blocking antigens). To challenge mice immunized with chimeric Pf antigens we also made dual transgenic parasites (Pf_antigen gene in Pb parasite). Another experimental vaccine combination of Pf_DNAJ and Pf_SLTRiP chimera (DNAJT-SLTRiP)is also being developed.

Drug discovery:

a) Novel fluorinated piperazine based-amino acid derivatives as antiplasmodial agents; Twenty novel analogues of fluorinated, N-(3-hydroxy-1- phenyl-4-(4-phenylpiperazin-1-yl)-alkyl)-amides containing different amino acids were designed and synthesized and tested for antimalarial activity

and host toxicity. Two hits 12c and 12e showed efficacy against Pf-3D7 strain with IC50 values of 0.696± 0.0462μM and 0.9377± 0.0461μM, respectively.

b) Multistage and transmission-blocking tubulin targeting antimalarial; Plasmodial Microtubules (MTs) play a crucial role during parasite proliferation, growth, and transmission, which render them highly desirable targets for the development of next-generation chemotherapeutics. Towards this, we evaluated the antimalarial activity of Tubulin targeting compounds received from the Medicines for Malaria Venture (MMV) "Pathogen Box" against the human malaria parasite. At nanomolar concentrations, the filtered-out compounds exhibited pronounced multistage antimalarial effects across the parasite life cycle.

c) Host-targeted therapy is a new direction for infectious disease drug development and aims to interfere with host molecules, pathways or networks that are required for infection or contribute to disease. Advances in our understanding of host pathways involved in parasite development and pathogenic mechanisms in malaria could facilitate the development of host-targeted interventions against Plasmodium infection / malaria disease. We tested malaria liverstage parasite development in MEF2C (a host transcription factor) overexpressing HepG2 cell line. We found that the parasite load is directly proportional to expression levels of MEF2C. Furthermore, overexpression of MEF2C stimulates the expression of lipid like molecules which creates immunosuppressive environment and enhances susceptibility of host.

Publications

Original peer-reviewed articles

1. Upadhyay C, Bhattacharya S, Kumar S, Kumar D, Bhadula N, Rathi B*, Singh AP*, Poonam* (2023) Novel fluorinated piperazine based-amino acid derivatives as antiplasmodial agents: Synthesis, bioactivity and computational studies. **Chem Biol Lett.** 10:543.
2. Singh SK, Shree A, Verma S, Singh K, Kumar K, Srivastava V, Singh R, Saxena S, Singh AP, Pandey A, Verma PK* (2023) The nuclear effector ArPEC25 from the necrotrophic fungus *Ascochyta rabiei* targets the chickpea transcription factor CaβLIM1a and negatively modulates lignin biosynthesis for host susceptibility. **Plant Cell.** 35: 1134–1159.
3. Kumar S, Sharma N, Dantas W, Nascimento JCF do, Maus H, Ronaldo Oliveira R, Pandit U, Singh AP, Schirmeister T, Panwar P, Pena L, Singh P, Rathi B*. (2022) A potent candidate against Zika virus infection: Synthesis, bioactivity, radiolabeling and biodistribution studies. **New J Chem.** doi:10.1039/D2NJ02482A
4. Kumari G, Jain R, Sah RK , Kalia I, Vashistha M , Singh P, Singh AP , Samby K, Burrows J, Singh S*(2022) Multistage and transmission-blocking tubulin targeting antimalarial discovered from the open access MMV Pathogen Box. **Biochem Pharmacol.** doi: 10.1016/j.bcp.2022.115154
5. Gupta Y, Sharma N, Singh S, Romero JG, Rajendran V, Mogire RM, Mathur R, Kashif M, Beach J, Jeske W, Poonam, Ogutu B, Kanzok SM, Akala HM, Jennifer Legac J, Rosenthal PJ, Rademacher DJ, Durvasula R, Singh AP, Rathi B*, Kempaiah P* (2022) The multistage antimalarial compound Calxinin perturbates *P. falciparum* Calcium homeostasis by targeting a unique ion channel **Pharmaceutics.**14: 1371.

[* Corresponding author]

Patent

1. Rathi B, Singh S, Mounce B, Poonam, Kempaih P, Singh AP, Durvasula R. Hydroxyethylamine based Piperazine compounds, methods of producing and using the same for treating disease. (US Patent No. 17/347,720 Granted on 01.11.2022) ***[Patents Granted]***

Fine tuning of immune signaling pathways

Soumen Basak

Principal Investigator	**Soumen Basak**
Project Associate	Bhawan Chugh (PA-1)
Project Fellow	Syed Yusuf Mian (SRF)
Ph.D. Students	Manti Kumar Saha Alvina Deka Naveen Kumar Sk Asif Ali Swapnava Basu
Collaborators	Alexander Hoffmann (Univ. of California, Los Angeles, USA) Abhyudai Singh (Univ. of Delaware, USA) Guruprasad R. Medigeshi (THSTI-Faridabad) Amit Awasthi (THSTI-Faridabad) Bhabatosh Das (THSTI-Faridabad) James Gomes (IIT-Delhi) Manidipa Banerjee (IIT-Delhi) Shilpak Chatterjee (IICB-Kolkata) 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 crosstalks 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 canonical and non-canonical NF-kB pathways and those beyond NF-kB signaling. We are mechanistically characterizing crosstalk mechanisms integrating cellular pathways within a network and exploring if such crosstalks has 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.

Publications

Original peer-reviewed articles

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

2. Ratra Y, Kumar N, Saha MK, Bharadwaj C, Chongtham C, Bais SS, Medigeshi G, Arimbasseri GA, Basak S* (2022) A vitamin D-RelB/NF-κB pathway limits Chandipura virus multiplication by rewiring the homeostatic state of autoregulatory Type 1 IFN-IRF7 signaling. **J Immunol.** 209:559-568.

3. Chowdhury S, Kar A, Bhowmik D, Gautam A, Basak D, Sarkar I, Ghosh P, Sarkar D, Deka A, Chakraborty P, Mukhopadhyay A, Mehrotra S, Basak S, Paul S, Chatterjee S (2022) Intracellular acetyl CoA potentiates the therapeutic efficacy of antitumor CD8+ T Cells. **Cancer Res.** 82:2640-2655.

[*Corresponding Author]

Understanding the role of Interferon Regulatory Factors in dendritic cell development

Prafullakumar Tailor

Principal Investigator	**Prafullakumar B. Tailor**
Project Scientist	Yadhu Sharma
Ph.D. Students	Annesa Das Ramya Venkataraman Ajay Kumar Anshul Kushwaha Jawahar P (Since July 2023) Shalini Kumari (Since July 2023)
Collaborators	Nirupama Trehanpati (ILBS, New Delhi) Himanshu Sinha (IIT-M, Chennai) Yashwant Kumar (THSTI, Faridabad)

The DC subsets are collection of heterogeneous populations that are broadly categorized into plasmacytoid DCs (pDCs) and classical DCs (cDCs) represented by the phenotypically diverse cDC subsets; cDC1 ($CD8a^+/CD103^+CD11b^-SIRPa^-$) and cDC2 ($CD4^+/CD103^-CD11b^+ SIRPa^+$). Each DC subtypes are characterized by surface markers, gene expression patterns and unique functions. We are interested in understanding the mechanisms of DC subtype development and their specific functions. Members of Interferon regulatory factors (IRFs) 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. Recently, we have initiated study towards improving existing CAR-T cell therapy and developing newer strategies for cancer immunotherapy.

Establishing and improvising novel CAR-T cell strategies

Immunotherapy is considered to be the fourth pillar of cancer therapy wherein recently Chimeric Antigen Receptor (CAR) T cell technology has revolutionized the treatment of hematologic malignancies such as leukemia and lymphoma. Despite development of various generation of the CAR constructs, CAR-T cell therapy is still at the nascent stage and have tremendous scope for progress especially for treating solid tumors. Towards developing tools and techniques for fostering advancement of CAR T-cell therapy, we begin by establishing CD19 specific CAR-T cell technologies in our laboratory. We employed a second generation anti-CD19-28z CAR construct specific to human CD19 surface marker. The extracellular domain comprised of the anti-CD19 scFv, derived from FMC63 mouse hybridoma line secreting human anti-CD19 monoclonal antibodies. The CAR construct was initially cloned into a GFP-tagged retroviral vector with MSCV backbone for transducing T cells. Since the transduction of primary T cells was poor with retroviral gene transfer, we employed the lentiviral vector towards achieving the desired efficiency. Anti-CD19 CAR-T cells were co-cultured with in house developed Luc^+ Raji cells and the cytotoxicity was assessed by decrease in the cell associated luciferase

activity. With the competency to produce functional anti-CD19 CAR T cells, potential of these cells can now be interrogated in a pre-clinical setting. With the aim of improving, we will modify the CD19 CAR construct to develop newer third generation CARs.

Publication

Original peer-reviewed article

1. Kumari S, Chakraborty S, Ahmed M, Kumar V, Tailor P, Biswal BK (2022) Identification of probable inhibitors for the DNA polymerase of the Monkeypox virus through the virtual screening approach. **Int J Biol Macromol**. 229:515-528.

T-cell immunity to virus infection and vaccination

Nimesh Gupta

Principal Investigator	**Nimesh Gupta**
Project Associates	Sathi Mallick
Project Fellows	Dharmendra Singh Mohammad Islamuddin Rajesh Vikkurthi Anupama Pai Riddhita Deb Ruchi Sharma
Ph.D. Students	Asgar Ansari Bhushan Nikam Someshwar Nath Jha Suvechchha Pandit Bhanu Pratap Singh
Collaborators	Naveet Wig (AIIMS, New Delhi) Manish Soneja (AIIMS, New Delhi) Poonam Coshic (AIIMS, New Delhi) Siraj Khan (RMRC, Assam) Anmol Chandele (ICGEB, New Delhi) Neel Bhavesh (ICGEB, New Delhi) Shinjini Bhatnagar (THSTI, Faridabad) Ravi Mishra (IMTECH, Chandigarh) Shane Crotty (LJI, California) Alessandro Sette (LJI, California) Alain Townsend (MRC, Oxford) Etienne Joly (IPSB, Toulouse) Santiswarup Singha (NII, New Delhi) Debasisa Mohanty (NII, New Delhi)

Vaccines are the most cost-effective preventive measures against infectious diseases. The goal of our lab is to understand the development of long-term sustained humoral immunity and provide foundational knowledge for the rational design of human vaccines. Specifically, our research is focused on understanding the biology of CD4+ T cells, mainly “follicular T helper (Tfh) cells”, in the settings of long-term immunological memory. This is exemplified by the research program on virus infection vs human vaccination, which provides a unique opportunity to identify the positive attributes of protective immunity.

Biology of Tfh cells in long-lasting protective immunity

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

In this program, we are investigating the longitudinal cohorts of JE (Japanese encephalitis) virus infection and SA14-14-2 JE vaccine. We found that ~18% of the individuals do not mount antibody response to the vaccine. Interestingly, Tfh cells in non-seroconvertors were functionally impaired in inducing humoral immunity. The in-depth investigations highlighted the implication of metabolites that suppress Tfh cells leading to no humoral response to vaccine (*Figure 1*).

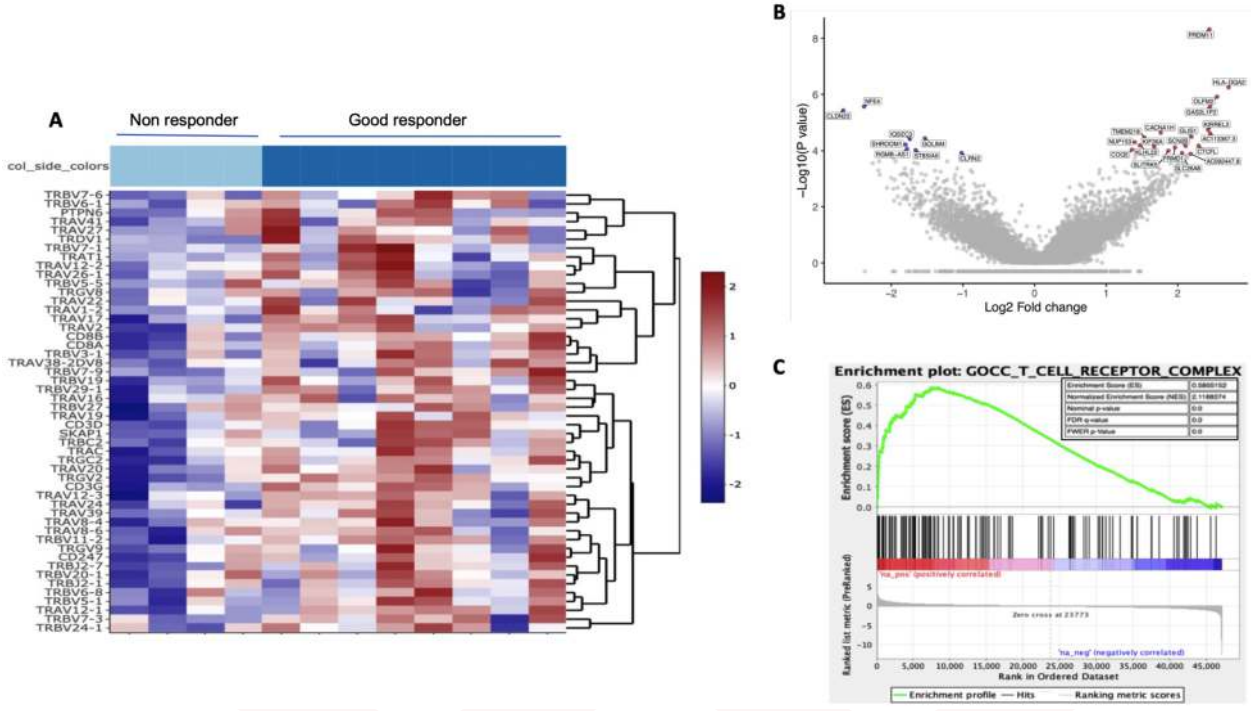


Figure 1. Bulk RNASeq analyses of the PBMCs from good responders vs. non-seroconvertors (non-responders) at Day 7 post-vaccination. (A) Gene set enrichment analyses between the two groups, (B) Differential gene expression and (C) Enrichment plot. (Unpublished data)

We are now progressing to delineate the mechanism by which identified metabolites are suppressing immune response to vaccine. In this duration, we have also developed animal models and human T-cell assays for testing JE vaccine candidates.

Biology of Tfh cells in COVID-19 infection and vaccination

We substantially contributed in understanding the T-cell immunity to Covid-19 infection and vaccination. We examined the immunological effectiveness of the indigenous Covid-19 vaccine *Covaxin*™, and compared it with the immune memory acquired after infection. We found that the vaccine induced robust immune memory that was comparable with that following infection in the levels of antibodies, memory B cells and memory T cells. Although the SARS-CoV-2 variants may substantially impact the vaccine-induced antibodies, the $CD4^+$ T-cell responses were highly preserved (*Figure* 2). We also found that the vaccine can induce functional Tfh cells like infection (*Nature Microbiology, 2022*).

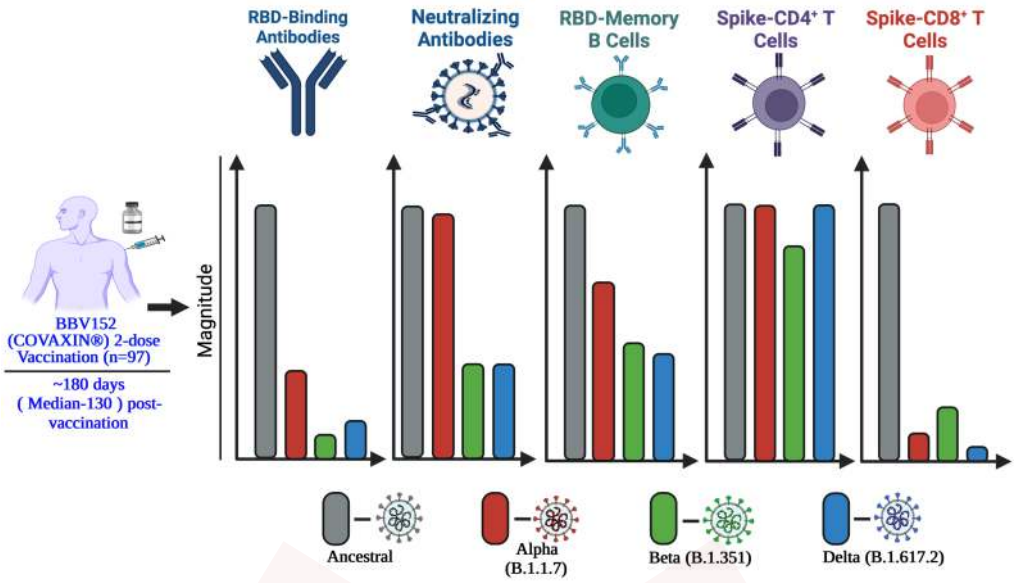


Figure 2. The study determined the immune memory and breadth of immune reactivity after immunization with COVID-19 vaccine "Covaxin", and compared it with the recovery after natural infection. (*Vikkurthi, R et.al., 2022. Nature Microbiology*).

Function of Tfh cells in humoral immunity establishment to dengue virus

Here, our attempts are focused on understanding the immunological basis of humoral response to dengue virus. We identified a novel subset of $CD4^+$ T cells that is accumulated in severe dengue. In a landmark contribution to the field, we have developed the method to study the mechanistic framework of human T-B cell cross-talk *(Cell Reports Methods, 2022; Patent-202111003148) (Figure 3).*

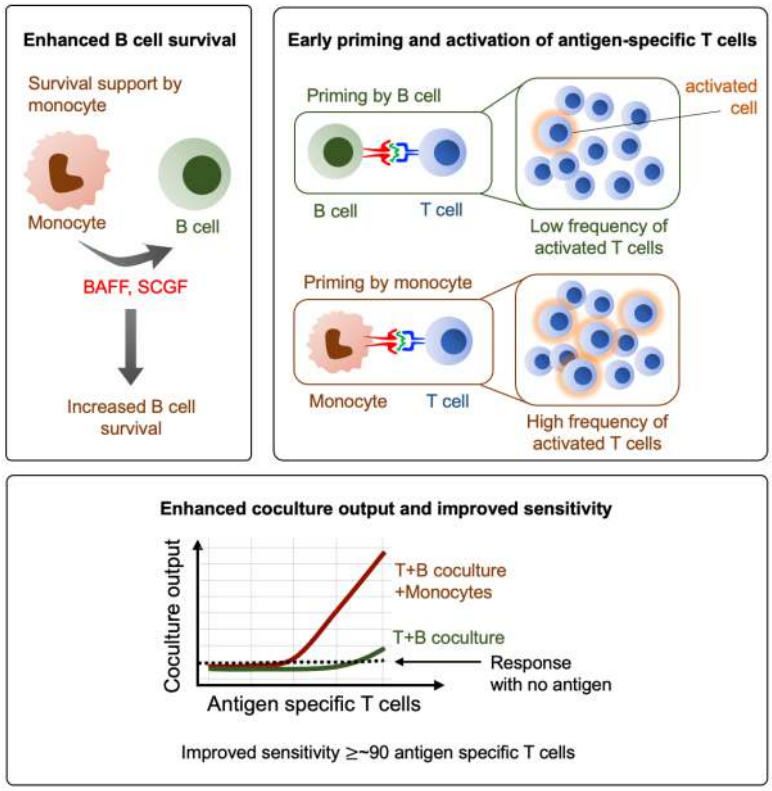


Figure 3. A new method to understand the mechanism of T-B cell cross-talk and to determine the humoral immunity function of T cells, at an antigen-specific level (*Ansari, A et.al., 2022. Cell Reports Methods*)

Utilizing this method, we demonstrated that the newly identified subset help the B cells and drives the exaggerated plasmablasts and antibody response. Because an excessive plasmablasts differentiation and poor quality antibodies are associated with severe dengue, our work reveal a crucial immune axis in dengue that has an important implication for the dengue vaccine development.

Human Immune Monitoring and T-cell Immunoassay Platform

As a translational component, we have established a *"Human Immune Monitoring and T-cell Immunoassay"* platform, with applications for the advanced immunological human trials of vaccines *(Figure 4)*.

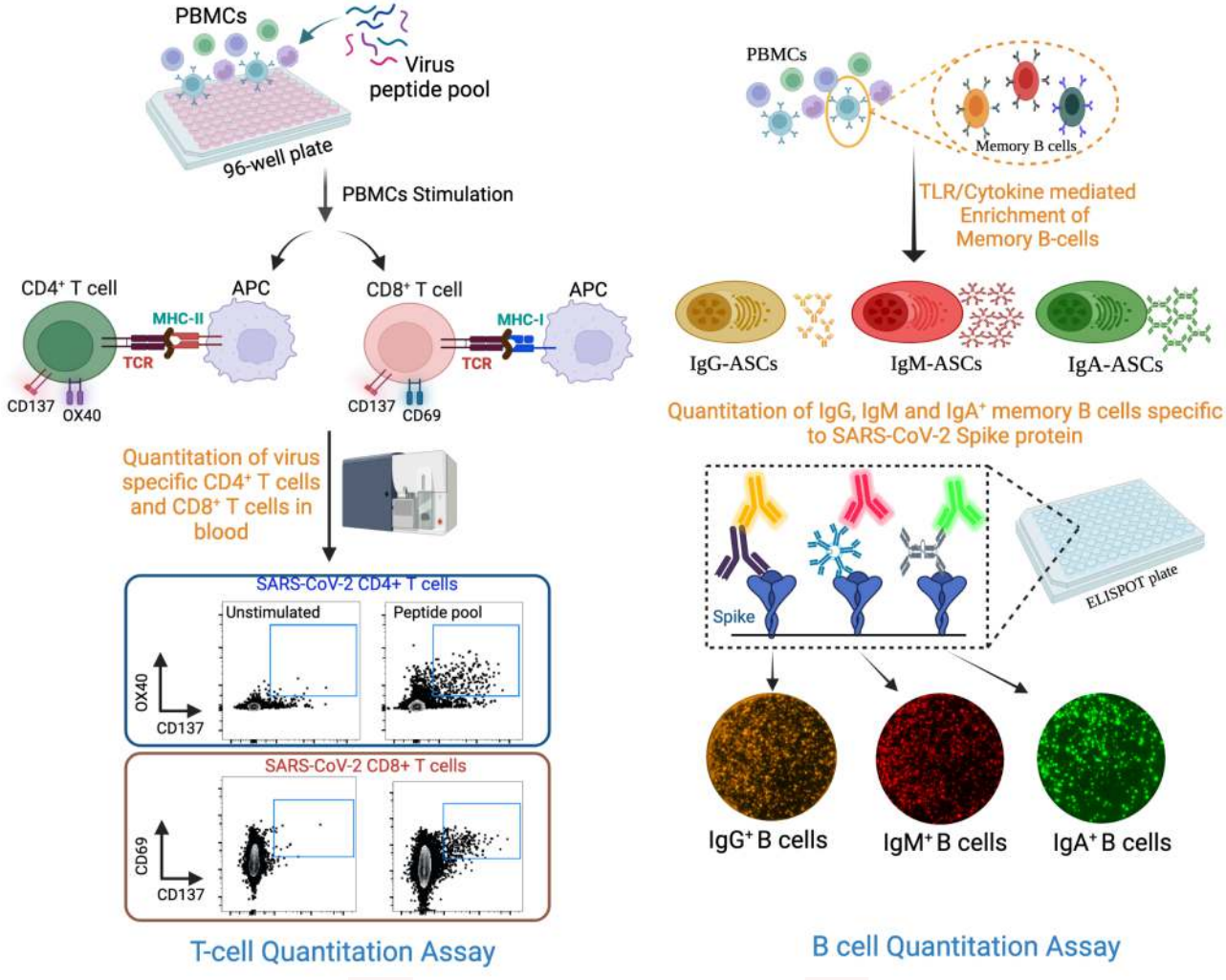


Figure 4. The human Immune Monitoring and T-cell Immunoassay platform offers advanced human immunology techniques for clinical trials of vaccines, biotherapeutics and antivirals. The image depicts the assay for the quantitation of virus-specific T cells and B cells in human blood.

During the Covid-19 pandemic, the platform was instrumental in generating scientific evidence for the T-cell immunity to Covid-19 vaccines and supported the policymaking. When the vaccine efficacy studies were not feasible, our platform was instrumental in conducting the immuno-bridging phase 3 clinical trial under industry-academia partnership for testing intranasal Covid-19 vaccine "iNCOVACC".

Publications

Original peer-reviewed articles

1. Vikkurthi R, Ansari A, Pai AR, Jha SN, Sachan S, Pandit S, Nikam B, Kalia A, Jit BP, Parray HA, Singh S, Kshetrapal P, Wadhwa N, Shrivastava T, Coshic P, Kumar S, Sharma P, Sharma N, Taneja J, Pandey AK, Sharma A, Thiruvengadam R, Grifoni A, Weiskopf D, Sette A, Bhatnagar A, Gupta N* (2022) Inactivated virus vaccine BBV152/Covaxin elicits robust cellular immune memory to SARS-CoV-2 and variants of concern. **Nat Microbiol** 7: 974-985.

2. Ansari A, Sachan S, Jit BP, Sharma A, Coshic P, Sette A, Weiskopf D, Gupta N* (2022) An efficient immunoassay for B cell help function of SARS-CoV-2 specific memory $CD4^+$ T cells. **Cell Rep Methods.** 2: 100224.

[*Corresponding author].

Patent

1. Gupta N, Sachan S. A dengue virus follicular T helper (Tfh) cell specific peptide megapool and its use thereof (Indian Patent Application No. 202211046391. Filed on 16.08.2022).

Awards / Fellowships

1. Mid-Career Scientist Oration Award for the Year-2022 conferred by the Indian Immunology Society for contribution in the area of "T cell immunity to vaccines".

Understanding Immune response to infections in humans

Veena S. Patil

Principal Investigator	**Veena S. Patil**
Project Fellow	Somdeb Chattopadhyay (SRF)
Ph.D. Students	Raunak Kar Kirti Sharma Rakhi Panwar Sonanjali Aneja Shreya Sinha
Collaborators	Avinash Bajaj (RCB, Faridabad) Aneeshkumar A.G. (NII, New Delhi) Anjali Sharma, (VMMC/Safdarjung Hospital, New Delhi) Jeeva Sankar (AIIMS, New Delhi) Ramesh Agarwal (AIIMS, New Delhi)

Research in our lab focuses on understanding the development of immune response to infections in humans by studying the regulation of global gene expression patterns uniquely associated with a pathogen, immune cell-type and/ disease stage using multi-omics and immunological tools. Two of the ongoing programs in the lab are described below.

Project 1: Systems biology approaches to understand the biology of human CD4+ helper T cells with cytotoxic potential (CD4-CTLs) in viral infections

In this project, we propose to understand the functional properties of circulating CD4-CTLs generated in response to different viral infections and define the molecular mechanisms that drive the development and differentiation of CD4-CTLs. We combine immunological tools with both bulk and single-cell multi-omics (RNA-Seq, ATAC-Seq, TCR-Seq and limited proteomics) to understand T cell memory development and maintenance. Our single-cell multi-omics data on antigen-specific memory T cells for viral infections, shows different flavours of memory T cells.

Characterization of CMV-specific T cells: The latent human Cytomegalovirus (hCMV) infection can pose a serious threat of reactivation and disease occurrence in immune-compromised individuals, as well as burdens the immune system in immune-competent individuals. Though, T cells are at the core of the protective immune response to hCMV infection, a detailed characterization of different T cell subsets involved in protection against the hCMV infection is lacking. We analyzed the single-cell transcriptomes and T cell antigen receptor (TCR) repertoires of over 8000 hCMV-reactive peripheral T cells isolated from different memory compartments. The hCMV-reactive T cells were highly heterogeneous and consisted of different developmental memory and functional T cell subsets such as, the long-term memory precursors and effectors, T helper-17, T regulatory cells (T_{REGs}) and cytotoxic T lymphocytes (CTLs). The hCMV-antigen specific T_{REGs} were enriched for molecules linked to their suppressive function and interferon response genes. The CTLs were of two types, the pre-effector and

effector like. Of particular interest was the mixture of both CD4-CTLs and CD8-CTLs in both the pre-effector and effector cytotoxic clusters, suggesting that both CD4-CTLs and CD8-CTLs share transcriptomic signatures. The huge TCR clonal expansion of both the cytotoxic clusters imply their predominant role in protective immune response to CMV. Further the clonotype sharing between the CTL clusters and the long-term memory clusters, indicate potential progenitors of CD4-CTLs. Together our study has identified many subsets of hCMV-specific memory T cells that may have implication in better understanding the hCMV-specific T cell immunity to design vaccination strategies and therapeutics.

Project 2: Understanding the dynamic changes in gene expression patterns of immune cell types associated with neonatal sepsis

The host immune response to neonatal sepsis is very poorly understood. We are analysing the dynamic change in immune cell proportions and the associated immune cell-type specific gene expression patterns in the context of sepsis in neonates in India. The results obtained from this study will provide better understanding of the stage- and pathogen-specific immune response to neonatal sepsis and hence design better therapeutic interventions. We are currently building the longitudinal cohort of PBMCs samples at different stages of sepsis in neonates.

Publication

Original peer-reviewed article

1. Verma P, Arora A, Rana K, Mehta D, Kar R, Verma V, Srikanth CV, Patil VS, Bajaj A (2022) Gemini lipid nanoparticle (GLNP)-mediated oral delivery of TNF-α siRNA mitigates gut inflammation via inhibiting the differentiation of CD4+ T cells. **Nanoscale.** 14:14717-14731

Integration of nutritional therapy with innate and adaptive immunity in infectious disease model

Tanmay Majumdar

Principal Investigator	**Tanmay Majumdar**
Project Associates	Santosh Kumar (SERB-NPDF) Anupamjeet Kaur (SERB project)
Ph.D. Student	Geetika Kumari Amit Kumar
Collaborators	Anil Kumar Pandey (ESIC Medical College & Hospital, Faridabad) Shailendra Mani (DBT-THSTI, Faridabad) Rakesh Kundu (Visva-Bharati University,West Bengal) Umesh Prasad Singh (CSIR-IICB, Kolkata)

I. Dynamics of T-cell subsets in toxoplasmosis

My research focus revolves around developing translational strategies for intervening in chronic human diseases by promoting a balanced immune response and reducing inflammation through the manipulation of the gut microbiota. Specifically, I am interested in investigating the role of nutrients in bridging the innate and adaptive immune systems. Understanding these mechanisms is crucial for treating inflammatory diseases that arise as a consequence of microbial infections. The primary objective of our research is to utilize this knowledge to design therapeutic and preventive strategies against pathogens that pose a significant threat to human health.

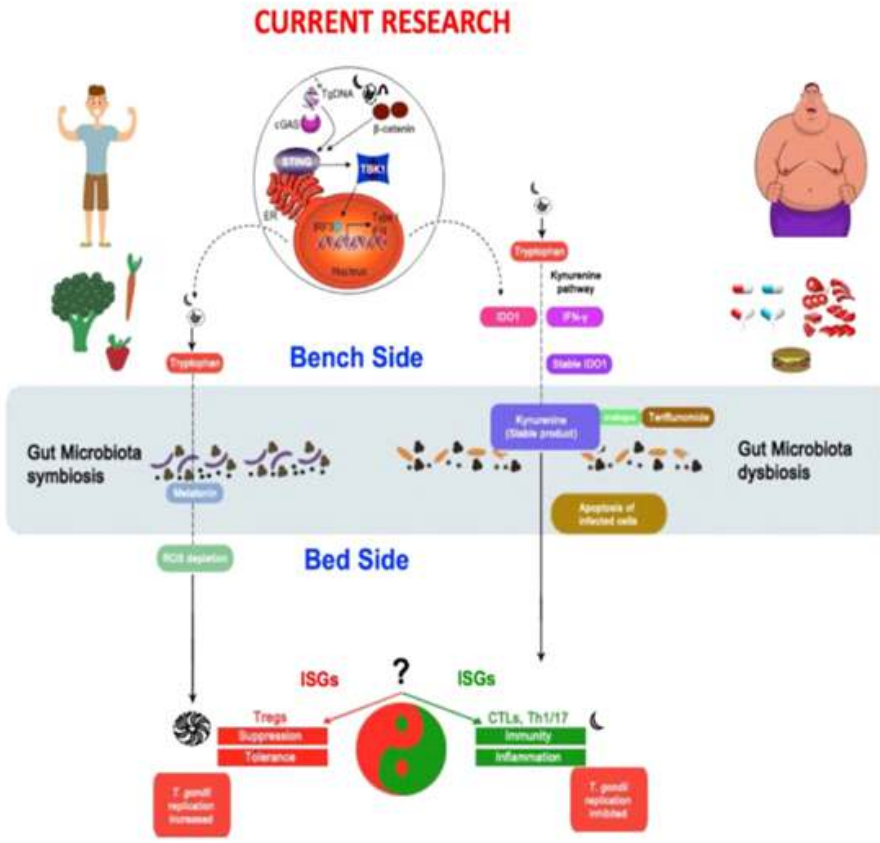
In our studies, we have discovered that *Toxoplasma gondii* exploits the β-catenin pathway, specifically by phosphorylating β-catenin at the S552 position, to facilitate its replication. By employing a specific inhibitor targeting this pathway, we observed a significant improvement in the survival of infected mice. Infected mice generate an inflammatory environment mediated by various immune cell subsets such as Th1/Tc1, Th9/Tc9, and Th17/Tc17, which promote the smooth replication of the parasites. This inflammatory milieu facilitates the dissemination of the parasites both locally (in the colon and small intestine) and distally (in the spleen and brain) within the infected mice. Notably, both lymphocytes, such as T-cells, and antigen-presenting cells, like macrophages, exhibit evidence of parasitemia.

By disrupting the expression of β-catenin using an inhibitor, we were able to prevent the inflammatory response and instead induce a tolerant immune response mediated by IL4-induced Th2/Tc2 cells. This shift culminated in a protective immune response against the parasites.

II. Microbiome-based nutritional therapy: A new arsenal against *Toxoplasma gondii* treatment-induced obesity

This project explores the impact of *Toxoplasma gondii* infection on the coordination between the gut microbiota and metabolic cycles, proposing that an altered microbiome population during treatment for persistent *T. gondii* infection may contribute to metabolic dysfunction and chronic inflammatory

diseases such as obesity. Within this context, the study aims to investigate the interplay between symbionts and pathobionts, which determine whether tolerance (Treg/Tr1/Breg/Br) or inflammation (Th1/Th17/Inflammatory B1) develops during the infection process. The chronic infection disrupts the balance, leading to uncontrolled inflammation that contributes to the obesity epidemic. To address this issue, this translational study will examine the potential of probiotics in restoring microbiota symbiosis and developing a novel class of anti-inflammatory small molecules that can combat *T. gondii*-induced obesity while considering the impact on the microbiome flora (Figure 1).



Through our research, we have identified that the phosphorylation of β-catenin plays a crucial role in facilitating the smooth replication of *T. gondii* within the host. To enhance the survivability of infected mice, we explored the potential of Wnt inhibitors to limit the expression of β-catenin. By inhibiting the Wnt pathway, we observed a significant improvement in the ability of infected mice to combat the infection and increase their chances of survival.

The ongoing and future research projects are detailed below.

i. Role of microbiome in parasites infection

ii. Role of macrophages in T-cells differentiation in course of parasites infection

Publication

Original peer-reviewed article

1. Nag S, Mandal S, Majumdar T, Mukhopadhyay S, Kundu R. (2023) FFA-Fetuin-A regulates DPP-IV expression in pancreatic beta cells through TLR4-NFkB pathway. **Biochem Biophys Res Commun.** 647:55-61.

Understanding the sources and mediators of meta-inflammation that aggravate inflammatory bowel disease (IBD) pathogenesis during Obesity/Lean Metabolic Obesity (LMO)

Devram Sampat Ghorpade

Principal Investigator	**Devram Sampat Ghorpade**
Project Fellow	Shubham Sharma
Ph.D. Students	Chayanika Gogoi Mohammad Athar Mehraj Ratulananda Bhadury
Collaborators	Vineet Ahuja (AIIMS, New Delhi) Gayatri Ramakrishna (ILBS, New Delhi) Jaswinder Singh Maras (ILBS, New Delhi)

Meta-inflammatory metabolic disorders are on the high rise with limited therapeutic interventions. In particular, parallel epidemics of diabesity and inflammatory bowel disease are alarming. Detailed understanding of the etiological triggers of meta-inflammation and illustration of pathophysiological mechanisms are the areas of research focus in our laboratory. Our efforts are directed to uncover organokine-mediated multi-organs cross-talks among liver, pancreas, muscle, adipose tissues, etc. The theme of our research group is to identify novel organokines and delineate the bio-functional roles of such organokines in meta-inflammatory metabolic disorders like diabesity, inflammatory diseases, cancers, etc. Homeostasis is the ability of the body to resist the physiological fluctuations around a homeostatic set point that maintains body functioning. Defect in the homeostatic regulatory mechanism is the underlying cause of various diseases. In the case of glucose homeostasis, over a period of day, feeding and fasting fluctuate the blood glucose levels around a physiological range (100 mg/dl). Breakdown in the physiological mechanisms to regulate the blood glucose levels in the physiological range results in diabetes. This necessitates the need to understand glucose homeostasis in greater depth.

Liver plays a central role in maintaining normoglycemia during the feeding and fasting phases. Postprandial spike in glucose levels is sensed by the liver which leads to enhanced GLUT2-mediated transport of glucose into the liver. These glucose molecules are utilized by hepatocytes to meet energy demand and excess is stored as glycogen. During the energy-demanding phase of fasting, the liver quickly supplies glucose by mobilizing glycogen stores to glucose and/or synthesizing neo-glucose from precursor amino acids. In either glucose surplus or glucose-deficit conditions, in a healthy individual, a state of normoglycemia is achieved by coordinated regulation of synthesis and degradation of receptors, transcription factors, and enzymes involved in glycolysis, gluconeogenesis, glycogenolysis, and glycogenesis. This suggests the existence of a biphasic nature of glucose homeostasis viz. active phase followed by the resolution phase. During the active phase, the cascade of bio-enzymatic reactions is activated either to utilize or produce glucose. The calm-down phase or resolution phase is marked by the downregulation of transcriptional activity, enzymatic activity, and post-translational regulation of key genes and/or proteins that are super-active during the active phase. The net result is the maintenance of normoglycemia in the body. The active phase of glucose utilization is mediated by glucose sensors (GLUT2, LRH1), glycolytic enzymes (GCK, PFK1, L-PK, etc.), and

transcription factors (ChREBP, SREBP1c, etc.), while gluconeogenesis active phase is governed by PGC1α, FOXO-1, FBP, G6PC, and GLUT2. To validate the biphasic nature of glucose homeostasis, we recapitulated the feeding and fasting phase in a mouse model and analyzed the active and resolution phase of glucose homeostasis. Our data demonstrate that glucose homeostasis is not a single-step process rather it is a biphasic, active phase followed by a resolution phase. We have identified 3 key molecules CRELD2, MANF, and LEAP-2 that could resolve the active phase of glucose homeostasis in the liver. The gluco-metabolic conditioners, CRELD2 MANF, and LEAP-2 open up an avenue to develop better therapeutic regimes for diabesity. The work related to identifying roles for these secretory hepatokines in IBD pathogenesis is underway.

CHEMICAL BIOLOGY, BIOCHEMISTRY AND STRUCTURAL BIOLOGY

Enzymes regulation and its importance in biology

Apurba Kumar Sau

Principal Investigator	Apurba Kumar Sau
Ph.D. Students	Sowmiya Gupta Ditsa Sarkar Monika Mittal Divya Rashmi Anjali Kalia Anirban Molla Pratiti Bakshi Dorle Archan Mukund
Collaborators	Saumitra Das (IISc, Bangalore) Shashank Deep (IIT-Delhi, New Delhi) Samudrala Gourinath (JNU, New Delhi) Shahid M Nayeem (AMU, Aligarh)

Enzymes regulation and its importance in biology

The conformational change of the W79-containing region along with the H-bond of W79 stimulates GMP formation

Although W79 of hGBP1 stimulates GMP formation, its underlying basis was not clearly understood. Here, we show that W79 stimulates GTPase activity leading to enhanced GMP formation through its side chain H-bonding contact with the main chain carbonyl of K76. It is also interesting to note that the W79-containing region undergoes solvent exposure after the cleavage of gamma phosphate. Thus, we suggest that the above H-bond along with the solvent exposure of W79 redirects the catalytic loop toward the beta phosphate after the cleavage of gamma phosphate for enhanced GMP formation

Stimulated GMP formation is crucial for anti HCV activity

To explore whether the stimulated GMP formation by hGBP1 is essential for anti HCV activity, we transfected the expression plasmids of wild-type hGBP1 and its tryptophan into alanine mutants in Huh7.1 cells. These cells were infected with the JFH1 strain of HCV and RNA levels were measured. The expression of wild-type protein leads to the suppression of the HCV-RNA (approximately 75%), indicating its antiviral activity against HCV. The W79A mutant, which is defective by having reduced GMP formation, virtually did not suppress HCV-RNA expression. However, the W114A mutant, which showed further stimulated GMP formation compared to the wild-type (% GMP in wild-type hGBP1 and W114A mutant was 84% and 95%, respectively), displayed more reduction in HCV-RNA (75 vs. 95%). Two other mutants decreased the HCV-RNA levels to some extent. These results suggest that the stimulated GMP formation by hGBP1 is mainly important for suppression of HCV proliferation.

Glu155 of the nonconserved motif in H. pylori arginase interacts with Ser152 and plays a role in catalytic function

To explore the role of Glu155 in catalytic function, the crystal structure of *H. pylori* Mn^{2+}-arginase was examined. The carboxylate group of Glu155 makes contact only with the hydroxyl group of Ser152 and forms an H-bond. To examine the role of this contact in catalytic function, a Ser152Ala mutant was prepared and its kinetic assay was performed. The catalytic efficiency for the Ser152Ala mutant was reduced by 4.3-fold compared to that of wild-type, where the k_{cat} value was primarily affected without altering the magnitude of $K_{0.5}$ (26% of wild-type activity). This suggests that the interaction of Glu155 with Ser152 plays a role in catalytic function. As reported, the mutation of Glu155 to Ala leads to a complete loss of catalytic activity. If Glu155 makes contact only with Ser152, one may anticipate a complete loss of catalytic activity in the Ser152Ala mutant. However, the observation of 26% of wild-type activity in the Ser152Ala mutant suggests that Glu155 may also interact with other residue(s). Thus, the crystal structure of the *H. pylori* Mn^{2+}-protein cannot fully explain the role of Glu155 in catalytic function.

Publication

Original peer-reviewed article

1. Mittal M, Kausar T, Rajan S, Rashmi D and Sau AK* (2023) Difference in catalytic loop repositioning leads to GMP variation between two human GBP homologues. **Biochemistry** 62:1509–1526.

[* Corresponding Author]

Molecular modelling of proteins and protein-ligand complexes using knowledge-based approaches and all atom simulations

Debasisa Mohanty

Principal Investigator	**Debasisa Mohanty**
Project Associates	Sonali Srivastava Sanjeet Mahtha
Project Fellows	Vikas Kumar Apratim Kumar Pandey
Ph.D. Students	Sana Amir Akshay Khanduja Ankita Pal Sapna Pal Suresh Kumar V (RCB-NII) Shweta Mahapatra
Collaborators	Rajesh S. Gokhale (IISER-Pune) Aneeshkumar A.G. (NII, New Delhi) Pushkar Sharma (NII, New Delhi) Rajesh S. Gokhale (IISER, Pune) Ranjana Arya (JNU, New Delhi) Manju Bansal (IISc, Bangalore)

The objectives of the major ongoing projects are **(A)** *In silico* identification of small ORFs by mining of bacterial genomes and human microbiome, **(B)** Structure based analysis of oncogenic mutations in EGFR kinase and development of small molecule inhibitors for targeting mutant kinases, **(C)** Identification of novel resistance associated mutations in *Mycobacterium tuberculosis* and analysis of the structural basis of drug resistance.

In silico identification and functional annotation of smORFs

Machine learning based method has been developed for identification and automated functional classification of smORFs in bacterial genomes and human microbiome. This method can assign function for 7 categories, namely, Antimicrobial proteins, Antitoxin type 2, Metal-binding, RNA-binding, Toxin type 1, Toxin type 2 and Ribosomal proteins. It was encouraging to note that, the models had 10 Fold Cross Validation ROC-AUC in the range of 0.84 to 0.97 and (Precision-Recall) PR-AUC in the range 0.66 to 0.97. These results indicate that our computational method can not only identify smORFs, but also predict their functions with reasonable accuracy. We have used ProsmORF-pred and ML based function prediction utility for identification and functional annotation of smORFs in human microbiome.

Structure based analysis of oncogenic mutations in EGFR kinase

Molecular dynamics (MD) simulation studies have provided mechanistic insight into how oncogenic mutations increase the population of active conformation of EGFR kinase, promoting aberrant phosphorylation by EGFR which is associated with cancer. These results have provided insight into the structural basis of the drug resistance in EGFR. We have attempted to understand how binding of allosteric inhibitors to the mutant EGFR kinases can potentially shift the population of conformers from active to inactive state. Several micro second scale MD simulations have been performed on native EGFR in inactive state, mutant EGFR (L858R/T790M) in inactive state, and allosteric inhibitor (EAI001) bound mutant EGFR (L858R/T790M). Our simulation provides insight into how allosteric inhibitor EAI001 helps in shifting the equilibrium towards inactive state. Hence, design of high affinity allosteric ligands can lead to potent EGFR inhibitors.

Identification of novel resistance associated mutations in Mycobacterium tuberculosis

The ML model developed for genotypic prediction of drug resistance (DR) utilizes the entire genome sequence. Hence, it can potentially identify new resistance markers. Therefore, attempt was made to identify both known and new markers of DR by using DeepShap (a method based on Shaplay algorithm) as well as feature importance of various mutations derived from XGBoost algorithm. It was encouraging to note that apart from known resistance associated mutations in the coding and non-coding regions, several new resistance associated mutations could be identified in both coding as well as non-coding regions. For ethambutol the ML model not only identified new resistance associated mutation Arg738Gln in the known DR associated gene embC, but also several novel mutations (His166Arg and Glu288Lys) were predicted in genes like *trmD* and *Rv2067c*, suggesting their association with DR. Since AI based methods like Alphfold2 and ESMFold have been able to predict high confidence 3D structures for majority of the *Mtb* proteome, work is currently ongoing to map newly identified DR mutations onto 3D structures for deciphering structural basis of their DR association.

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[* Corresponding Author]

To develop strategies for making sensors and actuators for biological processes

Pramod K. Upadhyay

Principal Investigator	**Pramod K. Upadhyay**
Project Fellow	Gargi Roy
Ph.D. Students	Prakriti Sinha K Varsha Mohan
Collaborators	Sangeeta Bhaskar (NII, New Delhi) P. Nagarajan (NII, New Delhi) S. Ramakrishnan (AIIMS, New Delhi) R. Lodha (AIIMS, New Delhi) Manisha Agarwal (Dr Shroff Charity Eye Hospital, Delhi) Vaishali Bhardwaj (RML Hospital, New Delhi) Kiran Chaudhary (RML Hospital, New Delhi)

The utility of Reprogrammed Monocytes (RM) as a cell-based therapy in sepsis

Sepsis is the unregulated systemic immune response to infection, resulting in symptoms of physiologic, pathologic, biochemical abnormalities and organ dysfunction. In severe bacterial infections such as in sepsis, the immune homeostasis between inflammatory and anti-inflammatory is compromised causing severe damage to organs while trying to clear the heightened infection. This condition leads to impaired interconnections between innate immune pathways and cytokines production, as well as dampens body's ability to counter invading pathogens.

Since RM's has immunomodulatory properties, we explored its potential for managing sepsis.

RM exhibits reduced immunogenicity

To understand the immunogenic nature of RM, the expression of the key immune antigen HLA-DR was determined by flow cytometry. The analysis showed that 7.88% of cells in RM cultures expressed HLA-DR antigen with an MFI of 195.3 compared to 12.4% of cells, MFI = 725.3, in monocytes; indicating a significant reduction HLA-DR molecules expression. The reduced immunogenicity of RM was further confirmed by evaluating their potential to induce lymphocyte proliferation in an *in-vitro* MLR experiment. The analysis showed that PBMC proliferation induced by RM (6.02 ± 0.91%) was significantly lower as compared to lymphocyte proliferation induced by corresponding monocytes (14.8 ± 1.96%). Furthermore, the time kinetic analysis at 24hrs, 48hrs and 72hrs of MLR culture did not show any significant change in lymphocyte proliferation.

Investigation on sepsis patients

For deciphering the effect of RM on septic PBMCs, peripheral blood samples were collected from sepsis patients admitted in the Departments of Medicine, Ram Manohar Lohia Hospital. Only patients which were given a qSOFA scoring of ≥2 were characterized as septic. Twenty-eight sepsis patient samples

(13M/15F, Median age 50 Years) were collected and processed. Twenty healthy controls were recruited at NII (11M/9F, Median age 28 Years).

RM exhibits its protective effect by modulating the host cell behaviour

To evaluate the protective effect of RM in sepsis, a co-culture of RM and patient derived PBMCs was established and studied. The RM culture were initiated 6 days prior to the collection of sepsis blood sample and a transwell co-culture of RM with patient PBMCs were setup.

The ROS levels by patient PBMCs was evaluated after their 24h co-culture with RM. The flow cytometric analysis showed that RM induced reduction in ROS production by patient PBMCs. The number of PBMCs generating ROS as well the ROS concentration both showed a trend of reduction in cocultures.

The reduced inflammatory behavior of patient PBMCs was further checked by quantifying the concentration of pro-inflammatory cytokines in the 24h co-culture supernatants. A trend of reduced levels of IL6, IL8, MCP1 and IL1β, further suggested the modulation of inflammatory behavior of patient PBMCs by RM.

The apoptotic profiling of patient derived PBMCs co-culture of RM, was done by Annexin V staining and followed by flow cytometric analysis. The apoptosis profiling showed a trend of increase in percent of Annexin-V- PI- viable cells and reduction in AnnexinV+ PI+ necrotic cell population in RM-PBMC cocultures.

Publications

Original peer-reviewed article

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[* Corresponding Author]

Chemical Glycobiology: Glycoform modulation, carbohydrate-based drug design and glycomics

Srinivasa-Gopalan Sampathkumar

Principal Investigator	**Srinivasa-Gopalan Sampathkumar**
Ph.D. Students	Anam Tasneem Shubham Parashar Charu Tanya Jain R. Abhiraj Simran Aittan Aishwarya Ranjan
Collaborators	Sriram Neelamegham (SUNY, Buffalo, USA) N.G. Ramesh (IIT-Delhi, New Delhi) Vinay Kumar Nandicoori (NII, New Delhi / CCMB, Hyderabad) Ayub Qadri (NII, New Delhi) Kanwaljit Kaur (NII, New Delhi) P. Nagarajan (NII, New Delhi) Madhumalar Arumugam (Jamia Milia Islamia, New Delhi) Kaisar Raza (Central University of Rajasthan, Ajmer)

A. Tools for the modulation of glycans

Sialoglycans, particularly sialyl-Lewis-X (sLeX/CD15s), are involved in leukocyte homing and extravasation through interactions with E-selectin (CD62E) (**Figure 1**). In our exploration for *N*-acetyl-D-mannosamine (ManNAc) analogues as metabolic precursors with novel biological properties, we designed *N*-(cycloalkyl)carbonyl derivatives. We hypothesized that the cycloalkyl moieties might be relatively more permissible for metabolic processing compared to their *N*-(alkyl)carbonyl (straight chain) counterparts due to steric hindrance. The *N*-cycloalkyl moieties might be able to fine-tune sialoglycan-protein interactions and modulate cellular processes.

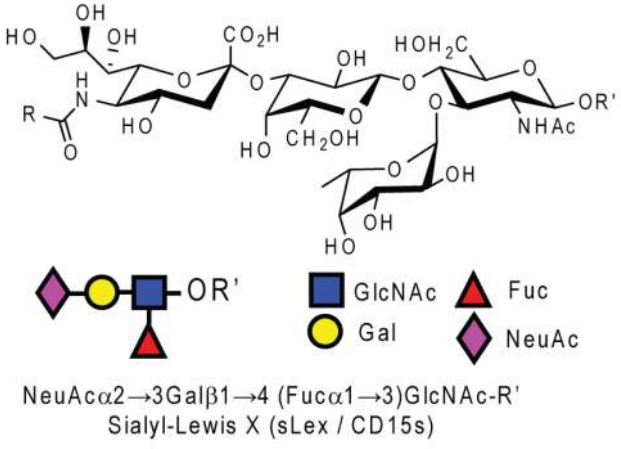

Figure 1. Engineering of sialyl Lewis-X (sLeX / CD15s) epitopes using metabolic precursors enhances cell adhesion to E-selectin. Both the chemical structure and symbol nomenclature for glycans (SNFG) are shown for sLeX. GlcNAc, N-acetyl-D-glucosamine; Gal, D-galactose; Fuc, L-fucose; NeuAc, N-acetyl-D-neuraminic acid.

A panel of peracetylated analogues of ManNAc, carrying *N*-cyclopropanoyl (**1a**) and *N*-cyclobutanoyl (**1b**), *N*-azidoacetyl- derivative (**1c**), *N*-acetyl (**1d**), *N*-propanoyl (**1e**), *N*-butanoyl (**1f**), and *N*-pentanoyl (**1g**) derivatives were synthesized and evaluated in mammalian cells. The C2 epimer, *N*-acetyl-D-glucosamine (GlcNAc) analogues, *N*-cyclopropanoyl (**2a**) and *N*-cyclobutanoyl (**2b**) were employed as controls.

Estimation of sLeX using anti-CD15s (clone CSLEX1) antibody by flow cytometry in HL-60 (human acute myeloid leukemia) cells incubated with ManNAc analogues showed that **1b**, but not the other analogues, increased the levels of sLeX by three-fold. The binding of E-selectin-Fc (CD62E) chimera was increased by 40-50% upon treatment with **1b**, but not in controls. Probing of the respective immunoprecipitates with anti-CD15s antibody showed enhanced levels of sLeX on three glycoproteins, *viz.,* CD162/PSGL1, CD44, and CD43, with maximal increase observed for treatment with **1b** followed by **1g**.

Treatment with **1b** showed a three-fold increase in the number of adherent HL-60 cells, compared to controls, on E-selectin coated surfaces. It is plausible that either the sLeX carrying the N-cyclobutanoyl-D-neuraminic acid (sLeX-Cb) has additional direct contacts with E-selectin or sLeX-Cb presents higher proportion of bioactive conformations due to remote substituent effects. Molecular dynamics simulations, in collaboration with Arumugam's group, results showed that sLeX-Cb displayed a higher proportion of bioactive conformer populations compared to sLeX. Our results highlight the importance of the remote *N*-acyl moiety of NeuAc in sLeX in governing the ensemble of bioactive conformations and carbohydrate-based drug design in general (Ref: Tasneem, A., *et al., Biorxiv,* doi: https://www.biorxiv.org/content/10.1101/2021.12.22.473788v2. Studies on *in vivo* effects for leukocyte migration and homing are currently underway.

A. Metabolic engineering of glycoconjugates in mycobacteria

Mycobacterial glycocalyx consists of mycolyl arabinogalactan peptidoglycan (mAGP) complex, trehalose di- and mono-mycolates, and sulfo-glycolipids. Genetic methods have shed light on the functions of various genes for the survival, virulence, and latency of mycobacteria. However, direct methods for the analysis of glycoconjugates have been few and far between. We have identified a simple monosaccharide analogue of GlcNAc, viz., 2-azido-2-deoxy-D-glucose (2AzGlc) for engineering of glycoconjugates of *Mycobacterium smegmatis,* in collaboration with Nandicoori's group.

Mycobacteria were cultured in the presence of various azido-group carrying monosaccharides, subjected to strain-promoted azide-alkyne cycloaddition (SPAAC) using dibenzocyclooctyne-cyanine 5 (DBCO-Cy5), and analyzed by flow cytometry and confocal microscopy. Strikingly, we observed robust expression of azido-groups upon incubation with the free monosaccharide 2AzGlc, but not with the corresponding peracetylated derivative. Interestingly, incubation of *E. coli* with 2AzGlc did not result in surface expression of azido-glycoconjugates suggesting bacterial selectivity. Evaluations on the applications of this glycan labelling methodology are currently underway.

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[* Corresponding Author]

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Structural studies on proteins, dynamics and ligand interactions using NMR

Monica Sundd

Principal Investigator	**Monica Sundd**
Ph.D. Students	Vijay Kumar Sonika Bhatnagar Rashima Prem Shivani Karalia Debodyuti Sadhukhan Shivangi Vaish
Collaborators	Suman Kundu (Delhi University- Delhi) Ashok Kumar Patel (IIT Delhi, New Delhi) Suman Jain (AIIMS- Delhi, New Delhi) Faizan Ahmed (JMI, New Delhi)

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.

Understanding the structure-function of the enzymes involved in lipoic acid modification

Lipoic acid is a hydrophobic cofactor, essential for the function of mitochondrial dehyrogenases *viz.* pyruvate dehydrogenase complex (PDHc), 2-oxoglutarate dehydrogenase, glycine cleavage system (GCS), branched-chain keto acid dehydrogenases and 2-oxoadipate dehydrogenase. These are multimeric enzymes with a conserved lipoyl domain, that serves as a substrate for lipoic acid modification. Lipoyl lysine acts as a "swinging arm", helping to shuttle intermediates between the active site of multienzyme complexes.

In the presence of free lipoate or octanoate, the cofactor is salvaged from the environment by lipoate-protein ligase A (LplA) and transferred to a lipoyl domain by an ATP dependent process. In lipoic acid deficient environments, Lipoate protein ligase B (LipB) also known as Lipoyl-octanoyl transferase catalyzes the first biosynthetic step of lipoic acid synthesis using C_8-ACP (a product of FAS) as a substrate. The two enzymes lipoylate the same dehydrogenases, using an entirely different mechanism. LplA uses free lipoic acid for modification, while LipB synthesizes it *de novo.* LipB functions as a cysteine/lysine dyad acyltransferase, forming a covalent octanoyl-LipB thioester intermediate by the transfer of octanoyl- chain from C_8-ACP (acyl carrier protein) to the catalytic Cys of LipB. Subsequently, the thioester bond is attacked by the ε-amino group of the lipoyl lysine, resulting in C_{8}-modification of the latter. In the subsequent step, octanoyl group covalently tethered to the lipoyl domain

of a dehydrogenase is converted to lipoic acid in the presence of LipA (lipoyl synthase) by insertion of 2 sulphur atoms.

In higher eukaryotes including humans, LplA is absent, and LipB is the only modifying enzyme liable for all lipoic acid modifications. Genetic mutation of this gene or any upstream fatty acid pathway gene results in a variety of neurological disorders, underscoring the need to understand the structure and function of LipB at the molecular level. Moreover, the biosynthetic enzyme LipB is not fully characterized, and the mechanistic understanding of its substrates is also sparse. Therefore, we have carried out an in-depth study on this enzyme. Using enzyme assays and NMR, we show that LipB has preference for the modified acyl carrier protein (ACP) in the following order C_{8}-ACP>Holo-ACP>Apo-ACP. As the enzyme displayed high affinity for C_{8}- chain and the phosphopantetheine arm, present in C_{8}- and holo-ACP respectively, we tested whether it could use C_{8}-CoA as a substrate. Our results suggest that the enzyme can indeed use C_{8}-CoA as a substrate and prefers it over its cognate substrate C_{8}-ACP. Using site-directed mutagenesis, we also identified an RGG loop present near the active site cavity of LipB, that allosterically regulates its activity. Furthermore, using NMR we show that LipB interacts with adenosine as well as the 3'5'-diphosphate of CoA. ^{31}P NMR experiments on wild-type, and various mutants confirm that the 3'-phosphate of CoA primarily interacts with the active site residue Lys 135 of LipB.

Taken together, our studies show that the biosynthetic enzyme LipB can use C_{8}-CoA as a substrate, in addition to C_{8}-ACP. These findings might be helpful in the treatment of patients with FAS mutations and related disorders.

Publications

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[*Co-corresponding author]

Therapeutic interventions for chronic diseases

Sarika Gupta

Principal Investigator	**Sarika Gupta**
Inspire Faculty	Priyanka Shukla
Project Associates	Sudhir Kumar Kavita Solanki
Ph.D. Students	Shikha Salhotra Kajal Kamble Gangaram Aishwarya Nilakhe Moh. Azad Arundhati Karmakar Sumnil Bhola
Collaborators	Bipin K. Gupta (NPL, New Delhi) Gyan Prakash Modi (IIT-BHU, Banaras) Naveen Kumar (IIT-Ropar, Ropar)

ARL6IP5 Ameliorates α-Synuclein Burden by Inducing Autophagy via Preventing Ubiquitination and Degradation of ATG1

Parkinson's Disease is the second most common neurodegenerative disorder, currently affecting ~9.6M elderly people worldwide and its prevalence is expected to double in the next 30 years. PD features both motor symptoms like bradykinesia, rigidity, or rest tremor and non-motor symptoms like cognitive impairment and/or sensory alterations. It is characterized by selective loss of dopamine neurons in substantia nigra pars compacta and intracellular inclusions of the Lewy body and Lewy neurites composed of a-synuclein and polyubiquitinated proteins. The cellular burden of Lewy-body and neuritis depends on the number of aggregates generated and cleared. Smaller cytosolic aggregates can be degraded by the proteasomal system, however, larger aggregates of synuclein can only be removed by either chaperon-mediated or macro-autophagy. Autophagy plays an essential role not only in protein degradation and recycling but also in replenishing nutrients and removal of damaged organelles. Though both the ubiquitin-proteasome system and autophagy could clear ubiquitinated substrates, however, autophagy is the only way to remove large protein aggregates or damaged organelles. Unlike other mitotic cells, neurons cannot get rid of aggregates and damaged organelles by cell division to disperse harmful substances. Being post-mitotic cells, neurons are the most vulnerable cells of CNS in most lysosomal disorders, indicating that neurons might rely on autophagy even more heavily than other cells to maintain protein homeostasis. Another challenge is the physically distinct localization of two important components of autophagy i.e. autophagic vacuoles generated in axons should travel long distances to the cell body where lysosomes are mainly present. The situation gets worse with age as neurons are gradually losing the capacity to efficiently transport and clear the waste generated at axons and dendrites, eventually leading to abnormal accumulation of autophagic substrate. Altogether these abnormalities affect neuronal physiology and synaptic transmission. This indicates that neurons are

prone to suffer from autophagic proteolytic damage. Although recent research has increased our understanding of the process of autophagy in neurons and identified various proteins (LRRK2, PINK, etc) that are mutated in PD and stalled the process of autophagy. However, a large majority, 85–90%, of PD cases are sporadic in nature therefore, identifying a downstream regulator of autophagy, that gets modulated by α-synuclein (the major component of Lewy bodies) would be of great significance, as they can, potentially reveal the underlying processes that are central to all forms of PD. We investigated the regulator of pre-autophagosome formation. More than 30 autophagy-related proteins have been identified as directly participating in the autophagy process. Proteins regulating the process of autophagy are much more numerous and unknown. To address this, in our present study, we identified a novel regulator (ARL6IP5) of neuronal autophagy and showed that the level of ARL6IP5 decreases in the brain with age and in Parkinson's disease in mice and humans. Moreover, a cellular model of PD (Wild type and A53T mutant α-synuclein overexpression) has also shown decreased levels of ARL6IP5. ARL6IP5 overexpression reduces α-synuclein aggregate burden and improves cell survival in an A53T model of Parkinson's disease. Interestingly, detailed mechanistic studies revealed that ARL6IP5 is an autophagy inducer. ARL6IP5 enhances Rab1-dependent autophagosome initiation and elongation by stabilizing free ATG12. We report for the first time that α-synuclein downregulates ARL6IP5 to inhibit the autophagy-dependent clearance of toxic aggregates that exacerbate neurodegeneration.

Publications

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Structural and dynamic studies of antigen-antibody and host-pathogen interactions

G Senthil Kumar

Principal Investigator	**G Senthil Kumar**
Project Fellow	Johnson Samuel
Ph.D. Student	Rahul Yadav
Collaborator	Chandrakumar Appayee (IIT Gandhinagar, Gandhinagar) K.R. Mahendran (RCGB, Trivandrum) Arumugam Madhumalar (JMI, New Delhi) Wolfgang Peti (UConn Health Center, USA) Matteo Ceccarelli (University of Cagliari, Italy)

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.

Objectives

A. Structural/Dynamic studies on antigen-antibody interactions:

In this project, the molecular basis for the antigen-antibody interaction 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 m ediating 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?

Publication

Original peer-reviewed article

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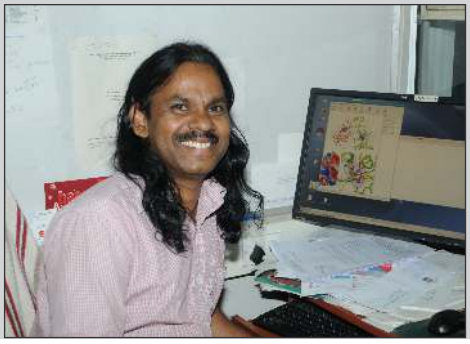

Designing new anti-TB molecules through structural biology approach

Bichitra Kumar Biswal

Principal Investigator	**Bichitra Kumar Biswal**
Ph.D. Students	Indu Bhatia Sayan Chakraborty Mohammed Ahmad Satish Tiwari Deepsikha Kar Swati Kumari Varun Kumar Mohini
Collaborators	Nisheeth Agarwal (THSTI, Faridabad) Ramandeep Singh (THSTI, Faridabad) Amit Pandey (THSTI, Faridabad)

My laboratory majorly aims at deriving mechanistic understandings of *Mycobacterium tuberculosis (Mtb)*, the organism that causes human tuberculosis (TB), metabolic pathways particularly the *de novo* Histidine (His) production. Further, we intent to design/develop novel anti-TB small molecules through exploiting the results of this study. Briefly, *Mtb* biosynthesizes His *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 model combined with its absence in humans makes this pathway an important anti-TB drug target. Our major focus in recent years has been in designing novel anti-TB molecules targeting *Mtb* His pathway enzymes primarily through a structure-guided approach.

Designing anti-TB molecules

Over the past three decades, plant IGPD (imidazole glycerol phosphate dehydratase, also known as HisB), an enzyme that catalyzes the sixth step of the His pathway, has been an important herbicide target. A plethora of studies particularly in the area of developing potent herbicides targeting IGPD has led to the discovery of an ample number of small molecules. These studies showed that triazole and imidazole scaffold compounds are promising IGPD inhibitors. The availability of such a wealth of information provides a basis to examine whether triazole and imidazole scaffold inhibitors exhibit anti-TB potency by inhibiting the function of the His pathway of *Mtb*. Our earlier studies and reports from other groups suggest that triazole and imidazole derivatives compounds have better prospects of inhibiting the function of IGPD. The 3D experimental structure of this enzyme from *Mtb* has been elucidated by us and from other organisms by others. The results from our recent high resolution structural study show that the functional unit of the enzyme is a 24-mer with 24 identical active sites. By utilizing these structural information in the inhibitors design; we constructed a number of triazole derivative compounds and calculated the binding affinity of each of these compounds. The binding scores together with the physiological properties suggested that these molecules exhibited high anti-TB potential. In order to pursue this further, a few of these molecules were procured and *in vitro* and *in vivo* efficacies were investigated.

High resolution crystal structure of the enzyme-inhibitor complex showed that each inhibitor binds at the active site of the enzyme (**Figure 1**). The two active site manganese atoms are coordinated with

the two nitrogen atoms of the triazole ring. The active site is made up of mainly histidine-rich amino acids. Based on cytotoxicity and *in-vitro* macrophage clearance data, we tested for their efficacy against *Mtb* in an animal model of TB infection. We observed that a triazole compound showed a significant lowering of the bacterial burden in both lungs and spleen relative to the untreated animals. Interestingly, supplementation of histidine in mice treated with this compound restored the bacterial burden to the untreated levels further validating the fact that the decrease in the bacterial load observed in the treated mice was a result of reduced biosynthesis of histidine. Our study demonstrated that abolishing the function of His biosynthesis represents a new means of curtailing TB infection.

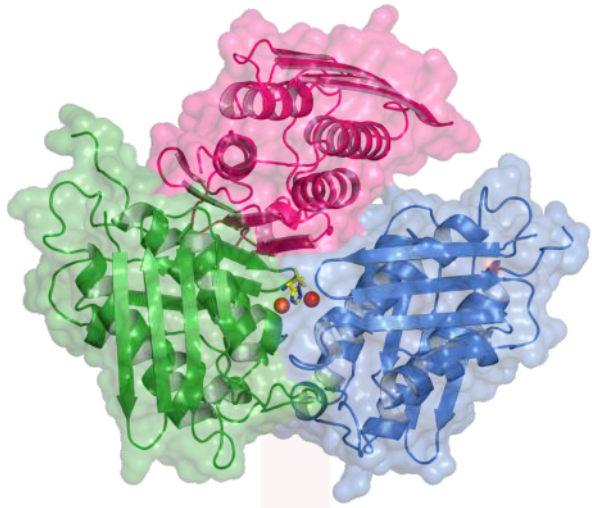

Figure 1. The high resolution crystal structure of HisB/inhibitor complex showed the binding of a triazole compound (in stick model with carbon atoms in yellow) in the enzyme's active site. Three subunits whose interface forms the active site are shown in green, magenta and blue colors. Two manganese atoms in the active site pocket are depicted as red spheres.

Publications

Original peer-reviewed articles

1. Ahuja R, Srichandan S, Jairam Meena J, Biswal BK, Panda AK (2023) Immunogenicity evaluation of thermostable microparticles entrapping receptor binding domain of SARS-CoV-2 by single point administration. **J Pharm Sci.** 112: 1664-1670.
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4. Pandey M, Tiwari S, Johri S, Biswal BK, Sharma C, Pandey AK (2022) Investigating a putative transcriptional regulatory protein encoded by Rv1719 gene of *Mycobacterium tuberculosis.* **Protein J.** 41:424-433.

[* Corresponding Authors]

Awards / Fellowships

TATA innovation fellowship (29.03.2023) for the year 2022-23 by DBT, India. For translational research in the areas of human Tuberculosis and COVID-19 employing innovative scientific and platform technologies.

Biophysical and biochemical characterization of *Leishmania Mexicana* phosphoglycerate kinase: an enzyme in the glycolytic pathway of parasitic protozoa

Vidya Raghunathan

Principal Investigator **Vidya Raghunathan**

Trypanosomatida cause deadly diseases in humans. Of the various biochemical pathways in trypanosomatida, glycolysis, has received special attention because of being sequestered in peroxisome like organelles critical for the survival of the parasites.

Proteins like Phosphoglycerate kinase are critical housekeeping metabolic enzymes and traditionally been a 'touch me not' for potential targets in drug research. However the pressures of survival and evolutionary changes are faced by entire cellular machinery and occur at many levels of individual protein secondary or tertiary structure. It is these, changing roles that allow a protein to maintain its biological activity while also rendering new roles that can potentially give insight on how to design inhibitory drugs. Protein folding is an old problem with new intrigues: in it lies the entire coded history of a protein's evolution. *Leishmania* PGK isoforms has some distinct structural features, as PGKB and PGKC differ primarily in the presence of a long extension at the C-terminus of PGKC. Drug development efforts can be targeted, either at the glycosome itself or at the enzymes present within them for which, targeting unique structural features is critical. We are interested to apply structural biological methods and enzymology to study the behavior of PGK isoforms in *Leishmania* sp.

Biophysical and biochemical characterization of PGK from other Leishmania species such as *L. donovani* and *L. major* has been included in the scope of work. Additionally we are working on immunologic link of PGK derived metabolites. PGKC has been suggested to have additional functions in the glycosome of *Leishmania* through our studies. We are interested to ask if such additional functions for PGK is there in immune cells because, already, one glycolytic enzyme, GAPDH has been found to play a role in controlling production of IFNg in TH1 cells and another hexokinase has been shown to moonlight as a NLRP3 regulator (NOD-LRR- and pyrin domain-containing 3) in macrophages.

So far no one has linked PGK to any immunoregulatory molecules, but because it can feed into important signaling pathways a link is possible. An important amino acid biosynthesis pathway, the serine biosynthetic pathway is fed by a product of phosphoglycerate kinase enzymatic reaction and could be coupled to pathways activated during increased energy requirements.

FUTURE PLANS FOR NEXT 5 YEARS

Our contributions have been towards appreciation of multifunctionality of proteins and how they happen in evolution. This has led us to ask new questions on the importance of Immunometabolism especially in reference to *Leishmania* infection. Structural analyses are revealing the function of different isoforms of *Leishmania*-derived phosphoglycerate kinase, work that may lead to the development of new drugs. In HIV infection and progression certain epistatic interactions in the HIV protease effect its rate of evolvability demonstrating how key interaction between residues on a protein surface act as key signals. Similar to this we found key interactions in glycosomal PGK that may lead to it having a key role within glycosome unlike the cytoplasmic counterpart.

The abstract of our work on the epistatic interactions in PGKC and role of GXXXG motif at the C-terminus received critical appreciation in Parasitology 2018, Paris, France.

Our present day knowledge reveals, importantly, that many biosynthetic pathways branch out from glycolysis and thus this pathway is important for cellular proliferation. Metabolites (either directly or indirectly linked to glycolysis) function as signaling molecules reinforcing the idea that metabolism is part of the cellular signaling network. Cellular metabolism is an area just being opened up. Our new challenge would be to understand the role of phosphoglycerate kinase in the metabolic signaling network especially with regards to infection and disease.

Immunometabolism should be given an important look over especially with regards to phosphoglycerate kinase. GAPDH, another enzyme of the glycolytic pathway has already been found to link to the aerobic glycolysis and release/inhibition of interferong. Is would be particularly useful to see if PGK is also somehow linked to aerobic glycolysis. It is well known that not just glucose but another carbohydrate mannan feeds into the glycolytic cycle of Leishmania. Could mannan be linked to aerobic glycolysis and if so how? The basis for the idea that phosphoglycerate kinase may be have an immunometablic role is that metabolites released by PGK in Leishmania such as 3-PG feed into signaling pathways like the serine metabolism pathway. Just like the unravelling of the laws of heredity, the laws of mutation and their exact relation to functional adapatability in proteins remains to be understood.

GENETICS CELL SIGNALING AND CANCER BIOLOGY

Cellular and molecular biology of human cancer

Anil Suri

Principal Investigator	**Anil Suri**
Consultant	Nirmala Jagadish
Project Fellows	Surbhi Arora Pooja Marsheena Nelleri
Collaborators	T. Rajkumar (Cancer Institute (WIA), Chennai) G.K. Rath (IRCH, NCI-AIIMS, New Delhi) Sridevi Veluswami (Cancer Institute (WIA), Chennai) R. Swaminathan (Cancer Institute (WIA), Chennai) Shirley Sunder Singh (Cancer Institute (WIA), Chennai) J.B. Sharma (AIIMS, New Delhi) D.N. Sharma (IRCH, AIIMS, New Delhi) Amlesh Seth (AIIMS, New Delhi) Alok Thakar (AIIMS, New Delhi) Ashish Suri (AIIMS, New Delhi) Govind Makharia (AIIMS, New Delhi) V. Suri (AIIMS, New Delhi) N. Singh (AIIMS, New Delhi) Prabhjot Singh (AIIMS, New Delhi) S. Upreti (Govt. Doon Medical College, Dehradun) Rajeev Sood (RMLH, New Delhi) Anju Gupta (VIMHANS, New Delhi) V. Swarankar (MGH,Jaipur) Hemant Malhotra (SRCC, MGH, Jaipur) Swati Garg (MGH,Jaipur) T.C. Sadasukhi (MGH, Jaipur) Ajay Yadav (MGH, Jaipur) Nitin Khunteta (MGH, Jaipur) Anand Mohan (MGH, Jaipur) Shweta Sharma (MGH, Jaipur) Sumit Goyal (MGH, Jaipur) Neha Sethi (MGH, Jaipur)

Our focus is addressed on SPAG9 for the assessment of early detection, disease risk, prognosis, and novel treatment modalities such as immunotherapy as well as disease recurrence.

A. Human clinical trials in cervical cancer patients stage IIIb Phase 2, [DCGI approval: 03 March 2015; CTRI/2016/12/007530]

Phase 2 Human clinical trials (54 patients) to assess the efficacy of Dendritic cells primed with either patient's own tumor lysate or using rSPAG9 protein in stage IIIB cervical cancer were carried out in collaboration at Cancer Institute, Adyar, Chennai. Cancer patients were being followed till December 2022.

B. Human clinical trials in ovarian cancer patients stage IV (recurrent/metastatic) who have failed two line of systemic therapies [DCGI approval: 4th March, 2020; 22nd January 2022; CTRI/2020/11/029436]

All SOPs were standardized at NII and were transferred to Cancer Institute, Adyar, Chennai.

C. Early detection, diagnosis and follow-up of the treated cervical and ovarian cancer patients: Site CCI, SRCC, MGMCH Jaipur

Blood samples were collected from cervical and ovarian cancer patients and healthy volunteers. Totally, blood samples have been collected from 239 ovarian cancer patients, 200 cervical cancer patients and 200 healthy volunteers. A total of 210 ovarian cancer patients,167 cervical cancer patients and 200 healthy control sera samples were evaluated for anti-SPAG9 antibodies. There was significant difference in mean absorption value in different stages and grades of ovarian cancer and cervical cancer as compared to healthy controls.

Award:

Dr. Anil Suri received an award-"Excellence in Science" in view of outstanding vision, dedication and commitment during long and distinguished career spanning many decades, which has had a major impact on health care, cancer care and cancer control Award conferred by Immuno-Oncology Society of India during 4th Annual Congress of Immuno-Oncology Society of India [I-OSICON 2023] 20th to 22nd January, 2023 at Jaipur, India.

Deciphering the role of cell signaling in *Mycobacterium tuberculosis (Mtb)* biology

Vinay Kumar Nandicoori

Principal Investigator	**Vinay Kumar Nandicoori**
Postdoctoral Fellow	Saba Naz
Ph.D. Students	Biplab Singha Sidra Khan Yogita Kapoor (CCMB) Priyadarshini Sanyal (CCMB) Abhishek Saha (CCMB) Amit Chattopadhaya (CCMB) Sutashree Nath (CCMB) Asis Khuntia (CCMB)
Collaborators	Umesh Varshney (IISc, Bangalore) Dhiraj Kumar (ICGEB, New Delhi) Aneeshkumar A.G. (NII, New Delhi) Yogendra Singh (IGIB, Delhi) Tej Sowpati (CCMB, Hyderabad)

GWAS and functional studies implicate a role for altered DNA repair in the evolution of drug resistance in *Mycobacterium tuberculosis.*

The acquisition of drug resistance in *Mtb* has evoked a precarious situation worldwide. Prolonged treatment duration, high drug toxicity, and the expensive drug regimen pose a challenge for treating the MDR and XDR-TB. Despite well-known mechanisms of drug resistance, in 10-40% of the clinical isolates of *Mtb*, drug resistance cannot be determined by the mutations in the direct targets of antibiotics, implying the presence of hitherto unknown mechanisms that foster the development of resistance in *Mtb*. In a quest of identifying genetic triggers that aids in the evolution of antibiotic resistance in *Mtb*, we performed GWAS using global data set of 2237 clinical strains that consist of antibiotic susceptible, MDR and XDR. Interestingly, we have identified mutations in the multiple DNA repair genes of *Mtb* that are associated strongly with the MDR phenotype. Functional validation of the identified mutations of DNA repair enzymes revealed that perturbation in the DNA repair mechanisms results in the enhanced survival of strains in the presence of antibiotics *ex vivo* and *in vivo*.

GWAS unveils mutations in the DNA repair genes.

To identify the genetic determinants contributing to the development of antibiotic resistance in *Mtb*, we performed genome-wide association analysis using whole-genome sequences of clinical strains from 9 published studies. We identified ~160,000 Single Nucleotide Polymorphism (SNPs) and indels after mapping the short reads on the reference *Rv* genome. After setting the adjusted p-value cut-off at 10^{-5}, we identified 188 mutations, including 24 intergenic regions that correlated with the multi-drug resistance. Among the 188 genes, ~45% of mutations resulted in non-synonymous changes, whereas ~33% resulted

in synonymous changes, 14% were identified in the upstream gene variant, and 8% possess stop/frameshift mutations. In addition to the mutations described above, we identified novel mutations in base excision repair (BER), nucleotide excision repair (NER), and homologous recombination (HR) pathway genes, *mutY, uvrA, uvrB,* and *recF* that are strongly associated with the MDR and XDR-TB).

Mutations in DNA repair genes result in the loss of function.

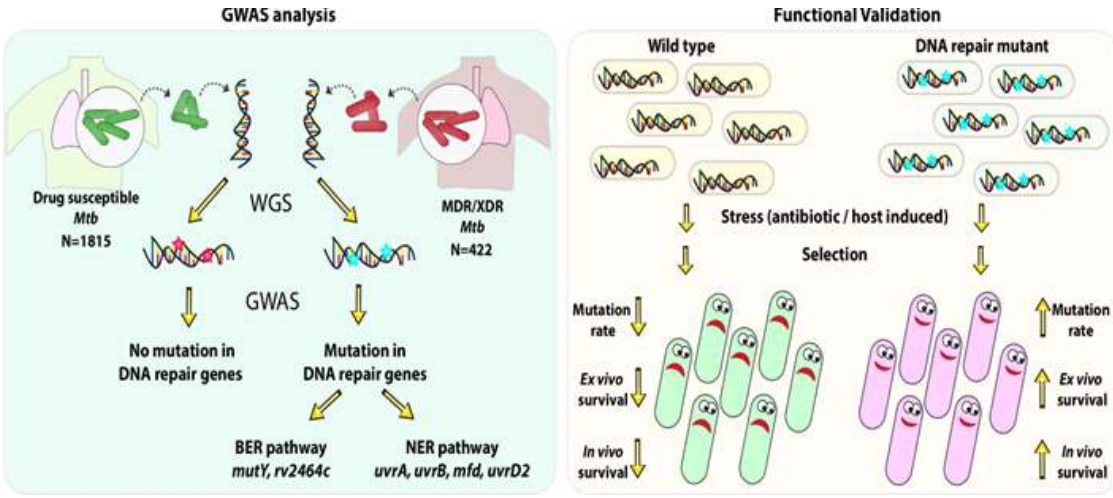
MutY is a 302 amino acid (aa) long adenosine DNA glycosylase encoded by rv3589. Oxidative damage to the DNA results in the formation of 7,8-dihydro 8-oxoguanine (8-oxoG) that can pair with guanine (G) or adenine (A). If left unrepaired, this would lead to C→G or C→A mutations in the genome. The GWAS analysis identified **Arg262Gln** mutation at the C-terminal region of the MutY. To decipher the biological role of the identified variant, we cloned *Mtb mutY* and performed site-directed mutagenesis to generate the mutant allele. Wild type and mutant *mutY* genes subcloned in an integrative *Mtb* shuttle vector. We generated the gene replacement mutant of *mutY* in laboratory strain H37Rv. Constructs were electroporated into *Mycobacterium tuberculosis mutY* mutant strain (*Mtb* D*mutY*) to generate *Mtb*D*mutY::mutY,* and *Mtb*D*mutY::mutY*-R262Q strains. We determined the mutation frequency in the presence of rifampicin and isoniazid. The data suggested that variant of *mutY* identified in the GWAS compromised its function.

The variant of *mutY* confers survival advantage *ex vivo*.

To ascertain the role of the identified variant of *mutY*, we evaluated the survival of *Rv, Rv*D*mutY,* *Rv*D*mutY::mutY*, and *Rv*D*mutY::mutY*-R262Q in the peritoneal macrophages. We did not observe any difference in the survival. We hypothesized that the evolution of strain to become antibiotic-resistant required continued antibiotic and host-directed stress. Therefore, we infected peritoneal macrophages in the absence or presence of the antibiotics. The bacteria recovered were cultured *in vitro* for 5 days and used for the next round of infection. The process was repeated for three rounds, and CFUs were enumerated at 4 and 96 h post-infection (p.i) during the fourth round of infection. *Rv*D*mutY* and *Rv*D*mutY::mutY*-R262Q exhibited better survival in the absence of antibiotics compared with Rv and *Rv*D*mutY::mutY*. We observed a log-fold advantage for *Rv*D*mutY* and *Rv*D*mutY::mutY*-R262Q compared with *Rv or Rv*D*mutY::mutY* in the presence of rifampicin or ciprofloxacin. Results suggest that antibiotic pressure in the host drives the acquisition of mutations, resulting in better survival of the strains.

MutY* variant exhibits enhanced survival *in vivo

Upon entering the host macrophages, *Mtb* encounters multiple stresses that impede its growth. To survive and grow in such a hostile environment, *Mtb* employs multiple defense mechanisms. An auxiliary mechanism used by the pathogen is to accumulate mutations in its genome that improve its ability to combat antibiotic and host-induced stress. We asked if the variant mutations identified in DNA repair genes are one such auxiliary mechanism? To test this hypothesis, we performed guinea pig infection experiments. 56 p.i, *Rv*D*mutY, Rv*D*mutY::mutY*-R262Q strains showed ~5 fold superior survival than *Rv Rv*D*mutY::mutY*, suggesting that the variant mutant identified indeed confers advantage. Next, we determined the survival ability of *Rv*D*mutY, Rv*D*mutY::mutY*, and *Rv*D*mutY::mutY*-R262Q, when competed against wild type Rv strain. The data clearly showed that *mutY* deletion or complementation with the variant confers a survival advantage to the pathogen. Collectively, results show that variant mutations identified in DNA repair genes using GWAS, abrogate their function and contribute to better survival under antibiotic/host stress conditions.



Model. Model depicts the analysis and subsequent validation. GWAS revealed mutation in three DNA repair pathway genes in MDR/XDR strains. Based on GWAS, we proposed that mutations in DNA repair genes contribute towards the evolution of antibiotic resistance in *Mtb.* Functional validation was performed using the gene replacement mutants of BER and NER pathway genes in *msm* and *Mtb. In vitro, ex vivo* and *in vivo* experiments show that compromised DNA repair pathway leads to evolution of MDR/XDR-TB.

Publications

Original peer-reviewed articles

1. Naz S, Paritosh K, Sanyal P, Khan S, Singh Y, Varshney U, Nandicoori VK* (2023) GWAS and functional studies suggest a role for altered DNA repair in the evolution of drug resistance in *Mycobacterium tuberculosis.* **Elife.** 12:e75860.

2. Singha B, Behera D, Khan MZ, Singh NK, Sowpati DT, Gopal B, Nandicoori VK* (2023) The unique N-terminal region of Mycobacterium tuberculosis sigma factor A plays a dominant role in the essential function of this protein. **J Biol Chem.** 299:102933.

3. Gupta S, Arora A, Saini V, Mehta D, Khan MZ, Mishra DK, Yavvari PS, Singh A, Gupta SK, Srivastava A, Kumar Y, Verma V, Nandicoori VK, Bajaj A (2022) Hydrophobicity of Cholic Acid-Derived Amphiphiles Dictates the Antimicrobial Specificity. **ACS Biomater Sci Eng.** 8:4996-5007.

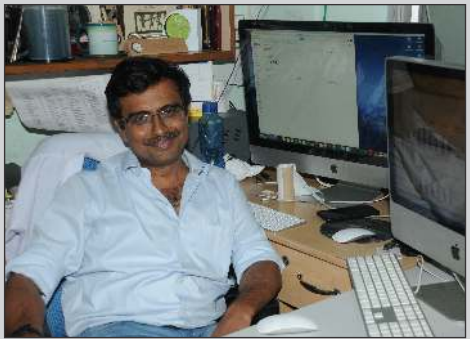
4. Kemp SA, Cheng MTK, Hamilton WL, Kamelian K; Indian SARS-CoV-2 Genomics Consortium (INSACOG); Singh S, Rakshit P, Agrawal A, Illingworth CJR, Gupta RK. (2022) Transmission of B.1.617.2 Delta variant between vaccinated healthcare workers. **Sci Rep.** 12:10492.

5. Naz S, Dabral S, Kumar D, Nandicoori VK* (2022) Protocol for ex vivo competition and sequencing of mycobacterium isolated from infected guinea pigs. **STAR Protoc**. 3:101804.

6. Kumar S, Khan MZ, Khandelwal N, Chongtham C, Singha B, Dabla A, Behera D, Singh A, Gopal B, Arimbasseri GA, Kamat SS, Nandicoori VK* (2022) Mycobacterium tuberculosis Transcription Factor EmbR Regulates the Expression of Key Virulence Factors That Aid in *ex vivo* and *in vivo* Survival. **mBio.**13:e0383621.

7. Soman S, Chattopadhyay S, Ram S, Nandicoori VK, Arimbasseri GA* (2023) Codon optimality has minimal effect on determining translation efficiency in *Mycobacterium tuberculosis.* **Sci Rep.** 13:415.

[* Corresponding Author]



Determining the signalling and repair pathways that are altered during genomic instability in nucleus and mitochondria

Sagar Sengupta

Principal Investigator	**Sagar Sengupta**
Project Fellows	Vandana Sharma Baishali Chakraborty
Ph.D. Students	Aamir Khan Ritu Agrawal Aftab Mohammed Rimpy Arun Savita Tavleen Kaur
Collaborators	Arnab Mukhopadhyay (NII, New Delhi) Avinash Bajaj (RCB, Faridabad) Patrick Legembre (Universite de Rennes, France) Tapas Kumar Kundu (JNCASR, Bangalore) Ullas Kolthur (TIFR, Mumbai) S.V.S Deo (AIIMS, New Delhi)

Mutations in RECQL4 cause three different disorders with distinct yet overlapping phenotypes, namely RAPADILINO, Baller-Gerold and Rothmund-Thomson syndrome. RECQL4 is constitutively present in the mitochondria in asynchronously growing cells. Human cells lacking mitochondrial RECQL4 exhibit increased reactive oxygen species (ROS), mtDNA mutations and altered metabolism phenotype which leads to cancer predisposition.

Mitochondria are vital organelle for energy production in eukaryotic cells, ATP generation through oxidative phosphorylation. Most precursor mitochondrial proteins containing the mitochondrial localization signal (MLS) are recognized by Tom20 and enter into the mitochondrial matrix using a complex machinery involving multiple proteins and membrane potential. Recent studies have implicated the role of ubiquitylation in mitochondrial protein import. MITOL is a mitochondrial E3 ligase present on the mitochondrial outer membrane. It is an important regulator of mitochondrial dynamics and quality control.

We report that RECQL4 is ubiquitylated by MITOL, at two lysine residues (K1101, K1154) via K6 linkage. This hampers the interaction of RECQL4 with Tom20, thereby restricting its entry into mitochondria. Thus, RECQL4 2K mutant (where both K1101 and K1154 are mutated) has increased entry into mitochondria and demonstrate enhanced mtDNA replication. Further, all three tested RTS patient mutants are hyper-ubiquitylated by MITOL and form insoluble aggregate-like structures on the outer mitochondrial surface. Three RTS mutants cannot enter mitochondria and show decreased mtDNA replication. However depletion of MITOL allows the RTS mutants to enter mitochondria and these cells show increased mtDNA replication. Increased accumulation of hyper-ubiquitylated RECQL4 outside

the mitochondria potentiates the cells towards mitophagy. Hence, regulating the turnover of RECQL4 by MITOL may have a therapeutic effect on RTS patients.

Publications

Original peer-reviewed articles

1. Hussain M, Saifi S, Mohammed A, Sengupta S* (2022) Protocol to detect in vitro and in cell ubiquitylation of mitochondrial DNA polymerase gamma by mitochondrial E3 ligase MITOL. **STAR Protoc.** 3:101710.

[* Corresponding Author]

Patents

1. Methods for decreasing resistance to chemotherapy. (U.S. National Stage Application No. 63/426,360)

2. DNA damage dependent microRNA signature for cancers, methods and uses related thereto (PCT Application number PCT/IN2020/050776; U.S. National Stage Application No. 17/998,888)

Awards / Fellowships

January 2023 : Awarded Professor Vishwa Nath Memorial Lecture by Indian National Science Association (INSA)

January 2023 : 8th Prof. G. K. Manna Memorial Award Lecture by All India Congress of Genetics and Genomics

Epigenetic regulation of the eukaryotic genome: Role of CTCF and enhancers in organizing chromatin

Madhulika Srivastava

Principal Investigator	**Madhulika Srivastava**
Project Associate	Monika Yadav
Project Fellow	Nidhi Bhasin
Ph.D. Student	Khushboo
Collaborators	Karl Pfeifer (NIH, Bethesda) Devinder Sehgal (NII, New Delhi)

Nuclear processes depend on interactions between cis acting regulatory elements and trans-acting factors and are intricately regulated by chromatin structure and organization. The dynamism of these interactions and the mechanistic diversity by which they are regulated, is intriguingly complex. CTCF, a DNA binding protein with multifunctional attributes, is an important contributor to chromatin organization. Additionally, intranuclear positions of genes with respect to various components of the nucleus are dynamic albeit non-random.

Antigen receptor (AgR) loci like Igh, TCRa/d, TCRb etc., serve as useful models to understand the interdependence of chromatin organization and gene regulation as transcription and VDJ recombination at these loci are precisely regulated by appropriate enhancer-promoter interactions and resultant epigenetic alterations at the nucleosomal level. Further, spatial proximity of V, D and J segments is necessary prior to RAG mediated VDJ recombination even though they are separated by vast linear distances on the genome. To decipher the nature of chromatin organization and its dynamics during development, we are investigating the regulation of transcription and VDJ recombination at murine TCRb locus.

Role of CTCF in chromatin organization

CTCF has thousands of binding sites in mammalian genomes and influences higher order chromatin organization. It has been suggested that chromatin extrusion through cohesion ring leads to formation of chromatin loops and CTCF bound to CTCF Binding Sites (CBS), impedes the chromatin extrusion depending on CBS orientation. Understanding about the role and mechanisms of CTCF based higher order chromatin organization has emerged based largely on quest to understand transcriptional regulation. In addition, higher order chromatin organization and the role of CTCF therein, is also critically important for VDJ recombination at AgR loci.

Murine TCRb, spanning about 700kb DNA, has 21 CTCF binding sites (CBS). In previous years, we have investigated the role of CTCF based chromatin organization in regulation of TCRb locus by ChIP-qPCR and Chromosome Conformation Capture analysis (3C-qPCR). Our analysis suggests that CBS interspersed amongst V segments act as punctuating marks during process of chromatin extrusion for defining dynamic chromatin loops that facilitate VDJ recombination.

Mechanisms underlying enhancer activity

Several genes have been observed to undergo significant changes in intranuclear positions during differentiation. Combination of genomic, biochemical and microscopic technologies have enhanced our understanding substantially. Yet much remains to be learnt about the principles and mechanisms underlying nuclear organization and mechanisms that link it to gene regulation. How intranuclear position of genetic loci changes during development remains an intriguing question. Enhancers, being vanguards of gene regulation, are likely candidates that might contribute to this phenomenon. While they are critical regulators of chromatin accessibility at AgR loci, their role in context of large-scale chromosomal reorganization is relatively less explored.

TCRb locus is precisely regulated during development for transcription as well as VDJ recombination. Our analysis of various aspects of the dynamic nuclear organization of murine TCRb locus, visualized by 3D-DNA FISH analysis, revealed that that TCRb locus gets located out of the chromosome territory (CT) specifically in developing thymocytes. Importantly, CRISPR/Cas9 based deletion mutagenesis demonstrated a novel role of enhancer Eb in this process. These 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 ANC-INC model of nuclear organization.

The observed enhancer dependent repositioning of the target locus highlights a novel aspect pertaining to activity of enhancers which may contribute to their ability to regulate gene expression and adds to the diversity of mechanisms underlying enhancer activity. It also provides strong genetic evidence that demonstrates an important role of enhancers in nuclear organization. Further, it suggests relevance of repositioning of the locus for regulation of VDJ recombination – an aspect worthy of being examined at other antigen receptor loci.

Role of cell signaling in eukaryotic development

Pushkar Sharma

Principal Investigator	**Pushkar Sharma**
Ph.D. Students	Rahul Singh Rawat Akanksha Rawat Komal Monika Singh Annu Nagar Ankita Paraste Meenakshi
Collaborators	Debasisa Mohanty (NII, New Delhi) G.A. Aneeshkumar (NII, New Delhi) T.S. Keshava Prasad (Yenepoya University, Mangalore) Rita Tewari (University of Nottingham, UK)

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. Here are some of the highlights of our research in these areas:

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

i. Role and regulation of parasite invasion by protein kinase PfPK2 in Plasmodium falciparum.

PfPK2 was found to play a role in host eythrocyte invasion. In order to decipher mechanisms via which it regulates this process, it was important to identify its parasitic targets. To this end, comparative phosphoproteomics studies were performed. It was interesting to note that several proteins with well-defined or proposed function in invasion exhibited significant changes in phosphorylation, which included proteins involved in signalling pathways and glideosome complex. The above-mentioned family of proteins were of special interest as they are likely to be relevant for the function of PfPK2 in host RBC invasion.

Interestingly, PfPK2 depletion prevented phosphorylation of gunaylyl cyclase (GCα), which is involved in generating second messenger cGMP. cGMP signalling regulates host RBC invasion as well as egress in *P. falciparum.* Several proteins implicated in phosphoinositide (PIP) metabolism and or downstream effectors of PIP signalling were aberrantly phosphorylated upon PfPK2 depletion. Strikingly, PfPK2-depletion caused almost a 2-fold decrease in cGMP formation upon PfPK2 depletion indicating its role in the synthesis of this second messenger. Previously, regulation calcium release in *P. falciparum* by cGMP was reported. Therefore, the role of PfPK2 in calcium release was investigated and PfPK2 depletion prevented the release of calcium from intraparasitic stores.

Collectively, these studies shed light on a novel signalling pathway in malaria parasite in which PfPK2 is an upstream regulator of key events like cGMP synthesis, which in turn is critical for calcium release. Given these second messengers are critical for host RBC invasion, explains the role of PfPK2 in this process.

ii. Regulation of parasite division by signalling and protein phosphorylation.

In human erythrocytes, asynchronous division of malaria parasite yields a multinucleated synctium as cell division takes place only after segmentation of individual merozoites. Not only the process of cell division is different from typical mitosis, the cell cycle regulators of the *Plasmodium* are distinct from mammalian counterpart. Therefore, role of essential cell cycle related protein kinases and phosphatases is being investigated to get deeper insights into molecular mechanisms involved in parasite division.

Previously, a role of PfPPM2-which is an essential protein phosphatase-in parasite division was reported. In order to elucidate the mechanism via which PfPPM2 interplays with cellular processes of the parasite, it was important to identify its putative downstream targets by comparative phosphoproteomics. A mass spectrometry-based quantitative phosphoproteomic approach was used to measure differences in the phosphorylation state of proteins upon PfPPM2 knockdown. Since PfPPM2 is a phosphatase, the proteins that exhibited significant increase in phosphorylation state upon its depletion were of specific interest. Interestingly, two major classes of proteins that exhibited altered phosphorylation were implicated in chromatin remodelling/organization and protein translation.

Several proteins related to protein synthesis were differentially phosphorylated, which included eukaryotic translation initiation factor 2-alpha kinase (PK4) and eukaryotic translation initiation factor 3 subunit C. Previous studies have indicated that PK4 is one of the major candidate kinases for the phosphorylation of eIFa at a site conserved in most organisms, which is critical for stalling protein synthesis. Strikingly, PfPPM2 depletion resulted in eIF2a phosphorylation. In addition, protein synthesis was severely impaired suggesting that PfPPM2 regulates protein synthesis in the parasite. Given that protein synthesis is important for cell division, it is possible that PfPPM2 may regulate it via its ability to aberrantly activate PK4, which in turn phosphorylates eIF2a.

We also found proteins implicated in chormatin remodelling to be influenced by PfPPM2, which have been implicated in sexual differentiation of the parasite. Corroboratively, PfPPM2 was also found to play a role in asexual to sexual conversion of the parasite by possibly regulating these proteins.

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

We are interested in the identification of miRNA that may target cell cycle related genes in response to Ab_{42} in Alzheimer's Disease (AD) as we are interested in their role in the aberrant regulation of neuronal cell cycle in CRNA. Detailed investigations were performed on two of these-miR-449a and miR-16-5p-that are expressed at lower level in neurons from transgenic Alzheimer's Disease mouse model APP/PS1 (TgAD). Previously, it was reported that these miRNA promote neuronal differentiation by suppressing the neuronal cell cycle and they prevent CRNA by suppressing the expression of key cell cycle proteins cyclin D1 and cdc25A. We investigated the status of CRNA in TgAD mice upon overexpression of miR449 and found that impaired miR-449a expression may contribute to CRNA in TgAD mice, which was prevented by overexpressing this miRNA in the cortex of these animals. Importantly, these results corroborated well with the observed reversal of defects in learning and memory in TgAD mice upon microinjection of lentivirus expressing this miRNA. Collectively, these and other findings raised the possibility of therapeutic use of miR-449a for AD.

Publications

Original peer reviewed article

1. Rawat RR, Bansal P and Sharma P* (2022) A VPS15-like kinase regulates apicoplast biogenesis and autophagy by promoting PI3P generation in *Toxoplasma gondii.* **PLoS Pathogens.**18:e1010922.

[* Corresponding Author]

Patents

Applications Filed

1. Sharma P and Chauhan M. Itch mutants for the treatment of memory and learning defects (Indian Patent Application Number: 202211052973 filed on 16.9.2022).
2. Sharma P and Chauhan M. miR449a as a therapeutic for neurodegenerative disorders (Indian Patent Application Number: 202211052962 filed on 16.9.2022)
3. Sharma P and Chauhan M. Clomipramine for the treatment of Alzheimer's Disease (US Patent Application Number: 17751613 filed on 23.05.2022)

Award / Fellowship

JC Bose Fellowship awarded by SERB was renewed for a second term of five years.

The role of tumor suppressors in stress response

Sanjeev Das

Principal Investigator	**Sanjeev Das**
Project Fellows	Adarsh Nair Amit Kumar Gauri Chopra
Ph.D. Students	Rohini Tamang Witty Tyagi Anita Nandi Mohammad Irfan
Collaborators	Jayanta Bhattacharyya (IIT-Delhi, Delhi) Sandeep Saxena (JNU, New Delhi) Subeer Majumdar (NIAB, Hyderabad)

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.

Objectives

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

HDAC5 belongs to the class IIa HDAC subfamily. HDAC5 has been observed to be upregulated in several cancers. The molecular mechanisms underlying the role of HDAC5 attributed to its deacetylase activity in tumorigenesis are not well understood. Using proteomics approach we have now identified SATB1 as a novel substrate of HDAC5. HDAC5 binds to and deacetylates SATB1 at the conserved lysine 411 residue. Furthermore, dynamic regulation of acetylation at this site is determined by TIP60 acetyltransferase. We also established that HDAC5-mediated deacetylation is critical for SATB1-dependent downregulation of key tumor suppressor genes. Unacetylated SATB1 also represses SDHA induced epigenetic remodeling and anti-proliferative transcriptional program. Thus, SATB1 spurs malignant phenotype in a HDAC5-dependent manner. Additionally, elevated HDAC5 levels correlate with reduced acetylated SATB1 levels in increasing grades of lung adenocarcinoma. These findings highlight the pivotal role of HDAC5 in tumorigenesis and provide novel mechanistic insight into SATB1 regulation.

B. Investigating the role of PKM2 in tumorigenesis

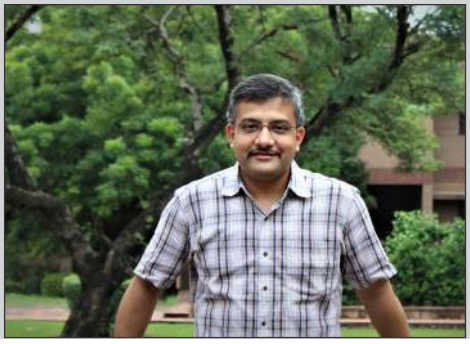
Most cancer cells expresses high levels of PKM2 as it augments aerobic glycolysis and provides a discerning advantage for tumor growth. Thus PKM2 is reported to be upregulated in multiple cancer types. However, the molecular details of mechanisms by which PKM2 harmonizes high energy demands

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. We examined the functions of PKM2, as regulator of RNA binding protein Matrin 3 upon mitogenic stimulation. We observed that EGFR-induced nuclear localization of PKM2 brings about phosphorylation of Matrin 3. RNA binding proteins (RBPs) have been reported to associate with mRNAs to form ribonucleoprotein complexes in the cell and play crucial role in stability, biogenesis, transport and localization of mRNA post-transcriptionally. As PKM2 has been reported to mediate epithelial to mesenchymal transition (EMT), we plan to investigate whether PKM2-Matrin 3 axis can regulate the genes involved in EMT pathway.

Publication

Original peer-reviewed article

1. Barnwal A, Das S, Bhattacharyya J (2023) Repurposing Ponatinib as a PD-L1 inhibitor revealed by drug repurposing screening and validation by *in vitro* and *in vivo* experiments. **ACS Pharmacol Transl Sci**. 6:281-289.



Elucidating the molecular mechanisms of aging and innate immunity using *Caenorhabditis elegans* as a model system

Arnab Mukhopadhyay

Principal Investigator	**Arnab Mukhopadhyay**
Ph.D. Students	Gautam Chandra Sarkar Tripti Nair Umanshi Rautela Sabnam Sahin Rahman Simran Motwani Jasleen Kaur
Collaborators	Sagar Sengupta (NII, New Delhi) Avinash Bajaj (RCB, Faridabad) Ujjaini Dasgupta (Amity University, Haryana) Kausik Chakraborty (CSIR-IGIB, New Delhi) Sanjeev Galande (Shiv Nadar University, Delhi-NCR) Mahesh J. Kulkarni (CSIR-NCL, Pune) D.S. Reddy (CSIR-NCL, Pune)

Our laboratory employs a combination of genetics, genomics, and molecular biology techniques in *Caenorhabditis elegans* to investigate the signaling events that trigger changes in gene expression during the aging process. We are examining how the micronutrient composition of the diet influences life history traits, and how animals have evolved regulatory mechanisms to counteract them. We are also interested in investigating how organisms detect DNA damage in somatic cells and regulate germline development and reproductive aging, with a focus on the role of nutrient sensing pathways in these processes.

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

Knockdown (KD) of *cyclin D* in low IIS mutant *daf-2(-)* worms led to germ cell arrest at the pachytene stage of meiosis I and sterility that was dependent on DAF-16/FOXO transcription factor. The pachytene cell numbers decreased upon *cyclin D* KD in *daf-2(-)* only, but not in *daf-16(-);daf-2(-)*. Surprisingly, KD of *cyclin D* only in germ cells of *daf-2(-)* worms did not lead to arrest. Interestingly, depletion of *cyclin D* only in the somatic vulva tissue (egg laying apparatus) led to pachytene arrest of germ cells and sterility in the *daf-2(-)* worms in a cell non-autonomous manner. In line with this observation, *Cyclin D* depletion only in the vulval tissues of wild-type worms resulted in poor oocyte quality, decreased reproductive span, and increased incidences of uterine tumour.

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

The physiological benefits observed in the *flr-4* vitamin B12-dependent longevity model is associated with the upregulation of cytoprotective gene expression (CyTP) downstream of the p38-MAPK

pathway. We found that expressing p38MKK/SEK-1 specifically in the intestine was sufficient to rescue both the life span and osmotic stress tolerance of the *flr-4(-)* worms. On the other hand, the one-carbon cycle (1C) enzyme methionine synthase/*metr-1* (needs vitamin B12 as a cofactor) was required only in the neurons. These results point to a role of neuron-gut signaling axis in the vitamin B12-dependent phenotypes of *flr-4(-)*. Using an RNAi screen, we showed the role of serotonin in this process, working downstream of the 1C in the neurons.

C. Deciphering the role of TORC2 in development and aging

We found that TORC2 mutant *rict-1(-)* possesses a higher osmotic stress tolerance (OST) and increased life span on HT115 (high B12 diet) or B12-supplemented OP50, compared to OP50 (low B12 diet), a phenotype similar to the *flr-4(-)*. Consequently, KD of crucial 1C genes, *metr-1* and *mtrr-1* abrogated the increased OST and life span of the *rict-1(-)* grown on HT115. Also, knocking down components of the p38-MAPK pathway rescinded *rict-1(-)* phenotypes on HT115, similar to *flr-4(-)*. Previous reports suggest the role of Phosphatidylcholine (PC) in inhibiting the p38-MAPK pathway. Supplementation of choline in the HT115 diet suppressed the OST and longevity of *rict-1(-)* without affecting wild-type worms. Next, we lowered the levels of PC by knocking down the Kennedy pathway enzymes required for PC synthesis. This intervention in the *rict-1(-)* on OP50 diet increased OST, while the wild-type worms did not exhibit any change.

Publication

Original peer-reviewed article

1. Garg A, Alam M, Bai S, Dandawate M, Kumari N, Gupta S, Agrawal U, Nagarajan P, Reddy DS, Kulkarni MJ, Mukhopadhyay A* (2023) Protective Effects of Rifampicin and Its Analog Rifampicin Quinone in a Mouse Model of Obesity-Induced Type 2 Diabetes. **ACS Pharmacol Transl Sci.** 6: 253–269

Role of metabolism-mediated gene regulation in development and disease

G AneeshkumarArimbasseri

Principal Investigator	**G. Aneeshkumar Arimbasseri**
Inspire Faculty Fellow	Archana Pant
Project Fellows	Mohtashim Rosh S. Jayalakshmi
Ph.D. Students	Neha Jawla Chen Chongtham Trisha Biswas Vaidehee Shubhu Khare Namaste Kumari
Collaborators	Veena Patil (NII, New Delhi) Suchitra D. Gopinath (THSTI, Faridabad) Jaswinder Singh (ILBS, New Delhi) Senbagavalli Prakash Babu (JIPMER, Puducherry) Debasisa Mohanty (NII, New Delhi) Vinay K. Nandicoori (CCMB, Hyderabad) Pushkar Sharma (NII, New Delhi)

Vitamin D affects muscle mass by modulating pancreatic insulin response.

Our laboratory's central theme is understanding metabolic derangements in different forms of malnutrition. We currently try to understand vitamin D's different roles under various metabolic conditions. Even though vitamin D receptor expression is minimal in skeletal muscles, vitamin D is an essential micronutrient for muscle function. However, the molecular and metabolic mechanisms of muscle vitamin D dependence were unknown. We have recently shown that in the absence of vitamin D signaling, glycogen synthase and glycogen phosphorylase are deregulated in skeletal muscle, leading to glycogen accumulation. We have also reported that this defect could be suppressed by rewiring the metabolism of VDRKO mice by providing a fat-enriched diet, leading to muscle mass restoration. In particular, we have identified that a milk-based high-fat diet (MBD) could restore muscle mass and systemic glucose homeostasis in VDRKO mice.

In contrast, a lard-based high-fat diet (HFD) could only restore muscle energy metabolism, but not muscle mass. Moreover, HFD leads to hyperglycemia. We analyzed pancreatic insulin synthesis and secretion in WT and VDRKO mice to address these issues. We found that VDRKO mice had deficient blood insulin levels, and there was no change even after a challenge with glucose. However, the VDRKO mice fed with MBD could restore insulin levels to that of WT.

On the other hand, the VDRKO mice fed with HFD failed to show any signal for insulin in the pancreas. These results indicate that when subjected to a high-fat diet, vitamin D is essential for insulin synthesis by pancreatic beta cells. Thus, milk-based diets restore muscle mass even without vitamin D by increasing the pancreatic insulin response.

Antibiotics that target bacterial ribosomes induce cell death in Th2 cells.

Apart from the 13 protein-coding genes, the mitochondrial genome codes for 20 tRNA genes and rRNA genes, enabling the mitochondrially encoded genes to be translated within the mitochondria. The mitochondrial ribosome resembles the bacterial ribosomes, and the antibiotics that target bacterial ribosomes are known to inhibit mitochondrial translation as well. Mitochondrial function is essential for T cell activation and effector functions in response to pathogens. We probed how the mitochondrial translation inhibiting antibiotics affect T-cell activation and differentiation. Our data show that inhibition of mitochondrial translation leads to decreased proliferation and effector functions of T cells. Differentiation of naïve CD4+ T cells into Th1, Th2, or Treg lineages was unaffected by inhibition of mitochondrial translation. However, Th2 cells undergo increased apoptosis when subjected to mitochondrial translation inhibition. This is associated with increased expression of Foxo1 and the pro-apoptotic genes Bim and Puma. Further, we show these differences relate to inherent metabolic differences between Th1 and Th2 cells. Though mitochondrial oxygen consumption is similar for Th1 and Th2 cells, the latter exhibit significantly lower basal and compensatory glycolysis, suggesting they depend more on mitochondrial OXPHOS.

Publications

Original peer-reviewed articles

1. Soman S, Chattopadhyay S, Ram S, Nandicoori VK, Arimbasseri GA* (2023) Codon optimality has minimal effect on determining translation efficiency in *Mycobacterium tuberculosis.* **Sci Rep.** 13:415.

2. Dev G, Chawla AS, Gupta S, Bal V, George A, Rath S, Arimbasseri GA* (2022) Differential Regulation of Two Arms of mTORC1 pathway fine-tunes global protein synthesis in resting B lymphocytes. **Int J Mol Sci.** 23:16017.

3. Ratra Y, Kumar N, Saha MK, Bharadwaj C, Chongtham C, Bais SS, Medigeshi G, Arimbasseri GA, Basak S (2022) A Vitamin D-RelB/NF-κB Pathway Limits Chandipura virus multiplication by rewiring the homeostatic state of autoregulatory Type 1 IFN-IRF7 Signaling. **J Immunol.** 209: 559–568.

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[* Corresponding Author]

Towards understanding the role of gut microbiota and their metabolites in the causation and treatment of colorectal cancer

Anil Kumar

Principal Investigator	**Anil Kumar**
Project Associates	Payal Gulati (MK Bhan Fellow) Manish Kushwaha
Ph.D. Students	Anuradha Gupta Govind Prakash
Collaborators	Govind K Makharia (AIIMS, New Delhi) Virendra Kumar (AIIMS, New Delhi) Pratima Solanki (JNU, New Delhi) P. Nagarajan (NII, New Delhi)

We are working on understanding the events leading to development of colorectal cancer (CRC) through microbial metabolites which may provide novel insight into pathology and potentially lead to new therapeutic modalities targeting the microbiota. Development of aptamer/MIP based sensor/biosensor for detection of gut bacteria and their metabolites is also going-on in the laboratory.

A. ***Metabolomic analysis of human colorectal cancer biopsies***

In this research activity, we carried out a comprehensive metabolomic analysis of colorectal cancer tissue samples from patient relative to adjacent nontumor tissues. The tissue samples were collected from 10 patients diagnosed with CRC undergoing colonoscopy at All India Institute of Medical Sciences (AIIMS). GC-MS based metabolomic study of tissue samples was performed to identify different potential metabolic biomarkers in patients with CRC. There was a separation between CRC patients and adjacent tissue, and differential metabolites were identified in the study. Out of 115 metabolites found in tumor and adjacent tissue only five were found in significantly decreased concentration in tumor tissue.

B. ***Quantifying gut microbiota derived 4-ethylphenyl sulphate by developing sensor***

The 4-ethylphenyl sulfate (4-EPS) has been considered as a well-known gut microbiota-derived metabolite. For quantifying the 4-EPS in human body fluids such as urine, an electrochemical sensor was developed using a polydopamine (PDA) based molecularly imprinted polymer (MIP) technique. The synthesized PDA-MIP was characterized by fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM) techniques. The PDA-MIP was drop casted on the surface of screen-printed carbon electrode (SPCE) to fabricate an electrochemical sensor. The developed PDA-MIP/SPCE sensor showed a broad linear detection range of 0.1-300 ng/mL with a high sensitivity of 153.88 μA(log (ng/mL))$^{-1}$cm^{-2} and a low limit of detection (LOD) of 0.018 ng/mL.

Publications

Original peer-reviewed articles

1. Jalandra R, Makharia GK, Sharma M, Kumar A* (2023) Inflammatory and deleterious role of gut microbiota-derived trimethylamine on colon cells. **Front Immunol.** doi:10.3389 /fimmu. 2022.1101429.

2. Verma D, Sajwan RK, Lakshmi GBVS, Kumar A*, Solanki P* (2022) A Molecularly imprinted polymer based on novel polyaniline–zinc sulfide nanocomposite for electrochemical detection of trimethylamine n-oxide. Environ. **Sci Nano.** 9:3992-4006.

3. Dalal N, Dhiman TK, Lakshmi GBVS, Singh AK, Solanki PR, Kumar A* (2022) MIP based sensor for detection of gut microbiota-derived Indoxyl Sulfate using PANI-Graphene-NiS2. **Mater Today Chem.** doi:10.1016/j.mtchem.2022.10115.

4. Jalandra R, Lakshmi GBVS, Dhiman TK, Sharma M, Kumar A*, Solanki PR* (2023) MIP based sensor for detection of gut microbiota derived Trimethylamine. **J Electrochem Soc.** doi: 10.1149/1945-7111/acb7a3.

[*Corresponding author]

Reviews

1. Vadhel A, Bashir S, Mir AH, Girdhar M, Sharma D, Kumar A, Malik T, Mohan A (2023) Opium alkaloids, biosynthesis, pharmacology and association with cancer occurrence. **Open Biol.** doi: 10.1098/rsob.22.0355.

2. Yadav AK, Verma D, Dalal N, Kumar A, Solanki PR (2022) Molecularly imprinted polymer-based nanodiagnostics for clinically pertinent bacteria and virus detection for future pandemics. **Biosens Bioelectron.** doi:10.1016/j.biosx.2022.100257.

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4. Tabassum Z, Mohan A, Mamidi N, Khosla A, Kumar A, Solanki PR, Malik T, Girdhar M (2023) Recent trends in nanocomposite packaging films utilising waste generated biopolymers: industrial symbiosis and its implication in sustainability. **IET Nanobiotechnol.** doi:10.1049/nbt2.12122.

Book Chapters

1. Solanki PR, Kumar A, Singh RP, Singh J, Singh KR (2023) Nanotechnological Aspects for Next-Generation Wound Management (Editors, Elsevier) https://www.elsevier.com/books/nanotechnological-aspects-for-next-generation-woundmanagement/solanki/978-0-323-99165-0. 2.

2. Rathee G, Bartwal G, Rathee J, Kumar A, Solanki PR (2022) Nanobiosensor for mycotoxin detection in foodstuff. In: Nanobiosensors for Environmental Monitoring (Eds. Singh RP, Ukhurebor KE, Singh J, Adetunji CO, Singh KR.) **Springer Cham.** doi: 10.1007/978-3-031-16106-3_12.

Patents

1. Jalandra R, Lakshmi GBVS, Solanki P, Kumar A. Electrochemical sensor for quantifying trimethylamine (TMA).(Indian Patent Application Number:202311001213 Filed on 05.01.2023)

2. Solanki P, Chahuan D and Kumar A. Nanomaterials based biosensor device for Vitamin-D detection. (Indian Patent Number: 426928. Granted on 27.3.2023)

Nanotechnology-based immunotherapeutic platform for cancer

Santiswarup Singha

Principal Investigator	**Santiswarup Singha**
Project Fellows	Richa Pahuja Arpita Das Aayush Raj Tyagi
Ph.D. Students	Khushboo Chaudhury Arnab Kumar Sahoo Antara Mondal Faisal Jamal
Collaborators	Nimesh Gupta (NII, New Delhi) Devinder Sehgal (NII, New Delhi) Devram Ghorpade (NII, New Delhi) Sandipan Halder (VNIT, Nagpur) Ashis Kumar Dhara (NIT, Durgapur)

The theme of our research is to develop nanotechnology-based immunotherapeutic platform to reprogram the immune responses against cancer. The antigen presentation ability of professional antigen-presenting cells (APCs) is heavily compromised resulting in T-cell-mediated suboptimal immune responses. We have formulated mesoporous silica particles that empower professional APCs to induce tumor-specific CD8+ T-cells dominating immune responses. We are investigating whether these CD8+ T-cells dominating immune responses can be harvested to formulate nano-immunotherapeutics for restricting tumor growth and metastasis. Additionally, we reprogram the antigen presentation ability of tumor cells for promoting the production of the TAA-derived defective ribosomal product (DRiP) and subsequently, to enhance the peptide (carrying tumor-specific mutations) presentation on the class-I major histocompatibility complex (MHC) to activate tumor-specific CD8+ T-cells. However, inducing sustainable T-cell activation and expansion still remains one of the major challenges to achieving therapeutic benefits. To address this challenge, we formulate nano-scale artificial APCs, capable of displaying multiple copies of tumor-specific peptide-major histocompatibility complex (p-MHC) and co-stimulatory molecules to engage tumor antigen-specific T-cells for inducing sustainable activation and expansion. We are optimizing the formulation of artificial APCs considering molecular density, flexibility, and directional presentation of p-MHC as critical parameters for inducing sustainable cognate T-cell activation. Our preliminary data indicate a threshold density of p-MHC required for activation and expansion of antigen-specific T-cells both *in-vitro* and *in-vivo*. We identified that T-cells that are expanded by high valency (# p-MHC per nanoparticle) artificial APCs (but not the low valency artificial APCs) could effectively restrict the growth of the aggressive mouse melanoma cancer. We have also developed p-MHC-based tetramer for identifying antigen-specific T-cells to evaluate the efficiency of these therapeutic avenues.

PUBLICATIONS

Original peer-reviewed articles

1. Ahuja R, Shelly A, Meena J, Singh M, Sehgal D, Panda AK (2022) Enhanced immunogenicity of recombinant pneumococcal protein delivered using thermostable polymer particles. **Mater Today Commun.** 32:103894.

2. Ahuja R, Srichandan S, Jairam Meena J, Biswal BK, Panda AK (2023) Immunogenicity evaluation of thermostable microparticles entrapping receptor binding domain of SARS- CoV-2 by single point administration. **J Pharm Sci.** 112:1664-1670.

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11. Dalal N, Dhiman TK, Lakshmi GBVS, Singh AK, Solanki PR, Kumar A* (2022) MIP based sensor for detection of gut microbiota-derived Indoxyl Sulfate using PANI- Graphene-NiS2. **Mater Today Chem.** doi: 10.1016/ j.mtchem.2022.10115. [*Corresponding author]

12. Das S, Saha T, Yadav S, Shaha C* (2022) A novel role of secretory cytosolic tryparedoxin peroxidase in delaying apoptosis of Leishmania-infected macrophages. **Mol Cell Biol.** doi:10.1128/mcb.00081- 22. [*Corresponding author]

13. Dev G, Chawla AS, Gupta S, Bal V, George A, Rath S, Arimbasseri GA* (2022) Differential regulation of two arms of mTORC1 pathway fine-tunes global protein synthesis in resting B lymphocytes. **Int J Mol Sci.** 23:16017. [*Corresponding author]

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17. Gupta I, Shankrit S, Narta K, Ghazi M, Grover R, Pandey R, Kar HK, Menon SM, Gupta A, Yenamandra VK, Singh A, Mukerji M, Mukhopadhyay A, Rani R, Gokhale RS, Dash D, Natarajan VT (2022) Whole exome-sequencing of vitiligo lesions indicate lower burden of somatic variations: implications in risk for non-melanoma skin cancers. **J Invest Dermatol.** doi: 10.1016/j.jid.2022.11.018.

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22. Hussain M, Saifi S, Mohammed A, Sengupta S* (2022) Protocol to detect in vitro and in cell ubiquitylation of mitochondrial DNA polymerase gamma by mitochondrial E3 ligase MITOL. **STAR Protoc.** 3:101710. [*Corresponding author]

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PATENTS AND TECHNOLOGY TRANSFER

1. Gupta S, Vijayan V. Peptide complex with immunomodulatory and anti-inflammatory function. [US Patent Number: 11447534. Granted on 20.09.2022]

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4. Nandicoori VK, Soni V, Yogeeswari P, Sriram D. Depletion of *M. tuberculosis* GlmU from infected murine lungs effects the clearance of the pathogen. [Indian Patent Number: 413180. Granted on 30.11.2022]

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6. Sharma N, Deshmukh SK, Kaushik H, Rupa P, Mathur DD, Garg LC. Development of secretory expression based DNA vaccine against ε-toxin of *Clostridium perfringens.* [Indian Patent Number: 397563. Granted on 25.05.2022]

7. Singh A, Verma J, Ahuja R, Panda AK. A composite scaffold and method of preparation thereof. [Indian Patent Number: 420141. Granted on 01.02.2023]

8. Solanki P, Chahuan D, Kumar A. Nanomaterials based biosensor device for Vitamin-D detection. [Indian Patent Number: 426928. Granted on 27.03.2023]

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11. Gupta N, Sachan S. A dengue virus follicular T helper (Tfh) cell specific peptide megapool and its use thereof. [Indian Patent Application Number: 202211046391. Filed on 16.08.2022]

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17. Sengupta S. Methods for decreasing resistance to chemotherapy. [US Patent Application Number: 63/426,360. Filed on 17.11.2022]

18. Sharma P, Chauhan M. Clomipramine for the treatment of Alzheimer's Disease. [US Patent Application Number: 17751613. Filed on 23.05.2023]

19. Sharma P, Chauhan M. Itch mutants for the treatment of memory and learning defects. [Indian Patent Application Number: 202211052962. Filed on 16.09.2022]

20. Sharma P, Chauhan M. MiR449a as a therapeutic for neurodegenerative disorders. [Indian Patent Application Number: 202211052962. Filed on 16.09.2022]

Technology Transfer

The following patented technologies have been transferred to the Centre for Cancer Immunotherapy (CCI), Sri Ram Cancer & Superspeciality Centre (SRCC), Mahatma Gandhi Medical College and Hospital, A unit of Mahatma Gandhi University of Medical Sciences and Technology (MGUMST), Jaipur.

1. Suri A. Novel cancer associated antibodies and their use in cancer therapy. [Indian Patent Number: 295616, Granted on 09.04.2018]

2. Suri A. Novel immunotherapeutic method for treatment of cancer. [Indian Patent Number: 284087, Granted on 08.06.2017]

3. Suri A. Immunotherapeutic composition. [Indian Patent Number: 286707, Granted on 08.06.2017]

AWARDS, DISTINCTIONS AND FELLOWSHIPS

- **Dr. Anil Suri** received an "Excellence in Science" award in view of outstanding vision, dedication, and commitment during a long and distinguished career spanning many decades, which has had a major impact on health care, cancer care, and cancer control. The award was conferred by the Immuno-Oncology Society of India during its 4th Annual Congress (20-23 January 2023).
- **Dr. Bichitra Biswal** was awarded the TATA Innovation Fellowship (2022-23) by the Department of Biotechnology, Government of India.
- **Dr. Nimesh Gupta** was conferred the Mid-Career Scientist Oration Award (2022) by the Indian Immunology Society for contributions in the area of 'T Cell Immunity to Vaccines'.
- **Dr. Pushkar Sharma** was awarded the JC Bose Fellowship for a second term of 5 years.
- **Dr. Sagar Sengupta** was awarded the Professor Vishwa Nath Memorial Lecture by the Indian National Science Association (INSA) and the 8th Prof. G. K. Manna Memorial Award Lecture by the All India Congress of Genetics and Genomics in January 2023.
- **Ms. Alvina Deka** (Ph.D. scholar from Dr. Soumen Basak's laboratory) was presented the 'Best Speaker Award' at the 49th Annual Conference of the Indian Immunology Society (IMMUNOCON-2022) organized jointly by the Departments of Translational & Regenerative Medicine and Immunopathology, in the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, 23-26 November 2023.
- **Ms. Charu Chauhan** (Ph.D. scholar from Dr. S-Gopalan Sampathkumar's laboratory) was presented the 'Young Scientist and Best Poster Presentation' awards at the International Carbohydrate Conference (CARBO-XXXVI) on Emerging Trends in Glycochemistry, Glycobiology & Technology held at Department of Chemistry, IIT Bombay, Mumbai, 5-7 December 2022.
- **Dr. Ekjot Kaur** (from Dr Sagar Sengupta's group) was awarded the DBT/Wellcome Trust India Alliance Early Career Fellowship in the year 2022.
- **Ms. Kritee Mehdiratta** (Ph.D. scholar of Dr Rajesh Gokhale) was elected as one of the 8 finalists for the prestigious Inspiring Science Award 2023 for her publication titled, "Kupyaphores are zinc homeostatic metallophores required for colonization of *Mycobacterium tuberculosis*".
- **Ms. Nishu Dalal** (Ph.D. scholar from Dr. Anil Kumar's laboratory) received 'CCI-Excellence Award for Best Oral Presentation' at the 3rd World Congress on Translational Cancer Research and Immunotherapy held at Jaipur by Mahatma Gandhi University of Medical Sciences and Technology, 3-5 February 2023.

- **Ms. Ritu Agrawal** (Ph.D. scholar from Dr. Sagar Sengupta's laboratory) received 'Best Poster Award' at the 5th International Chromosome Stability Meeting 2022 held by IISER, TVM and JNCASR at Bengaluru, 14-18 December 2022. She was also presented a poster award at the 42 Annual Conference of the Indian Association of Cancer Research 2023 by ACTREC, TMC at Mumbai, 12-16 January 2023.

- **Mr. Sachin Kushwah** (Ph.D. scholar from Dr. Devinder Sehgal's laboratory) received the 'Oral Presentation Award' at the workshop on "Monoclonal Antibodies -an emerging era in biologicals: Principles of production, applications in immunodiagnostics and therapeutics" held at Institute of Advanced Virology, Trivandrum, Kerala, 8-9 December 2022

- **Ms. Simran Aittan** (Ph.D. scholar from Dr. S-Gopalan Sampathkumar's laboratory) was presented the 'Best Poster Presentation' award at the International Carbohydrate Conference (CARBO-XXXVI) on Emerging Trends in Glycochemistry, Glycobiology & Technology held at Department of Chemistry, IIT Bombay, Mumbai, 5-7 December 2022.

- **Ms. Tanya Jain** (Ph.D. scholar from Dr. S-Gopalan Sampathkumar's laboratory) was presented the 'Best Poster Presentation' award at the International Carbohydrate Conference (CARBO-XXXVI) on Emerging Trends in Glycochemistry, Glycobiology & Technology held at Department of Chemistry, IIT Bombay, Mumbai, 5-7 December 2022.

Ph.D. DEGREES AWARDED TO NII SCHOLARS

Twenty-seven scholars of the Institute were awarded the degree of Doctor of Philosophy by Jawaharlal Nehru University on the completion of their work.

S. No.	Student's Name	Topic of Research	Guide
1	Ms. Shalini Verma	Acyl-Coenzyme A binding proteins of *Leishmania major*: Comparative studies of their structure and function	Dr. Monica Sundd
2	Ms. Yashika Ratra	Investigating the crosstalk between non-canonical NF-κB signaling and the anti-viral pathways	Dr. Soumen Basak
3	Ms. Priya Gupta	In silico analysis of signaling and Protein-Protein Interaction (PPI) networks in *P. falciparum*	Dr. Debasisa Mohanty
4	Ms. Tripti Nair	Characterization of a micronutrient-driven diet-gene pair that regulates stress response and lifespan in *Caenorhabditis elegans*	Dr. Arnab Mukhopadhyay
5	Ms. K Varsha Mohan	Effects of immune dysregulation and development of disease regulating strategies for Retinitis Pigmentosa	Dr. Sangeeta Bhaskar
6	Ms. Moumita Sarkar	Deciphering the interplay between ovarian steroids and chorionic gonadotropin in tumorigenesis	Dr. B.K. Biswal
7	Ms. Shikha Salhotra	Characterisation of Arl6ip5/JWA/GTRAP3-18 as a cholesterol binding protein: Role in cholesterol homeostasis and related disorders	Dr. Sarika Gupta
8	Ms. Prakriti Sinha	Understanding the role of monocytes in Hepatitis B infection and exploring its potential for gene-based biomarkers	Dr. Sangeeta Bhaskar
9	Ms. Shagufta Jahan	Evaluation of preventive and therapeutic potential of a novel compound in a mouse model of Alzheimer's disease	Dr. Sarika Gupta
10	Ms. Annesa Das	Understanding the transcriptional regulation of dendritic cell differentiation and innate immune responses by Interferon Regulatory Factor 8	Dr. Prafullakumar B. Tailor
11	Ms. Ditsa Sarkar	Biochemical and biophysical investigation of *Helicobacter pylori* N-carbamoylputrescine amidase, an enzyme involved in polyamine biosynthesis	Dr. Apurba K. Sau

S. No.	Student's Name	Topic of Research	Guide
12	Mr. Lalit	To study the macrophage function and underlying mechanisms in TB-IRIS development using T cell -deficient mice as animal model	Dr. Sangeeta Bhaskar
13	Mr. Uday Aditya Sarkar	NF-kappa B activating pathways in multiple myeloma	Dr. Soumen Basak
14	Mr. Gautam Chandra Sarkar	Investigating the role of cdk-12 in aging and germline development under conditions of low insulin signaling	Dr. Arnab Mukhopadhyay
15	Ms. Ayushi Jain	Evaluation of long noncoding RNA mediated regulation of sertoli cell function	Dr. Sanjeev Das
16	Ms. Monika Yadav	Characterization of cis- and trans-acting factors that govern chromatin architecture at murine TCRb locus	Dr. Madhulika Srivastava
17	Ms. Hema Sori	Molecular dissection of antibody response against glycoconjugate	Dr. Devinder Sehgal
18	Mr. Biplab Singha	Deciphering the regulation of sigma factor A mediated transcription in *Mycobacterium tuberculosis*	Dr. Vinay K. Nandicoori
19	Ms. Indu	Structural and biochemical studies of a membrane protein Rv2903c from *Mycobacterium tuberculosis*	Dr. B.K. Biswal
20	Ms. Anamica Das	Dissecting the role of vitamin D receptor signalling on skeletal muscle function	Dr. Aneeshkumar A. G.
21	Mr. Gagan Dev	Regulation of protein synthesis in resting state lymphocytes	Dr. Aneeshkumar A. G.
22	Ms. Shilpa Sachan	Phenotypic and functional properties of follicular T helper cells in dengue	Dr. Nimesh Gupta
23	Ms. Sowmiya Gupta	Understanding the role of different domains of hGBP3 and its splice variant hGBP3ΔC in antiviral activity	Dr. Apurba K. Sau
24	Ms. Garima	Understanding the phosphopantetheinyl transferase and acyl carrier protein of fungal type I fatty acid synthase	Dr. Monica Sundd
25	Ms. Gargi	To understand the underlying mechanism by which MIP regulates the function of T cells to prevent tumor growth	Dr. Sangeeta Bhaskar

S. No.	Student's Name	Topic of Research	Guide
26	Mr. Anush Chakraborty	Understanding the immunotherapeutic potential of different formulations of *Mycobacterium indicus pranii* in mouse tumor model	Dr. Sangeeta Bhaskar
27	Mr. Mohammed Ahmad	Structural and biochemical studies of enolase from *Mycobacterium tuberculosis*	Dr. B.K. Biswal

SCIENTIFIC LECTURES

International Day of Immunology

Prof. Apurva Sarin delivering her lecture on International Day of Immunology at NII

The 29th of April is celebrated as the Day of Immunology worldwide with the aim to strengthen the public's awareness about immunology and its impact on individuals as well as public health and well-being. The Institute celebrated the day by hosting a public talk by Prof. Apruva Sarin from the Institute for Stem Cell Science and Regenerative Medicine. Prof. Sarin spoke about “Metabolic Signaling Underpinning Cell Fate Decisions".

Foundation Day Lecture

Prof. Sylviane Muller delivering the Foundation Day Lecture at NII

The 36th Foundation Day of NII was celebrated on 6th October 2022. The foundation day lecture was delivered by Prof. Sylviane Muller, Director of the Strasbourg Institute for Drug Development and Discovery (IMS), Strasbourg, France, and Emeritus Research Director CNRS. Prof. Muller delivered a lecture on “Mechanism Guided Novel Therapies for Treating Systemic Lupus Erythematous and other Auto-Inflammatory Diseases.” During her address, she lauded the deep-rooted scientific excellence of NII and the enthusiasm of the gathering. The foundation day celebration was also attended by a delegation of immunologists and scientists from CNRS, France.

SCIENCE FESTIVALS, EXPOSITIONS AND SYMPOSIA

Biotech Startup Expo 2022

The NII contingent at the Biotech Startup Expo 2022

The Department of Biotechnology with the Biotechnology Industry Research Assistance Council (BIRAC) organized Biotech Startup Expo on 9th-10th June 2022 at Pragati Maidan, New Delhi. This expo was a part of the celebrations of 10 years of BIRAC. The expo showcased startups, biotech incubation centers, and various other national and international programs. The faculty, students, and staff of NII attended the expo. NII's work was displayed in a dedicated stall through posters and demonstrations. Notably, Dr. Nimesh Gupta and his students demonstrated a rapid COVID-antibody test using recombinant RBD protein and blood samples of visitors at the stall.

International Science Festival (IISF) 2022

Dr. Jitendra Singh, Honorable Minister of State (IC) of the Ministry of Science and Technology (right) interacting with Dr. Debasisa Mohanty, Director NII; Dr. Nimesh Gupta, Scientist NII; and Mr. Pradeep Chawla, FAO, NII (left to right) at IISF 2022
Dr. Nimesh Gupta and Dr. Neerja Wadhwa conducting a quiz for school students at IISF 2022

A glimpse of the activities at the NII stall at IISF 2022

The International Science Festival 2022(IISF) held at MANIT Bhopal from 21st-24th January 2023 was a grand celebration of science. IISF aimed to bridge the gap between scientific advancements and society. NII actively participated in the event by presenting posters, demonstrating experiments, and organizing a quiz for school students. NII showcased a range of informative and visually captivating posters, which gave the visitors a glimpse of the history of NII and the research that is carried out at the institute. These posters covered diverse topics related to the working principle of vaccination, the importance of vaccine evaluation prior to mass vaccination, targeting metabolic pathway molecules of *Mycobacterium tuberculosis*, drug target discovery, nanoparticle-based artificial antigen-presenting cells to induce anti-tumor immunity and more. Additionally, NII actively engaged with the audience by conducting live experiments at their exhibition stall. Scientists from various labs demonstrated agglutination-based assay to find COVID-19 specific antibodies in the blood and a qualitative test for loading of tumor-associated antigen into the nanoparticles. By showcasing the biological processes of fertilization, implantation, and development, NII initiated comprehensive sex education among school students. Since school students actively participated at IISF, NII engaged with this young audience by organizing a vaccine quiz. The quiz aimed to test the students' scientific knowledge and promote a scientific temper as well as a spirit of healthy competition. Winners of the quiz were duly rewarded with prizes and certificates as a token of recognition. By actively connecting science with society, NII contributed to the overall objective of the IISF and helped inspire a new generation of scientific enthusiasts.

Ph.D. students presenting their posters on National Science Day

The visitors and NII staff, students, and faculty together on National Science Day

The National Science Day 2023 was celebrated with great enthusiasm and fervor on 28th February–marking the day of the discovery of the Raman Effect. Events of the day showcased the scientific research conducted at NII and highlighted the day-to-day impact of frontier research in immunology and biomedicine. As part of our Science Setu outreach activities, we invited various colleges and undergraduate (UG) students to participate in the day-long event. About 12 colleges from Delhi-NCR, including 14 teachers/professors and about 80 undergraduate students, attended the event. A young investigator symposium, organized and chaired by NII Ph.D. scholars, was held in the forenoon where the final year Ph.D. scholars presented their work in five-minute flash-talk presentations (21 presentations). This was followed by a poster session, consisting of 51 posters by both Ph.D. scholars and short-term trainees, along with lunch and tea. The poster session was well-attended by everyone at NII as well as the UG students. A panel of 10 external expert members was invited to evaluate the posters for clarity and content of presentations by the Ph.D. scholars. In the afternoon, a Quiz program was held by the NII Ph.D. scholars for the UG students, which elicited both excitement and engagement. The teachers/professors from the colleges, Quiz winners, and poster presentation awardees were honored with a specially designed memento of a porcelain mug carrying the NII emblem.

Symposia on Opportunities for Frontier Research Collaborations by the Human Frontier Science Program (HFSP)

The delegates from HFSPO with the organizers and participants

Pavel Kabat, Secretary General HFSPO (right) with Dr. Pushkar Sharma, Scientist, NII

Dr. Debasisa Mohanty, Director NII and Guntram Bauer, Director of Science Policy and Communications, HFSPO addressing the gathering

In February 2023, the Human Frontier Science Program Organization (HFSPO) and the Ministry of Science and Technology, Government of India promoted a series of symposia in leading Indian research institutions in the Life Sciences. The events started at NII on the 10th of February to discuss "Opportunities for Frontier Research Collaborations by the Human Frontier Science Program". Pavel Kabat, Secretary General HFSPO and Guntram Bauer, Director of Science Policy and Communications, HFSPO addressed the gathering about HFSPO programs. The awardee perspective was shared by Rishikesh Narayanan, IISc Bengaluru; Anupam Sengupta, University of Luxembourg; and Rahul Roy, IISc Bengaluru.

India has been part of the HFSPO for several years, and this series of symposia at different locations in the country provided detailed information on HFSP programs to the Indian research community. The goal was to foster new opportunities for international collaboration among Indian research institutions and scientists while providing opportunities for interaction with HFSP personnel and awardees.

I-CONNECT: Vaccines and Therapeutics

A poster for the virtual session on "Vaccines and Therapeutics" under i-CONNECT

The Ministry of Science and Technology supported a series of iconic 75 Industry Connect ('i'-Connect) events to showcase the achievements in various S&T areas. The purpose of these events is to forge partnerships with industry in thematic/focus areas. Under the aegis of 'i'-Connect, NII hosted a virtual session on "Vaccines and Therapeutics" on 16th June 2022. Dr. Sagar Sengupta, NII; Dr. Nimesh Gupta, NII; Dr. Aneeshkumar, NII; Dr. Sarika Gupta, NII; and Dr Bakulesh Khamar, Cadila Pharmaceuticals presented at the session. The talks were followed by a panel discussion on "Academia-Industry Partnership for Innovation in Frontiers of Biomedicine" with Dr. Bakulesh Khamar; Dr. Parul Ganju, Ahammune; Dr. Arnab Mukhopadhyay, NII; and Dr. Devinder Sehgal, NII joining in as panelists.

INSTITUTIONAL EVENTS AND VISITS

Mental Health Awareness Week

Dr. Paramjeet Singh, Psychiatrist, Pushpawati Singhania Research Institute, New Delhi delivering a lecture during Mental Health Awareness Week

During the Mental Health Awareness Week on 20th April 2022 NII invited Dr. Paramjeet Singh, Psychiatrist, Pushpawati Singhania Research Institute, New Delhi to talk to the faculty, staff, and students about the importance of mental health and why taking care of it is the need of the hour. The interaction aimed at addressing issues like stress at the workplace and mental health post-pandemic.

National Cyber Security Awareness

Colonel Binoj Koshy, ADG, UIDAI and Dr. Debasisa Mohanty, Director NII (left to right)

On 21st October 2022, Colonel Binoj Koshy, ADG (Technical), Information Security Division, Unique Identification Authority of India (UIDAI) delivered a lecture on Cyber Security at NII. The lecture was attended by faculty, staff, and students of NII.

Health Check-Up Camp on World Health Day

The team from Pushpawati Singhania Research Institute, New Delhi with Ms. Chandresh Bhagtani (center), Administrative Officer, NII

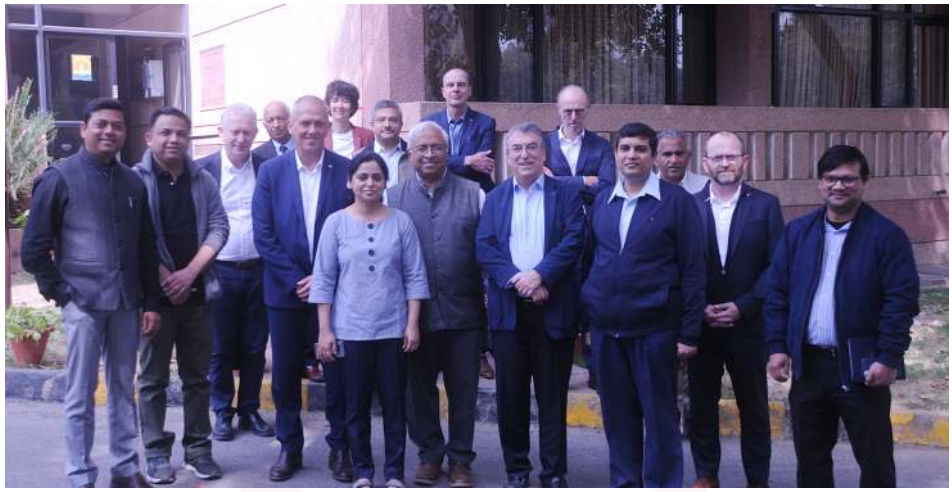
On the occasion of World Health Day (7th April 2022), a free health check-up camp was organized in the institute with the support of the Pushpawati Singhania Research Institute, New Delhi. Complementary health-profile tests and consultations were made available to the faculty, staff, and students of NII.

Visit of Veterinarian Officers from The Indian Army

Veterinary officers from the Indian Army with the Director and staff of NII

On 18th January 2023, seven veterinary officers from the Indian Army, enrolled in the National Diploma in Equine Husbandry, Medicine, and Surgery at RVC Centre and College in Meerut Cantonment, visited the Transgenic Facility, Primate Research Facility, Small Animal Facility and Central Instrumentation Facility of NII. The objective of their visit was to understand advanced reproductive technologies such as in vitro fertilization, transgenic technology, embryo manipulation, embryo biotechnology, DNA recombination, and genetic engineering. The officers gained insights into the comprehensive care and management of small animals and primates. They were also exposed to state-of-the-art equipment and technologies used in research and diagnostics. During their visit, the officers engaged in various discussions and interactive sessions related to the subject. This visit provided the veterinarian officers with valuable exposure to cutting-edge technologies, equipping them with the necessary skills and knowledge to apply these advancements in their future endeavors in animal health, breeding programs, and overall veterinary services, ensuring they stay at the forefront of veterinary science in the Indian Army.

Visit of CNRS Delegates



CNRS delegates with the Director and faculty of NII

In February 2023, NII hosted Prof Antoine Petit, President, CNRS, France and the delegates from CNRS. The group discussed opportunities for future collaborations between the scientists from NII and CNRS.

Farewell of Ph.D. 2017 Batch

As the graduate students of 2017 crossed the Rubicon, NII bid them a fond farewell. A tree was planted on the campus to mark the memory of their time at NII and a farewell dinner followed.

The 2017 Ph.D. batch of NII with the Director, faculty, and Senior Manager of NII

Vigilance Awareness Week

The Vigilance Awareness Week was observed at the Institute from 31st October to 6th November 2022. A banner announcing the observance of Vigilance Awareness Week was put up at the main entrance of the Institute, and placards bearing slogans against corruption were displayed. A pledge to fight corruption was taken by the NII community on 31st October 2022. The integrity pledge was taken on the Central Vigilance Commission website by members of the community. An essay-writing competition was organized on 2nd November 2022 on the theme of "Corruption-Free India for a Developed Nation". Shri T. P. Sharma, Under Secretary Central Vigilance Commission delivered a lecture on 5th November on the theme of Vigilance Awareness Week 2022.

Dr. D. K. Vashisht, Senior Manager NII with the members of the administration department at the observance of Vigilance Awareness Week

TRAINING AND WORKSHOPS

Workshop on Computational Analyses of Transcriptomics Data

Dr. Debasisa Mohanty, Dr. Devinder Sehgal, Dr. Arnab Mukhopadhyay, Dr. Soumen Basak, and Dr. Rintu Kutum with the participants of the workshop

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 conducted a workshop on "Computational Analyses of Transcriptomics Data" for its Ph.D. students and scholars. Prof. Shandar Ahmad and Dr. Rintu Kutum were the resource persons for the workshop, which consisted of sixteen sessions spread over eight weeks from 20th May to 22nd July 2022. The workshop was designed to combine theoretical and hands-on sessions training the students in transcriptomics data analysis and open-source scientific computing.

SCIENCE SETU

A glimpse of science setu activities undertaken at NII

School students and their teachers visiting NII under the SRIJAN program with the Director and faculty of NII

NII engages with the public at large through activities, events, and interactions to bridge the gap between science and society. Under the Science Setu program, NII regularly welcomes students and teachers from undergraduate colleges into its campus and labs. For better implementation of the Science Setu program, MoUs have been signed with several Delhi University colleges. Scientists of NII regularly visit schools and colleges for interactions and talks. Students from both schools and colleges visit NII to see the research and instrumentation facilities and interact with scientists and researchers. In addition, NII also accepts short-term trainees from colleges who join labs to get hands-on experience in research in immunology and biomedicine.

Among the various Science Setu activities notable was the SRIJAN open day held at the Institute on 27th July 2022. Around 90 school students ranging from class 6th to 11th of the National Talent Search Program of Vidyarthi Vigyan Manthan (VVM) under the aegis of VIBHA attended the open day with great enthusiasm and engaged with scientific zeal. The students visited the state-of-art research instrumentation facility of the Institute. The students and project staff of NII engaged with the students on various topics such as fluorophores and chromatography, proteins and amino acids, computational biology, the immune system, parasitic diseases, and animal models.

ANNUAL GENERAL MEETING (AGM) OF SOCIETIES

NII hosted the Annual General Meeting of the Societies of all DBT autonomous institutes from 1st to 2nd December, 2022. The meeting was chaired by Dr. Jitendra Singh, Honorable Minister of State (IC) of the Ministry of Science and Technology, who serves as the President of the Societies. The Minister reviewed the progress made by the institutions and urged them to promote a sustainable startup culture by engaging with industry. He also emphasized the importance of collaborations and partnerships among the institutions.

Dr. Jitendra Singh (right), Honorable Minister of State (IC) of the Ministry of Science and Technology with Dr. Rajesh Gokhale (center), Secretary DBT, and Dr. Debasisa Mohanty (left), Director, NII

Annual General Meeting of societies in progress at NII

Dr. Jitendra Singh, Honorable Minister of State (IC) of the Ministry of Science and Technology at the AGM of the societies of DBT autonomous institutes with the institute heads and other functionaries

INVITED SEMINARS

S.No.	Topic	Speaker	Date
1	Metabolic signaling underpinning cell fate decisions	Prof. Apurva Sarin Institute for Stem Cell Science and Regenerative Medicine, Bengaluru	29.04.2022
2	Engineering immunology using chemistry and AI	Dr. Gaurav Chopra Department of Chemistry, Purdue University, USA	25.05.2022
3	SIRT6 - A potential therapeutic target for treating cardiac lipotoxicity	Dr. Ravi Sundaresan Indian Institute of Science, Bengaluru	05.08.2022
4	Epigenome reprogramming during a response to immunotherapy and cell therapy	Dr. Kunal Rai Anderson Cancer Centre, Harvard Medical School, Boston, USA	10.08.2022
5	Designing drugs to target resistance	Prof. Sanjay V. Malhotra Oregon Health & Sciences University, Portland, USA	22.08.2022
6	Bacterial odors as molecular patterns for *Caenorhabditis elegans*	Dr. Varsha Singh Department of Molecular Reproduction, Development & Genetics, Indian Institute of Sciences, Bengaluru	02.09.2022
7	Rational design by computational tools as a strategy to search for therapeutic effectors	Dr. Santiago Di Lella IQUIBICEN-Argentinian National Research Council School of Exact and Natural Sciences, Universidad de Buenos Aires, Argentina	27.09.2022
8	Outside-in integrin signaling in hematopoiesis: The journey so far and the way forward	Dr. Satish Khurana School of Biology, Indian Institute of Science Education and Research, Thiruvananthapuram	30.09.2022
9	A chemical biology approach toward understanding a human neurological disorder	Dr. Siddhesh Kamat Indian Institute of Science Education and Research, Pune	21.10.2022
10	High-throughput screening for novel antimicrobials against atypical Acinetobacter baumannii	Prof. Indranil Biswas Department of Microbiology, Molecular Genetics and Immunology, University of Kansas Medical Center, Kansas, USA	15.11.2022

S.No.	Topic	Speaker	Date
11	T-cell immunity to chronic infections and solid tumors	Dr. Vandana Kalia Division of Hematology and Oncology, University of Washington School of Medicine, USA	21.11.2022
12	Glycan engineering in studies of SARS-CoV-2 infectivity and inflammatory diseases	Prof. Sriram Neelamegham Department of Chemical and Biological Engineering, State University of New York at Buffalo, USA	28.11.2022
13	Sexual harassment at workplace: Approach, prevention, prohibition, and redressal	Prof. Ritu Gupta National Law University, Delhi	07.11.2022
14	Decoding honey badger and firefox: The hidden half of the MYC story in human cancer	Prof. Anindya Bagchi Tumor Initiation and Maintenance Program, Sanford Burnham Prebys Medical Discovery Institute La Jolla, USA	04.01.2023
15	When Immunity cause mischief: Meeting the challenge of rebalancing the immune response pattern to virus infection	Prof. Barry T. Rouse University of Tennessee, USA	06.02.2023
16	Regulation of the magnitude and time to resolution of the immune response	Prof. Sourav Ghosh Yale University, USA	06.02.2023
17	From lysosome perturbation to tissue regeneration: A story of serendipitous discovery	Dr. Santosh Chauhan CSIR- Centre for Cellular and Molecular Biology, Hyderabad	20.02.2023
18	Design of antibiotics that target the essential biotin biosynthetic pathway in Mycobacteria	Prof. Courtney C. Aldrich Department of Medical Chemistry, University of Minnesota, USA	20.02.2023
19	Epigenetic dysregulation and enhancer malfunction in human pathophysiology	Prof. Debabrata Chakravarti Professor Feinberg School of Medicine, Northwestern University, USA	21.02.2023
20	How do RNP condensates disassemble?	Dr. Purusharth I. Rajyaguru Department of Biochemistry, Indian Institute of Science, Bangalore	14.03.2023

GRADUATE STUDENT SEMINAR SERIES (PHD 2018 BATCH)

S.No.	Topic	Speaker	Date
1	Identification and analysis of smORFs in bacterial genomes	Mr. Akshay Kumar	07.04.2022
2	Elucidating the roles of host transcription factors in malaria liver stage parasite development	Ms. Pooja	21.04.2022
3	Targeting an essential metabolic pathway to design new anti- TB compounds	Mr. Satish Tiwari	21.04.2022
4	Somatic cyclin D ensures reproductive fitness	Ms. Umanshi Rautela	28.04.2022
5	Investigating the role of p53 and DREAM complex in the regulation of BLM helicase transcription	Ms. Ritu Agarwal	28.04.2022
6	Understanding the role of a key protein phosphatase in signaling and development of malaria parasite	Ms. Akanksha Rawat	05.05.2022
7	Anti-tumor response of MIP involves direct effect on cancer cells	Ms. Bharti Swami	05.05.2022
8	Acylation induced conformational heterogeneity in invasion associated ACP (IacP)	Ms. Rashima Prem	12.05.2022
9	Mechanistic understanding of *Mycobacterium tuberculosis* infection of hepatocytes	Mr. Binayak Sarkar	12.05.2022
10	Mechanistic understanding of role of mitochondrial translation in T cell activation and differentiation	Ms. Neha Jawla	26.05.2022
11	Structure and function of glycosylation of pre melanosomal protein (PMEL/ gp100) in melanogenesis	Ms. Tanya Jain	26.05.2022
12	Dysregulation of bone remodeling in Alzheimer's disease	Ms. Aishwarya Nilakhe	02.06.2022
13	Understanding the role of Cyclin F in tumorigenesis	Ms. Rohini Tamang	02.06.2022
14	Understanding the mechanism of lower GMP formation in large GTPase, hGBP3	Ms. Divya Rashmi	16.06.2022
15	Investigating dendritic cell- intrinsic role of non-canonical NF-kB pathway in gut inflammation	Ms. Alvina Deka	16.06.2022
16	Regulation of malaria parasite division by protein kinases	Ms. Monika Singh	23.06.2022
17	Human Metabolic phenotypes of responses to the live attenuated SA-14-14-2 Japanese encephalitis vaccine	Mr. Bhushan Nikam	23.06.2022

INVITED TALKS DELIVERED BY NII FACULTY

S.No.	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organization	Date
1	Dr. Devinder Sehgal	Capturing the bug with NETs	Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi (Under the Summer Undergraduate Research Programme 2022)	24 June 2022
2	Dr. Devinder Sehgal	Learning immunology from monoclonal antibodies	Workshop titled 'Monoclonal antibodies: Principles of production, applications in immunodiagnostics and therapeutics' at Institute of Advanced Virology, Thiruvananthapuram	8-9 December 2022
3	Dr. Anil Kumar	Intellectual property rights and their relevance to science and society	School of Bioengineering & Bio-Sciences, Lovely Professional University, Jalandhar	18 February 2023
4	Dr. Anil Kumar	Metabolic and genotoxic effect of gut microbiota-derived trimethylamine (TMA) on colon cells	3rd World Congress on Translational Cancer Research and Immunotherapy at Centre for Cancer Immunotherapy (CCI), Sri Ram Cancer Superspeciality Center (SRCC), Mahatma Gandhi Medical College and Hospital, Jaipur	3-5 February 2023
5	Dr. Anil Kumar	Emerging role of microbiota in human health and diseases	UGC-sponsored Online Refresher Course in Biological Science (Interdisciplinary) for University and College Teachers by Bharathidasan University,Tamil Nadu	14 July 2022
6	Dr. Anil Kumar	IPRs for science and society	Faculty Development Program on Entrepreneurship, Intellectual Property Rights, Start-ups, and Innovation, School of Bioengineering & Bio-Sciences, Lovely Professional University, Jalandhar	15 July 2022
7	Dr. Anil Kumar	Gut microbiota-derived meta bolites as potential biomarkers in different diseases	62nd Annual International Conference of the Association of Microbiologists of India (AMI), University of Mysore	22 September 2022
8	Dr. Apurba Kumar Sau	Underlying basis for stimulated GMP formation in human large GTPases and its effect on antiviral activity	Proteomics Society, India and International Conference on Proteins and Proteomics by Indian Institute of Chemical Biology, Kolkata.	3-5 November 2022
9	Dr. Veena S. Patil	Human CD4-CTL memory subset in infectious diseases: Lessons from multi-omics	Immunocon 2022: 48th Annual Meeting of Indian Immunology Society, Post-graduate Institute of Medical Education and Research, Chandigarh	8-9 July 2022
10	Dr. Veena S. Patil	Unraveling the heterogeneity in T- cell memory subsets using single-cell multi-omics	Roadshow by 10X genomics on "See biology in new ways with single cell and spatial technologies"	26 July 2022
11	Dr. Veena S. Patil	Understanding immunology in the genomics era.	25th Genvision 2023, Indian Institute of Technology Bombay	21-22 January 2023

S.No.	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organization	Date
12	Dr. Veena S. Patil	Applications of high dimensional biology in advancing translational research: Latest trends and way forward	Panel discussion at BD PARADIGM meet	24 February 2023
13	Dr. Pushkar Sharma	Signaling pathways in apicomplexan parasites	Birla Institute of Technology and Science, Hyderabad	12 November 2022
14	Dr. Rahul Pal	Disorders of proliferation: Analysis of novel pathways and targets	Birla Institute of Technology and Science, Pilani, Rajasthan	3 December 2022
15	Dr. Nimesh Gupta	A deep dive into the immunology of vaccine	All India Institute of Medical Sciences, New Delhi	29 April 2022
16	Dr. Nimesh Gupta	Immunology of vaccine	Varahamihira Science Forum, Tamil Nadu	28 May 2022
17	Dr. Nimesh Gupta	An efficient immunoassay for qualitative assessment of T cells: A new parameter for vaccine evaluation	Indian Immunology Society, Banaras Hindu University, Varanasi	9 July 2022
18	Dr. Nimesh Gupta	How immunology will lead the development of future vaccines : Lessons and tips for the successful expedition	India Vaccine Leaders Conclave, Mumbai	25 August 2022
19	Dr. Nimesh Gupta	A Tfh-like T helper subset drives antibody responses to dengue virus	International Union of Biochemistry and Molecular Biology, Regional Centre for Biotechnology, Faridabad	17 November 2022
20	Dr. Nimesh Gupta	T cells in virus infection and vaccination: Lessons for vaccine development	Association of Clinical Biochemists of India, New Delhi	24 November 2022
21	Dr. Nimesh Gupta	T cells immunity in infection and vaccination	Indian Immunology Society, Chandigarh	25 November 2022
22	Dr. Nimesh Gupta	Variants, boosters and the future of COVID-19 vaccines	Venkateshwara College, Delhi University, New Delhi	10 January 2023
23	Dr. Nimesh Gupta	T cell immunity to COVID-19 vaccine	Maharaja Sayajiroa University of Baroda	6 January 2023
24	Dr. Nimesh Gupta	Development of T-cell based bioassays	Indian Institute of Chemical Technology, Mumbai	3 February 2023
25	Dr. Nimesh Gupta	Vaccine immunology: Lessons for the development of future vaccines	Mahatma Gandhi Medical College and Research Institute, Puducherry	9 February 2023
26	Dr. Nimesh Gupta	Immunology and vaccine development: How to deploy immunology for developing highly effective, durable-immunity and broadly-protective vaccines	Vaccine Summit, Pune	28 March 2023

S.No.	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organization	Date
27	Dr. Sarika Gupta	Panel Discussion at the Global Pharma, Healthcare & Technology Expo & Summit 2023	Global Pharma, Healthcare & Technology Expo & Summit Co-Hosted with Pharma Trends Expo & Summit Healthcare Trends Expo & Summit– 2023 at Hyatt Centric, New Delhi, India	16 February 2023
28	Dr. Agam Prasad Singh	Malaria pathology, virulence, resistance and vaccines	Human Resource Development Centre, JNU, New Delhi	30 September 2022
29	Dr. Agam Prasad Singh	Session chair of "Sustainable development" session	International Conference on Integrative Chemistry, Biology & Translational Medicine, 2nd International symposium, New Delhi, India	8 December 2022
30	Dr. Agam Prasad Singh	Session coordinator of "New directions in synthesis & medicinal chemistry" session	International Conference on Integrative Chemistry, Biology & Translational Medicine, 2nd International symposium, New Delhi, India	8 December 2022
31	Dr. Agam Prasad Singh	Novel multi-stage active antimalarial	International conference on Infectious diseases: Management, control and prevention	12 December 2022
32	Dr. Monica Sundd	Protein-ligand interactions using NMR	Department of Pharmaceutical chemistry, Jamia Hamdard University, New Delhi	31 October 2022
33	Dr. Sanjeev Das	Understanding new paradigms in cancer metabolism	Recent Trends in Cancer Research and Precision Medicine 2022, Indian Institute of Technology, Kanpur, India	15 December 2022
34	Dr. Sagar Sengupta	Behind the lens…looking at another world	Banaras Hindu University, Banaras, India	26 April 2022
35	Dr. Sagar Sengupta	DNA Damage Sensitive MicroRNAs: A sensitive tool for detection of early stage colon cancer	Vaccines and Therapeutics, i-CONNECT, National Institute of Immunology, New Delhi, India	16 June 2022
36	Dr. Sagar Sengupta	DNA Damage Sensitive MicroRNAs: A sensitive tool for detection of early stage colon cancer	Biological Research in Frontier Areas Symposium, Bhabha Atomic Research Centre, Mumbai, India	25 July 2022
37	Dr. Sagar Sengupta	MITOL-dependent ubiquitylation negatively regulates the entry of PolgA into mitochondria	Cell Biology Conference and International Symposium, Indian Society of Cell Biology, University of Kashmir, Srinagar, Jammu and Kashmir, India	2 September 2022
38	Dr. Sagar Sengupta	Trying to reach the bed from the bench: the gap remains	Tata Institute of Fundamental Research, Hyderabad, India	11 November 2022
39	Dr. Sagar Sengupta	MITOL dependent ubiquitylation negatively regulates the entry of proteins involved in mitochondrial replication into mitochondria	91st Annual Meeting of Society of Biological Chemists, India	9 December 2022

S.No.	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organization	Date
40	Dr. Sagar Sengupta	Disruption of chromatin remodeling leads to chemosensitivity and adjunct therapy in colon cancer	Biological Transactions: From Molecules to Organisms (BTMO 2023), Indian Institute of Science, Bengaluru	20 January 2023
41	Dr. Sagar Sengupta	Disruption of chromatin remodeling leads to chemosensitivity and adjunct therapy in colon cancer	An Interdisciplinary Approach to Biological Sciences (IABS 2023), Indian Association for the Cultivation of Science, Kolkata	1 February 2023
42	Dr. Sagar Sengupta	Efforts to make functional mitochondrial replication machinery in AdPEO patients	Royal Society Yusuf Hamied Workshop for India and the UK	24 February 2023
43	Dr. Sagar Sengupta	DNA Damage Sensitive MicroRNAs: a sensitive tool for detection of early stage colon cancer	Emerging Materials in Cancer Therapy, Indian Institute of Technology, Kharagpur	24 March 2023
44	Dr. Tanmay Majumdar	Host-directed therapy against pan-SARS-CoV-2 variants	91st Annual Meeting of Society of Biological Chemists, India	10 December 2022
45	Dr. Soumen Basak	Intestinal inflammation gone awry - a role of NF-kappaB cross talks	Frontiers in Biology Symposium, Indian Institute of Science Education and Research Thiruvananthapuram	29 Apr-1 May 2022
46	Dr. Soumen Basak	A RelB NF-kappaB-type-1 IFN signaling axis in antiviral vitamin D functions	Departmental Seminar, Indian Institute of Technology, Mandi (online)	14 May 2022
47	Dr. Soumen Basak	Probing crosstalk between immune signaling pathways: A bottoms-up systems biology approach	Workshop on Modeling Biological Systems, Ashoka University, Sonipat (online)	26 April-2 May 2022
48	Dr. Soumen Basak	Intestinal inflammation: Molecular mechanisms	One-day symposium on Inflammation, Translational Health Science and Technology Institute, Faridabad	14 July 2022
49	Dr. Soumen Basak	NF-κB signaling in gut inflammation: Role in IECs and DCs	Annual meeting, The Society of Inflammation Research, National Centre for Cell Science, Pune	24-25 September 2022
50	Dr. Soumen Basak	A RelB NF-kappaB-type-1 IFN signaling axis in antiviral vitamin D function	National Science Day, Central University of Rajasthan (online)	28 February 2023
51	Dr. G. Senthil Kumar	Protein dynamics by solution NMR spectroscopy: Dynamic activation and regulation of MAPK p38	International ICGEB-DBT workshop on “NMR spectroscopy for drug development and biomarker discovery”, International Centre for Genetics Engineering and Biotechnology, New Delhi	27 April 2022

S.No.	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organization	Date
52	Dr. G. Senthil Kumar	Protein structure and function	Ramjas College, New Delhi	24 May 2022
53	Dr. G. Senthil Kumar	Solution NMR studies of penicillin binding protein PBP5	XXVIII Annual symposium of the NMR society of India (NMRS 2023), Indian Institute of Science Education and Research Berhampur, 24-27th February 2023	25 February 2023
54	Dr. G. Senthil Kumar	NMR of proteins	Central University of Karnataka, Kalaburagi	15 March 2023
55	Dr. Arnab Mukhopadhyay	The struggle to maintain a normal life: a worm's perspective	School of Interdisciplinary Research (SiRE) Symposium, Indian Institute of Technology Delhi	13 April 2022
56	Dr. Arnab Mukhopadhyay	Interspecies interactions regulate longevity in *Caenorhabditis elegans*	Frontiers In Modern Biology (FIMB) Symposium; Indian Institute of Science Education and Research Kolkata	22 January 2023
57	Dr. Arnab Mukhopadhyay	Longevity is regulated by interspecies interactions: the story of a worm and its diet	Hansraj college, New Delhi	17 March 2023
58	Dr. Devram Sampat Ghorpade	Poster presentation at Ramalingaswami Re-Entry Fellowship & MK Bhan-Young Researcher Fellowship Joint Conclave	Rajiv Gandhi Centre for Biotechnology (RGCB) Thycaud, Thiruvananthapuram, Kerala	2 December 2022
59	Dr. G. Aneeshkumar Arimbasseri	Vitamin D modulates skeletal muscle fuel choice	Advanced Research Unit on Metabolism, Development, & Aging symposium, Tata Institute of Fundamental Research, Hyderabad	17 March 2023
60	Dr. G. Aneeshkumar Arimbasseri	From yeast chromatin to vitamin D in mice	Centre for Cellular & Molecular Biology, Hyderabad	22 February 2023
61	Dr. G. Aneeshkumar Arimbasseri	Vitamin D modulates skeletal muscle fuel choice and pancreatic insulin response to orchestrate metabolic plasticity	42nd Mahabaleswar Seminars: Mitochondria and Metabolism, Indian Institute of Science Education and Research, Pune	15 February 2023
62	Dr. Debasisa Mohanty	*In silico* identification of bioactive secondary metabolites from human microbiome	Guha Research Conference (GRC) 2021, Nainital	21 April 2022
63	Dr. Debasisa Mohanty	Molecular dynamics simulations for deciphering structure and dynamics of kinases	Centre for Development of Advanced Computing, Pune	5 July 2022
64	Dr. Debasisa Mohanty	Designing allosteric inhibitors for PfCDPK1 by combining atomistic simulations with machine learning	Dr B. R. Ambedkar Center for Biomedical Research, Delhi University	4 November 2022

S.No.	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organization	Date
65	Dr. Debasisa Mohanty	Machine learning based approach for identification of novel resistance associated mutations in *Mycobacterium tuberculosis* and analysis of the structural basis of drug resistance	Ashoka University, Sonipat, Haryana	11 November 2022
66	Dr. Debasisa Mohanty	Machine learning based methods for identification of novel bioactive secondary metabolites by mining of bacterial genomes & human microbiome	National Institute of Pharmaceutical Education and Research, Mohali	12 November 2022
67	Dr. Debasisa Mohanty	Recent advances in applications of AI/ML for drug discovery & protein design: Implications for Chem-Bio defense	Defense Research Development Establishment, Gwalior	16 November 2022
68	Dr. Debasisa Mohanty	Mining of bacterial genomes & human microbiome for identification of novel small ORFs and prediction of their putative function.	International Centre for Genetic Engineering & Biotechnology, New Delhi	24 November 2022
69	Dr. Debasisa Mohanty	Computational methods for identification of novel bioactive secondary metabolites by mining of bacterial genomes & human microbiome	91st Annual Meeting of the Society of Biological Chemists (India) 2022, Sister Nivedita University, Kolkata	11 December 2022
70	Dr. Debasisa Mohanty	Designing novel inhibitors for EGFR kinase by combining atomistic simulations with machine learning	Centre for Development of Advanced Computing, Pune	28 February 2023
71	Dr. Debasisa Mohanty	Valedictory address in the Science Innovation Festival	National Science Centre, New Delhi	26 March 2023
72	Dr. Srinivasa-Gopalan Sampathkumar	Modulation of glycosylation *in vitro* and *in vivo*.	Guha Research Conference (GRC) 2021	25 April 2022
73	Dr. Srinivasa-Gopalan Sampathkumar	Pharmacological modulation of cell adhesion through engineering of sialyl-Lewis-X (sLeX/ CD15s).	Indian Academy of Biomedical Sciences (IABS) Conference at University of Mysore, Mysuru	8 September 2022
74	Dr. Srinivasa-Gopalan Sampathkumar	Modulation of sLeX/ CD15s expression and cell adhesion induced by N-acetyl-D-mannosamine analogues	CARBO-XXXVI at the Indian Institute of Technology Bombay (IIT-B), Mumbai	6 December 2022

S.No.	Scientist	Title	Organizer/ Name of Institute/ College/ School/ Organization	Date
75	Dr. Bichitra Kumar Biswal	Designing new anti-TB molecules through structure-guided approach	Translational Health Science and Technology Institute, Faridabad	25 March 2023
76	Dr. Bichitra Kumar Biswal	Designing novel anti-TB molecules through structural biology approach	Utkal University, Bhubaneswar	10 February 2023
77	Dr. Bichitra Kumar Biswal	X-ray crystallography to drug discovery including some fundamental aspects of symmetry	Jamia Millia Islamia University, New Delhi	18 January 2023
78	Dr. Bichitra Kumar Biswal	Identifying new anti-TB molecules targeting Histidine biosynthesis	University of Delhi, North Campus	8 December 2022

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 (ÄKTA flux 6), fast performance liquid chromatography (ÄKTA Avant 150, NGC Chromatography System BIO-RAD), multiplex immunoassay system (Bio-plex 200, BIO-RAD), chemi-luminescence imaging system (Azure 600), real-time 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 post-translational modification using state-of-art mass spectrometry. The major equipment at this facility are Thermo LTQ LC-MS/MS, TSQ Altis Plus Triple Quadrupole MS, and Orbitrap Exploris 240 MS.

Other advanced analytical facilities that aid multidisciplinary research at NII include transmission microscopy, scanning electron microscopy (Carl Zeiss EVO Ls10), confocal microscopy (Zeiss LSM 980), NMR spectrometer (Bruker Avance III 700 MHz), a dual-wavelength X-ray generator for X-ray crystallography, various flow cytometers, micro-computed tomography (Quantum GX2 micro-CT, Perkin- Elmer), Nano String, high-throughput DNA sequencer, and small animal imaging system (Lago X, Spectral Instruments Imaging).

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 112 mouse strains, four rat strains, and one stock of rabbits.

The breeding of all defined strains is maintained in a three-tier system: the Foundation Stock (FS), Pedigreed Expansion Stock (PES), and 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 GM 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 Primate Research Centre 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. We have 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-ups. 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 center 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 center 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 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 in 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 reports 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 the 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 other 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:

- Construction of a new quarantine facility
- Replacement of the cooling coil of the Air Handling Units (AHUs)

- Restoration and upgradation of staff quarters and laboratories in the NII campus as well as the staff quarters in Dwarka
- Supply, installation, testing, and commissioning of a 100Kwp rooftop grid sharing solar system at NII
- Upgradation of the Building Management System at NII
- Upgradation of the main building's raw water and soft water pumping system
- Repairing of the child 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
- Fortification over the windows of the Primate Research Centre

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
- Re-carpeting and repairing internal roads at NII campus
- 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 old SAF at NII
- Supply, installation, testing, and commissioning of a 2*400 sq mm LT cable for and renovation of electrical/civil infrastructure of the Primate Research Centre
- Replacement of AHU of the auditorium of NII
- Upgradation of the swimming pool at NII

Library and Documentation Services

The Library and Documentation Department is a service-oriented supportive unit that works as an Information Repository and Dissemination Centre. It provides information support to the scientific staff, researchers, administrative, and technical staff of the institute, using both archival and contemporary digital resources.

The library has a rich collection of books and journals; many resources are accessible online by scientific staff and students. NII is a member of the DeLCON consortium project of the Department of Biotechnology. The library coordinates procedures (online) for the subscription of journals and e-books databases as well as processes the payment of journal publication charges. The library has automated all its housekeeping activities. A searchable database, Web-Online Public Access Catalogue (Web-OPAC), is being maintained.

The library has been involved in compiling, designing, and printing the Parliamentary and Scientific Annual Reports of the institute in Hindi and English. The library prepares monthly pictorial research publications and bibliometrics reports. It helps in collecting, compiling, editing, designing, and printing various reports of the Institute such as the RAP-SAC report and the institutional workshop reports, and submitting documentation for the Scientific Industrial Research Organization registration.

Information on subscriptions of e-journals and e-books, new procurements. and publications are regularly updated on the NII website. The NII library has an Institutional Digital Repository (IDR) that can be searched for full-text articles published from 2008 onwards. The library also conducts an

induction program for newcomers, as well as holds workshops on various subjects such as the use of software for the detection of plagiarism.

The library undertakes all the binding and photocopying work of the Institute. It houses a collection of Hindi books (including those dealing with administrative practices) and magazines, which has been set up for popularizing the language. Thirty-seven books have been added to the library collection over the past year.

Academic and Training Services

The activities of the Academic and Training Department can be categorized under three major groups: students 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 disbursal of fellowships of scholars.

The Institute takes in scientists who have been awarded independent fellowships from the following institutions/organizations 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 under-graduate students of different colleges under the Science Setu program. 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 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 collusion 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.

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 center facilitates day-to-day troubleshooting, maintenance, and anti-virus support of about 850 PCs and other peripheral devices. In addition, the center 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 center also helps organize and conduct virtual meetings and lectures.

NOTABLE ACTIVITIES

SUMMARY OF NOTABLE ACTIVITIES

Academic Courses, Training Programs 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 program through a national-level examination followed by interviews.

The Ph.D. program of the Institute has been running since the academic year 1986-87. In the year 2022-23, twenty-two students were admitted into the program. To date, 551 students have been awarded their Ph.D. degree through NII including the 27 students who obtained their degree in the academic year 2022-23 available in **Annexure-III**.

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

Publications

Ninety-three research articles were published in the year of 2022-2023. Of these publications, seventy-five were published in journals as peer-reviewed research articles and the rest as reviews/ proceedings. Details of these articles are available in **Annexure-I.**

Patents and Technology Transfer

The Institute has a policy of protecting the 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 eleven patent applications, while nine patents were granted. Details of these patents are available in **Annexure-II.** Three patented technologies were transferred in 2022-23.

Lectures/Talks Delivered and Papers Presented on Invitation

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 programs in India and abroad.

Lectures/Seminars by Visiting Scientists and Ph.D. Graduate Students

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 also deliver a seminar in their field of study. During 2022-2023, thirty-seven seminars were organized in the campus , which includes graduate student's and invited seminar. These seminars were attended not only by the scholars and scientists of the Institute but also by investigators from other institutions.

Anti-Terrorism Day

Anti-Terrorism Day was observed on 21st May 2022. 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, all forms of terrorism and violence. We pledge to uphold and promote peace, social harmony and understanding among all fellow human beings and fight the forces of disruption threatening human lives and values".

Sadbhawna Diwas

To promote national integration and communal harmony among peoples of all religions, languages, and regions, Sadbhawna Diwas is observed on the 20th of August, which is the birth anniversary of Late Shri Rajiv Gandhi. On Sadbhawna 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, the birth anniversary of Late Shri Sardar Vallabhbhai Patel, was observed on 31st October 2022. 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."

Independence Day

Independence Day was celebrated on 15th August 2022 in the Institute. The event was marked by a message from the Director, followed by the singing of the National Anthem by the students of NII and children of the staff of the Institute.

The Director hoisting the flag on Independence Day

Rendition of the National Anthem

International Women's Day

International Women's Day celebrates the social, economic, cultural, and political achievements of women. On 2nd March 2023, our Institute organized a self-defense training workshop. The workshop was conducted by Ms. Kiran Sethi and Mr. Shiv Kumar Kohli, experts in self-defense techniques. Aimed at empowering staff and students, the workshop dealt in skills of personal safety and confidence. Participants learned practical techniques and strategies for self-defense. This initiative exemplified the commitment of the institute to create a safe and inclusive environment while celebrating the spirit and success of women on an institutional platform.

Self-defense workshop in progress with Ms. Kiran Sethi

International Yoga Day

The practice of yoga greatly aids in promoting both physical and mental well-being. On 27th September 2014, during his speech at the UN General Assembly, the Hon'ble Prime Minister Narendra Modi proposed that June 21st (the summer solstice, the longest day of the year) will be observed and celebrated as 'International Yoga Day' to raise awareness about the benefits of practicing yoga. Yoga Day was celebrated on 21st June 2022 in the Institute. Ms. Indu Sharma, Assistant Professor, Morarji Desai National Institute of Yoga delivered a lecture on 'Yoga for Day-to-Day Life'. She was accompanied by Ms. Neetu Yadav who held a yoga session for the staff and students of NII.

Yoga demonstration in progress at NII auditorium

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 of the economically weaker sections.

Representation of Persons with Benchmark Disabilities

The Institute follows reservation guidelines for persons with benchmark disabilities as per the 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 in official work, a Hindi Pakhwara (Hindi Fortnight) was celebrated in the Institute with great zeal from 16th September to 30th October 2022. During this period, various Hindi competitions such as Hindi Sulekh (Hindi Writing), Hindi Nibandh (Hindi Essay), Hindi Shrutlekh (Hindi Dictation), Hindi Saamanyagyaan (Hindi general knowledge), Hindi Vaad Pratiwaad (Hindi Debate), Hindi Vayavhaarik (Hindi noting and drafting), and Hindi Kavita (Hindi poetry) were organized. A large number of 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.
- The Institute has implemented the Government of India incentive scheme for writing notes and drafts originally in Hindi. An incentive scheme for encouraging the writing of articles and research papers in Hindi on scientific and technical subjects was also implemented.
- The fifth edition of NII's in-house Hindi magazine "JAIPRATIRAKSHA DARPAN" is under preparation and will be published shortly.

RTI ANNUAL RETURN INFORMATION SYSTEM (2022-2023)

Report on Receipt and Monthly Disposal of RTI Cases (2022-2023)

S.No	Year	Month	Opening Balance	Receipt	Disposed	Closing Balance
1	2022	April	433	2	1	435
2	2022	May	435	1	1	436
3	2022	June	436	4	2	440
4	2022	July	440	1	4	441
5	2022	August	441	5	4	446
6	2022	Sept	446	6	1	452
7	2022	Oct	452	4	5	456
8	2022	Nov	456	3	5	459
9	2022	Dec	459	9	5	468
10	2023	Jan	468	5	7	473
11	2023	Feb	473	0	4	473
12	2023	March	473	3	3	476
	Total			**43**		

Total RTI cases disposed as on 31st March 2023 = 43

RTI ANNUAL RETURN INFORMATION SYSTEM (2022 -2023)

ANNUAL RETURN FORM
Year 2022-23 (up to March 2023)
Insert Mode (New Return)

	Opening balance AS ON 1-04-2022	**Received during the Year 2022-2023 (including cases transferred to other Public Authority)**	**No. of cases transferred to other Public Authority**	**Decisions where request/appeals rejects/appeals rejected**	**Decision where requests/appeals accepted**
Request	0	43	0	0	43
First Appeal	0	6	0	0	6

No. of cases where disciplinary action taken against any Officer	NIL

No. of CAPIOs designated	No. of CPIO 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	9	11	24	Others
									8				

Amount Charges Collected (in Rs)		
Registration Fee Amount	Additional Fee & Any other charges	Penalties Amount
100	-	-

Last date of uploading the pro-active disclosures on the website of PA	http://www.nii.res.in/others/right information on 25.03.2023.

ORGANIZATIONS

COMMITTEES OF THE INSTITUTE

(As on 31.03.2023)

NII SOCIETY

Dr. Jitendra Singh
President
Hon'ble Minister of State (Independent Charge)
of Science & Technology and Earth Sciences
Government of India

Sh. Saurabh Bharadwaj
Minister, Health and Family Welfare
Government of NCT of Delhi
(Minister-in-charge of the Department handling biotechnology matters in the State where respective AI is situated (NCT of Delhi, in case of NII))

Dr. Rajesh S. Gokhale
Secretary
Department of Biotechnology
Ministry of Science & Technology
Government of India, New Delhi

Dr. Rajiv Bahl
Secretary
Department of Health Research
(DHR) and DG (ICMR)
Government of India, New Delhi

Dr. N. Kalaiselvi
Secretary
Department of Scientific & Industrial Research
(DSIR) and DG (CSIR)
Government of India, New Delhi

Principal Secretary in charge
Department handling Biotechnology matters in the State where AI is situated
(NCT of Delhi, in case of NII)

Sh. Vishvajit Sahay
Additional Secretary & Financial Advisor
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

Prof. Y. K. Gupta
President
All India Institute of Medical Science, Bhopal

Prof. M. Jagadesh Kumar
Chairman
University Grant Commission, New Delhi

Dr. Rajesh Jain
Chairperson & Managing Director
Panacea Biotech, New Delhi

Prof. G. Padmanaban
Former Director
Indian Institute of Science (IISc), Bengaluru

Dr. Subeer S. Majumdar
Director General
Gujarat Biotechnology University, Gujarat

Dr. Senapathy `Kris' Gopalakrishnan
Co-founder
Infosys Ltd, Bengaluru

Dr. Debasisa Mohanty
Director
National Institute of Immunology, New Delhi

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, Dr. Ram Manohar Lohia Institute of Medical Sciences (RMLIMS), Lucknow and Professor, Department of Hematology
Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGI), Lucknow

Dr. Anurag Agrawal
Dean, Trivedi School of Biosciences, 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
Professor of Pathology
Dr. Ram Manohar Lohia Hospital (RML) Hospital and Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS), New Delhi

Dr. Kakali Dey Dasgupta
Nodal Officer of NII in DBT and
Scientist-E, 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

Dr. Suchita Ninawe
Ex-Officio
Scientist-'G'/H level officer
Department of Biotechnology
Government of India, New Delhi

Dr. Pushkar Sharma
Director (Addition Charge)
National Institute of Immunology
New Delhi

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

Prof. Amita Aggarwal
Head
Department of Clinical Immunology and Rheumatology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow

Dr. Sudhir Gupta
Prof. of Medicine,
Pathology and Laboratory Medicine and Microbiology and Molecular Genetics, Chief Division of Basic and Clinical Immunology
University of California, Irvine, USA

Prof. (Dr.) Trinad Chakraborty
Professor of Medical Microbiology and Director, Institute of Medical Microbiology
Justus-Liebig University Faculty of Medicine
35392, Giessen, Germany

Prof. Shubhada V. Chiplunkar
Former Director
Advance Centre for Treatment Research & Education in Cancer
(ACTREC) Tata Memorial Centre, Kharghar, Navi Mumbai

RESEARCH AREA PANEL

Dr. Rajan Sankaranarayana
Outstanding Scientist
Structural Biology Laboratory
CSIR-Centre for Cellular and Molecular Biology (CCMB)
Uppal Road, Hyderabad

Dr. Souvik Maiti
Director
CSIR-Institute of Genomics and Integrative Biology
Sukhdev Vihar, Mathura Road
New Delhi

Prof. R. Sankararamakrishnan
Department of Biological Sciences & Bioengineering (BSBE)
Indian Institute of Technology
Kalyanpur, Kanpur

Dr. Dinakar M. Salunke
Former Director
International Centre for Genetic Engineering and Biotechnology (ICGEB)
Aruna Asaf Ali Marg, New Delhi

Dr. Sharmila A. Bapat
Scientist-G
National Centre for Cell Science (NCCS)
NCCS Complex, Pune University Campus
Ganeshkhind, Pune

Prof. V. Nagaraja
Honorary Professor
Department of Microbiology and Cell Biology
Indian Institute of Science (IISc)
CV Raman Rd, Bengaluru
Karnataka

Dr. Shantanu Chowdhury
Senior Principal Scientist (Functional Genomics)
CSIR-Institute of Genomics and Integrative Biology (IGIB)
Sukhdev Vihar, Mathura Road
New Delhi

Dr. Lolitika Mandal
Associate Professor, Biological Sciences
Indian Institute of Science Education and Research (IISER)
Knowledge City, Sector 81, Mohali
PO, Sahibzada Ajit Singh Nagar
Punjab

Dr. Sathees C. Raghavan
Professor
Department of Biochemistry
Indian Institute of Science (IISc)
CV Raman Rd, Bengaluru
Karnataka

Prof. Apurva Sarin
Former Director
Institute of Stem Cell Science and Regenerative Medicine (inSTEM)
National Centre for Biological Sciences
Bellary Road, Bangalore

Prof. Yogendra Singh
Professor
Department of Zoology
University of Delhi, Delhi

Dr. Mohan Wani
Scientist 'G'
National Centre for Cell Science Complex
Savitribai Phule Pune University Campus
Ganeshkhind Road Pune

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

FINANCE COMMITTEE

Sh. Vishvajit Sahay
Chairperson
Additional Secretary & Financial Adviser
Department of Biotechnology
Ministry of Science & Technology
Block-2, 6th-8th Floor, CGO Complex,
Lodhi Road,
New Delhi

Dr. Suchita Ninawe
Scientist-G
Department of Biotechnology
Ministry of Science & Technology
Block-2, 6th-8th Floor, CGO Complex,
Lodhi Road,
New Delhi

Dr. Subhra Chakraborty
Director
National Institute of Plant Genome Research
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 Accountants 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 Offcer
National Institute of Immunology
New Delhi

BUILDING COMMITTEE

Sh. 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, ICGEB
Member (Ex-Officio)
Ex-Officio Director
ICGEB
New Delhi

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

Dr. Agam P. Singh
Member
Staff Scientist-VI
National Institute of Immunology
New Delhi

Sh. 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. Subrata Sinha
Department of Biochemistry
All India Institute of Medical Sciences
New Delhi

Prof. Yogendra Singh
Department of Zoology
University of Delhi
New Delhi

Prof. Ajay Kumar Saxena
School of of Life Sciences
Jawaharlal Nehru University
New Delhi

Prof. B. R. Panda
School of Biotechnology
Jawaharlal Nehru University
New Delhi

Prof. Ajay Kumar Dubey
Special Invitee
Rector
Jawaharlal Nehru University
New Delhi

Dr. Monica Sundd
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Sanjeev Das
Staff Scientist
National Institute of Immunology
New Delhi

INSTITUTIONAL ANIMAL ETHICS COMMITTEE

Dr. Devinder Sehgal
Chairperson
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Pravin Kumar Atul
CPCSEA Main Nominee
National Institute of Malaria Research
New Delhi

Dr. Krushnarvind Babalbhai Patel
CPCSEA Link Nominee
Institute of Liver and Biliary Sciences
New Delhi

Dr. Suresh Kumar Dwarikadheesh
CPCSEA nominated Member
National Institute of Biologicals (NIB)
Noida

Dr. Kakali Purkayashtha
CPCSEA nominated Member
All India Institute of Medical Sciences
New Delhi

Dr. P. Nagarajan
Member Secretary
Staff Scientist
National Institute of Immunology
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
Senior Technical Officer
National Institute of Immunology
New Delhi

INSTITUTIONAL BIO-SAFETY COMMITTEE

Dr. Arnab Mukhopadhyay
Chairman
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Soumen Basak
Member Secretary
Staff Scientist
National Institute of Immunology
New Delhi

Prof. Krishnamurthy Natarajan
DBT nominee
Jawaharlal Nehru University
New Delhi

Dr. Mohammed Faruq
Bio-safety Officer
IGIB
New Delhi

Dr. Dhiraj Kumar
International Centre for Genetics and
Engineering Biotechnology
New Delhi

Dr. Prafullakumar B. Tailor
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Sarika Gupta
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Devram Ghorpade
Staff Scientist
National Institute of Immunology
New Delhi

INSTITUTIONAL HUMAN ETHICS COMMITTEE

Prof. Subrata Sinha
Chairman
All India Institute of Medical Sciences
New Delhi

Dr. Shinjini Bhatnagar
Translational Health Science & Technology
Institute
Faridabad

Dr. Sandeep Mathur
All India Institute of Medical Sciences
New Delhi

Dr. Goutam Bhattacharya
K & S Partners
Intellectual Property Attorneys
Gurugram

Maj. Gen B. S. Dhillon (VSM)
201 Rose Apartments
Gurugram

Sh. Sudhir Patwal
National Institute of Plant Genome Research
New Delhi

Dr. Nimesh Gupta
Staff Scientist
National Institute of Immunology
New Delhi

Dr. Rahul Pal
Member Secretary
Staff Scientist
National Institute of Immunology,
New Delhi

STAFF OF THE INSTITUTE

(As on 31.03.2023)

SCIENTIFIC STAFF

Core & 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-VI

Dr. Bichitra K. Biswal, Staff Scientist-VI

Dr. S. Gopalan Sampathkumar,
Staff Scientist-VI

Dr. Arnab Mukhopadhyay, 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-V

Dr. Vidya Raghunathan, Staff Scientist-V

Dr. Nimesh Gupta, Staff Scientist-V

Dr. Aneeshkumar A.G., Staff Scientist-V

Dr. Veena S. Patil, Staff Scientist-IV

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. Ankita Varshney, Staff Scientist-III

Dr. Sangeeta Bhaskar, Staff Scientist-VII
(Superannuated on 30.09.2022)

Emeritus Scientists

Dr. Pramod K. Upadhyay

Dr. Rahul Pal

Professor of Eminence

Dr. Anil Kumar Suri (Relieved on 03.10.2022)

Scientist (Project)
Dr. Yadhu Sharma
Project Scientist III
Dr. Sonali Shrivasatava
Project Scientist I

DBT –RA Programme
Dr. Shabnam

DST- Inspire Faculty Award
Dr. Ekjot Kaur
Dr. Priyanaka Shukla
Dr. Archana Pant

DST –SERB (Young Scientist)
Dr. Savita Yadav
Dr. Santosh Kumar
Dr. Priya Rani

ICMR-RA
Dr. Swati Priya

ICMR-SRF
Sh. Mohd. Kashif
Ms. Yashika Ratra
Sh. Gautam Chandra Sarkar
Sh. Amir Khan
Sh. Nafees Ansari

DBT BIO Care Women
Dr. Aditi Varshney

DST WOSA Scientist
Dr. Nidhi Chaudhary

MK Bhan Research Fellow
Dr. Payal Gulati

INSA Visiting Scientist
Dr. Pooja Gulati

TARE Fellowship
Dr. Vivek Srivastava

Project Associate
Ms. Supriya Rautela
Ms. Mohtashim Rosh
Sh. Manish Kushwaha
Ms. Bhawna

Project Assistant
Ms. Pooja Pal
Ms. Shaveta Sharma
Sh. Satyendra Singh
Ms. Amandeep

Research Associate III
Dr. Rajesh Anand

Research Associate II
Dr. Mallick Sathi N. N Sima

Research Associate I
Dr. Kritee Mehdiratta
Dr. Anupamjeet Kaur

Research Associate
Dr. Monika Yadav

Senior Research Fellows
Ms. Deepa Kale
Sh. Pradeep Ganguly
Dr. Syed Yusuf Mian
Sh. Shams Tabrez
Dr. Richa Pahuja
Ms. Charu Garg
Ms. Sana Amir
Sh. Asgar Ansari
Ms. Kajal Gangaram Kamble
Ms. Ranijisha K. R.
Sh. Yatish R. Thakare
Sh. Somdeb Chattopadhyay

Junior Research Fellows
Ms. Nishu
Ms. Arpita Das
Sh. Rahul Singh Rawat
Sh. Shubham Sharma
Ms. Vandana Sharma
Ms. Baishali Chakraborty
Sh. Johnson Samuel
Ms. Nidhi Bhasin

Consultant Level II
Ms. Richa Arya

Consultant Level I
Sh. Ravi Kant Pal

Scientific Administrative Assistant
Ms. Priyanshu Ananad

Senior Project Assistant (Technical)
Sh. Apratim Kumar Pandey
Ms. Jyotsna

Technician
Sh. Vivek Kr .Pandey

Technical Assistant (Project)
Sh. Mahfuj Hasan
Ms. S. Jayalakshami

Non-Human Primate Handler
Sh. Manoj
Sh. Mukesh

Lab. Assistant/Technician
Sh. Rajkumar Mane

Field Assistant (Project)
Sh. Himanshu

Ph.D. SCHOLARS

Mr. Amir Khan
Mr. Bhushan Dilip Dhamale
Mr. Sayan Chakaraborty
Mr. Sumit Murmu
Mr. Vijay Kumar
Mr. Asgar Ansari
Ms. Charu
Ms. Jyotsna
Ms. Kamble Kajal Gangaram
Mr. Manti Kumar Saha
Ms. Monika Mittal
Ms. Ramya Venkataraman
Mr. Sachin Kushwaha
Ms. Sana Amir
Ms. Sidra Khan
Ms. Sonika Bhatnagar
Ms. Akanksha Rawat
Ms. Alvina Deka
Mr. Akshay Khanduja
Ms. Bharati Swami
Mr. Bhushan Sanjay Nikam
Mr. Binayak Sarkar
Ms. Divya Rashmi
Ms. Monika Singh
Ms. Neha
Ms. Pooja
Ms. Rashima Prem
Ms. Ritu Agrawal
Ms. Rohini Tamang
Mr. Satish Tiwari
Ms. Tanya Jain
Ms. Umanshi Rautela
Ms. Nilakhe Aishwarya Shrikant
Mr. Abhiraj R
Mr. Aftab Mohammed
Ms. Ankita Pal
Ms. Antara Mondal
Ms. Chandrima Bharadwaj
Mr. Chen Chongtham
Ms. Deepsikha Kar
Ms. Anjali Kalia
Ms. Shivani Karalia
Ms. Komal
Mr. Mohit Yadav
Mr. Naveen Kumar
Ms. Rashmi Sanjay Bhosale
Mr. Raunak Kar
Ms. Rimpy Arun
Ms. Sabnam Sahin Rahman
Ms. Sapna Pal
Ms. Shabnam
Ms. Shreya Bhattacharya
Mr. Someshwar Nath Jha
Mr. Soumya Banerjee
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. Rashi Mittal
Ms. Savita
Ms. Shaikh Zikra Arkam
Ms. Simran Aittan
Ms. Simran Motwani
Ms. Summaiya Khan
Ms. Suvechchha Pandit
Ms. Swati Kumari
Ms. Trisha Biswas
Ms. Anita Nandi
Ms. Ankita Paraste
Mr. Anshul Kushwaha
Ms. Chayanika Gogoi
Mr. Faisal Jamal
Ms. Geetika Kumari Ramesh Chandra
Mr. Jashobanta Behera
Ms. Jasleen Kaur
Ms. KM Anuradha Gupta
Mr. Mohammad Athar Mehraj
Ms. Namaste Kumari
Ms. Neha Gupta
Ms. Pratiti Bakshi
Ms. Rakhi
Ms. Shweta Mahapatra
Ms. Sonanjali Aneja
Ms. Tavleen Kaur
Mr. Varun Kumar
Ms. Tuba Anjum Usmani
Ms. Aishwarya Rajan
Mr. Amit Kumar
Ms. Arundhati Karmakar
Mr. Bhanu Pratap Singh
Ms. Debodyuti Sadhukhan
Ms. Dorle Archana Mukund
Mr. Govind Prakash
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

TECHNICAL STAFF

Senior Technical Officers
Sh. Adner Bobin
(Superannuated on 31.05.2022)
Sh. Ajay Kumar Sharma
(Superannuated on 31.12.2022)
Ms. Sweety Batra
Ms. Rekha Rani
Ms. Sushma Nagpal
Dr. Neerja Wadhwa
Dr. Archana Ranjan

Technical Officer-II
Sh. Dayanand
(Superannuated on 30.06.2022)
Ms. Neetu Kunj
Sh. Ranbir Singh
Sh. Md Aslam
Sh. Ashok Kumar
Sh. Ram Bodh
Sh. Rajit Ram
Sh. Kevlanand
Sh. Inderjit Singh
Sh. Chanderdeep Roy
Sh. Sunder Singh Bisht
Sh. Dhramvir Singh
Sh. Roshan Lal
Sh. Birender Kumar
Sh. K.P. Pandey
Sh. Khim Singh
Sh. Nihal Singh
Sh. Pritam Chand
Sh. Manoj Kumar
Sh. Kumod Kumar
Sh. Deshraj
Sh. Kunwar Singh
Sh. Mahesh Roy
Sh. Sudipta Das

Technical Officer-I
Sh. Ravi Ranjan Kumar
s/o Sh. Vijay Kumar
Sh. Ravi Ranjan Kumar
s/o Sh. Shivajee Prasad
Sh. Ankit Sharma
Sh. Pankaj Kumar Mahto
Sh. Vimlesh Singh
Ms. Sarojini Minj
Sh. T. Khaling
Sh. Raghav Ram

Technician-I
Sh. Rajkumar Peddipaga
(Date of demise- 19.08.2022)
Sh. Kiran Pal
(Date of demise- 17.07.2022)
Sh. Ajay Bansal
Sh. Vijendra Kumar
Sh. Nand Lal Arya
Sh. Rakesh Kumar
Sh. Birender Roy
Sh. Puran Singh
Sh. Shahnawaj Haider
Sh. Rajesh K. Meena
Sh. Naresh Kumar
Sh. Anand Prakash Toppo
Sh. Babu Lal Meena

Technician-II
Sh. Vineet Singh
Sh. Pankaj Kumar
Sh. Surender Singh Rawat
Sh. Sonu Gupta
Sh. Arun Lal

Skilled Work Assistant
Sh. Vijay Pal
(Superannuated on 31.01.2023)
Sh. Raj Kumar
Sh. Bhan Singh
Sh. Amarnath Prasad
Sh. Hemant
Ms. Monika

ACADEMIC CELL

Administrative Officer
Sh. Madan Mohan

Section Officer
Ms. Sanju Bisht

Skilled Work Assistant
Ms. Rupinder Kaur

COMPUTER & BIOSTATISTICS

Senior Technical Officer
Sh. M.S.V.V.S Rao
(Superannuated on 30.09.2022)
Ms. Sunita Sachdev

Technical Officer-II
Sh. Naveen Chander

Skilled Work Assistant
Sh. Gaurav Kumar Ravi

ENGINEERING, MAINTENANCE AND INSTRUMENTATION

Executive Engineers
Sh. Raj Kamal Singh
(Superannuated on 30.09.2022)
Sh. Harendra Singh

Senior Technical Officer
Sh. Mukesh Chander

Assistant Engineers
Sh. Iswari Prasad Sharma
(Superannuated on 30.06.2022)
Sh. Amarnath Sah
Sh. Sooraj Prakash
Sh. Ranbir Singh
Sh. R.K. Bharadwaj
Sh. R.K. Sharma
Sh. Yogesh Kr. Tripathi
Sh. Vinod Kumar Panchal
Sh. Mahabeer Singh Panwar

Technical Officer-I
Sh. Sharwan Kumar

Management Assistant
Sh. Mohan S Negi

Technician-I
Sh. Akshyay Kumar Behra
Sh. Pramod Yadav
Sh. Amarnath Gope
Sh. Sanish Kumar

Technician-II
Sh. Rajiv Kumar
Sh. Deen Mohd
Sh. Shashi Bhushan Kumar

Skilled Work Assistants
Sh. Krishna P Gaudel
Sh. Hukum Singh
Sh. Prabhu Dayal
Sh. Ram Prasad

Tradesman (Plumber)
Sh. Praveen Kumar

LIBRARY & DOCUMENTATION SERVICES

Documentation Officer
Ms. Prachi S. Deshpande
(On Deputation)

Senior Technical Officers
Ms. Meenakshi
Sh. Ranjiv Mahajan

Technical Officer II (Documentation)
Sh. Phunglianpau

Technical Officer II
Sh. Satish K Sharma

Technician I
Sh. Babu Lal
(Superannuated on 30.09.2022)

PRIMATE RESEARCH CENTRE

Senior Technical Officer (Vet)
Dr. Surender Singh

Senior Technical Officer
Sh. H. S. Sarna

Technical Officers II
Sh. J.P. Bhardwaj
(Superannuated on 30.11.2022)
Sh. Rajesh Kumar

Skilled Work Assistants
Sh. Shambhu Kumar Bhagat
Sh. Deepak Kumar

SMALL ANIMAL FACILITY

Technical Officer II
Sh. Mohan K Mandal
(Superannuated on 30.03.2023)
Sh. Sadhu Ram
Sh. Surender Singh
Sh. Shailendra K. Arindkar
Sh. Dinesh CPS Negi
Sh. Kapoor Chand

Technician I
Sh. Jaglal Thakur
Sh. Mukesh Kumar
Sh. Subhash Chand Dogra
Sh. Yash Pal
Sh. Abhinav Kumar
Sh. Suraj Kumar

Skilled Work Assistant
Sh. Prem Chand
(Superannuated on 30.03.2023)
Sh. Kuldeep Kumar
Sh. Nand Kishore
Sh. Ram Bhool
Sh. Ram Dev Yadav
Sh. Ram Surat
Sh. Subhash Chand III
Sh. Krishen

ADMINISTRATIVE STAFF

General Administration
Senior Manager
Dr. D.K. Vashist

Manager (A&E)
Ms. Anju Sarkar

Administrative Officers
Ms. Chandresh Bhagtani
Sh. Mahender Pal Singh

Section Officers
Ms. Sheela Satija
(Superannuated on 30.04.2022)
Ms. Daisy Sapra
Sh. Siddharth Sharma

Management Assistants
Sh. Sant Lal
Ms. Neha
Sh. Sandeep Patil
Sh. Deepak Yadav
Sh. Virender Singh Kandoria
Sh. Alam Singh
Sh. Darwan Singh

Junior Translator
Ms. Nisha

Junior Assistant II
Sh. Atyush Kumar

Drivers
Sh. Satyabir Singh
(Superannuated on 31.05.2022)
Sh. Madan Lal
Sh. Suti Prakash
Sh. Mahender Singh

Skilled Work Assistants
Sh. Dinesh Singh
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
Finance & Accounts Officer
Sh. Pradeep Chawla

Section Officers
Sh. Rakesh Satija
(Superanuuated on 30.06.2022)
Sh. Suresh C. Chandel
Sh. Aslam Ali

Management Assistant
Sh. Harinarayan Kumar

Technician I
Sh. Brahm Dev

Skilled Work Assistant
Sh. Naveen Negi

STORES & PURCHASE

Store and Purchase Officer
Sh. Padam Singh Rawat

Accounts Officer
Sh. Dev Dutt Sharma

Section Officer
Sh. Dharambir

Management Assistant
Sh. Ramswaroop Meena

Junior Assistant I
Sh. Debarshi Deb

Skilled Work Assistant
Sh. Balraj
(Supernnuated on 31.05.2022)

PATENT CELL
Dr. Anil Kumar

Section Officer
Sh. Om Prakash

Six Months Project Trainee 2022-2023.

S.NO.	NAME	D.O.J	LAB IN-CHARGE
1	Mr. Mohan Tripathi	27-04-2022	Dr. Pramod K. Upadhyay
2	Ms. Tamanna	09-05-2022	Dr. Aneeshkumar A.G.
3	Ms. Nancy	13-05-2022	Dr. Soumen Basak
4	Ms. Sampita Sarkar	17-05-2022	Dr. S. Gopalan Sampathkumar
5	Ms. Ankita Mondal	17-05-2022	Dr. Soumen Basak
6	Ms. Sreya Prasanna Kumar	27-05-2022	Dr. Sagar Sengupta
7	Mr. Deep Bansal	01-06-2022	Dr. Prafullakumar B. Tailor
8	Ms. Grishma Kulkarni	01-06-2022	Dr. Nimesh Gupta
9	Ms. Khushi Mahajan	06-06-2022	Dr. Devinder Sehgal
10	Ms. Ridhima Raina	06-06-2022	Dr. S. Gopalan Sampathkumar
11	Mr. Aryan Gupta	10-06-2022	Dr. S. Gopalan Sampathkumar
12	Ms. Shruti Gupta	13-06-2022	Dr. Arnab Mukhopadhyay
13	Ms. T. Naga Keerthana	13-06-2022	Dr. Arnab Mukhopadhyay
14	Ms. Vanshika Madan	15-06-2022	Dr. Anil Kumar
15	Ms. Himani Singh	15-06-2022	Dr. Bichitra K. Biswal
16	Ms. Asha Prajapati	15-06-2022	Dr. Bichitra K. Biswal
17	Mr. Mayank Jha	15-06-2022	Dr. Anil Kumar
18	Mr. Sumit Chauhan	16-06-2022	Dr. Anil Kumar
19	Ms. Ayushi Chaudhary	17-06-2022	Dr. Arnab Mukhopadhyay
20	Mr. Subhankar Dey	20-06-2022	Dr. Anil Kumar
21	Ms. Aakriti Beniwal	20-06-2022	Dr. Anil Kumar
22	Ms. Mansi Chaturvedi	22-06-2022	Dr. Aneeshkumar A.G.
23	Ms. Aditi Singh	27-06-2022	Dr. Santiswarup Singha
24	Ms. Reeva Garg	27-06-2022	Dr. Tanmay Majumdar
25	Ms. Sakshi Gupta	01-07-2022	Dr. Pramod K. Upadhyay
26	Ms. Simran Shabir	01-07-2022	Dr. Sarika Gupta
27	Ms. Dhrana Bagul	04-07-2022	Dr. Anil Kumar
28	Ms. Dewaunshi Hemat Panchakshari	04-07-2022	Dr. Senthil Kumar
29	Ms. Nandini	05-07-2022	Dr. Senthil Kumar
30	Ms. Kanika Sharma	05-07-2022	Dr. Nimesh Gupta
31	Mr. Vadant Soni	07-07-2022	Dr. Anil Kumar
32	Ms. Durga Devi B.	08-07-2022	Dr. Sarika Gupta
33	Mr. Gokul. S.	08-07-2022	Dr. Devram Ghorpade
34	Ms. Swat	08-07-2022	Dr. P. Nagarajan
35	Ms. Ishita	11-07-2022	Dr. Debasisa Mohanty
36	Ms. Ankita	15-07-2022	Dr. Apurba K. Sau
37	Mr. Rushikesh	08.08.2022	Dr. Apurba K. Sau
38	Ms. Yeshika Tanwar	18-07-2022	Dr. Sagar Sengupta
39	Dr. Mamta	15-09-2022	Dr. Debasisa Mohanty
40	Dr. Mudit Agarwal	13-10-2022	Dr. Veena S. Patil
41	Dr. Pooja Gulati	31-10-2022	Dr. Debasisa Mohanty
42	Ms. Bhagyasri T.	14-11-2022	Dr. Arnab Mukhopadhyay

43	Mr. Rohan Nagpal	15-12-2022	Dr. Bichitra K. Biswal
44	Ms. Shradha Gupta	15-12-2022	Dr. Bichitra K. Biswal
45	Ms. Simar Kalra	15-12-2022	Dr. Bichitra K. Biswal
46	Ms. Bhawana Sharma	02-01-2023	Dr. Senthil Kumar
47	Ms. Babita	02-01-2023	Dr. Arnab Mukhopadhyay
48	Ms. Rasanpreet Kaur	02-01-2023	Dr. Devinder Sehgal
49	Mr. Manish Kumar Tiwari	02-01-2023	Dr. S. Gopalan Sampathkumar
50	Ms. Manisha Upadhyay	02-01-2023	Dr. Ankita Varshney
51	Ms. Ishika Singh	02-01-2023	Dr. Senthil Kumar
52	Ms. Swekcha	02-01-2023	Dr. Prafullakumar B. Tailor
53	Ms. Shadi Rezaei	02-01-2023	Dr. Anil Kumar
54	Ms. Vaibhavi Yelane	04-01-2023	Dr. Devram Ghorpade
55	Ms. C.S. Aswani Anil Kumar	04-01-2023	Dr. Tanmay Majumdar
56	Mr. Puranjaya Pancholi	05-01-2023	Dr. Pushkar Sharma
57	Ms. Eisha Pandey	05-01-2023	Dr. Sarika Gupta
58	Ms. M. Keerthana	05-01-2023	Dr. Agam P. Singh
59	Ms. Shreya Bhattachariyee	06-01-2023	Dr. Arnab Mukhopadhyay
60	Ms. Sumran Karamchandani	06-01-2023	Dr. Pushkar Sharma
61	Ms. Parvati Girinath	09-01-2023	Dr. Sarika Gupta
62	Ms. CH Jahnavi	09-01-2023	Dr. Apurba K. Sau
63	Ms. Priya Soni	09-01-2023	Dr. P. Nagaranjan
64	Ms. Simran	09-01-2023	Dr. Ankita Varshaney
65	Ms. Shahzeela Fatima	10-01-2023	Dr. Nimesh Gupta
66	Ms. Sonam Gupta	10-01-2023	Dr. Anil Kumar
67	Ms. Sukirti Shivpuri	16-01-2023	Dr. Tanmay Majumdar
68	Ms. Proorva Bhargava	17-01-2023	Dr. Veena S. Patil
69	Ms. Lavanya Chaudhary	18-01-2023	Dr. Soumen Basak
70	Ms. Aditi Sharma	18-01-2023	Dr. Aneeshkumar A.G.
71	Ms. Mansi Chaturvedi	24-01-2023	Dr. Aneeshkumar A.G.
72	Mr. Medini Mohan Das	06-02-2023	Dr. Anil Kumar
73	Ms. Azeen Zehra	07-02-2023	Dr. Bichitra K. Biswal
74	Ms. Nukala Vanditha	01-03-2023	Dr. Anil Kumar
75	Ms. Rachamadaga Sai	01-03-2023	Dr. Arnab Mukhopadhyay

Photographs/images on the front cover and separators are contributed by

Ms. Aishwarya Nilakhe, PhD Scholar and Mr. Phunglianpau, Technical Officer-II.

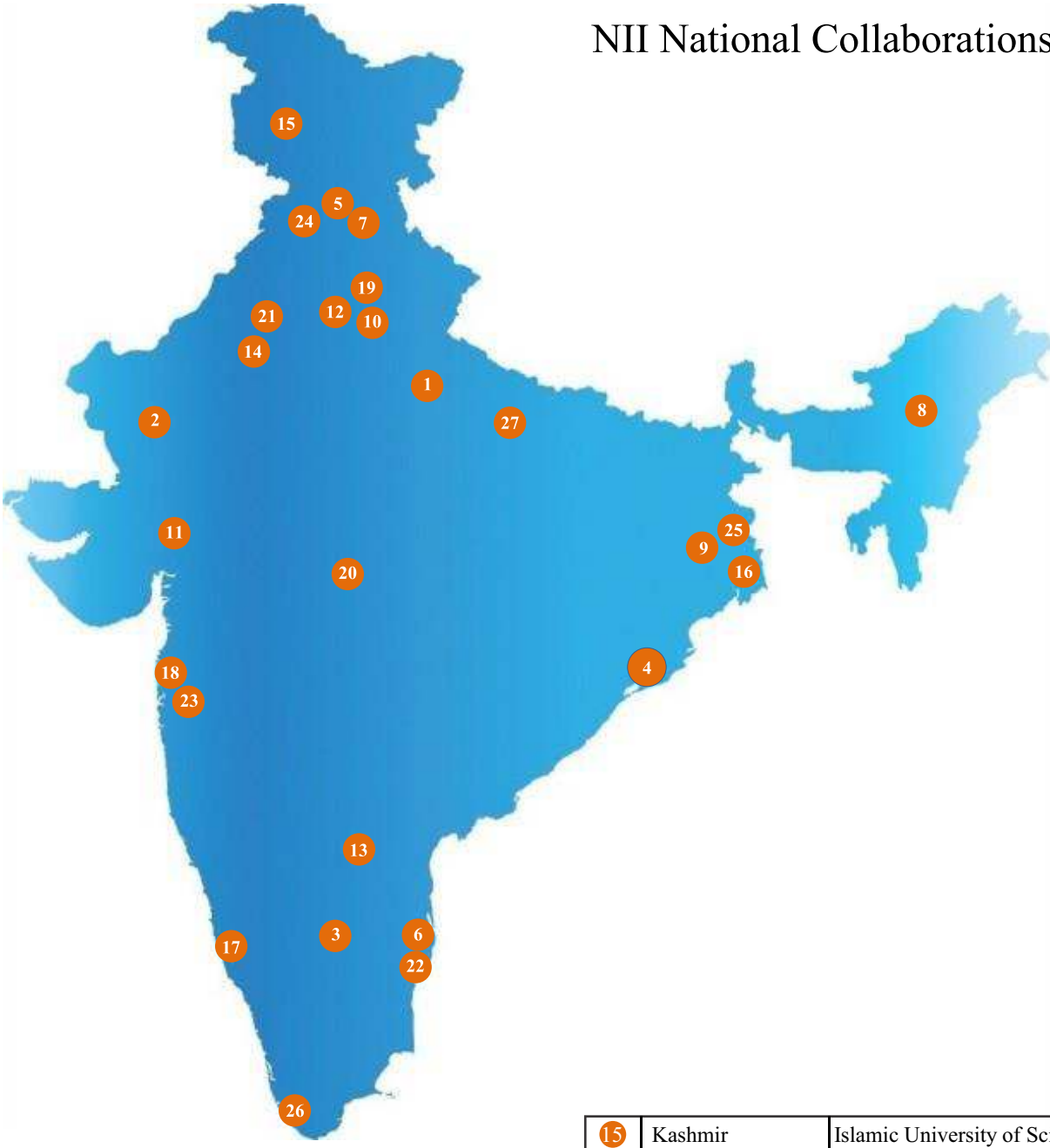
Cover page design by. Dr. Banya Kar, Public Relations Officer.

A PAGE FROM HISTORY

Shri K. R. Narayanan (Minister of State for Science & Technology, Atomic Energy, Space, Electronics, Ocean Development) inaugurating the NII Swimming Pool on 21st July, 1989. Prof. G. P. Talwar (Director, NII) & Mrs. Talwar and Mr. SM Bose (Senior Manager, NII) and other NII Staff were also present.

NII COLLABORATIONS

NII National Collaborations



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2	Ajmer	Central University of Rajasthan
3	Bangalore	IISc, JNCASR
4	Bhubaneswar	ILS, RMRC
5	Chandigarh	MTECH
6	Chennai	IIT-M, Cancer Institute (WIA)
7	Dehradun	Govt. Doon Medical College
8	Dibrugarh	RMRC
9	Durgapur	NIT
10	Faridabad	THSTI, RCB, ESIC Medical College & Hospital
11	Gandhinagar	IIT Gandhinagar
12	Gurugram	Amity University
13	Hyderabad	CCMB, NIAB
14	Jaipur	MGH

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20	Nagpur	VNIT
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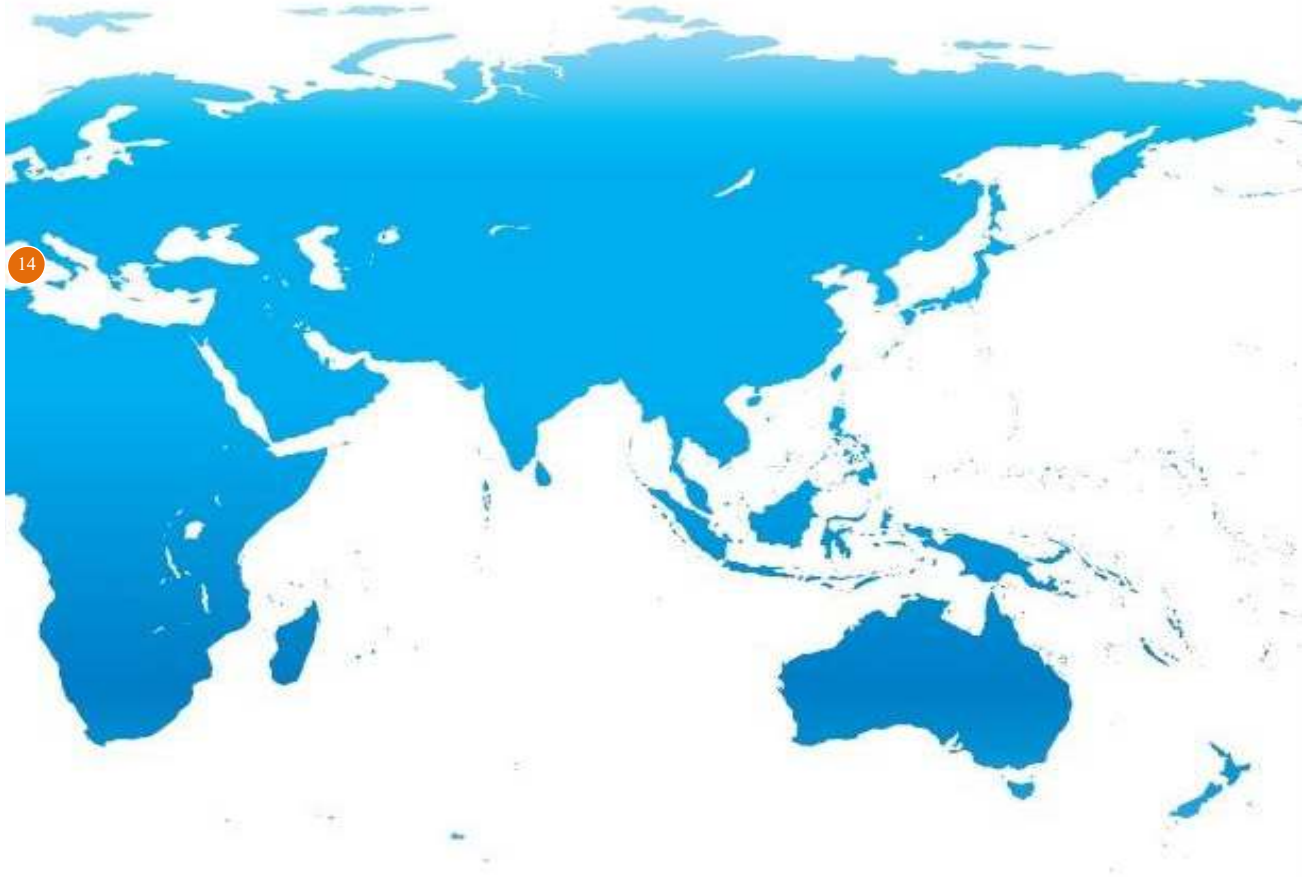
22	Puducherry	JIPMER
23	Pune	CSIR-NCL, IISER
24	Ropar	IIT-Ropar
25	Shantiniketan	Visva-Bharati University
26	Thiruvananthapuram	IAV, RGCB
27	Vanarasi	IIT-BHU

NII International Collaborations

1	Alexander Hoffmann (University of California, Los Angeles, USA)
2	Shane Crotty & Alessandro Sette (La Jolla Instiute for Immunology, California, USA)
3	Tom Rothstein (Western Michigan University, USA)
4	Prakasha Kempaiah (Mayo Clinic, Florida, USA)
5	Karl Pfeifer (National Institutes of Health, Bethesda, USA)
6	Sriram Neelamegham (State University of New York, Buffalo, USA)
7	Abhyudai Singh (Universty of Delaware, USA)
8	Wolfgang Peti (UConn Health Center, USA)
9	Rita Tewari (University of Nottingham, UK)
10	Alain Townsend (MRC, Oxford, United Kingdom)
11	Ilpo Huhtaniemi (Imperial College, London)
12	Patrick Legembre (Universite de Rennes, France)
13	Etienne Joly (IPSB, Toulouse, France)
14	Matteo Ceccarelli (University of Cagliari, Italy)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NATIONAL INSTITUTE OF IMMUNOLOGY
(An autonomous research institute under the Department of Biotechnology (DBT), Government of India)
Aruna Asaf Ali Marg, New Delhi - 10067, India
Phone: 91 11-267117121, 26717145; Fax: 91 11-26742125 / 91 11-26742626
www.nii.res.in