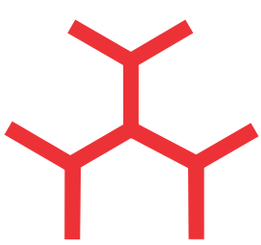
National Institute of Immunology
राष्ट्रीय प्रतिरक्षाविज्ञान संस्थान

2021-22 ANNUAL REPORT

NATIONAL INSTITUTE OF IMMUNOLOGY



ANNUAL REPORT
2021-22

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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

Overview

The last couple of years have been particularly hard, and we have striven to emerge from the restrictions the pandemic has placed upon us all. I would like to express my gratitude to all the members of NII community who have gone beyond the call of duty to ensure the smooth functioning of the institute, often at considerable personal discomfort. Through the pandemic, NII conducted training programmes for medical and technical professionals from all across the country. The hands-on courses imparted skills required to carry out qPCR diagnostic tests for human pathogens. In addition, NII routinely carries out qPCR tests for SARS-CoV-2 on samples received from various hospitals as a service to the nation. NII is also contributing to genome sequencing of SARS-CoV-2 samples.

We continue to reach out school and college students to motivate and introduce them to modern areas of biological research. As part of the Science Setu initiative, members of the NII faculty present their work as well as other topics of scientific relevance to undergraduate and postgraduate students from across the country. We also hosted several post-graduate students from for their internship.

The administrative and technical support we receive is exceptional, and has contributed in no small way to our growth. The Institute is blessed with talented faculty, forever striving to exceed and excel. Without their aptitude and drive, little could be achieved. Graduate students and other research scholars are the driving force behind all our work, and the life-blood of campus life.

We remain forever in the debt to the members of our Research Area Panel / Scientific Advisory Committee. Appraisals and critiques are gratefully received, and acted upon.

We are grateful to the Department of Biotechnology for all the technical and administrative inputs it provides; their counsel serves to guide us on our journey.

Research Highlights

It is a pleasure and a privilege to present the Annual Report of the Institute for the year 2021-22. While we seek to shed light on basic biological mechanisms and processes, we also strive to develop new tools and aids that can help alleviate the ills that inflict us. It is our constant endeavour to contribute to finding solutions to critical diseases that affect human kind. In line this, research at NII is focused on three broad areas:

1. **Immunity and Infection**
2. **Chemical Biology, Biochemistry and Structural Biology**
3. **Genetics, Cell Signaling and Cancer Biology**

A summary of some of the highlights of recent research carried out at NII is presented here.

Immunity and Infection

Ongoing work seeks to gain insights into how *Mycobacterium indicus pranii* (MIP) induced its anti-tumor effects. MIP administration caused a significant decrease in levels of tumor-associated Tregs, effects caused by reduced concentrations of tumoral CCL22. MIP treatment was found to

reduce metastasis, possibly due to lower expression of tumoral MMP2, MMP9, VEGF and PDGF.

Tumor-associated βhCG has been associated with poor prognosis in cancer patients. Interestingly, βhCG can be detected in circulation in women post-menopause, a time during which the incidence of several cancers also registers an increase. In βhCG transgenic mice, ovariectomy constituted an additional pro-tumorigenic signal, and progesterone had anti-tumor effects; associated molecular signatures were identified. Analysis of online databases revealed correlates between the expression of identified genes and poor prognosis in post-menopausal patients.

Efforts are being made to understand the molecular evolution of anti-polysaccharide antibody responses. Analysis of a panel of pneumococcal capsular polysaccharide type 14-specific and carrier-specific monoclonal antibodies indicated that anti-polysaccharide responses are initially restricted, and later diversify. In contrast, anti-carrier responses also demonstrate diversity in the initial phases..

Malaria continues to be a major global health burden and currently known vaccines exhibit limited efficacy. *Plasmodium* proteins that are introduced into the hepatocyte cytosol could constitute novel vaccine antigens and / or drug targets. Studies are now aimed at delineating the minimal protective antigenic regions of several newly identified antigens. A novel pathway involving protein kinase Pf CDPK7 was dissected in the human malaria parasite which regulates biosynthesis of major phospholipids and regulates parasite development.

Biochemistry, genetics and computational modeling have been employed to elucidate cross-regulatory mechanisms and crosstalk in health and disease. Such coordinated approaches are critical for better understanding of concomitant pathways activated as a consequence of feedback and feed-forward loops. Cues that activate specific sets of gene-expression programs are being elucidated. In this context, work has focused on the crosstalk between noncanonical and canonical NF- κB signaling. It appears that such crosstalk fuels intestinal inflammation, both in mice and humans. Agents that interrupt such crosstalk could have therapeutic potential.

Dendritic cells act as critical antigen presenting cells, and the influence of diet on immune responses is being increasingly recognized. l-methionine was shown to influence plasmacytoid dendritic cell (pDC) development *in vivo,* and diet-driven differences were observed between hypermethylated regions of DNA from pDCs and classical DCs. Specific single-point mutations in interferon regulatory factor genes were demonstrated to result in defective pDC maturation as well as diminished interferon-mediated responses and anti-viral immunity.

Work aimed at understanding the biology and function of follicular T helper (Tfh) cells as they relate to anti-viral immunity has continued. In this regard, responses to vaccination as well as to natural infection are being compared. Currently, studies focus on Japanese encephalitis and SARS-CoV-2. Factors affecting antibody responses, as well as memory response, to dengue virus are also being elucidated.

Pathways that influence the generation and maintenance of T cell memory to microbes are being delineated. To this end, immunological assays and several multi-omics technologies are being employed. Molecular signatures of memory T cells specific for different microbial antigens appear to vary quite substantially. Work also seeks to further elucidate the immune responses in neonates during episodes of sepsis.

Chemical Biology, Biochemistry and Structural Biology

The study of enzyme action is providing novel insights into their function. For example, amino acid residues critical for GMP formation by hGBP1 have been identified. Mechanistic insight into the catalysis mediated by *Helicobacter pylori*

arginase have also been obtained, and a novel inhibitor was identified.

Solution NMR studies on acyl carrier protein (ACP) from *S. cerevisiae* have helped in elucidating mechanism of acyl chain sequestration by fungal FAS. Chemical shift perturbation studies in combination with site directed mutagenesis have unraveled the role of specific glycine residues present in the $^{188}GX_2GX_3G^{195}$ motif in the formation of a unique hydrophobic cavity which can potentially facilitate acyl chain sequestration in ScACP.

The utility of bioinformatic approaches in modern biology continues to be enumerated. Using RiPPMiner-Genome, a program for genome mining developed at NII, over a thousand cross-linked chemical structures were identified, after analysis of more than ten thousand whole genome sequences from human microbiota. Besides allowing classification into distinct ribosomally-synthesized and post-translationally modified peptide (RiPP) families, further analysis also permitted the assigning of putative function to some of these peptides. In other work, molecular dynamics studies have led to the designing of high-affinity peptide inhibitors aimed at blocking the interaction of the receptor binding domain of the spike protein of SARS-CoV-2 with the ACE2 receptor.

Gylcan moieties play significant roles in all aspects of biology. For example, the interaction of E-selectin with sialyl-Lewis-X determines the efficiency of leukocyte extravasation, and glycan-selectin interactions influence the course of atherosclerosis. HexNAc analogues, designed to modify the hydrophobic properties of sialoglycans, were synthesized. One amongst such analogues enhanced cellular expression of sialyl-Lewis-X, increasing cell adhesion. Such studies can further understanding of cell trafficking and can also aid in the development of new therapeutics.

The histidine biosynthesis pathway in *Mycobacterium tuberculosis* constitutes an interesting drug target. Based on high-resolution X-ray structures of HisB, several triazole and imidazole scaffold inhibitors have been designed; co-crystal structures of HisB-inhibitor complexes have also been characterized. Some of these inhibitors have been found to be non-toxic, and reduce the load of mycobacteria in macrophage infection models *in vitro*.

Data suggests that patients of Alzheimer's Disease demonstrate bone loss. Studies indicate that treatment with osteocalcin (a protein synthesized by osteoblasts) has neuroprotective effects in an animal model of the disease; brain Ab42 levels are reduced, accompanied by improvements in cognitive function. Exploration of the "brain-bone axis" therefore has the potential to result in significant therapeutic benefits. Study of cell cycle-related neuronal apoptosis has revealed that some miRNAs which were shown to suppress the cycle are aberrantly expressed in neurons from a mouse model for Alzheimer's Disease and two of these were shown to protect neuronal cell death.

Genetics, Cell Signaling and Cancer Biology

Tuberculosis continues to extract a heavy toll in terms of both morbidity and mortality. Transcription factors essential for *Mtb* survival are being identified. One such factor AosR, works to dampen oxidative and nitrosative stress, thus promoting mycobacterial growth. The molecular events involved in synthesis of a novel class of compounds that sequester zinc from the host and contribute to disease pathogenesis was dissected.

The role of enhancers in large scale chromosomal reorganization is being elucidated. In particular, the enhancer Eb of the *TCRb* locus appears to contribute to the repositioning of the *TCBb* locus, a process that may facilitate VDJ recombination.

Signalling and trafficking events in apicomplexan parasites are being elucidated. TgVPS15, a *Toxoplasma gondii* orthologue of eukaryotic VPS15, was found to regulate both biogenesis in the steady state and autophagy under nutrient-limiting conditions.

Work on SPAG-9, a cancer-testis antigen identified at NII, has continued. Phase II clinical trials are ongoing in patients of cervical cancer (Stage II). Clinical trials are also ongoing in patients of ovarian cancer (Stage IV). Patients are injected with autologous dendritic cells primed with either patient's own tumor lysate or with recombinant SPAG9.

Colon cancer is widely prevalent; diagnosis often relies on hospital procedures like colonoscopy and PET scans. Six microRNAs were found to be upregulated in colon cancer, as early as in Stage I; an inverse correlation was observed with survival. Such microRNA can constitute prominent biomarkers for diagnosis and prognosis.

Defects in tumor suppressors can drive oncogenesis. The cancer-testis antigen PRAMEF2, a biomarker of several cancers, was found to promote the degradation of LATS1 kinase, resulting in the upmodulation of several tumor-associated genes.

Caenorhabditis elegans is being employed as a model system to study the molecular basis of aging. Specifically, whether specific dietary interventions can influence the aging process is being assessed, and whether repurposed drugs can be employed as therapeutics in diabetes-related illnesses is being determined.

Mechanisms by which micronutrients and macronutrients connect protein homeostasis and energy metabolism are being elucidated. In skeletal muscles, the essentiality of vitamin D for the utilization of glucose as an energy source was established; absence of the vitamin D receptor caused muscle atrophy.

Increasing evidence suggests that microbial metabolites play a role in the progression of colorectal cancer. Indoxyl sulfate affected the cell cycle progression of human epithelial adenocarcinoma cell lines. Additionally, a sensitive and precise sensor has been developed for the detection of trimethylamine in human fluids.

In a new initiative, nano-scale artificial antigen presenting cells, capable of displaying tumor-specific peptide-MHCs and co-stimulatory molecules, are being formulated. Chemical synthesis of gold nano-spheres, gold-nanorods, as well as iron oxide, silica, and mesoporous silica nanoparticles has been standardized. The influence of molecular density, flexibility, and directional presentation of coated tumor-specific p-MHC and co-stimulatory molecules on function will be assessed.

Pushkar Sharma
Director (Additional Charge)

Date : 1st June, 2022

RESEARCH REPORTS

IMMUNITY & INFECTION

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

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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 are being studied. Role of macrophages in TB-IRIS development was also analyzed.

Analysis of the role of regulatory T cells in MIP mediated anti-tumor activity

Tregs promote tumor growth by down-regulating the anti-tumor immune response. Significant reduction in the frequency of Treg cells infiltration in tumor microenvironment was observed in MIP treated mice. Treg cell reduction was a consequence of reduced intra-tumoral CCL22 in MIP treated tumors. Further, higher expression of intra-tumoral IFN-α was observed in the MIP treated group. MIP treatment could not decrease the percentage of Tregs as well as CCL22 level in TME of IFNR1 KO mice and also no reduction in tumor volume was observed in MIP treated IFNR1 KO mice unlike WT mice, providing evidence of important role of IFN-α in MIP mediated anti-tumor activity.

Role of MIP on metastasis and angiogenesis in murine melanoma model

It was observed that after one month of B16F10 s.c.tumor implantation, the number of metastatic nodules in the lungs of MIP treated mice were significantly less as compared to control, untreated group. Differentially expressed genes and factors responsible for metastasis and angiogenesis in control and MIP treated mice were measured *in vitro*, where CXCR4 expression was found to be reduced in the MIP treated group. MMPs are one of the important factors allowing the tumor cells to migrate through the blood vessels and lymphatics. MIP treated tumors showed lower expression of MMP2 and 9 as compared to control. VEGF and PDGF were also found to be down-regulated by MIP, which is a soluble factor secreted from the tumor cells and contributes to the invasion and migration of tumor cells. Another important observation was that MIP delays the tumor growth and metastasis in a PPARγ dependent manner. Further detailed studies are underway to fully understand the mechanism.

Publication

Original peer-reviewed article

1. Pal L, Nandani R, Kumar P, Swami B, Roy G and Bhaskar S*(2021) Macrophages are the key players in promoting hyper-inflammatory response in a mouse model of TB-IRIS. **Front Immunol**.doi: 10.3389/fimmu.2021.775177. [*Corresponding author]

Disorders of proliferation: Analysis of novel pathways and targets

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Human chorionic gonadotropin (hCG) and systemic autoimmunity

Pregnancy is associated with lupus "flares".

Apoptotic blebs elicited by different drugs demonstrated differential presence of autoantigens. Co-incubation of lupus splenocytes with hCG and specific blebs induced increases in phosphorylation of signaling intermediates and secretion of autoantibodies, providing mechanistic insight into the hormone's links with autoreactive responses.

Hemoglobin (Hb) and lupus

Free Hb is inflammatory, and is efficiently scavenged; clearance mechanisms can be overwhelmed in certain disease states.

Peripheral blood mononuclear cells from SLE patients secreted higher levels of lupus-associated cytokines upon Hb incubation. Co-incubation of Hb and apoptotic blebs with splenocytes from lupus-prone mice revealed synergies in secretion of cytokines and autoantibodies. Infusion of Hb into such mice induced early-onset glomerulosclerosis.

Neutralization of Hb could therefore have beneficial effects.

The incidence of several cancers increases post-menopause.

βhCG can be detected in circulation post-menopause. In βhCG transgenic mice, ovariectomy constituted an additional pro-tumorigenic signal, and had anti-tumor effects; RNA-seq identified associated molecular signatures. Analysis of TCGA databases revealed correlates between the expression of identified genes and poor prognosis in post-menopausal.

βhCG could serve as a prognostic indicator in post-menopausal women, and treatment with progesterone may prove beneficial.

Publications

Original peer-reviewed articles

1. Sharma H, Bose A, Sachdeva R, Malik M, Kumar U, Pal R* (2022) Haemoglobin drives inflammation and initiates antigen spread and nephritis in lupus. **Immunology**165:122-140. [*Corresponding author]

2. Gupta A, Vats A, Ghosal A, Mandal K, Sarkar R, Bhattacharya I, Das S, Pal R, Majumdar SS (2022) Follicle-stimulating hormone-

mediated decline in miR-92a-3p expression in pubertal mice Sertoli cells is crucial for germ cell differentiation and fertility. **Cell Mol Life Sci**. doi: 10.1007/s00018-022-04174-9.

Microbial interface biology and associated host immune response

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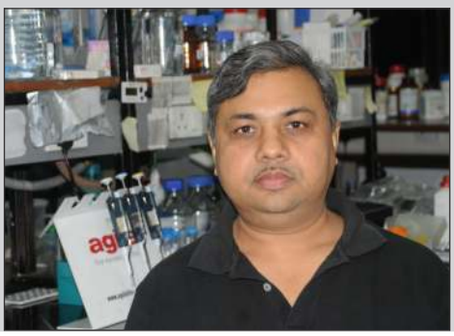
We are interested in understanding how anti-polysaccharide antibody response evolves over time in mice immunized with a model glycoconjugate vaccine PCP14-CRM_{197} (pneumococcal capsular polysaccharide type 14 conjugated to CRM_{197}, a nontoxic variant of diphtheria toxin). In order to understand the molecular characteristics of the anti-PCP14 antibody response, we generated PCP14- and CRM_{197}-specific monoclonal antibodies (mAbs) using hybridoma technique from mice immunized with one and three doses of the glycoconjugate. We generated 18 anti-PCP14 and 11 anti-CRM_{197} mAbs from primary immunization, and 12 anti-PCP14 and 26 anti-CRM_{197} mAbs from mice that received three doses of the glycoconjugate vaccine. Interestingly, all mAbs, barring 14, were of IgM/κ isotype.The nucleotide sequences of the heavy and light chains were analyzed for VH, DH, JH, VL and JL gene usage, HCDR3 and LCDR3 length and sequence. Our preliminary findings from the analysis of the 19 heavy and 44 light chain sequences suggest that the primary anti-polysaccharide antibody response induced against glycoconjugate is very restricted and it becomes more diverse with booster shots. In contrast to the anti-polysaccharide response, the antibody response to the carrier protein in glycoconjugate-immunized mice is diverse in both primary and tertiary response.



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

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Plasmodium species introduce effector molecules into hepatocyte cytosol to manipulate host metabolic and /or signaling pathways for its own benefit. We aim to identify, new parasite molecules that affect the host cellular processes. Such parasite proteins are potential antigens and should be evaluated for their vaccine potential or possibly as drug targets.

Malaria vaccines, malaria drug/ inhibitor and target discovery

Characterization of malaria vaccine candidates

To find the Pb DNAJ and Pf SLTRiP protective regions and T cell epitopes, we have expressed recombinant protein sub fragments (S1, S2, S3, S4, S5, for immunization of mice and subsequent challenge with Pf/Pb transgenic parasites.These experiments will narrow down minimal protective regions.

Malaria vaccine development

Plan is to generate Pf-antigen in Pb transgenic parasites as well as express, purify Pf-DNAJ:Pf-CSP chimeric protein for preclinical studies. All plasmid constructs for transfection have been made. Once ready these transgenic parasites will be used for homologous challenge of mice immunized with respective Pf-antigens. For protein expression gene was codon optimized and then synthesized chemically. Desired regions were PCR amplified and cloned into pSS1 expression vector. Verified construct was transformed in competent *L. lactis* and grown in a fermenter and supernatant containing desired protein was used for purification using NiNTA and HiTRAP-HP ion exchange columns. High purity protein was recovered.

Malaria drug discovery

A series of novel morpholine analogs were synthesized and tested for antimalarial potency. Although the compounds did not exhibit high potency against the malaria parasite their

tolerance for normal cells up to 2 mM combined with negligible lysis in RBCs up to 100 mM concentration were notable observations.

Publications

Original peer-reviewed articles

1. Kumari V, Prasad KM, Kalia I, Sindhu G, Dixit R, Rawat DS, Singh OP, Singh AP,Pandey KC (2022) Dissecting the role of *Plasmodium* Metacaspase-2 in malaria gametogenesis and sporogony. **Emerg Microbes Infect**. 11:938-955.

2. Kalia I, Anand R, Quadiri A, Bhattacharya S, Sahoo B, Singh AP* (2021) *Plasmodium berghei*-Released Factor, PbTIP, modulates the host innate immune responses **Front Immunol**. doi: 10.3389/fimmu.2021.699887. [*Corresponding author]

3. Kashif M, Quadiri A, Singh AP* (2021) Essential role of a *Plasmodium berghei* heat shock protein (PBANKA_0938300) in gametocyte development. **Sci Rep**. doi: 10.1038/s41598-021-03059-4. [*Corresponding author]

4. Upadhyay C, Sharma N, Kumar S, Sharma P, Fontinha D, Chhikara B, Mukherjee B, Kumar D, Prudêncio M, Singh AP, Singh P (2022) Synthesis of new analogs of morpholine and their antiplasmodial evaluation against human malaria parasite *Plasmodium* falciparum. **New J Chem**. 46:250-262.

5. Sharma PK, Kalia I, Kaushik V, Brünnert D, Quadiri A, Kashif M, Chahar K, Agarwal A, Singh AP*, Goyal P* (2021) STK35L1 regulates Plasmodium infection and expression of cell cycle genes during liver stage of malaria. **Exp Cell Res**. doi:https://doi.org/10.1016/j.yexcr.2021.112764. [*Corresponding authors]

6. Kumari V, Pandey R, Srinivasan E, Kalia I, Singh AP, Saxena AK, Rajaekaran R, Gupta D, Pandey KC (2021) *P. falciparum* Metacaspase-2 capture its natural substrate in a non-canonical way. **J Biochem**. doi:https://doi.org/10.1093/jb/mvab086.

7. Sharma N, Kashif M, Singh V, Fontinha D, Mukherjee B, Dhruv K, Singh S, Prudêncio M, Singh AP*, Brijesh R* (2021) Novel antiplasmodial compounds leveraged with multistage potency against Parasite *Plasmodium falciparum*: *In vitro, in vivo* evaluations and pharmacokinetic studies. **J Med Chem**. 64:8666-8683. [*Corresponding authors]

8. Pandey I, Quadiri A, Wadi I, Pillai CR, Singh AP*, Das A* (2021) Conserved Plasmodium protein (PF3D7_0406000) of unknown function, in-silico analysis and cellular localization. **Infect Genet Evol**. Doi: 10.1016/j.meegid.2021.104848. [*Corresponding authors]

Patent

1. Rathi B, Singh S, Mounce B, Poonam, Kempaih P, Singh AP, Durvasula R. Hydroxiethyamine based piperazine compounds, methods of producing and using the same for treating disease. [US Patent Application Number 17/347,720. Filed on 15.6.2021]

Fine tuning of immune signaling pathways

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Extracellular cues engage discrete cell signaling pathways to activate specific sets of transcription factors, which trigger distinct gene-expression programs. However, these pathways are known to be physically and functionally interlinked within the cellular network. More so, in their anatomic niche, mammalian cells receive signals from a variety of stimuli that generate plausible crosstalks between concomitantly activated pathways. Combining biochemistry, genetics, and computational modeling, we have been characterizing these cross-regulatory mechanisms and elucidating their role in physiology and diseases. We are particularly investigating how the so-called "immune-organogenic" noncanonical NF-κB pathway crosstalks with inflammatory canonical NF-κB signaling and the anti-viral type1-interferon axis. Our recent study demonstrated that NF-κB crosstalks fuel aberrant intestinal inflammation in colitogenic mice and in inflammatory bowel disease patients. We also found a role of the NF-κB system in linking micronutrients to anti-viral immunity. We argue that our work bear promises for therapeutic interventions in human ailments targeting signaling crosstalks.

Publications

Original peer-reviewed articles

1. Chawla M, Mukherjee T, Deka A, Chatterjee B, Sarkar UA, Singh AK, Kedia S, Lum J, Dhillon MK, Banoth B, Biswas SK, Ahuja V, Basak S* (2021) An epithelial *Nfkb2* pathway exacerbates intestinal inflammation by supplementing latent RelA dimers to the canonical NF-κB module. **Proc Natl Acad Sci. (USA)** doi: 10.1073/pnas.2024828118. [*Corresponding author]

2. Mudgal R, Bharadwaj C, Dubey A, Choudhary S, Nagarajan P, Aggarwal M, Ratra Y, Basak S*, Tomar S* (2022) Selective estrogen receptor modulators limit alphavirus infection by targeting the viral capping enzyme nsP1. **Antimicrob Agents Chemother**.doi: 10.1128/AAC.01943-21. [*Corresponding authors]

Reviews/Proceedings

1. Mukherjee T#, Ratra Y#, Banoth B, Deka A, Polley S, Basak S* (2021) A kinase assay for measuring the activity of the NIK-IKK1 complex induced in the noncanonical NF-κB pathway. **Methods Mol Biol**. 2366:165-181.[#Joint first authors] [*Corresponding author]

Awards / Fellowships

Elected as a Fellow of the Indian National Science Academy (INSA, New Delhi). In recognition of Dr. Basak's work in developing an understanding of the fundamental principle underlying signaling pathway crosstalk and in revealing physiological and the pathophysiological consequences of such cross-regulatory NF-κB controls.

Understanding the role of Interferon Regulatory Factors in dendritic cell development and innate immunity

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P. Nagarajan (NII, New Delhi)
S. Paul Oh (BNI, AZ, USA)

Methionine- and Choline-deficient diet identifies an essential role for DNA methylation in plasmacytoid dendritic cell biology

Diet plays an important role in lifestyle disorders associated with the disturbed immune system. During the study of methionine- and choline-deficient diet–induced nonalcoholic fatty liver disease, we observed a specific decrease in the plasmacytoid dendritic cell (pDC) fraction from murine spleens. We identified that l-methionine supplementation correlates with representation of the pDC fraction. We demonstrated that supplementation of methionine-deficient medium with S-adenosylmethionine (SAM), a key methyl donor, reverses the defect in pDC development. Based on our observed effect of SAM and zebularine on DC subset development, we sought to clarify the role of DNA methylation in pDC biology and hence performed Whole-genome bisulfite sequencing analysis from the splenic DC subsets. Our study identified that pDCs display differentially hypermethylated regions (DMRs) in comparison with classical DC (cDC) subsets. Analysis of the DMRs suggested that association with the MAPK pathway such that its inhibition by chemical inhibitor U0126 guides DC development toward the pDC subtype. Our observation is physiologically relevant as Langerhan Cell Histiocytosis associated with constitutive MAPK signaling display reduced pDC proportions *(Blood 2021; 138:1237)*.

IRF8 and BATF3 interaction enhances the cDC1 specific Pfkfb3 gene expression

Development of diverse DC subtypes from a common progenitor population is tightly regulated by complex molecular inter-play between transcription factors. We had earlier demonstrated that *Bat f3* and *Id2* expression have a synergistic effect on the *Irf8* directed classical cDC1 development. Bi-FC and IP assays confirmed that IRF8 selectively interacts with BATF3 but not with ID2. Analysis of genome recruitment of IRF8-BATF3 complex at promoters and transcriptomics study from the cDC1 subtype led to identification of metabolically important *Pfkfb3* gene. We confirmed the direct regulation of *Pfkfb3*, a critical enzyme in glycolysis by IRF8-BATF3 complex in cDC1 biology.

Mutation in Irf8 gene *(Irf8 R294C)* impairs Type I IFN-mediated antiviral immune response by murine pDCs

pDCs are the key producers of type I interferons (IFNs), thus playing a critical role in antiviral immune responses. Previous studies indicated that the *Irf8R294C* (BxH2) mutation specifically abrogates development of cDC1 without affecting that of pDC. Our transcriptome analysis on sorted pDC populations by RNA-sequencing identified defect in *Ifnb* gene induction. Our results suggested that though the point mutation *Irf8R294C* did not affect pDC development, it led to defective type I IFN production, thus resulting in inefficient antiviral response. Further, analysis of *in vitro* FLDC cultures and in vivo mouse model, we observed that *Irf8R294C* mutation also led to defect in production of ISGs as well as defective upregulation of costimulatory molecules on pDCs in response to NDV infection (or CpG stimulation). Our study signifying that single point mutation in *(Irf8R294C)* severely compromised type I IFN-mediated immune response leading to impaired antiviral response.

Publications

Original peer-reviewed articles

1. Rawat BS, Venkataraman R, Budhwar R, Tailor P* (2022) Methionine- and choline-deficient diet identifies an essential role for DNA methylation in plasmacytoid dendritic cell biology **J Immunol**.208:881-897.[*Corresponding author]

2. Chauhan KS, Das A, Jaiswal H, Saha I, Kaushik M, Patel VK, Tailor P* (2021) IRF8 and BATF3 interaction enhances the cDC1 specific *Pfkfb3* gene expression. **Cell Immunol**.doi: 10.1016/ j.cellimm. 2021.104468.[*Corresponding author]

3. Das A, Chauhan KS, Kumar H, Tailor P* (2021) Mutation in *Irf8* gene *(Irf8R294C)* impairs Type I IFN-mediated antiviral immune response by murine pDCs. **Front Immunol**.doi: 10.3389/ fimmu.2021 .758190. [*Corresponding author]

4. Dwivedy A, Mariadasse R, Ahmad M, Chakraborty S, Kar D, Tiwari S, Mani S, Tailor P, Majumdar T, Jeyakanthan J, Biswal BK. (2021) Characterization of the NiRAN domain from RNA-dependent RNA polymerase provides insights into a potential therapeutic target against SARS-CoV-2. **PLoS Comput Biol**.doi: 10.1371/journal. pcbi.1009384.

5. Tripathi A, Singh Rawat B, Addya S, Surjit M, Tailor P, Vrati S, Banerjee A (2021) Lack of Interferon Regulatory Factor 8 associated with restricted IFN-gamma expression augmented Japanese Encephalitis Virus replication in the mouse brain. **J Virol**.doi: 10.1128/JVI.00406-21.

6. VermaP, Biswas S, Yadav N, Khatri A, Siddiqui H, Panda JJ, Rawat BS, Tailor P, Chauhan VS (2021) Delivery of a cancer-testis antigen-derived peptide using conformationally restricted dipeptide-based self-assembled nanotubes. **Mol Pharm**.18:3832-3842.

Patent

1. Majumdar T, Biswal BK, Tailor P. Methods and compositions for treating viral diseases using combination of drugs. [US Patent Application Number 17/241,130. Filed on 27.4.2021]

T cell immunity to virus infection and vaccines

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Our laboratory works in the area of viral immunology. We are interested in understanding the human immunological determinants of long-term sustained protective immunity developed against viruses. Major focus is to delineate the biology and function of a CD4 T cells subset "follicular T helper (Tfh) cells" in a long-lasting protective immunity. The global aim is to identify and harness the positive attributes of Tfh cells for the rational design of next generation vaccines. Here are some ongoing programs.

Tfh cells in long-lasting protective immunity in infection and vaccination

Here, we are studying the characteristics of immunological memory and clonotype diversity of Tfh cells in response to human vaccines. To determine the optimal traits of Tfh cells in long-lasting protective immunity, the vaccine responses are also compared with recovery from natural infection. To this, we are studying the longitudinal cohorts of infection and vaccination using our human immune monitoring and T-cell assay platform. Currently, we are investigating the cohorts of (i) Japanese encephalitis (JE) and SA14142 live attenuated JE vaccine and (ii) COVID-19 and inactivated SARS-CoV-2 vaccine.

Tfh cells in humoral immunity establishment to dengue virus

In this program, our attempts are focused on providing the insight into the determinants of antibody response to dengue virus. Here, we are exploring the biology of Tfh and related CD4+ T-cell subsets in acute dengue virus infection or virus-specific immune memory.

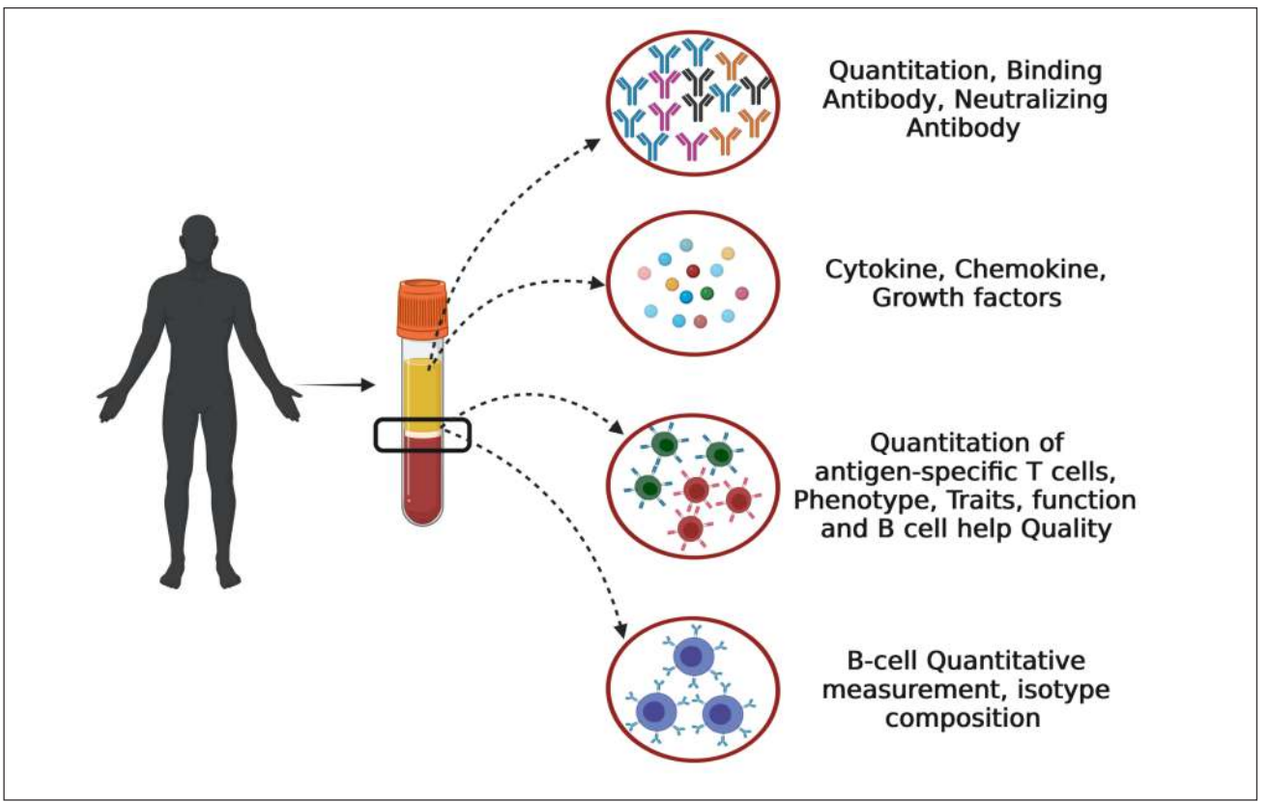

Figure 1: Human T-cell assay and immune monitoring platform. This platform includes the advanced human immunology techniques for studying the traits of T cells and the dynamics of cell-mediated and humoral immunity to vaccines and virus infection in antigen-specific settings.

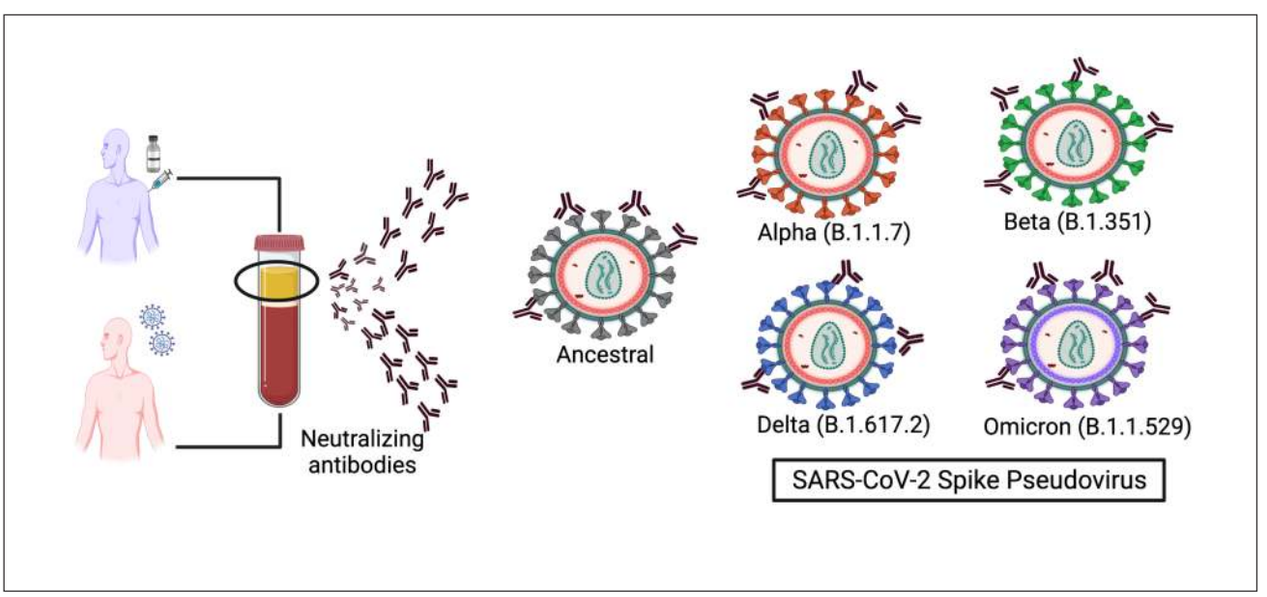

Figure 2. The SARS-CoV-2 Pseudovirus platform. The SARS-CoV-2-Spike expressing Pseudoviruses for ancestral virus and the variants of concern. It includes both the lentivirus based and the VSV-backbone based pseudoviruses for measuring the virus neutralizing antibodies in infection and vaccination in BSL-2 settings.

Publications

Original peer-reviewed articles

1. Thiruvengadam R, Awasthi A, Medigeshi G, Bhattacharya S, Mani S, Sivasubbu S, Shrivastava T, Samal S, Rathna Murugesan D, KoundinyaDesiraju B, Kshetrapal P, Pandey R, Scaria V, Kumar Malik P, Taneja J, Binayke A, Vohra T, Zaheer A, Rathore D, Ahmad Khan N, Shaman H, Ahmed S, Kumar R, Deshpande S, Subramani C, Wadhwa N, Gupta N, Pandey AK, Bhattacharya J, Agrawal A, Vrati S, Bhatnagar S, Garg PK (2022) Effectiveness of ChAdOx1 nCoV-19 vaccine against SARS-CoV-2 infection during the delta (B.1.617.2) variant surge in India: a test-negative, case-control study and a mechanistic study of post-vaccination immune responses. **Lancet Infect Dis**. 22:473-482.

2. Chauhan S, Rathore DK, Sachan S, Desmazes SL, Gupta N, Awasthi A, Vrati S, and Kalia M (2021) Japanese encephalitis virus infected human monocyte-derived dendritic cells activate a transcriptional network leading to an antiviral inflammatory response. **Front Immunology**.doi: 10.3389/fimmu.2021.638694.

Immune response to infections in humans

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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 (Figure 1).

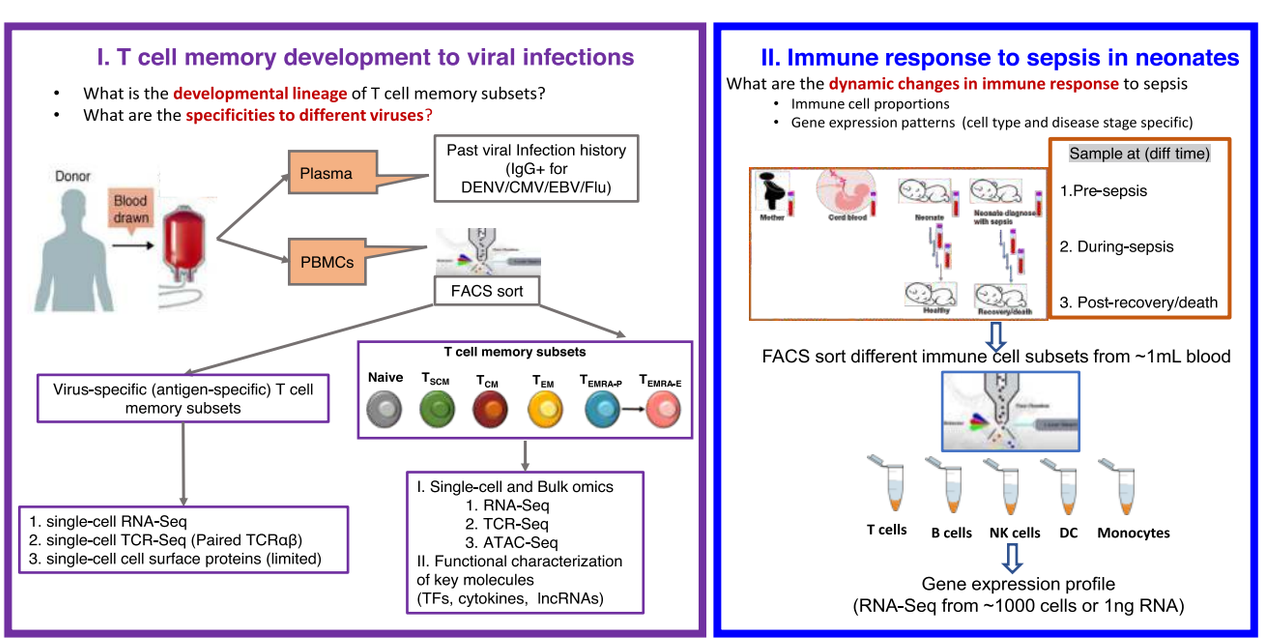

Figure 1. Multi-omics approaches to understand response to infections in humans.

T cell memory development to infectious diseases

The acquisition of immunological memory to infections is a hallmark of protective immunity and hence forms the basis for vaccinations. We are interested in understanding how the T cell memory is formed during the primary infection and maintained over the years to defend the subsequent secondary infection from the same pathogen. 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 shows different flavours of T cells to different viruses.

Immune response to sepsis in neonates

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.

Publications

Original peer-reviewed articles

1. Rana K, Pani T, Jha SK, Mehta D, Yadav P, Jain D, Pradhan MK, Mishra S, Kar R, Reshma GB, Srivastava A, Dasgupta U, Patil VS*, Bajaj A* (2022) Hydrogel-mediated topical delivery of steroids can effectively alleviate psoriasis via attenuating the autoimmune responses. **Nanoscale.** 14:3834-3848. [*Corresponding authors]

2. Kumar S, Pal S, Thakur J, Rani P, Rana K, Kar A, Kar R, Mehta D, Jha SM, Pradhan MS, Jain D, Rajput K, Mishra S, Ganguli M, Srivastava A, Dasgupta U, Patil VS, Bajaj A (2021) Nonimmunogenic hydrogel-mediated delivery of antibiotics outperforms clinically used formulations in mitigating wound infections. **ACS Appl Mater Interfaces**. 13:44041-44053.

3. Pal S, Soni V, Kumar S, Jha SM, Medatwal N, Rana K, Yadav P, Mehta D, Jain D, Sharma P, Kar R, Srivastava A, Patil VS, Dasgupta U, Nandicoori VK, Bajaj A (2021) A hydrogel-based implantable multidrug antitubercular formulation outperforms oral delivery. **Nanoscale**. 13:13225-13230.

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

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My research interest has been emergent to bolster translational disease intervention strategies through cutting-edge reconnaissance against important human infectious diseases by cultivating the balance between tolerance versus immunity, abrogating inflammation, mediated by the gut microbiome.

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

The project is based on the hypothesis that *Toxoplasma gondii* infection interferes with the synchronization between the gut microbiota and metabolic cycles.We raise the question of how an altered microbiome population might develop metabolic dysfunction while being treated for a persistent *T. gondii* infection, leading to obesity. Symbionts and pathobionts compete to determine whether there will be tolerance (Treg/Tr1/Breg/Br) or inflammation (Th1/Th17/Inflammatory B1) in the course of infection. Chronic infection causes uncontrolled inflammation, which fuels the obesity epidemic. This translational research will look at how probiotics work to improve the body and identify a novel class of anti-inflammatory small molecules based on the microbiome that can fight *T. gondii*-induced obesity (Figure 1).

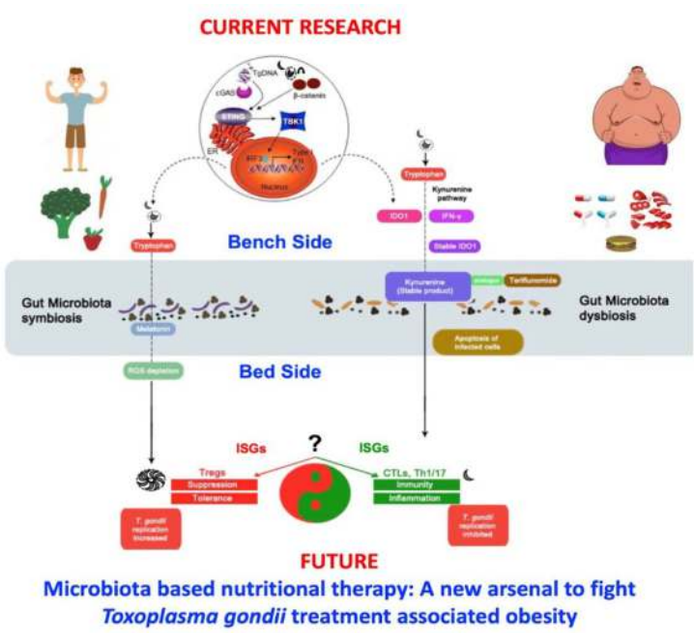

Figure 1. Climax population of microbiota, interacts intimately within the host, colonizes our body. These microbiotas include both symbionts and pathobionts which form commensal eubiosis consortium within the host body. The competition between symbionts vs pathobiont determines the dynamics between tolerance vs inflammation, and also the fate of the infection. Microbiota-based nutritional therapy may be an alternative therapeutic approach to control the infection as well as it can impede inflammatory disease like obesity.

- We have found that activation of Wnt molecule has facilitated *T. gondii* replication smoothly in the host. Use of Wnt inhibitor (JW55) recovered the mortality of *T. gondii* infected mice significantly.
- Infected mice lost their body weight significantly, however, treatment with Wnt inhibitor improved the body weight of parasites infected mice significantly.

Dynamics of T-cell subsets in toxoplasmosis

The human digestive tract is occupied by mucus and microbiome which maintain a tolerogenic microenvironment to escape unwanted immune responses. The enteric pathogen, *Toxoplasma gondii* takes the opportunity to replete its infection in this tolerogenic microenvironment in the gut.Antigen-presenting cells like dendritic cells (DCs) are the symphony for the immune tolerant process. IL-10 and TGF-ß released by DCs can develop the immunosuppressive microenvironment in the intestinal region. These immunosuppressive cytokines are under the control of several tolerogenic molecules such as indoleamine 2, 3-dioxygenase 1 (IDO1), cytotoxic T-lymphocyte associated protein 4 (CTLA4/CD152), and programmed cell death 1 (PD1), can facilitate *T. gondii* to colonize in the mucosal/immuno-tolerant site for fast replication and further dissemination in different organs.

Objectives

1. Understanding the role of tolerogenic molecules (IDO1, CTLA4, PD1) in differentiating T-cells subsets (Th1, Th2, Th9, Th17, Th22, Treg/Tr1, Tc1, Tc17 cells, etc.) using knockout mice.
2. Identifying the protective T-cells subsets which can thwart the parasite replication *in vivo*.
3. Subsequently, we propose to examine immunotherapeutic checkpoint strategy with inhibitors of IDO1, or CTLA4, or PD1 along with protective T-cells therapy for withdrawing the immunosuppressive tolerant microenvironment for circumventing the parasite infection.

Publications

Original peer-reviewed article

1. Dwivedy A,Mariadasse R, Ahmad M, Chakraborty S, Kar D, Tiwari S, BhattacharyyaS, Sonar S, Mani S, Tailor P, Majumdar T*, Jeyakanthan J*, Biswal BK* (2021) Characterization of the NiRAN domain from RNA-dependent RNA polymerase provides insights into a potential therapeutic target against SARS-CoV-2. **PLoS Comput Biol**.doi: 10.1371/journal.pcbi.1009384[*Corresponding authors]

Patent

1. Majumdar T, Biswal BK, Tailor P. Methods and compositions for treating viral diseases using combination of drugs. [US Patent Application Number: 17/241,130; Filed on: 27.04.2021]

Learning the homeostasis processes by virtue of multi-organ cross-talks in metabolic disorders

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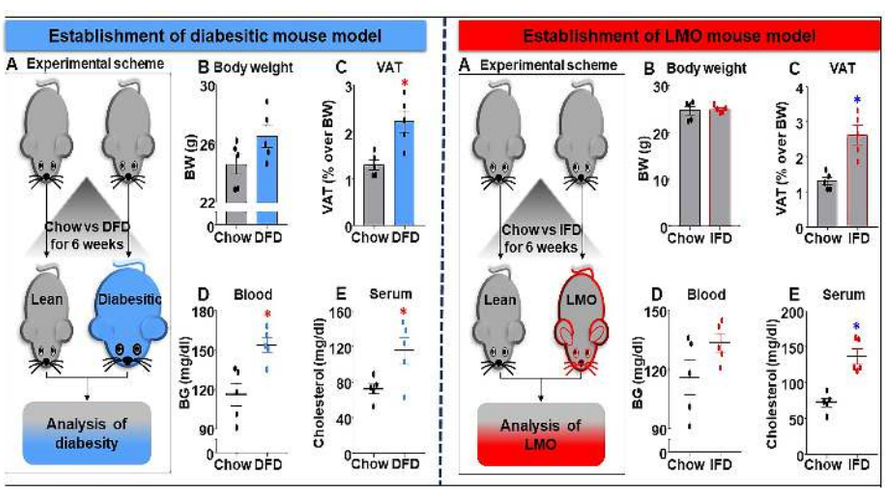
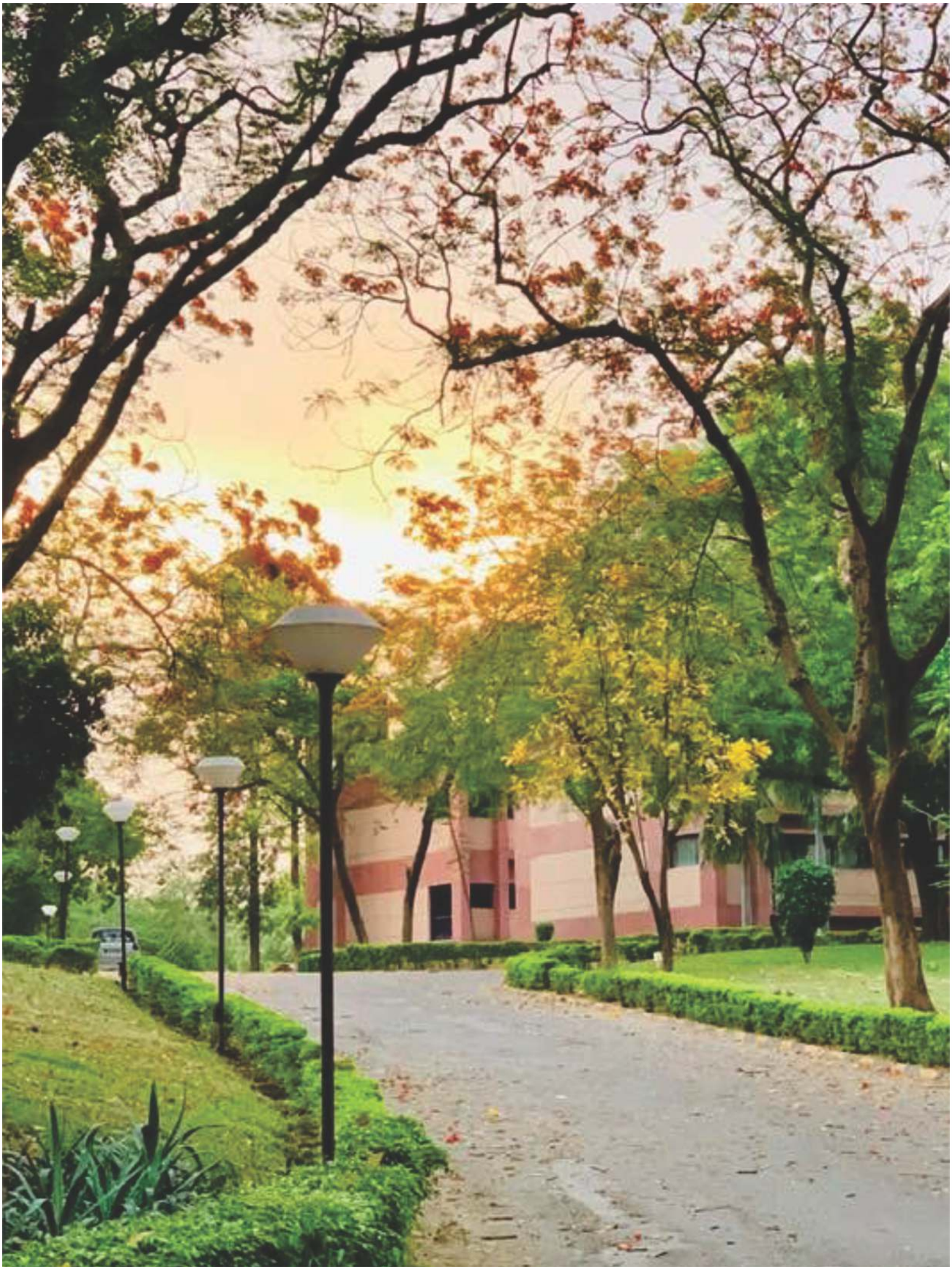
In our Immunoinflammation laboratory (IIL), we pursue the unique clinically relevant questions. By using the combination of *ex vivo* and *in vivo* models we are uncovering previously unknown homeostasis processes underlying metabolic disorders. At present we are working on diabesity which encompasses obesity-associated diabetes. Obesity and related diabetes cases are on the high rise and limited understanding of details of molecular processes compels the scientific community to identify key regulatory molecules that could be posed to newer therapeutic platforms. In parallel to the global rise of obesity-associated diabetes cases, the Indian subcontinent has a unique cohort of individuals that are not obese but are metabolically high risk to develop diabetes, cardiovascular diseases, IBD, etc. This cohort is termed lean but metabolically obese (LMO). India has the highest cases of LMO with prediabetes or diabetes. LMO-specific drugs or regimes to improve glucose tolerance and insulin resistance are the need of time.One of the important steps toward developing LMO-targeted therapies is to understand the details of regulatory processes underlying LMO development. In this context, we have invested our efforts to develop mouse models of global diabesity and India-subcontinent-specific LMO. Having these models at our facility facilitates our understanding of these metabolic disorders in detail and ensures uncovering of hidden secrets unique to these diseases.



C57bl/6j mice were fed either chow or diabesitic diet (DFD) or Indianized fat diet (IFD) for 6 weeks and the effects of DFD & IFD feeding on metabolic disturbances were evaluated. Measurement of body weight, VAT (% over BW), BG (mg/dl), and serum cholesterol of. N = 5 mice per group; mean ± s.e.m.; *, < 0.05 by paired t-test. BW: body weight, VAT: visceral adipose tissue, and BG: blood glucose.

CHEMICAL BIOLOGY, BIOCHEMISTRY AND STRUCTURAL BIOLOGY



Enzymes regulation and its importance in biology

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Enzymes regulation and its importance in biology

Stimulation of GMP formation in hGBP1 is mediated by W79

Despite several studies, the underlying mechanism of stimulated GMP formation by hGBP1 is not fully clarified. Here, we showed that W79 located after switch I stimulates GMP formation. We propose that the H-bond between the indole ring of W79 and the main chain carbonyl of K76 can reposition the active site after the first phosphate cleavage step through the movement of W79-containing region. We also observed a long-range effect of further enhanced GMP formation in the W114A mutant (W114 situated after switch II), which is mediated through W79, thereby highlighting W79 as a key regulator.

An evolutionary non-conserved motif in Helicobacter pylori arginase mediates positioning of the loop containing the catalytic residue for catalysis

Unlike other arginases, the *Helicobacter pylor*i homolog has a 13-residue non-conserved motif that is extremely crucial to function. However, the mechanistic basis for the role of this motif in catalytic function is less understood. Here, we showed that Glu155 of this stretch interacts with both Lys57 and Ser152, which are essential for positioning of the motif through Trp159. We found that the Lys57-Glu155-Ser152 interaction influences the positioning of the loop containing the catalytic His133 so that this His can participate in catalysis, thereby providing a mechanistic understanding into the role of this motif in catalytic function. We also found a new molecule, which specifically inhibits this enzyme.

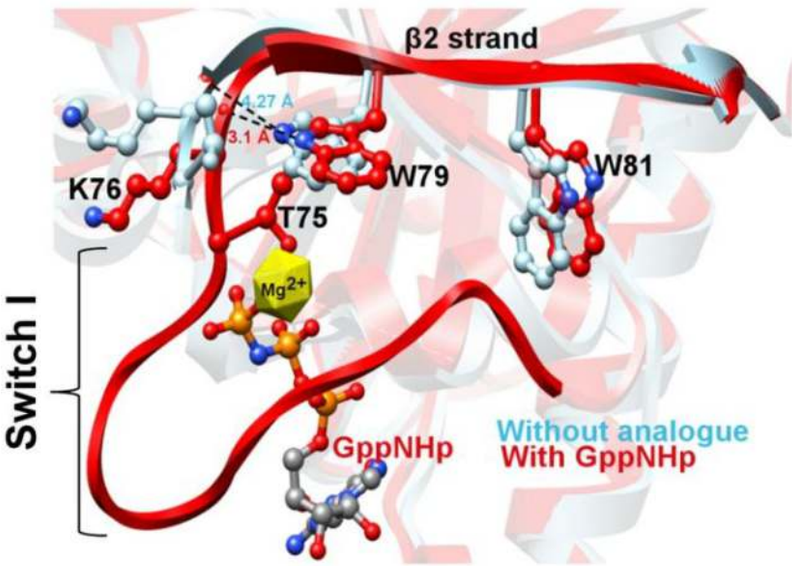

Figure 1. The H-bonding contact between the indole N of W79 and the main chain carbonyl of K76 in hGBP1 repositions the switch I containing catalytic loop for enhanced GMP formation.

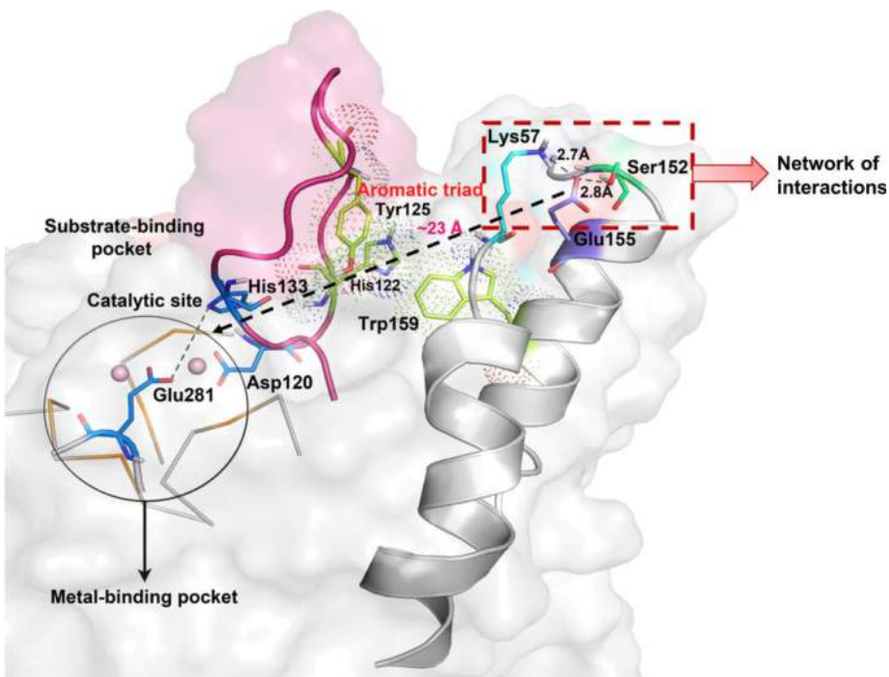

Figure 2. The long-range effect of interactions involving Lys57–Glu155–Ser152 on the positioning of the loop containing the catalytic His133 in *Helicobacter pylori* arginase.

Publication

Original peer-reviewed article

1. Sarkar D, Vijayan R, Gourinath S and Sau AK* (2022)A unique aromatic cluster near the active site of *H. pylori* CPA is essential for catalytic function. **Biophys J**. 121:248-262. [*Corresponding author]

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

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The specific objectives of the major ongoing projects are (A) *In silico* identification of novel biosynthetic pathways and small ORFs by mining of bacterial genomes and human microbiome, (B) Structure based analysis of mutations in genomes of SARS-CoV-2 variants and prediction of inhibitors for different drug targets.

Genome mining of human gut microbiome

Analysis of whole genome sequences of 10,648 isolates of human microbiota using RiPPMiner-Genome could successfully identify more than a thousand cross-linked chemical structures from four distinct RiPP families i.e. Lanthipeptides, Lassopeptides, Thiopeptides and Cyanobactins and core peptides for the remaining RiPP classes. Clustering of the predicted RiPPs with RiPPs with known function using sequence similarity network (SSN) as well as chemical fingerprints of cross-linked structures revealed that majorly RiPPs from Firmicutes (Lactobacillus intestinalis) cluster with known RiPPs associated with pore formation, cytolysis and anti-microbial property against *S. aureus, L. monocytogenes* and LABs, while RiPPs from Bacteroidetes and Proteobacteria do not cluster with known RiPPs. Apart from analyzing the capacity of microbiota for *de novo* biosynthesis of novel secondary metabolites like RiPPs, we have also analyzed the putative Xenobiotic Metabolizing Enzymes (XMEs) which can potentially affect activity of several drugs by altering their chemical structures.

Structure based analysis of mutations in SARS-CoV-2 and prediction of inhibitors for different drug targets

Multiple microsecond scale MD simulations have been carried out on RBD:hACE2, RBD:hACE2(glycosylated) and a number of peptide fragments in complex with RBD. The peptide fragments have been selected based on analysis of RBD:hACE2 crystal structures with the objective of identifying peptides which can bind with higher affinity compared to hACE2. Based on analysis of multiple MD trajectories, attempt has been made to trace the region of high

affinity as well as the combination of the binding partner residues which are utilizing the binding region more efficiently compared to others. Figure 1 shows three key regions on RBD which make crucial interactions with hACE2. The interaction foot-printing information has been utilized for the design of the peptide inhibitor to interrupt RBD.

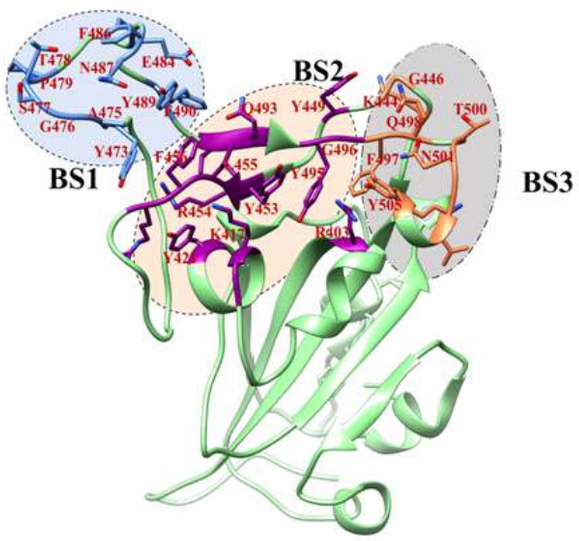

Figure 1. Sub-sites in the binding pocket of RBD where interactions can be optimized for design of high affinity peptide inhibitors.

Publications

Original peer-reviewed articles

1. Kumar P, Mohanty D* (2021) Development of a novel pharmacophore model guided by ensemble of waters and small molecule fragments bound to SARS-CoV-2 Main protease. **Mol Inform**. doi: 10.1002/minf.202100178.[*Corresponding author]

2. Mehdiratta K, Singh S, Sharma S, Bhosale RS, Choudhury R, Masal DP, Manocha A, Dhamale BD, Khan N, Vivekanand A, Sharma P, Ikeh M, Brown AC, Parish T, Ojha AK, Michael JS, Faruq M, Medigeshi GR, Mohanty D, Reddy DS, Natarajan VT, Kamat SS, Gokhale RS (2022) Kupyaphores are zinc homeostatic metallophores required for colonization of *Mycobacterium tuberculosis*. **Proc Natl Acad Sci. USA**. doi: 10.1073/pnas.2110293119.

To develop strategies for making sensors and actuators for biological processes

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Effects of immune dysregulation in Retinitis Pigmentosa

Retinitis Pigmentosa is a heritable ocular disease and it causes progressive photoreceptor degeneration due to genetic mutation.

Retinal Neuron like Cells (RNLCs) were generated by differentiating RP patients' own blood derived peripheral blood mononuclear cells to mimic patient condition to clinically characterize rate of degeneration and average rate of apoptosis of respective RNLCs was calculated.

The exome sequencing of DNA isolated from RP patient was performed to determine their source mutation and each mutation was matched with apoptosis profile of respective RNLCs.

A correlation between average rate of apoptosis and onset of retinal degeneration was observed.

Role of monocytes in Hepatitis B infection

Hepatitis B virus infection is a serious threat to public health. We focus on monocytes, its role in the disease and its utility for biomarkers in HBV infection.

Blood samples were obtained from 49 HBV patients and 10 healthy controls. RNA was extracted from CD14+ monocyte and sequenced.

The number of upregulated Differentially Expressed Genes were highest in the immune-tolerant, followed by inactive; the number of downregulated DEGs were highest in immune-clearance and acute sample. The pathway activation pattern is almost inverse between the immune-clearance and inactive carrier.

Publications

Original peer-reviewed article

1. Agarwal M, Gupta C,Varsha Mohan K,Upadhyay PK, Dhawan A, Jha V (2021) Adjunctive intravitreal anti-vascular endothelial growth factor and moxifloxacin therapy in management of intraocular tubercular granulomas.**Ocul Immunol Inflamm**. doi: 10.1080/09273948.2021.2002367.

Review

1. Jain K, Sinha P, Varsha Mohan K, Upadhyay PK* (2021) Mouse models of the humanized immune system. In: **Essentials Of Laboratory Animal Science: Principles And Practices** (Eds. Nagarajan P, Gudde R, Srinivasan R Springer Nature (Singapore) Pte Ltd). pp 725-742. doi: 10.1007/978-981-16-0987-9_30. [*Corresponding author]

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

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We strive to develop small molecules as tools for probing the role of glycosylation in immunological processes. Glycans provide major immunogenic epitopes such as blood group (A/B/H(O)) and Lewis antigens. Particularly sialyl-Lewis-X (sLeX/CD15s) is a branched tetrasaccharide moiety, viz., NeuAca2→6Galb1→4(Fuca1→3)GlcNAc-R, whose expression is limited to a subset of glycoproteins and gangliosides. Interactions of sLeX with E-selectin are critical for extravasation and response to inflammation. Defective cell adhesion is associated with Leukocyte adhesion deficiency (LAD) while dysregulated cell adhesion is associated with atherosclerosis.

In this context, we designed and synthesized HexNAc analogues carrying the N-(cycloalkyl)carbonyl moieties with the reasoning that the cycloalkyl moieties would be more sterically acceptable to metabolic processing compared to their *N*-alkylcarbonyl counterparts and would modify the hydrophobic properties of the sialoglycans. Among a panel of analogues evaluated, the peracetyl *N*-cyclobutanoyl-D-mannosamine was found to be metabolically processed through the sialic acid biosynthetic pathway and resulted in a four-fold enhancement of sLeX expression compared to the controls. Enhanced sLeX expression was manifested in increased cell adhesion to E-selectin. The ability to enhance sLeX expression in leukocytes would enable a fundamental understanding of the role of glycans in cell trafficking and open up promising avenues for therapeutic approaches for LAD.

Publication

Patent

1. Sampathkumar S.-G., Parashar S, Tasneem A, Rautela J. Hexosamine compounds and methods thereof. [Indian Patent Application Number: 202111026912/TEMP/E-1/30167/2021-DEL. Filed on 16.6.2021]

Structural studies on proteins, dynamics and ligand interactions using NMR

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Structure and function of the proteins/ezymes involved in the fatty acid biosynthesis pathway

Fungal FAS2 gene product has been recognized as a candidate target for drug intervention in Candida parapsilosis and C. albicans. Therefore, we selected S. cerevisiae acyl carrier protein (ACP) as a prototype to understand acyl chain sequestration by fungal FAS. Different ScACP acyl-intermediates were prepared enzymatically, to mimic the fatty acid elongation process *in vivo*. C_{8-} ($\delta C_{8-}\delta$Holo-), C_{10-} ($\delta C_{10-}\delta C_{8-}$) and C_{12-}*Sc*ACP ($\delta C_{12-}\delta C_{10-}$) amides displayed large perturbations in both proton (^{1}H) and nitrogen (^{15}N) dimension. Three glycines present within a ^{188}GX2GX3G^{195} motif in helix II displayed significant perturbations in C_{12}-*Sc*ACP. To uncover the role of the three glycines, Gly 188, Gly 191 and Gly 195 were mutated to valine, singly, as double and triple mutants. Reduction of chain sequestration was observed in the single mutants, while complete loss of chain engulfment was observed in the G188V/ G191V/ G195V*Sc*ACP triple mutant. Cast 3.0 server identified a cavity formed by Leu 187, Leu 190, Gly 191, Gly 195-Pro 198, Pro 201, Leu 209, and Phe 213 in compliance with our chemical shift perturbation data and glycine mutagenesis studies. The opening of this cavity lies between helix II and loop II. We speculate that this is the opening of the primary hydrophobic cavity of *Sc*ACP, not reported before.

Publications

Original peer-reviewed articles

1. Garima, Prem R, Yadav U, Sundd M* (2021) A GX2GX3G motif facilitates acyl chain sequestration by Saccharomyces cerevisiae acyl carrier protein. **J Biol Chem**.doi: 10.1016/j.jbc.2021.101394. [*Corresponding author]

2. Rajak MK, Bhatnagar S, Pandey S, Kumar S, Verma S, Patel AK, Sundd M* (2021) Leishmania major biotin protein ligase forms a unique cross-handshake dimer. **Acta Crystallogr D Struct Biol**. 77: 510-521. [*Corresponding author]

3. Meena VK, Kumar V, Karalia S, Garima, Sundd M* (2021) Ellagic acid modulates uninduced as well as mutation and metal-induced aggregation of a-synuclein: Implications for Parkinson's disease. **ACS Chem Neurosci**. 12:3598-3614. [*Corresponding author]

Review

Arya R, Dhembla C, Makde RD, Sundd M and Kundu S (2021) An overview of the fatty acid biosynthesis in the protozoan parasite Leishmania and its relevance as a drug target against leishmaniasis. **Mol Biochem Parasitol**. 246:111416.

Therapeutic interventions in chronic diseases

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Modulating brain-bone axis for ameliorating memory deficits in the 5XFAD mouse model of Alzheimer's disease

Initial studies in animals and humans suggest that osteocalcin supports brain health and enhances cognitive function. However, no detailed analysis is done to establish osteocalcin's role in modulating brain function. Moreover, people have yet to explore the brain-bone axis's potential for treating bone disorders and neurodegenerative diseases. Additionally, clinical data indicated an increased osteoporosis incidence and bone loss in Alzheimer's patients. The role of osteocalcin in the fetus's brain development and memory generation has been studied; however, its role in the adult brain has not yet been explored. To address this, we studied; however, its role in the adult brain has yet to be explored. To address this, we studied the effect of carboxylated osteocalcin, or Gla-OC, a vitamin K-dependent non-collagenous bone protein synthesized by bone-forming cells osteoblasts.During bone remodeling, the carboxylated osteocalcin is converted into the undercarboxylated OS and released into the blood. To understand the role of osteocalcin in the progression of AD, we used a humanized transgenic mouse model of AD, i.e., 5XFAD. Our extensive studies show that Gla-OC is a potent modulator of diseases involving amyloid deposits. Significant clearance of the amyloid deposit is observed in 5XFAD mice treated with Gla-OC, which is the prime reason for the reduction in levels of Abeta42 in brain samples. The effect is deemed positive, considering the improvement in other impaired cognitive functions brought about by amyloidosis.The effect of Gla-OC, as mentioned earlier, is validated by confirming the increase in the number and activity of astrocytes in the animals treated with Gla-OC. Elevation in the expression of amyloid uptake proteins like LRP-1 and CD36 and degradation of endocytosed Abeta42 by neprilysin and cathepsin is also

observed upon Gla-OC treatment. These effects are brought about by the impact of Gla-OC on the transcription factor TFEB. Another unexpected finding is the use of Gla-OC in the circulation, which has a neuroprotective function.Gla-OC also protects against tau pathology, as evidenced by the reduction of tau cleavage and phosphorylation in db/db mice. Gla-OC also improves the integrity of the blood-brain barrier via IGF-1. Thus, our study opens a new avenue to exploit the brain-bone axis for treating various neurodegenerative diseases.

Publications

Original peer-reviewed articles

1. Singh YP, Shankar G, Jahan S, Singh G, Kumar N, Barik A, Upadhyay P, Singh L, Kamble K, Singh GK, Tiwari S, Garg P, Gupta S, Modi G (2021) Further SAR studies on natural template based neuroprotective molecules for the treatment of Alzheimer's disease. **Bioorg Med Chem**.doi: 10.1016/j.bmc.2021.116385.

2. Papanai GS, Pal S, Pal P, Yadav BS, Garg P, Gupta S, Ansari SG, Gupta BK (2021) New insight into the growth of monolayer MoS2 flakes using an indigenously developed CVD setup: a study on shape evolution and spectroscopy. **Mater Chem Front**. 5:5429-5441.

Patents

1. Gupta S,Vijayan V. Peptide complex with immunomodulatory and anti-inflammatory function. [Indian Patent Number: 393755. Granted on 31.03.2022]

2. Gupta S, Ahmed I, Nilakhe A, Upadhyay P. Novel compound modulating GSK-3 activity. [US Patent Application Number: 17/463,717. Filed on 01.09.2021]

3. Gupta S, Upadhyay P. Formulation for modulating pain and inflammation and methods thereof. [Indian Patent Application Number: 202111021028. Filed on 11.05.2021]

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

G Senthil Kumar

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Research in our laboratory focuses on the characterization of structural, allosteric, and dynamic changes in antigen-antibody/host-pathogen interactions using the combination of solution NMR spectroscopy, X-ray crystallography along with various biochemical and biophysical techniques.

Structural/Dynamic studies on antigen-antibody interactions

In this project, we propose to identify and characterize the molecular basis for the antigen-antibody interaction betwen the glycoprotein E DIII domain of dengue viral protein and antibodies. Specifically, we are interested in the identification of additional unidentified epitopes using solution NMR spectroscopy, determination of structures of DIII domain in complex with antibodies using X-ray crystallography and the characterization of the role of dynamics in the interaction between the DIII domain of DENV serotypes and antibodies.

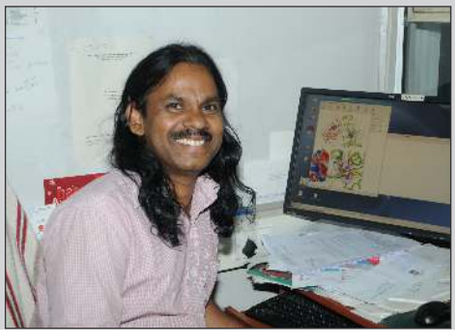
Molecular basis for host-pathogen interactions

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. Specifically, we are interested in the characterization of structural basis for the interaction of NS2A domain of DENV and calmodulin that dictates the viral replication process and the identification of the mode of interaction between SARS-CoV-2 nucleocapsid protein and protein phosphatase 1 (PP1) to identify how PP1 achieves substrate specificity and mediates the phosphoregulation of viral transcription.

Publication

Original peer-reviewed articles

1. Kumar GS*, Page R, Peti W (2021) ^{1}H,^{15}N and ^{13}C sequence specific backbone assignment of the MAP kinase binding domain of the dual specificity phosphatase 1 and its interaction with the MAPK p38. **Biomol NMR Assign**. 15:243-248 [*Corresponding author]



Structural and biochemical studies of *M. tuberculosis* proteins

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Ramandeep Singh (THSTI, Faridabad)

My laboratory majorly aims at deriving mechanistic understandings of *Mycobacterium tuberculosis (Mtb)* metabolic pathways particularly the Histidine (His) production and exploiting the results of this study for designing new anti-TB small molecules. Briefly, Mtbbiosynthesizes 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 combined with its absence in humans makes the enzymes of this pathway as important anti-TB drug targets. Using structural and biochemical studies of these enzymes particularly of HisB (Imidazole glycerol phosphate dehydratase), we have designed a number of triazole scaffold potent inhibitors against this enzyme. In another project, we focus on elucidating structural and biochemical properties of membrane associated proteases and enzymes of glycolysis pathway.

Designing anti-TB molecules through a structure guided approach

The essentiality of His pathway for *Mtb* to mount a sustained TB infection in mouse model suggests that the enzymes of this pathway constitute novel anti-TB drug targets. Therefore designing/ identifying small molecules disrupting the *Mtb* His biosynthesis deems a new strategy to curb TB infection. In this context, we have been pursuing structural and biochemical studies on the enzymes of this pathway. We have previously determined the high-resolution X-ray structures of HisB (also known as imidazole glycerol phosphate dehydratase), that catalyses the sixth step of the pathway and HisB-substrate (Imidazole glycerol phosphate; IGP) and HisB-triazole compound complexes. The functional unit of HisBis a 24-mer, exhibiting a 432 molecular symmetry.The overall tertiary structure of a monomeric HisB comprises a four-helix-bundle sandwiched between two four stranded β-sheets. The structure of HisB-IGP complex revealed that the imidazole ring of the IGP is anchored between the two active site Mn atoms and the rest of the substrate interacts mainly through either direct or water mediated hydrogen bondings with residues Glu21, Arg99, Glu180, Arg121 and Lys184 which protrude from three

separate protomers. Using this structural information and building on our previous studies we have designed a number of triazole and imidazole scaffold inhibitors and have carried out their structural, biochemical and inhibition studies. We have demonstrated that these triazole scaffold inhibitors exhibited minimum inhibitory concentration (MIC)99 values of approximately 20 - 30 µM range. The co-crystal structure of HisB-compound3 complex shows that the inhibitor inhibits the function of HisB competitively. We show that the inhibitor binds to the enzyme's active site, which is situated in the interface of the three monomers (Fig. 1). The triazole ring of the inhibitor is positioned between the two active site manganese atoms. The ring also makes metal mediated interactions with the active site histidine residues. The other portions of the molecule make hydrogen bonding interactions mainly with Asp, Arg, His and Glu, which protrude from the three subunits. Subsequently, we tested the potency of these inhibitors in killing *Mtb* in macrophage infection model. For this, H37Rv bacterial strain was grown in Middlebrooke 7H9 broth (Difco) supplemented with 10% Oleic Albumin Dextrose Catalase (OADC), 0.2% glycerol and 0.05% Tween-80 until the mid-log phase. Our studies showsome of these compounds are non-toxic in the macrophage cell line up to higher millimolar range and reduce the bacterial load in macrophage TB infection model approximately 1000 times. These results suggest inhibition of *Mtb* His pathway by triazole scaffold inhibitors represents a new way of curtailing TB infection in macrophage model.

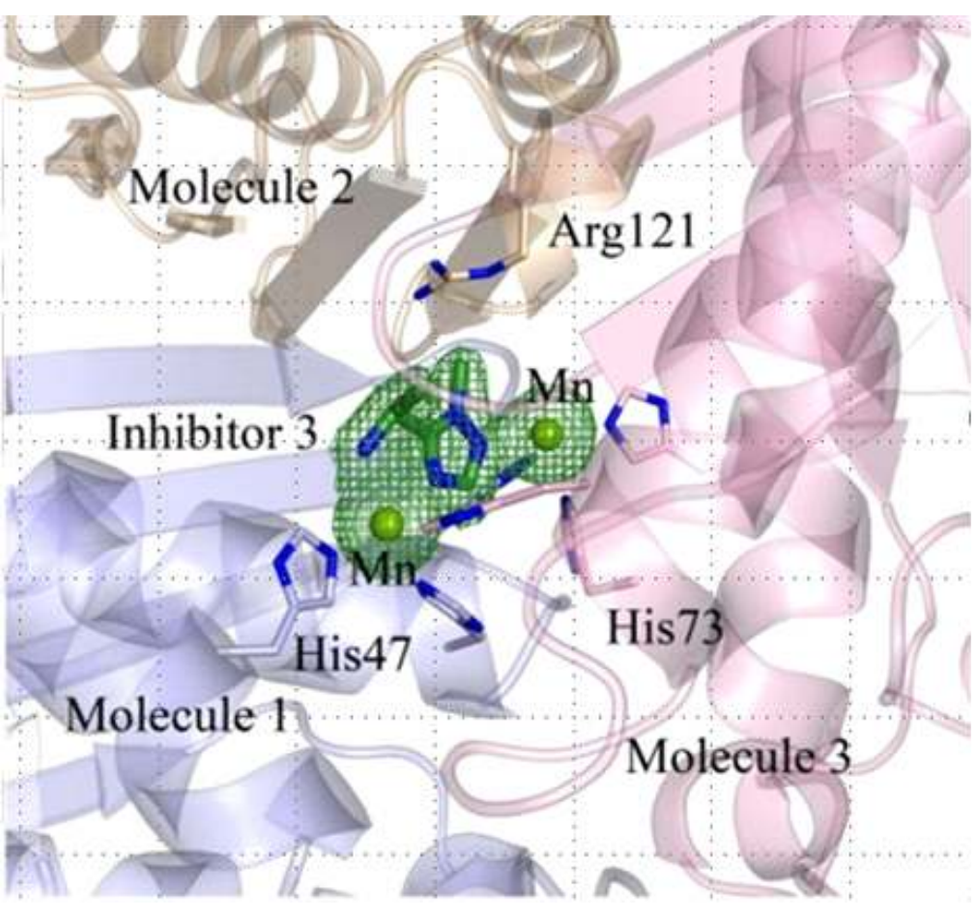

Figure 1. The difference Fourier |Fo| - |Fc| electron density map contour at the 3σ level for a molecule, Inhibitor 3, is shown in green with respective inhibitor in stick representation. Three subunits whose interface forms the active site are shown in violet, grey and pink colours. Also shown are the difference Fourier maps for two manganese atoms in the active site.

Publications

Original peer-reviewed articles

1. Kumar D, Jha B, Bhatia I, Ashraf A, Dwivedy A, Biswal BK* (2022) Characterization of a triazole scaffold compound as an inhibitor of *Mycobacterium tuberculosis* imidazoleglycerol-phosphate dehydratase. **Proteins**. 90:3-17. [*Corresponding author]

2. Dwivedy A, Mariadasse R, Ahmad M, Chakraborty S, Kar D, Tiwari S, Bhattacharya S, Sonar S, Mani S, Tailor P, Majumdar T*, Jeyakanthan J*, Biswal BK* (2021) Characterization of the NiRAN domain from RNA-dependent RNA polymerase provides insights into a potential therapeutic target against SARS-CoV-2. **PLoS Compt Biol**.doi:https://doi.org/10.1371/journal.pcbi.1009384. [*Corresponding authors]

3. Mariadasse R, Rajmichael R, Dwivedy A, Amala M, Ahmad M, Mutharasappan N, Biswal BK and Jeyakanthan J (2021) Characterization of putative transcriptional regulator (PH0140) and its distal homologue. **Cell Signal**.doi: 10.1016/j.cellsig.2021.110031.

Patent

1. Majumdar T, Biswal BK, Tailor P. Methods and compositions for treating viral diseases using combination of drugs. [US Patent Application Number: 17/241,130. Filed on 27.4.2021]

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.

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 use X-ray crystallography and related structural biological methods to study the PGK isoforms in *Leishmania spp*. Phosphoglycerate kinase (PGK) from *Leishmania spp.* which, exists in the cytoplasmic PGKB and glycosomal PGKC isoforms shows differences in biochemical properties. Computational analysis predicted the likelihood of a transmembrane helix only in the glycosomal isoform PGKC, of approximate length 20 residues in the 62-residue extension,ending at, arginine residues R471 and R472. From experimental studies using circular dichroism and NMR with deuterated sodium dodecyl sulfate, we find that the transmembrane helix spans residues 448 ± 2 -476 (Figure 1).

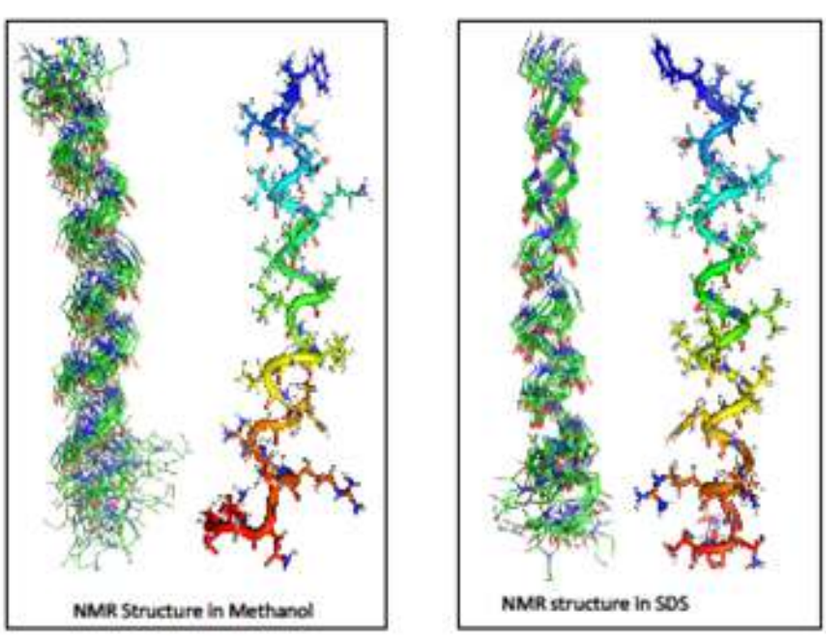

Figure 1

Further, we sought to establish the three-dimensional structure of PGKC_*Lmexicana* by homology modelling and biochemical data. We have a final theoretical 3-dimensional model of *L.Mexicana* PGKC (residues 1-479) that enables visualization of the GXXXG motif in the enzyme fold (Figure 2). While supporting our biochemical data, the docking interactions reveal new aspects of the tertiary fold of PGKC.

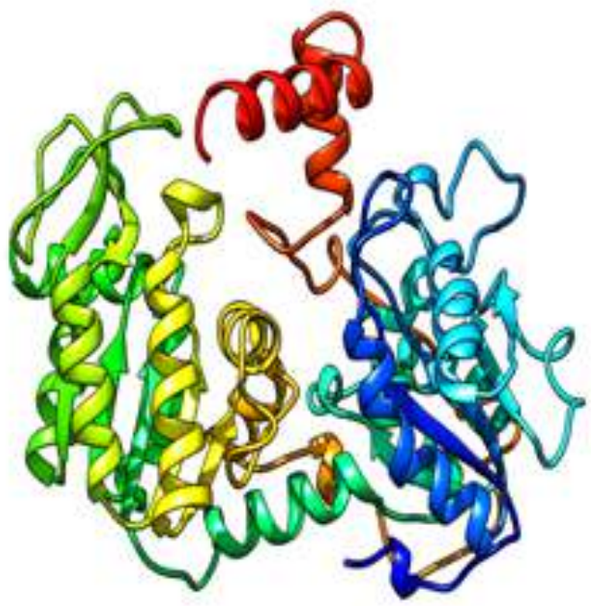

Figure 2

The helix which corresponds to TMS (Figure 1) is a discontinuous helix in the model shown in Figure 2. Furthermore, *GXXXG* motif such as is present in our case may have function in stabilizing the protein conformation given the sequence context such as the presence of neighboring β-branched residues. The hydrophobic patch that is formed by ^{462}LLIGIFIG^{469} may represent the localized epistatic interactions controlling the evolvability of PGKC. The perturbation leading to evolution of PGKC may be the drastic change in the environment of the protein, in this case the encapsulation in the glycosome. In the well-studied case of HIV-1 protease, epistatic interaction in mutation covariance cause high evolvability and drug resistance of the protease. The knowledge in this field is still scant and the exact role of epistatic pair-wise interactions or modularity on evolvability of function and robustness of a protein is not fully understood. We hypothesize a switch type of mechanism for the 63-mer between insertion into the membrane with the rest of PGKC in an open conformation to a closed conformation of PGKC_*Lmexicana* where the 63-mer stabilizes this conformation.

We are interested in the relevance of information theory (Shannon CE, 1948, Bell Sys Tech J, 27:379-423) used in developmental/ evolutionary/ genomics biology to protein folding. Coding in protein folding is symbolic but degenerate in that while one sequence does give one structure in the reverse similar folds can be generated from multiple sequences. The probabilistic nature of

protein structural code but not the sequence code is evident. The applications of this theory on protein structure/function evolution specifically in the case of PGK of *Leishmania* will be insightful. Residual entropy and shared entropy are unique to non-equilibrium probabilistic systems such as folded proteins, which serve as source of information for directing evolutionary changes of the structure. Information theory has application in evolution particularly with respect to mutations in proteins. RNA viruses like SARS-CoV-2 show high mutational rates which correlate with their infectivity.

Publication

Original peer reviewed article

1. Raghunathan V* (2021) How common is gain of function. **Acta Scientific Microbiology**. 4:30-34. [*Corresponding author]

GENETICS CELL SIGNALING AND CANCER BIOLOGY

Cellular and molecular biology of human cancer

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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.

Human clinical trials in cervical cancer patientsstageIIIb 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 are being followed till September 2022 before the codes will be broken.

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

Ovarian cancer is one of the most common gynaecologic cancers. Human clinical trials with dendritic cells primed with rSPAG9 protein in stage IV ovarian cancer were initiated in collaboration at Cancer Institute, Adyar, Chennai. Due to paucity of tumor lysate for trials, third arm of the trial was dropped and DCGI approval was obtained again on 22nd January 2022. All SOPs were standardized at NII and were transferred to Cancer Institute, Adyar, Chennai.

Publication

Original peer-reviewed article

1. Dhandapani H, Jayakumar H, Seetharaman A, Singh SS, Ganeshrajah S, Jagadish N, Suri A, Thangarajan R, Ramanathan P (2021) Dendritic cells matured with recombinant human sperm associated antigen 9 (rhSPAG9) induce CD4+, CD8+ T cells and activate NK cells: a potential candidate molecule for immunotherapy in cervical cancer. **Cancer Cell Int**.doi: 10.1186/s12935-021-01951-7.

Redox homeostasis in *Mycobacterium tuberculosis (Mtb)* is modulated by a novel actinomycetes-specific transcription factor

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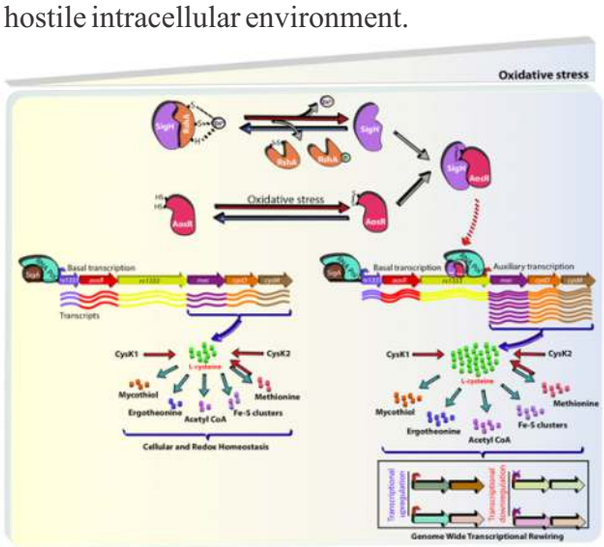
Mtb is an airborne pathogen that has co-evolved with its human host to establish the continual loop of inhalation, active to chronic infection, latency, dissemination to virtually any organ, and transmission to other individuals. *Mtb* has evolved diverse cellular processes in response to the multiple stresses it encounters within the infected host. We explored available TnSeq datasets to identify transcription factors (TFs) that are essential for *Mtb* survival inside the host. The analysis identified a single TF, Rv1332 (AosR), conserved across actinomycetes with a so-far uncharacterized function. AosR mitigates phagocyte-derived oxidative and nitrosative stress, thus promoting mycobacterial growth in the murine lungs and spleen. Oxidative stress induces formation of a single intra subunit disulphide bond in AosR, which in turn facilitates AosR interaction with an extracytoplasmic-function sigma factor, SigH. This leads to the specific upregulation of the CysM-dependent non-canonical cysteine biosynthesis pathway through an auxiliary intragenic stress-responsive promoter, an axis critical in detoxifying host-derived oxidative and nitrosative radicals. Failure to upregulate AosR-dependent cysteine biosynthesis during the redox stress causes differential expression of 6% of *Mtb* genes. Our study shows that the AosR-SigH pathway is critical for detoxifying host-derived oxidative and nitrosative radicals to enhance *Mtb* survival in the hostile intracellular environment.



Model depicting the proposed role of AosR during oxidative stress. In response to oxidative stress, SigH is liberated from its cognate anti-sigma factor (RshA) and an intramolecular disulfide bond is formed in the AosR. This subsequently results in oxidative stress-dependent interaction between AosR and SigH that together binds to an auxiliary promoter upstream of mec. Increased transcription of mec-cysO-cysM results in enhanced production of cysteine-derived antioxidant molecules. Increased production of cysteine through non-canonical cysteine biosynthesis protects mycobacteria cells from phagocyte-derived oxidative and nitrosative stress. Inhibition of this redox-regulatory circuit results in genome-wide transcription changes.

Publications

Original peer-reviewed articles

1. Khan MZ, Singha B, Ali MF, Taunk K, Rapole S, Gourinath S, Nandicoori VK* (2021) Redox homeostasis in *Mycobacterium tuberculosis* is modulated by a novel actinomycete-specific transcription factor. **EMBO J**.doi: 10.15252/embj.2020106111. [*Corresponding author]

2. Salini S, Bhat SG, Naz S, Natesh R, Kumar RA, Nandicoori VK, Kurthkoti K (2022) The error-prone polymerase DnaE2 mediates the evolution of antibiotic resistance in persister mycobacterial cells.**Antimicrob Agents Chemother**.doi: 10.1128/AAC.01773-21.

3. Gupta S, Mishra DK, Khan MZ, Saini V, Mehta D, Kumar S, Yadav A, Mitra M, Rani P, Singh M, Nandi CK, Das P, Ahuja V, Nandicoori VK, Bajaj A (2022) Development of a highly specific, selective, and sensitive fluorescent probe for detection of mycobacteria in human tissues. **Adv Healthc Mater**.doi: 10.1002/adhm.202102640.

4. Mlcochova P, Kemp SA, Dhar MS, Papa G, Meng B, Ferreira IATM, Datir R, Collier DA, Albecka A, Singh S, Pandey R, Brown J, Zhou J, Goonawardane N, Mishra S, Whittaker C, Mellan T, Marwal R, Datta M, Sengupta S, Ponnusamy K, Radhakrishnan VS, Abdullahi A, Charles O, Chattopadhyay P, Devi P, Caputo D, Peacock T, Wattal C, Goel N, Satwik A, Vaishya R, Agarwal M; Indian SARS-CoV-2 Genomics Consortium (INSACOG); Genotype to Phenotype Japan (G2P-Japan) Consortium; CITIID-NIHR BioResource COVID-19 Collaboration, Mavousian A, Lee JH, Bassi J, Silacci-Fegni C, Saliba C, Pinto D, Irie T, Yoshida I, Hamilton WL, Sato K, Bhatt S, Flaxman S, James LC, Corti D, Piccoli L, Barclay WS, Rakshit P, Agrawal A, Gupta RK (2021) SARS-CoV-2 B1.617.2 Delta variant replication and immune evasion. **Nature** 599:114-119.

5. Dhar MS, Marwal R, Vs R, Ponnusamy K, Jolly B, Bhoyar RC, Sardana V, Naushin S, Rophina M, Mellan TA, Mishra S, Whittaker C, Fatihi S, Datta M, Singh P, Sharma U, Ujjainiya R, Bhatheja N, Divakar MK, Singh MK, Imran M, Senthivel V, Maurya R, Jha N, Mehta P, A V, Sharma P, Vr A, Chaudhary U, Soni N, Thukral L, Flaxman S, Bhatt S, Pandey R, Dash D, Faruq M, Lall H, Gogia H, Madan P, Kulkarni S, Chauhan H, Sengupta S, Kabra S; Indian SARS-CoV-2 Genomics Consortium (INSACOG)‡, Gupta RK, Singh SK, Agrawal A, Rakshit P, Nandicoori V, Tallapaka KB, Sowpati DT, Thangaraj K, Bashyam MD, Dalal A, Sivasubbu S, Scaria V, Parida A, Raghav SK, Prasad P, Sarin A, Mayor S, Ramakrishnan U, Palakodeti D, Seshasayee ASN, Bhat M, Shouche Y, Pillai A, Dikid T, Das S, Maitra A, Chinnaswamy S, Biswas NK, Desai AS, Pattabiraman C, Manjunatha MV, Mani RS, Arunachal Udupi G, Abraham P, Atul PV, Cherian SS (2021) Genomic characterization and epidemiology of an emerging SARS-CoV2 variant in Delhi, India. **Science** 374:995-999.

6. Pal S, Soni V, Kumar S, Jha SK, Medatwal N, Rana K, Yadav P, Mehta D, Jain D, Sharma P, Kar R, Srivastava A, Patil VS, Dasgupta U, Nandicoori VK, Bajaj A (2021) A hydrogel-based implantable multidrug antitubercular formulation outperforms oral delivery. **Nanoscale**13:13225-13230.

7. Agarwal M, Soni V, Kumar S, Singha B, Nandicoori VK* (2021) Unique C-terminal extension and interactome of *Mycobacterium tuberculosis* GlmU impacts it's *in vivo* function and the survival of pathogen. **Biochem J**. 478:2081-2099. [*Corresponding author]

Determining the signaling and repair pathways that are altered in human cancer

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A DNA damage dependent miR signature can be a biomarker for detection of colon cancer

Colon cancer is one of the most common type of colon cancer – both in India and worldwide. According to the ICMR, it is the third most common cancer in men (663000 cases in 2014, 10.0% of all cancer cases) and the second most common in women (571000 cases in 2014, 9.4% of all cancer cases). In hospitals, patients with colon cancer are still detected either by CT colonography and colonoscopy or by immunohistochemistry which checks for the loss or gain of expression of certain proteins during colon cancer. Colon cancer recurrence is still detected only using the PET scans.

It has been now discovered that there are six microRNAs (which were named DNA damage sensitive microRNAs or DDSMs) which gets upregulated only in colon cancer cells. In the colon cancer cells the levels of the DDSMs depend on a single master regulator protein, named CDX2. Importantly the upregulated DDSMs target a group of cellular proteins which are essential to maintain the pristine name of our genetic material within each cell of our body. Hence due to the loss of these genome stabilizers, the cells have greater tendency to form cancers, as was shown in experiments = using mice models. Studies also provided definitive clues why in normal cells the levels DDSMs are low, which happens due to the repression of CDX2.

Expression analysis of the DDSMs was also done on publicly available datasets in The Cancer Genome Atlas (TCGA) and also in a cohort of colon cancer patients who had come to AIIMS, New Delhi for treatment. This involved 410 patient information present in TCGA and the biopsy materials of 54 patients from AIIMS, New Delhi. It was found that the DDSMs were all

upregulated even in Stage I colon cancer tissues and not in the surrounding normal tissues. The upregulation of the DDSMs persisted upto the final Stage IV colon cancer. More importantly increased expression of the DDSMs in the cancer patients decreased the probability of their survival. Hence it is believed that the identified DDSMs can serve as an invaluable biomarker for colon cancer early detection process.

Publications

Original peer-reviewed articles

1. Priya S, Kaur E, Kulshrestha S, Pandit A, Gross I, Kumar N, Agarwal H, Khan A, Shyam R, Bhagat P, Prabhu JS, Nagarajan P, Deo SVS, Bajaj A, Freund JN, Mukhopadhyay A, Sengupta S* (2021) CDX2 inducible microRNAs sustain colon cancer by targeting multiple DNA damage response pathway factors. **J Cell Sci**.doi: 10.1242/jcs.258601. [*Corresponding author]

2. Sreekanth V,Pal S,Kumar S,Komalla V,Yadav P,Shyam R,Sengupta S,Bajaj A (2021)Self-assembled supramolecular nanomicelles from bile acid-docetaxel conjugate are highly tolerable with improved therapeutic efficacy. **Biomater Sci**. 9: 5626-5639.

Patent

1. Sengupta S. DNA damage dependent microRNA signature for cancers, methods and uses related thereto. [PCT Application Number: PCT/IN2020/050776. Filed on 30.12.2021]

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

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Nuclear processes depend on dynamic interactions between *cis* acting regulatory elements and *trans*-acting factors and are intricately regulated by chromatin structure and organization. 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, a DNA binding protein with multifunctional attributes, is an important contributor to higher order chromatin organization. Previous analysis in the lab suggests that some of these may be important for establishment of recombination center (RC) while others, interspersed amongst V gene segments, might be important for bringing V segments in proximity of RC for VDJ recombination. Further, it suggested that chromatin extrusion shapes the chromatin loop organization conducive for VDJ recombination. We are currently investigating these aspects to delineate the role of CTCF in the regulation of *TCRb* locus.

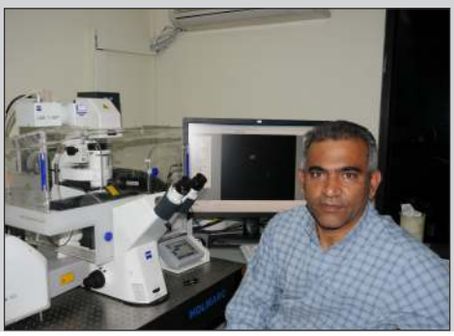
Mechanisms underlying enhancer activity

Although well established to regulate chromatin accessibility necessary for transcription, additional roles of enhancers in large scale chromosomal reorganization remain elusive Our analysis in developing lymphocytes and utilizing *CRISPR/Cas9* mutagenesis of *TCRb* locus demonstrated that enhancer Eb of *TCRb* locus is not important for influencing the intra-nuclear radial position or locus contraction but is critically required for repositioning of *TCRb* locus away from bulk of chromosome 6 territory which may facilitate VDJ recombination. Such 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.

Publication

Original peer-reviewed article

1. Yadav M, Jalan M, Srivastava M* (2022) Enhancer dependent repositioning of TCRb locus with respect to chromosome territory. **J Mol Biol**.doi: 10.1016/j.jmb.2022.167509. [*Corresponding author]



Role of cell signaling in eukaryotic development

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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:

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

a. Dual role of a putative VPS15-like kinase in Toxoplasma gondii

PI3P generation in most eukaryotes depends on class III PI3-Kinase, which in turn is regulated by a pseudokinase VPS15. Detailed studies were performed to elucidate the function of TgVPS15, a VPS15 orthologue, in *Toxoplasma gondii*.

We found that TgVPS15 has a dual function: it regulates apicoplast biogenesis during parasite intracellular development in steady state and under nutrient limiting conditions it regulates autophagy. For both these processes, its ability to promote PI3P formation, most likely via PI3-kinase VPS34, is critical. Even though TgVPS15 has features of pseudokinase, we found two residues in its kinase domain that were critical for its parasitic functions.

b. Dissection of the role of protein kinase PK2 in Plasmodium falciparum development

Plasmodium falciparum Protein kinase 2 (PfPK2) is indispensable for the growth of malaria parasite and is suggested to be a putative effector of calcium/calmodulin. Our recent studies suggested that PfPK2 may regulate host erythrocyte invasion as well as parasite maturation inside the host erythrocytes. We have performed quantitative phosphoproteomic studies to identify PfPK2 targets in the parasite to gain insights into the mechanism via which this kinase regulates invasion.

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

We found a role of miRNA miR-449a and miR16-5-p that are expressed at lower levels in neurons from mouse model for Alzheimer's Disease (AD). Our recent studies suggested that these miRNA promote neuronal differentiation by suppressing the neuronal cell cycle. The loss of their expression resulted in aberrant activation of the cell cycle leading to apoptosis. miR-449a may prevent CRNA by targeting cyclin D1 and CDC25 A. Interestingly, overexpression of miR-449a by using lentivirus in AD mouse model significantly reverted the defects in learning and memory.

Publication

Original peer reviewed article

1. Maurya R, Tripathi A, Kumar M, Antil N, Yamaryo-Botté Y, Kumar P, Bansal P, Doerig C, Botté CY, Prasad TSK, Sharma P* (2021) PI4-kinase and PfCDPK7 signaling regulate phospholipid biosynthesis in *Plasmodium falciparum*. **EMBO Rep**.doi: 10.15252/embr.202154022. [#Equal contribution; $Equal contribution; *Corresponding author]

The role of tumor suppressors in stress response

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The focus of the lab is to understand the function and regulation of tumor suppressors. Here, we report the work carried out on two proteins viz. PRAMEF2 and HDAC5 which determine tumorigenesis.

Unravelling the role of PRAMEF2 in tumorigenesis

PRAMEF2 belongs to the PRAME multigene family of cancer testis antigens, which serve as biomarkers for several cancers. However, the molecular mechanisms underlying its role in tumorigenesis remain unexplored. We have now established PRAMEF2 as a component of a Cullin 2-based E3 ligase complex. PRAMEF2 mediates polyubiquitylation of LATS1 kinase of the Hippo/YAP pathway. LATS1 degradation promotes enhanced nuclear accumulation of the transcriptional coactivator YAP, resulting in increased expression of proliferative and metastatic genes. These findings highlight the pivotal role of PRAMEF2 in tumorigenesis and provide novel mechanistic insight into YAP regulation.

Understanding the role of HDAC5 in transcriptional dysregulation during malignant transformation

Altered expression of HDAC5 has been linked to tumorigenesis.Limited non-histone substrate repertoire of HDAC5 restricts the understanding of its role as transcriptional regulator.Using proteomics approaches, we have now identified SATB1 as a novel substrate of HDAC5. We plan to delineatethe role of HDAC5-SATB1 axis in determining the expression transcription of genes involved in cancer-associated pathways.

Publications

Original peer-reviewed articles

1. Ghosh M ,Das S*(2021) PRAMEF2-mediated dynamic regulation of YAP signaling promotes tumorigenesis. **Proc Natl Acad Sci USA**doi: 10.1073/pnas.2105523118. [*Corresponding author]

2. Priyanka P, Sharma M, Das S and Saxena S (2021) The lncRNA HMS recruits RNA binding protein HuR to stabilize the 3'-UTR of *HOXC10* mRNA. **J Biol Chem**. doi: 10.1016/j.jbc.2021.100997.

3. Gupta A, Vats A, Ghosal A, Mandal K, Sarkar R, Bhattacharya I, Das S, Pal R, Majumdar SS (2022) Follicle-stimulating hormone-mediated decline in miR-92a-3p expression in pubertal mice Sertoli cells is crucial for germ cell differentiation and fertility. **Cell Mol Life Sci**.doi: 10.1007/s00018-022-04174-9.

4. Priyanka P, Sharma M, Das S and Saxena S (2022) E2F1-induced lncRNA, *EMSLR* regulates lncRNA *LncPRESS1*. **Sci Rep**.doi: 10.1038/s41598-022-06154-2.

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

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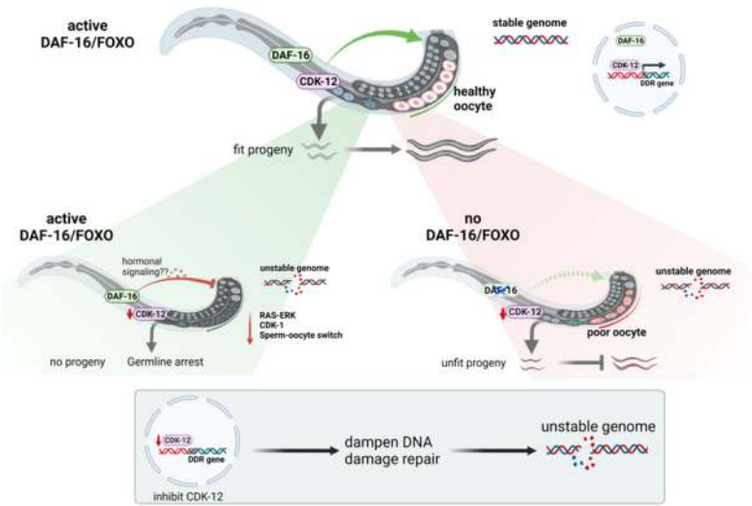
We use a combination of molecular genetics and genomics in *Caenorhabditis elegans* to reveal molecular basis of aging and age-related diseases. We are studying pro-longevity dietary interventions with health benefits. We are also interested in understanding how DNA damage in somatic cells regulate germline development and reproductive aging. Further, we are repurposing FDA-approved drugs to treat diabetes-related complications.

We showed that CDK-12 plays a pivotal role in the repair of damaged DNA. Therefore, knocking down *cdk-12* may lead to genomic instability that is sensed by activated DAF-16 in the *daf-2(-),* leading to germline arrest at pachytene stage of meiosis. Our other data support a role of DAF-16 in regulating DNA damage repair during lowered IIS, thereby promoting resistance to DNA damage, supporting growth and reproduction.

By genetically or pharmacologically manipulating the Phosphatidylcholine (PC) levels in *flr-4(-),* we showed that lower PC levels activate the p38 MAPK pathway. We also found that the B12 mechanism II may modulate PC levels through transcriptional modulation of PEMT/PMT-2 in the *flr-4(-)* grown on a B12-rich diet, thereby activating p38-MAPK pathway, increasing downstream CyTP gene expression, stress tolerance and life span.

Rifampicin-quinone (RIF-Q) that has 2-times less antibiotic activity than rifampicin, retained potent anti-glycating activity *in vitro*. The shortened life span of *C. elegans* grown on 2% glucose was increased on RIF-Q supplementation. RIF-Q treatment also improved glucose homeostasis under hyperglycemic conditions in *db/db* mice. Further experiments showed that RIF-Q treatment reduces diabetic nephropathy without causing hepatoxicity and major weight alterations.



Publications

Original peer-reviewed articles

1. Nair T, Chakraborty R, Singh P, Rahman SS, Bhaskar AK, Sengupta S and Mukhopadhyay A* (2021) Adaptive capacity to dietary Vitamin B12 levels is maintained by a gene-diet interaction that ensures optimal life span. **Aging Cell** doi: https://doi.org/10.1111/acel.13518). [*Corresponding author]

2. Kaushik N, Rastogi S, Verma S, Pandey D, Halder A, Mukhopadhyay A and Kumar N (2021) Transcriptome analysis of insulin signaling-associated transcription factors in *C. elegans* reveal their genome-wide target gene specificity and complexity. **Int J Mol Sci**. doi:https://doi.org/10.3390/ijms222212462.

3. Priya S, Kaur E, Kulshrestha S, Pandit A, Gross I, Kumar N, Agarwal H, Khan A, Shyam S, Bhagat P, Prabhu JS, Nagarajan P, Deo SVS, Bajaj A, Freund J-N, Mukhopadhyay A, Sengupta S (2021) CDX2 inducible microRNAs sustain colon cancer by targeting multiple DNA damage response pathway factors. **J Cell Sci**. doi: https://doi.org/10.1242/jcs.258601.

Role of metabolism-mediated gene regulation in development and disease

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Regulation of protein homeostasis and energy metabolism in skeletal muscles is intertwined: increased availability of nutrients tend to increase protein synthesis while a deficit in energy levels leads to increased protein degradation. Amino acids generated by protein degradation in turn contribute to energy homeostasis. Though disruption of this cross talk is observed in several diseases, the mechanisms by which these processes regulate each other at cellular and organismic level are not fully understood. Our research focuses on understanding various mechanisms by which micronutrients and macronutrients connect protein homeostasis and energy metabolism.

Vitamin D is a micronutrient well known to affect skeletal muscle, an organ that regulated systemic protein homeostasis, but the mechanisms by which vitamin D promotes muscle strength is not well known. Our study had shown that vitamin D is essential for skeletal muscles to utilize glucose as energy source; mice that lack vitamin D receptor shift the muscle metabolism to fatty acid oxidation. The underlying defect that causes this change is the accumulation of glycogen in the skeletal muscles, which is not available for energy production. The systemic energy deprivation that ensues as a result of this defect causes increased proteolysis and atrophy in skeletal muscles of VDRKO mice.

Publication

Original peer-reviewed article

1. Das A, Gopinath SD*, Arimbasseri GA* (2022) Systemic ablation of vitamin D receptor leads to skeletal muscle glycogen storage disorder in mice. **J Cachexia Sarcopenia Muscle** 13: 467-480. [*Corresponding authors]

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

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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. Developing bacteria/microbiota-based adjuvant *Immune checkpoint blockade (ICB)* therapy for treating the solid cancer (colorectal cancer) is another focus of the laboratory. Development of Aptamer/MIP based sensor/biosensor for detection of gut bacteria and their metabolites is also going-on in the laboratory.

Gut microbiota derived-metabolite indoxyl sulfate (IS) has deleterious effect on colonic epithelial cells

Present study dealt with the genotoxic and cytotoxic effect of indoxyl sulfate (IS) on human epithelial adenocarcinoma cell lines i.e., HCT-116 and HT-29. All tested subjects showed significant decrease in cell viability, cellular ATP content in time and dose dependent fashion and 10mM concentration of IS at 72hrs proved most cytotoxic to cells. IS also caused G2/M cell cycle arrest in concentration dependent manner and found most cytotoxic at 10mM (Figure 1).

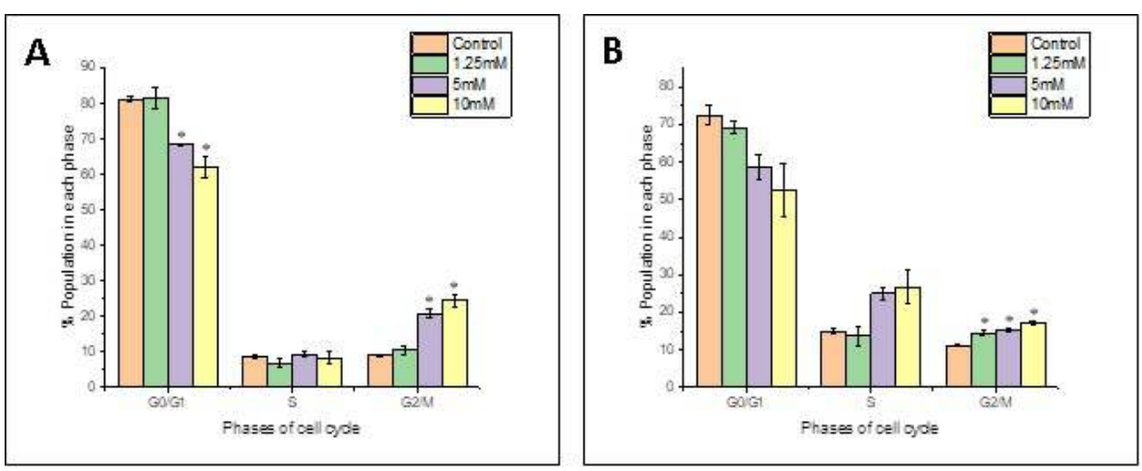

Figure 1. Effect of indoxyl sulfate on cell cycle progression of HCT-116 (A) and HT-29 (B)

Development of sensor for detecting gut microbiota derived Trimethylamine (TMA)

The early detection of TMA in bodily fluids is believed to be crucial in extrapolating thepathophysiology and treatment of a variety of disorders. With a sensitivity of 2.47 A mL ppm -1 cm -2, the MIP-based sensor was developed with a dynamic detection range of 1–15 ppm. The new sensor is simple to build and use and it can detect TMA in human fluids like urine with great precision.

Publication

Original peer-reviewed articles

1. Mohan A, Girdhar M, Kumar R, Chaturvedi HS, Vadhel A, Solanki P, Kumar A, Kumar D, Mamidi N (2021) Polyhydroxy butyrate-based nanocomposites for bone tissue engineering. **Pharmaceuticals**. doi:10.3390/ph14111163.

Reviews

1. Verma D, Yadav AK, Chaudhary N, Mukherjee MD, Kumar P, Kumar A*, Solanki PR (2021) Recent advances in understanding SARS-CoV-2 infection and updates on potential diagnostic and therapeutics for COVID-19. **Coronaviruses** doi: 10.2174/2666796703666220302143102. [*Corresponding author].

2. Yadav AK, Verma D, Chaudhary N, Kumar A, Solanki PR (2021) Aptamer based switches: A futuristic approach in *H. pylori* detection. **Materials Letters** doi: 10.1016/j.matlet.2021.131239.

Nanotechnology-based immunotherapeutic platform for cancer

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We are working on the development of nano-immunotherapeutics for reprogramming immune cells to induce sustainable anti-tumor immune responses. We formulate the nano-delivery platform to empower professional antigen-presenting cells (APCs) to process and present the tumor-associated antigen (TAA) in the context of the class-I/II major histocompatibility complex (MHC). Additionally, we design the nano-delivery platform for re-calibrating the proteostasis in the tumor cells to promote the presentation of peptides derived from the TAA in the context of class I MHC. These approaches have the potential to elicit anti-tumor immune responses through cytotoxic T-cell and T-helper cell activation and expansion. However, because of the complex tumor inhibitory mechanisms, the sustainability of T-cells responses is heavily compromised. To overcome this challenge, we are formulating nano-scale artificial APCs capable of displaying tumor-specific peptide-MHCs and co-stimulatory molecules. We have optimized the chemical synthesis of different types of gold (such as gold nano-sphere and gold-nanorod), iron oxide, silica, and mesoporous silica nanoparticles. Additionally, we have generated the Chinese hamster ovary-Suspension (CHO-S) cell clone capable of expressing Ova(257-264)-K^b class-I MHC. We will investigate key parameters such as molecular density, flexibility, and directional presentation of coated tumor-specific p-MHC and co-stimulatory molecules that govern the functionalities of nano-scale artificial APCs to induce anti-tumor T-cells responses.

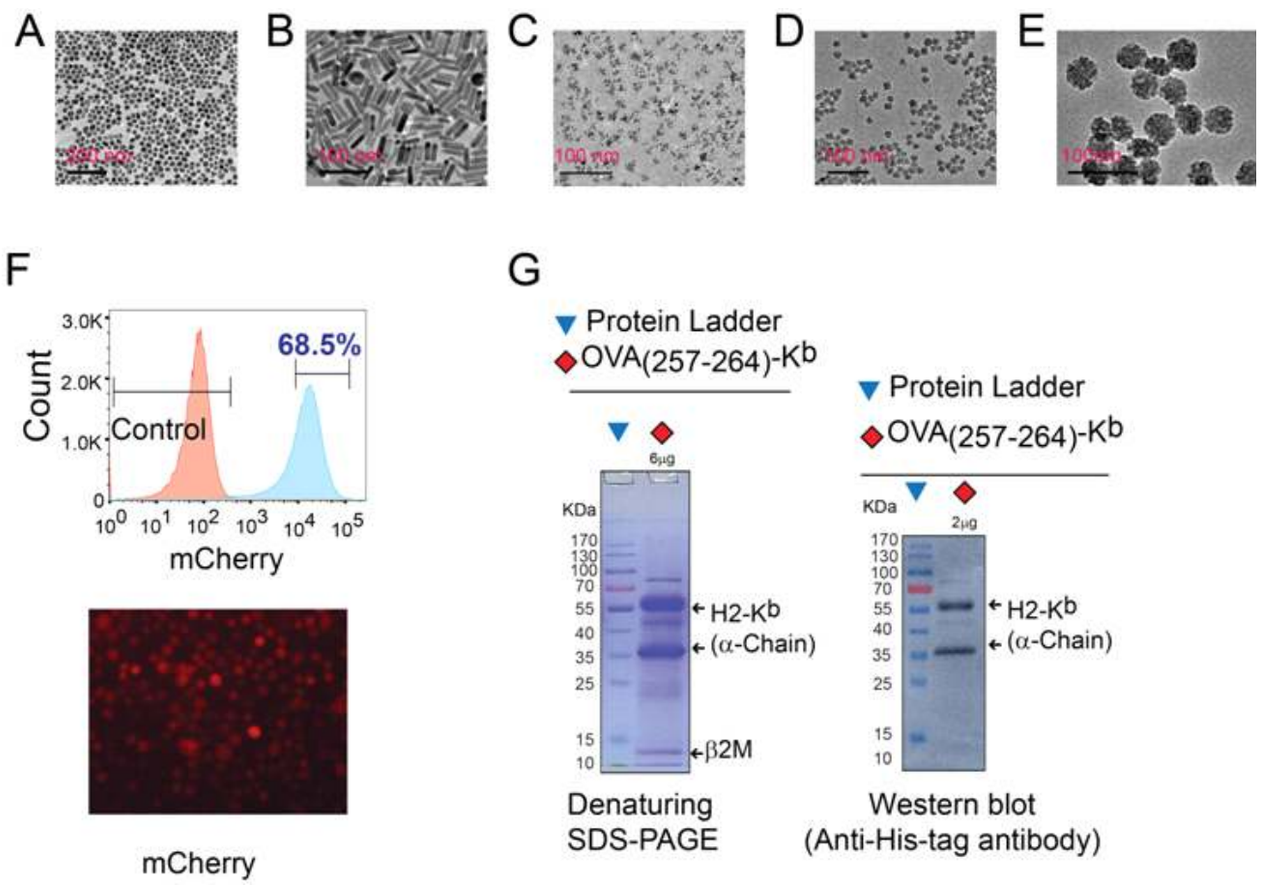

Figure legend

Chemical synthesis of nanoparticles and tumor-specific peptide-MHC production: Representative transmission electron microscopic images of A) gold nano-sphere B) gold nano-rod C) Iron-oxide nanoparticle D) silica nanoparticle E) mesoporous silica particle. F) Histogram profile (Top) and fluorescence microscopic image (bottom) of FACS-sorted Ova(257-264)-K^b CHO-S cells. G) Denaturing SDS PAGE (left) and western blot (right) of purified Ova(257-264)-K^b MHC.

PUBLICATIONS AND PATENTS

1. Agarwal M, Soni V, Kumar S, Singha B, Nandicoori VK*(2021) Unique C-terminal extension and interactome of *Mycobacterium tuberculosis* GlmU impacts it's *in vivo* function and the survival of pathogen. **Biochem J.** 478: 2081-2099.
2. Agarwal M, Gupta C, Mohan KV, Upadhyay PK, Dhawan A, Jha V (2021) Adjunctive intravitreal anti-vascular endothelial growth factor and moxifloxacin therapy in management of intraocular tubercular granulomas. **Ocul Immunol Inflamm.** doi: 10.1080/09273948.2021.2002367.
3. Ahuja R, Shelly A, Meena J, Panda AK* (2022) Microparticles entrapping pneumococcal protein SP0845 show improved immunogenicity and temperature stability. **Int J Biol Macromol.** 203: 661-670.
4. Ali A, Kumar V, Banerjea AC* (2021) STUB1/CHIP promotes ubiquitination and degradation of HIV-1 Vif to restore the cellular level of APOBEC3G protein. **Biochem Biophys Res Commun.** 574:27-32.
5. Arya RP, Lahon A, Patel AK(2021) Dengue virus induces interferon-β by activating RNA sensing pathways in megakaryocytes. **Immunol Lett.** 236:31-36.
6. Bhattacharya I, Sharma SS, Sarkar H, Gupta A, Pradhan BS, Majumdar SS*(2021) FSH mediated cAMP signalling upregulates the expression of Gα subunits in pubertal rat Sertoli cells. **Biochem Biophys Res Commun.** 569:100-105.
7. Chawla M, Mukherjee T, Deka A, Chatterjee B, Sarkar UA, Singh AK, Kedia S, Lum J, Dhillon MK, Banoth B, Biswas SK, Ahuja V, Basak S*(2021) An epithelial Nfkb2 pathway exacerbates intestinal inflammation by supplementing latent RelA dimers to the canonical NF-κB module. **Proc Natl Acad Sci USA.** doi: 10.1073/pnas.2024828118.
8. Chauhan D, Sri S, Kumar R, Panda AK, Solanki PR (2021) Evaluation of size, shape, and charge effect on the biological interaction and cellular uptake of cerium oxide nanostructures. **Nanotechnology.** doi: 10.1088/1361-6528/ac03d5.
9. Chauhan KS, Das A, Jaiswal H, Saha I, Kaushik M, Patel VK, Tailor P* (2022) IRF8 and BATF3 interaction enhances the cDC1 specific Pfkfb3 gene expression. **Cell Immunol.** 371:104468. doi:.1016/j.cellimm. 2021.104468.
10. Chauhan S, Rathore DK, Sachan S, Lacroix-Desmazes S, Gupta N, Awasthi A, Vrati S, Kalia M (2021) Japanese Encephalitis Virus Infected Human Monocyte-Derived Dendritic Cells Activate a Transcriptional Network Leading to an Antiviral Inflammatory Response. **Front Immunol.** doi: 10.3389/fimmu.2021.638694.
11. Das A, Gopinath SD, Arimbasseri GA* (2022) Systemic ablation of vitamin D receptor leads to skeletal muscle glycogen storage disorder in mice. **J Cachexia Sarcopenia Muscle.** 13: 467-480.
12. Das A, Chauhan KS, Kumar H, Tailor P* (2021) Mutation in Irf8 gene (Irf8R294C) impairs Type I IFN-mediated antiviral immune response by murine pDCs. **Front Immunol.** doi: 10.3389/fimmu.2021.758190.

13. Das S, SahaT, Shaha C (2021) Tissue / biofluid specific molecular cartography of *Leishmania donovani* infected BALB/c mice: deciphering systemic reprogramming. **Front Cell Infect Microbiol**. doi: 10.3389/fcimb.2021.694470

14. Dhar MS, Marwal R, Vs R, Ponnusamy K, Jolly B, Bhoyar RC, Sardana V, Naushin S, Rophina M, Mellan TA, Mishra S, Whittaker C, Fatihi S, Datta M, Singh P, Sharma U, Ujjainiya R, Bhatheja N, Divakar MK, Singh MK, Imran M, Senthivel V, Maurya R, Jha N, Mehta P, A V, Sharma P, Vr A, Chaudhary U, Soni N, Thukral L, Flaxman S, Bhatt S, Pandey R, Dash D, Faruq M, Lall H, Gogia H, Madan P, Kulkarni S, Chauhan H, Sengupta S, Kabra S; Indian SARS-CoV-2 Genomics Consortium (INSACOG)‡, Gupta RK, Singh SK, Agrawal A, Rakshit P, Nandicoori V, Tallapaka KB, Sowpati DT, Thangaraj K, Bashyam MD, Dalal A, Sivasubbu S, Scaria V, Parida A, Raghav SK, Prasad P, Sarin A, Mayor S, Ramakrishnan U, Palakodeti D, Seshasayee ASN, Bhat M, Shouche Y, Pillai A, Dikid T, Das S, Maitra A, Chinnaswamy S, Biswas NK, Desai AS, Pattabiraman C, Manjunatha MV, Mani RS, Arunachal Udupi G, Abraham P, Atul PV, Cherian SS (2021) Genomic characterization and epidemiology of an emerging SARS-CoV2 variant in Delhi, India. **Science.** 374:995-999.

15. Dutta D, Santhanam SK, Parween F, Ismaeel S, Qadri A*(2021) Membrane prohibitin forms a dynamic complex with p56lck to regulate T cell receptor signaling. **Immunol Lett.** 241:49-54.

16. Dhandapani H, Jayakumar H, Seetharaman A, Singh SS, Ganeshrajah S, Jagadish N, Suri A,Thangarajan R, Ramanathan P (2021) Dendritic cells matured with recombinant human sperm associated antigen 9 (rhSPAG9) induce CD4+, CD8+ T cells and activate NK cells: a potential candidate molecule for immunotherapy in cervical cancer. **Cancer Cell Int.** doi: 10.1186/s12935-021-01951-7.

17. Dwivedy A, Mariadasse R, Ahmad M, Chakraborty S, Kar D, Tiwari S, Bhattacharyya S, Sonar S, Mani S, Tailor P, Majumdar T*, Jeyakanthan J*, Biswal BK*(2021) Characterization of the NiRAN domain from RNA-dependent RNA polymerase provides insights into a potential therapeutic target against SARS-CoV-2. **PLoS Comput Biol.** doi:10.1371/ journal. pcbi.1009384.

18. Equbal Z*, Baligar PN, Srivastava M, Mukhopadhyay A* (2021) A two-stage process for differentiation of wharton's jelly-derived mesenchymal stem cells into neuronal-like cells. **Stem Cells Int.** doi: 10.1155/2021/6631651.

19. Garima, Prem R, Yadav U, Sundd M* (2021) A GX2GX3G motif facilitates acyl chain sequestration by *Saccharomyces cerevisiae* acyl carrier protein. **J Biol Chem.** doi: 10.1016/j.jbc.2021.101394.

20. Ghosh M, Das S*(2021) PRAMEF2-mediated dynamic regulation of YAP signaling promotes tumorigenesis. **Proc Natl Acad Sci USA.** doi: 10.1073/ pnas. 2105523118.

21. Gupta A, Mandal K, Singh P, Sarkar R, Majumdar SS*(2021) Declining levels of miR-382-3p at puberty trigger the onset of spermatogenesis. **Mol Ther Nucleic Acids.** 26:192-207.

22. Gupta A, Vats A, Ghosal A, Mandal K, Sarkar R, Bhattacharya I, Das S, Pal R, Majumdar SS*(2022) Follicle-stimulating hormone-mediated decline in miR-92a-3p expression in pubertal mice Sertoli cells is crucial for germ cell differentiation and fertility. **Cell Mol Life Sci.** doi: 10.1007/s00018-022-04174-9.

23. Gupta S, Mishra D, Khan MZ, Saini V, Mehta D, Kumar S, Yadav A, Mitra M, Rani P, Singh M, Nandi CK, Das P, Ahuja V, Nandicoori VK, Bajaj A(2022) Development of a highly specific, selective, and sensitive fluorescent probe for detection of mycobacteria in human tissues. **Adv Healthc Mater.** doi: 10.1002/ adhm.202102640.

24. Gupta SK*, Toor S, Minhas V, Chaudhary P, Raman M, Anoop S, Panda AK*(2022) Contraceptive efficacy of recombinant porcine zona proteins and fusion protein encompassing canine ZP3 fragment and GnRH in female beagle dogs. **Am J Reprod Immunol.** doi: 10.1111/aji.13536.

25. Hakiem OR, Batra JK* (2021) Role of HrcA in stress management in *Mycobacterium tuberculosis.* **J Appl Micro Biol.** 132: 3315-3326.

26. Ismaeel S, Qadri A*(2021) ATP release drives inflammation with lysophosphatidyl-choline. **Immuno Horizons.** 5:219-233.

27. Kalia I, Anand R, Quadiri A, Bhattacharya S, Sahoo B, Singh AP* (2021) *Plasmodium berghei*-Released Factor, PbTIP, modulates the host innate immune responses **Front Immunol.** doi: 10.3389/fimmu.2021. 699887.

28. Kashif M, Quadiri A, Singh AP* (2021) Essential role of a *Plasmodium berghei* heat shock protein (PBANKA_0938300) in gametocyte development. **Sci Rep.** doi: 10.1038/s41598-021-03059-4.

29. Kaushik N, Rastogi S, Verma S, Pandey D, Halder A, Mukhopadhyay A, Kumar N. (2021) Transcriptome analysis of insulin signaling-associated transcription factors in *C. elegans* reveal their genome-wide target genes specificity and complexity. **Int J Mol Sci.** doi: 10.3390/ijms222212462.

30. Khan MZ, Singha B, Ali MF, Taunk K, Rapole S, Gourinath S, Nandicoori VK* (2021) Redox homeostasis in *Mycobacterium tuberculosis* is modulated by a novel actinomycete-specific transcription factor. **EMBO J.** doi: 10.15252/embj. 2020106111.

31. Kumar D, Jha B, Bhatia I, Ashraf A, Dwivedy A, Biswal BK* (2021) Characterization of a triazole scaffold compound as an inhibitor of *Mycobacterium tuberculosis* midazoleglycerol -phosphate dehydratase. **Proteins.** 90: 3-17.

32. Kumar GS*, Page R, Peti W (2021) ^{1}H, ^{15}N and ^{13}C sequence specific backbone assignment of the MAP kinase binding domain of the dual specificity phosphatase 1 and its interaction with the MAPK p38. **Biomol NMR Assign.** 15: 243-248.

33. Kumar S, Pal S, Thakur J, Rani P, Rana K, Kar A, Kar R, Mehta D, Jha SK, Pradhan MK, Jain D, Rajput K, Mishra S, Ganguli M, Srivastava A, Dasgupta U, Patil VS, Bajaj A (2021) Nonimmunogenic hydrogel-mediated delivery of antibiotics outperforms clinically used formulations in mitigating wound infections. **ACS Appl Mater Interfaces.** 13:44041-44053.

34. Kumar P, Mohanty D*(2021) Development of a novel pharmacophore model guided by the ensemble of waters and small molecule fragments bound to SARS-COV-2 main protease. **Mol Inform.** doi: 10.1002/ minf.202100178.

35. Kumari V, Prasad KM, Kalia I, Sindhu G, Dixit R, Rawat DS, Singh OP, Singh AP, Pandey KC(2022) Dissecting the role of *Plasmodium Metacaspase*-2 in malaria gametogenesis and sporogony. **Emerg Microbes Infect.** 11: 938-955.

36. Kumari V, Pandey R, Srinivasan E, Kalia I, Singh AP, Saxena AK, Rajaekaran R, Gupta D, Pandey KC (2021) *P. falciparum metacaspase*-2 capture its natural substrate in a non-canonical way. **J Biochem.** doi:https:// doi.org/10.1093/jb/mvab086.

37. Lahon A, Arya RP, Banerjea AC*(2021) Dengue virus dysregulates master transcription factors and PI3K/AKT/mTOR signaling pathway in megakaryocytes. **Front Cell Infect Microbiol.** doi: 10.3389/ fcimb.2021.715208.

38. Mariadasse R, Rajmichael R, Dwivedy A, Amala M, Ahmad M, Mutharasappan N, Biswal BK, Jeyakanthan J (2021) Characterization of putative transcriptional regulator (PH0140) and its distal homologue. **Cell Signal.** doi: 10.1016/j.cell Signal. 2021.110031.

39. Maurya R, Tripathi A, Kumar M, Antil N, Yamaryo-Botté Y, Kumar P, Bansal P, Doerig C, Botté CY, Prasad TSK, Sharma P* (2021) PI4-kinase and PfCDPK7 signaling regulate phospholipid biosynthesis in *Plasmodium falciparum*. **EMBO Rep.** doi: 10.15252/embr.202154022.

40. Meena VK, Kumar V, Karalia S, Garima, Sundd M* (2021) Ellagic acid modulates uninduced as well as mutation and metal-induced aggregation of α-synuclein: implications for Parkinson's disease. **ACS Chem Neurosci.** 12:3598-3614.

41. Meena J, Goswami DG, Anish C, Panda AK* (2021) Cellular uptake of polylactide particles induces size dependent cytoskeletal remodeling in antigen presenting cells. **Biomater Sci.** doi: 10.1039/d1bm01312b.

42. Mehdiratta K, Singh S, Sharma S, Bhosale RS, Choudhury R, Masal DP, Manocha A, Dhamale BD, Khan N, Asokachandran V, Sharma P, Ikeh M, Brown AC, Parish T, Ojha AK, Michael JS, Faruq M, Medigeshi GR, Mohanty D, Reddy DS, Natarajan VT, Kamat SS, Gokhale RS*(2022) Kupyaphores are zinc homeostatic metallophores required for colonization of *Mycobacterium tuberculosis*. **Proc Natl Acad Sci USA.** doi: 10.1073/pnas.2110293119.

43. Mlcochova P, Kemp SA, Dhar MS, Papa G, Meng B, Ferreira IATM, Datir R, Collier DA, Albecka A, Singh S, Pandey R, Brown J, Zhou J, Goonawardane N, Mishra S, Whittaker C, Mellan T, Marwal R, Datta M, Sengupta S, Ponnusamy K, Radhakrishnan VS, Abdullahi A, Charles O, Chattopadhyay P, Devi P, Caputo D, Peacock T, Wattal C, Goel N, Satwik A, Vaishya R, Agarwal M; Indian SARS-CoV-2 Genomics Consortium (INSACOG); Genotype to Phenotype Japan (G2P-Japan) Consortium; CITIID-NIHR Bio-Resource COVID-19 Collaboration, Mavousian A, Lee JH, Bassi J, Silacci-Fegni C, Saliba C, Pinto D, Irie T, Yoshida I, Hamilton WL, Sato K, Bhatt S, Flaxman S, James LC, Corti D, Piccoli L, Barclay WS, Rakshit P, Agrawal A, Gupta RK (2021) SARS-CoV-2 B1.617.2 Delta variant replication and immune evasion. **Nature.** 599:114-119.

44. Mohan A, Girdhar M, Kumar R, Chaturvedi HS, Vadhel A, Solanki PR, Kumar A, Kumar D, Mamidi N (2021) Polyhydroxybutyrate-based nanocomposites for bone tissue engineering. **Pharmaceuticals.** doi: 10.3390/ph14111163.

45. Mudgal R, Bharadwaj C, Dubey A, Choudhary S, Nagarajan P, Aggarwal M, Ratra Y, Basak S*, Tomar S* (2022) Selective estrogen receptor modulators limit alphavirus infection by targeting the viral capping enzyme nsP1. **Antimicrob Agents Chemother.** doi: 10.1128/AAC.01943-21.

46. Nair T, Chakraborty R, Singh P, Rahman SS, Bhaskar AK, Sengupta S, Mukhopadhyay A*(2021) Adaptive capacity to dietary Vitamin B12 levels is maintained by a gene-diet interaction that ensures optimal life span. **Aging Cell.** doi.org/10.1111/acel.13518.

47. Pandey I, Quadiri A, Wadi I, Pillai CR, Singh AP*, Das A*. (2021) Conserved Plasmodium protein (PF3D7_0406000) of unknown function, in-silico analysis and cellular localization. **Infect Genet Evol.** doi: 10.1016/j.meegid.2021.104848.

48. Papanai GS, Pal S, Pal P, Yadav BS, Garg P, Gupta S, Ansari SG, Gupta BK (2021) New insight into the growth of monolayer MoS2 flakes using an indigenously developed CVD setup: a study on shape evolution and spectroscopy. **Mater Chem Front.** 5:5429-5441.

49. Pal L, Nandani R, Kumar P, Swami B, Roy G, Bhaskar S*(2021) Macrophages are the key players in promoting hyper-inflammatory response in a mouse model of TB-IRIS. **Front Immunol.** doi: 10.3389/ fimmu. 2021.775177.

50. Pal S, Soni V, Kumar S, Jha SK, Medatwal N, Rana K, Yadav P, Mehta D, Jain D, Sharma P, Kar R, Srivastava A, Patil VS, Dasgupta U, Nandicoori V K, Bajaj A (2021) A hydrogel-based implantable multidrug antitubercular formulation outperforms oral delivery. **Nanoscale.** 13:13225-13230.

51. Patil GS, Kinatukara P, Mondal S, Shambhavi S, Patel KD, Pramanik S, Dubey N, Narasimhan S, Madduri MK, Pal B, Gokhale RS, Sankaranarayanan R. (2021) A universal pocket in Fatty acyl-AMP ligases ensures redirection of fatty acid pool away from Coenzyme A-based activation. **eLife.** doi: 10.7554/eLife.70067.

52. Priya S, Kaur E, Kulshrestha S, Pandit A, Gross I, Kumar N, Agarwal H, Khan A, Shyam R, Bhagat P, Prabhu JS, Nagarajan P, Deo SVS, Bajaj A, Freund JN, Mukhopadhyay A, Sengupta S* (2021) CDX2 inducible microRNAs sustain colon cancer by targeting multiple DNA damage response pathway factors. **J Cell Sci.** doi: 10.1242/jcs.258601.

53. Priyanka P, Sharma M, Das S, Saxena S*(2021) The lncRNA HMS recruits RNA binding protein HuR to stabilize the 3'-UTR of HOXC10mRNA. **J Biol Chem.** doi: 10.1016/j.jbc.2021.100997.

54. Priyanka P, Sharma M, Das S, Saxena S* (2022) E2F1-induced lncRNA, EMSLR regulates lncRNA LncPRESS1. **Sci Rep.** doi:10.1038/s41598-022-06154-2.

55. Raja R, Wang C, Mishra R, Das A, Ali A, Banerjea AC* (2022) Host AKT-mediated phosphorylation of HIV-1 accessory protein Vif potentiates infectivity via enhanced degradation of the restriction factor APOBEC3G. **J Biol Chem.** doi:10.1016/j.jbc.2022.101805.

56. Rajak MK, Bhatnagar S, Pandey S, Kumar S, Verma S, Patel AK, Sundd M* (2021) Leishmania major biotin protein ligase forms a unique cross-handshake dimer. **Acta Crystallogr D Struct Biol.**77:510-521.

57. Raghunathan V* (2021) How common is gain of function. **Acta Scientific Microbiol.** 4:30-34.

58. Rana K, Pani T, Jha SK, Mehta D, Yadav P, Jain D, Pradhan MK, Mishra S, Kar R, G BR, Srivastava A, Dasgupta U, Patil VS*, Bajaj A* (2022) Hydrogel-mediated topical delivery of steroids can effectively alleviate psoriasis via attenuating the autoimmune responses. **Nanoscale.** 14:3834-3848.

59. Rawat BS, Venkataraman R, Budhwar R, Tailor P* (2022) Methionine- and choline-deficient diet identifies an essential role for DNA methylation in plasmacytoid dendritic cell biology. **J Immunol.** 208:881-897.

60. Salini S, Bhat SG, Naz S, Natesh R, Kumar RA, Nandicoori VK, Kurthkoti K (2022)The error-prone polymerase DnaE2 mediates the evolution of antibiotic resistance in persister mycobacterial cells. **Antimicrob Agents Chemother.** doi: 10.1128/AAC.01773-21.

61. Sarkar D, Vijayan R, Gourinath S, Sau AK* (2022) A unique aromatic cluster near the active site of *H. pylori* CPA is essential for catalytic function. **Biophys J.** 121: 248-262.

62. Sharma H, Bose A, Sachdeva R, Malik M, Kumar U, Pal R*(2022) Haemoglobin drives inflammation and initiates antigen spread and nephritis in lupus. **Immunology.** 165:122-140.

63. Sharma N, Kashif M, Singh V, Fontinha D, Mukherjee B, Kumar D, Singh S, Prudencio M, Singh AP*, Rathi B* (2021) Novel antiplasmodial compounds leveraged with multistage potency against the parasite *Plasmodium falciparum*: In vitro and in vivo evaluations and pharmacokinetic studies. **J Med Chem.** 64: 8666-8683.

64. Sharma PK, Kalia I, Kaushik V, Brünnert D, Quadiri A, Kashif M, Chahar KR, Agrawal A, Singh AP*, Goyal P* (2021) STK35L1 regulates host cell cycle-related genes and is essential for Plasmodium infection during the liver stage of malaria. **Exp Cell Res.** doi:10.1016/j.yexcr.2021.112764.

65. Singh YP, Shankar G, Jahan S, Singh G, Kumar N, Barik A, Upadhyay P, Singh L, Kamble K, Singh GK, Tiwari S, Garg P, Gupta S, Modi G (2021) Further SAR studies on natural template based neuroprotective molecules for the treatment of Alzheimer's disease. **Bioorg Med Chem.** doi: 10.1016/ j.bmc.2021.116385.

66. Singhvi P, Saneja A, Ahuja R, Panda AK* (2021) Solubilization and refolding of variety of inclusion body proteins using a novel formulation. **Int J Biol Macromol.** 193: 2352-2364.

67. Singhvi P, Verma J, Panwar N, Wani TQ, Singh A, Qudratullah M, Chakraborty A, Saneja A, Sarkar DP, Panda AK* (2021) Molecular attributes associated with refolding of inclusion body proteins using the freeze-thaw method. **Front Microbiol.** doi:10.3389/fmicb.2021.618559.

68. Sreekanth V, Pal S, Kumar S, Komalla V, Yadav P, Shyam R, Sengupta S, Bajaj A (2021) Self-assembled supramolecular nanomicelles from a bile acid-docetaxel conjugate are highly tolerable with improved therapeutic efficacy. **Biomater Sci.** 9:5626-5639.

69. Thiruvengadam R, Awasthi A, Medigeshi G, Bhattacharya S, Mani S, Sivasubbu S, Shrivastava T, Samal S, Rathna Murugesan D, KoundinyaDesiraju B, Kshetrapal P, Pandey R, Scaria V, Kumar Malik P, Aneja J, Binayke A, Vohra T, Zaheer A, Rathore D, Ahmad Khan N, Shaman H, Ahmed S, Kumar R, eshpande S, Subramani C,Wadhwa N, Gupta N, Pandey AK, Bhattacharya J, Agrawal A, Vrati S, Bhatnagar S, Garg PK; Department of Biotechnology India Consortium for COVID-19 research(2021) Effectiveness of ChAdOx1nCoV-19 vaccine against SARS-CoV-2 infection during the delta (B.1.617.2) variant surge in India: a test -negative, case-control study and a mechanistic study of post-vaccination immune responses. **Lancet Infect Dis.** doi:10.1016/S1473-3099(21) 00680-0.

70. Tiwari R, Ganguli N, Alam H, Sahu I, Vadivel CK, Sinha S, Patel S, Jamghare SN, Bane S, Thorat R, Majumdar SS, Vaidya MM (2021) Generation of a tissue-specific transgenic model for K8 phosphomutants: A tool to investigate the role of K8 phosphorylation during skin carcinogenesis *in vivo*. **Cell Biol Int.** 45:1720-1732.

71. Tripathi A, Rawat BS, Addya S, Surjit M, Tailor PB,Vrati S, Banerjee A (2021) Lack of Interferon Regulatory Factor 8 associated with restricted IFN-gamma expression augmented Japanese encephalitis virus replication in the mouse brain. **J Virol.** doi: 10.1128/JVI.00406-21.

72. Upadhyay C, Sharma N, Kumar S, Sharma P, Fontinha D, Chhikara B, Mukherjee B, Kumar D, Prudêncio M, Singh AP, Singh P (2022) Synthesis of new analogs of morpholine and their antiplasmodial evaluation against human malaria parasite *Plasmodium falciparum.* **New J Chem.** 46:250-262.

73. Verma P, Biswas S, Yadav N, Khatri A, Siddiqui H, Panda JJ, Rawat BS, Tailor P, Chauhan VS (2021) Delivery of a cancer-testis antigen-derived peptide using conformationally restricted dipeptide-based self-assembled nanotubes. **Mol Pharm.** 18:3832-3842.

74. Yadav M, Jalan M, Srivastava M* (2022) Enhancer dependent repositioning of TCRb locus with respect to the chromosome territory. **J Mol Biol.** doi:10.1016/ j.jmb. 2022.167509.

75. Yadav VK, Berger JM, Singh P, Nagarajan P, Karsenty G (2021) Embryonic osteocalcin signalling determines lifelong adrenal steroidogenesis and homeostasis in the mouse. **J Clin Invest.** doi:10.1172/ JCI153752.

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REVIEWS/PROCEEDINGS/BOOK CHAPTERS

1. Ali A, Mishra R, Kaur H, Banerjea AC*(2021) HIV-1 Tat: An update on transcriptional and non-transcriptional functions. **Biochimie.** 190:24-35.
2. Arya R, Dhembla C, Makde RD, Sundd M*, Kundu S* (2021) An overview of the fatty acid biosynthesis in the protozoan parasite Leishmania and its relevance as a drug target against leishmaniasis. **Mol Biochem Parasitol.** doi:10.1016/j.molbiopara. 2021.111416.
3. Jain K, Sinha P, Mohan K V, Upadhyay PK* (2021) Mouse models of the humanized immune system. In: **Essentials of Laboratory Animal Science: Principles and Practices.** Nagarajan P., Gudde R, Srinivasan, R. (Eds). Springer Nature Singapore. pp 725-742.
4. Lata S, Mishra R, Arya RP, Arora P, Lahon A, Banerjea AC*, Sood V. (2021) Where all the roads meet? A crossover prespective on host factors regulating SARS-CoV-2 infection. **J Mol Biol.** doi: 10.1016/j.jmb.2021.167403.
5. Mukherjee T, Ratra Y, Banoth B, Deka A, Polley S, Basak S* (2021) A kinase assay for measuring the activity of the NIK-IKK1 complex induced in the noncanonical NF-κB pathway. **Methods Mol Biol.** 2366:165-181. [Joint first authors]
6. Singhvi P, Panda AK* (2022) Solubilization and refolding of inclusion body proteins. **Methods Mol Biol.** 2406:371-387.
7. Verma D, Yadav AK, Chaudhary N, Mukherjee MD, Kumar P, Kumar A*, Solanki PR (2021) Recent advances in understanding SARS-CoV-2 infection and updates on potential diagnostic and therapeutics for COVID-19. **Coronaviruses.** doi: 10.2174/2666796703666220302143102.
8. Yadav AK, Verma D, Chaudhary N, Kumar A, Solanki PR (2021) Aptamer based switches: A futuristic approach in H. pylori detection. **Materials Letters.** doi:10.1016/j.matlet. 2021.131239.

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PATENTS

1. Gupta S, Upadhyay P. Formulation for modulating pain and inflammation and methods thereof. [Indian Patent Application Number: 202111021028. Filed on 11.05.2021]
2. Sampathkumar SG, Parashar S, Tasneem A, Rautela J. Hexosamine compounds and methods thereof. [Indian Patent Application Number: 202111026912/TEMP/E-1/30167/2021-DEL. Filed on 16.6.2021]
3. Gupta S, Vijayan V. Peptide complex with immunomodulatory and anti-inflammatory function. [Indian Application Patent Number: 393755. Granted on 31.03.2022]
4. Gupta S, Ahmed I, Nilakhe A, Upadhyay P. Novel compound modulating GSK-3 activity. [US Patent Application Number: 17/463,717. Filed on 01.09.2021]
5. Majumdar T, Biswal BK,Tailor P. Methods and compositions for treating viral diseases using combination of drugs. [US Patent Application Number: 17/241,130. Filed on 27.4.2021].
6. Rathi B, Singh S, Mounce B, Poonam, Kempaih P, Singh AP, Durvasula R. Hydroxiethyamine based Piperazine compounds, methods of producing and using the same for treating disease. [US Patent Application Number:17/347,720. Filed on 15.6.2021]
7. Sengupta S. DNA damage dependent microRNA signature for cancers, methods and uses related thereto. [PCT Application Number:PCT/IN2020/050776. Filed on 30.12.2021]

AWARDS AND DISTINCTIONS

- **Dr. Sanjeev Das** was selected as one of the seventy-five scientists under fifty shaping today's India.
- **Dr. Soumen Basak** was elected Fellow of the Indian National Science Academy.
- **Mr. Amandeep Vats** (a Ph.D. scholar from Dr. Subeer Majumdar's laboratory) received the third prize in the extempore speech competition conducted by Institute of Bioinformatics and Applied Biotechnology.
- **Ms. Ditsa Sarkar** (a Ph.D. scholar from Dr. A.K. Sau's laboratory) received both the Protein Society Anniversary Award and the Graduate Student Poster Award at an 35th International Symposium of the protein Society, USA, 7th-15th July, 2021.
- **Mr. Gautam Chandra Sarkar** (a Ph.D. scholar from Dr. Arnab Mukhopadhyay's laboratory) received a prize for his poster at the 90th Meeting of the Society of Biological Chemists (India).
- **Mr. Mohammed Ahmad** (a Ph.D. scholar from Dr. Bichtra K Biswal's laboratory) received the best poster prize at the 48th National Seminar on Crystallography.
- **Dr. Payal Gulati** was selected for the prestigious MK Bhan Fellowship under the mentorship of Dr. Anil Kumar.

Annexure-II

Ph.D. DEGREES AWARDED TO NII SCHOLARS

Nineteen 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	Mr. Inderjeet	Understanding the host immune system modulation by *Plasmodium* parasite	Dr. Agam P. Singh
2	Ms. Meenakshi Chawla	Investigating the role of the non-canonical *Nfkb2* pathway in chemically-induced mice models of colitis	Dr. Soumen Basak
3	Mr. Suresh Kumar	To elucidate the role of transcription factor EmbR in *Mycobacterium tuberculosis*	Dr. Vinay K. Nandicoori
4	Ms. Anam Ashraf	Dissecting the mechanistic properties of HisI (Rv1606) and the dynamics of histidine biosynthesis enzymes in *in-vivo* infection of *Mycobacterium tuberculosis*	Dr. B K Biswal
5	Mr. Bhupendra Singh Rawat	Understanding the diet induced modulation of dendritic cell homeostasis	Dr. Prafullakumar Tailor
6	Ms. Mamta Singh	Immunological evaluation of nanoparticles based Pneumococcal antigens	Dr. Amulya K. Panda
7	Mr. Amit Garg	Evaluation of the protective role of Rifampicin in diabetes using *Caenorhabditis elegans* and mice models of hyperglycemia	Dr. Arnab Mukhopadhyay
8	Mr. Parminder Singh	Molecular and therapeutic investigation into taurine regulation of bone mass	Dr. B.K. Biswal Dr. Amulya K. Panda
9	Ms. Gagandeep Kaur	Studying the impact of carbohydrate on the structured antibacterial peptides	Dr. Sangeeta Bhaskar Dr. Kanwal Jeet Kaur
10	Mr. Manoj Kumar Rajak	Biochemical and structural characterization of biotin protein ligase of *Leishmania major*	Dr. Monica Sundd
11	Mr. Vinod Kumar Meena	Investigation of small molecules as modulators of α-synuclein aggregation; relevance to Parkinson's disease	Dr. Monica Sundd
12	Ms. Priyanka	Dissecting the mechanism of long non-coding RNAs in regulating cell proliferation	Dr. Sanjeev Das Dr. Sandeep Saxena

S. No.	Student's Name	Topic of Research	Guide
13	Ms. Madhu Baghel	Understanding the role of osmotic stress in the process of osteogenesis	Dr. Amuya K. Panda
14	Mr. Deepak Kumar	Designing novel anti-TB inhibitors by targeting imidazole glycerol phosphate dehydratase (HisB) from *Mycobacterium tuberculosis*	Dr. B.K. Biswal
15	Mr. Rahul Ahuja	Improved immunogenicity of recombinant protein using biodegradable polymer particles	Dr. B.K. Biswal Dr. Amuya K. Panda
16	Mr. Md. Qudratullah	Improvement to the cow genome annotation through integrated transcriptomic and proteomic analysis	Dr. B.K. Biswal Dr. Amulya K. Panda
17	Mr. Amandeep Vats	Role of YAP in Sertoli cells	Dr. Sanjeev Das Dr. Subeer S. Majumdar
18	Ms. Alka Gupta	Micro RNA mediated gene regulation in developmental maturation of testicular Sertoli cells	Dr. Sanjeev Das Dr. Subeer S. Majumdar
19	Ms. Ahana Addhya	Investigations on the role of β-O-GlcNAc modification of nuclear/cytoplasmic protein in cellular functions	Dr. S. Gopalan Sampathkumar

LECTURES AND SEMINARS

Foundation Day Lecture

The 35th Foundation Day of NII was celebrated on October 6th, 2021. **Prof Shiv K. Sarin, (Vice Chancellor, ILBS, Delhi)** delivered a lecture on "Liver Fat Flames and Frames the Body."

Prof S.K. Sarin during his lecture

Prof. SK Sarin with the Director, NII and other scientists on the occasion

International Day of Immunology

On the occasion of the 'International Day of Immunology' NII organized a webinar on the theme of "Immunobiology of SARS-Cov-2" on 29th April, 2021. **Dr. Amit Awasti (THSTI, Faridabad)** delivered a lecture on "Pathophysiology of SARS-Cov-2 infection in an animal model" and **Dr. Dipyaman Ganguly (ICB, Kolkata)** spoke on "Immunological memory of SARS-Cov-2". **Dr. Bichitra Biswal (NII)** delivered a lecture on "Identifying potent inhibitors against the RNA dependent RNA polymerase of SARS-Cov-2". **Dr. Nimesh Gupta (NII)** talked about "Immunological memory of SARS-Cov-2".

CONFERENCE/SYMPOSIA/WORKSHOPS/MOU

SCIENCE FESTIVALS AND EXPOSITIONS

India International Science Festival - 2021

NII enthusiastically participated in the seventh **India International Science Festival (IISF) 2021** held at Goa from 10th-13th December, 2021. Students and teachers of several local schools (including Dr. Keshav Baliram Hedgewar Vidyamandir, Karapur-Tisk, Sankhali, Govt High School, Mormugao, Govt. High School, Shristhal, Conacona, Kudal High School, Shri Shadhanan Vidyalaya, and St. Annes High School) visited the NII stall. NII displayed posters on ongoing research projects and achievements of the institution. Short videos made were also displayed during the event. Ph.D. scholars and members of the NII Faculty described their research work in easy-to-understand language, which attracted the attention of many students, teachers and common people alike. Self-explanatory flyers, which shed additional light on the research programmes being carried out at NII, were appreciated as being interesting and informative. **Dr. P. Nagarajan, a Scientist at NII,** was on hand to explain the fundamentals of biology to school students. Interaction led to lots of interesting questions and lengthy discussions.

Students visiting the NII stall at IISF – 2021 and interacting with Dr. P. Nagarajan

Vigyan Sarvatra Poojyate: Mega Expo

The National Institute of Immunology participated enthusiastically in the **Mega Expo** held at the **Jawaharlal Nehru Stadium** from 22nd - 28th February, 2022, organized under the aegis of **Vigyan Sarvatra Pujyate.** Posters prepared by NII Ph.D. scholars, depicting information on cutting-edge research at NII, were put up. A screen displaying other details on on-going projects, as well as other institutional information of public interest, was also placed at the stall. The stall attracted a very good response from the general public, and several queries as regards the COVID-19 pandemic were responded to.

The NII stall at the Vigyan Sarvatra Poojyate Mega Expo

INTERNATIONAL SYMPOSIUM ON COVID-19

The **National Institute of Immunology (NII)** organized an online International Symposium ("Covid-19: Delta, Omicron and Beyond…") on the immunopathological aspects of the COVID-19 phenomenon from February 23rd- 25th,2022. Members of the faculty, Ph.D. students and scientific staff from about a dozen biotechnology Institutes, spread all across India, participated in the event. The primary objective was to particularly reach out to young students and researchers with the aim of cultivating and promoting scientific discussions in the area. The program was also streamed on YouTube to enable access by a wider audience. A host of international leaders participated in this event, including **Dr. Anurag Agarwal (Institute of Genomics and Integrative Biology), Dr. Galit Alter (Harvard Medical School), Dr. Alejandro Balazs (Harvard University), Dr. Gaurav Gaiha (Harvard University), Dr. Nimesh Gupta (National Institute of Immunology), Dr. Thirumala-Devi Kanneganti (St. Jude Children's Research Hospital), Dr. Shiv Pillai (Harvard University), Dr. Alessandro Sette (La Jolla Institute for Immunology), Dr. Alex Shalek (Massachusetts Institute of Technology), Dr. Alex Sigal (Africa Health Research Institute), Dr. Duane Wesemann (Harvard Medical School) and Dr. Somnath Dutta (Indian Institute of Science).** It was an exciting scientific feast.

A poster advertising the COVID-19 International Symposium

NATIONAL SCIENCE DAY

As part of the celebrations for National Science Day, **Prof. P Balaram, (Emeritus Professor, National Centre for Biological Science)** presented an online lecture on "Chemistry and biology in the age of corona virus" on 28th February, 2022. Ph.D. students, staff and members of the NII faculty participated enthusiastically in the proceedings, enlivened by Prof. Balram's deep appreciation of the history of scientific discoveries. Young researchers present posters describing their work on the occasion.

Poster Exhibition: Ph.D students presenting their posters on National Science Day

INTERNATIONAL WOMEN'S DAY

International Women's Day celebrates the social, economic, cultural, and political achievements of women. The day also marks a call to action for accelerating women's equality. It is a day to uplift one another, collaborate as a global community, as well as share stories and experiences. Specific areas of focus include technology, work, forging change, creatives, empowerment, health, and sport. To commemorate this special day the Institute organised a talk Dr. Rinku Sengupta Dhar (Head, Obstetrics and Gynaecology, Sitaram Bhartia Hospital) on "Celebration & Comprehension of Women's Health".

INTERNATIONAL YOGA DAY

The practice of yoga greatly aids in promoting physical and mental well-being. On September 27th, 2014, during his speech at the **UN General Assembly, Prime Minister Narendra Modi** proposed that June 21st (the summer solstice, the longest day of the year) be observed and celebrated as **'International Yoga Day',** with the objective of increasing awareness of the many benefits of practicing yoga. Due to the pandemics phase, Yoga Day was celebrated on 21st June on campus in online mode. Participants enjoyed the Yoga postures in solitude and have uploaded their videos on the site shared by the Govt of India.

TRAINING WORKSHOPS, MEMORANDUM OF UNDERSTANDING (MOU)

Molecular biology training for COVID-19 diagnosis

The Bill and Melinda Gates Foundation funded the training of medical and technical professionals as part of a national effort to scale up qRT-PCR-based testing for the detection of SARS-CoV-2, the causative agent of COVID-19. Viruses such as Dengue can also be detected by qRT-PCR. The training effort was coordinated by Foundation for Innovative New Diagnostics (FIND) organization. Training sessions at NII were initiated on October 5th, 2020 with participants hailing from different regions of Bihar; sessions concluded on April 17th, 2021. Cumulatively, training has been imparted to 54 students/ technicians.

The Director, NII addressing participants at the conclusion session of the training exercise

MoU

An MoU was signed between NII and the Institute of Bioresources and Sustainable Development (IBSD, Manipur, Imphal) for creation of a framework for collaboration between two Institutes.

The Director, NII, Dr. Pushkar Sharma, other Faculty members and the Dr. DK Vashisht (Senior Manager) along with Director of IBSD Prof. Pulok Kumar Mukherjee at the signing ceremony

ANNUAL GENERAL MEETING (AGM) OF SOCIETIES

NII hosted the AGM of the Societies of all DBT autonomous institutes on November 12th to 14th, 2021. The meeting was chaired by Dr. Jitendra Singh (Honourable Minister for Science and Technology) who serves as 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 working in a collaborative manner.

Dr. Jitendra Singh (Honourable Minister for Science) at the AGM of the Societies of DBT autonomous institutes, along with institute heads and other functionaries

INVITED SEMINARS

	Topic	Speaker	Date
1	COVID-19 in India: What models can do (and can't)	Prof. Gautam Menon, Ashoka University, Sonipat, Haryana	29.07.2021
2	Sialidases and sialoglycan foraging in dysbiotic vaginal microbiota	Dr. Kavita Agarwal University of California, USA	19.08.2021
3	Cancer associated H3.3G34 mutations may have a distinct role in genome instability	Dr. Rajesh Kumar Yadav All India Institute of Medical Sciences, Patna	29.09.2021
4	Protein-induced membrane remodeling-new insights from unbiased screens and in vitro reconstitution	Dr. Thomas Pucadyil Indian Institute of Science Education and Research, Pune, Maharastra	30.09.2021
5	Genome-wide in silico identification of transcription factor binding sites	Dr. Narendra Kumar Elucidata Data Consulting Private Limited, New Delhi	11.10.2021
6	Host-pathogen interaction of microbes and the concerning consequences	Dr. Vidya D. Negi National Institute of Technology, Rourkela, Odisha	13.10.2021
7	Altered metabolism a therapeutic target for cardiomyopathy in type 2 diabetes	Dr. Keshav Gopal Katz Group Centre, University of Alberta, Edmonton, Canada	18.10.2021
8	Health risk assessment of Xenobiotics	Dr. Atindra Kumar Pandey National Centre for Disease Control, New Delhi	20.10.2021
9	Deciphering the disease biology using functional genomics approach	Dr. Dilip Kumar SIgN, A-Star Institute, Singapore	25.10.2021
10	Quality control and assembly of the Nuclear Pore Complex: The Nuclear Gatekeeper	Dr. Sapan Borah Yale School of Medicine, Boyer Centre for Molecular Medicine, New Haven, CT, USA	27.10.2021
11	Serotonin - From mood to mitochondria	Dr. Vidita A. Vaidya Tata Institute of Fundamental Research, Mumbai, Maharastra	29.10.2021
12	Particulate antigen delivery for providing long term potent immune response	Dr. Jairam Meena National Institute of Immunology, New Delhi	1.11.2021

	Topic	Speaker	Date
13	Prognostic biomarkers of drug-induced liver injury (DILI) - Does immune system impact the outcome?	Dr. Md. Shabir Hussain Jawaharlal Nehru University, New Delhi	10.11.2021
14	Need of standardisation of immunity enhancers from plants	Dr. Payal Rani Maa Saraswati Institute, College of Pharmacy, Abohar, Punjab	15.11.2021
15	Gut Feeling: Gut-LIVER-brain axis in toxin-induced multiorgan inflammation	Dr. Ratanesh Kumar Seth University of South Carolina, Columbia, USA	17.11.2021
16	Helix invasive approach for targeting of duplex DNA and RNA for genetic therapy	Dr. Chhuttan L. Meena CSIR-National Chemical Laboratory (CSIR-NCL), Pune, Maharastra	22.11.2021
17	Structural and functional investigations of pathogen proteins involved in human disease	Dr. Sanjeev Kumar Michigan State University, East Lansing, Michigan, USA	24.11.2021
18	Oligonucleotide aptamers and SELEX Technology: Potential scope in biomedical sector	Dr. Jyoti Bala Rapture Biotech International Pvt Ltd Noida, Uttar Pradesh	29.11.2021
19	Organic peroxide as antimalarial agents	Dr.Ved Prakash Banasthali University, Rajasthan	01.12.2021
20	Therapeutic interventions in infectious diseases	Dr. Sukrat Sinha Nehru Gram Bharati University, Prayagraj, Uttar Pradesh	06.12.2021
21	Development of immune boosting beta glucan polymeric particles and its applications	Dr. Geetha Venkat IIT Madras, Chennai	08.12.2021
22	Exploring the therapeutic potential with the elucidation of the mechanisms of novel allenic fatty acids against cancer and covid-19 using molecular and metabolomic approaches	Dr. Ashish K. Choudhary New Delhi	13.12.2021
23	Aging of the immune system - from basic aspects to SARS-CoV-2 pandemic	Prof. Janko Nikolich-Zugich University of Arizona College of Medicine-Tucson, USA	13.12.2021
24	The role of mitochondria in cancer biology: Is there any connection?	Dr. Bhanupriya Awasthi AIIMS, New Delhi	15.12.2021
25	EHV-1 KyA immunization effectively protected CBA micr from pathogenic RacL11 challenge	Dr. Akhilesh Kumar Shakya All Indian Institute of Medical Sciences, Raebareli, Uttar Pradesh	22.12.2021
26	Mapping brain circuits mediating stress and cell trajectories using single-cell genomics	Dr. Naresh Hanchate University College, London, UK	27.01.2022

NII FACULTY AND Ph.D. SCHOLAR LECTURE SERIES

S. No	Topic	Lectures delivered by	Date
1	Computational biology for deciphering mutations for Sars-CoV-2 and design of novel antiviral inhibitors	Dr. Debasisa Mohanty	01.04.2021
2	Phenotypic and functional properties of follicular T helper cells in dengue A tale of two sortases	Ms. Shilpa Sachan Ph.D. Scholar, Batch 2016 Mr. Sumit Ph.D. Scholar, Batch 2016	08.04.2021
3	Effects of small molecules on amyloid formation Targeting the *Mtb* Histidyl tRNA synthetase	Mr. Vijay Kumar Ph.D. Scholar, Batch 2016 Mr. Sayan Chakraborty Ph.D. Scholar, Batch 2016	01.07.2021
4	Towards understanding the role of gut microbiota and their metabolites in the causation and treatment of colorectal cancer	Dr. Anil Kumar	08.07.2021
5	NF-kappaB activating pathways in multiple myeloma	Mr. Uday Aditya Sarkar Ph.D. Scholar, Batch 2016	15.07.2021
6	LncRNAs: From 'Junk' genetic material to frontline players in cancer Tuning the chords of life: Reproductive hormones and cancer	Ms. Priyanka Ph.D. Scholar, Batch 2016 Ms. Moumita Sarkar Ph.D. Scholar, Batch 2016	12.08.2021
7	Role of VPS15 in the development of Apicomplexan parasites Understanding the transcriptional regulation of DC differentiation and function by IRF8	Mr. Rahul Singh Rawat Ph.D. Scholar, Batch 2016 Ms. Annesa Das Ph.D. Scholar, Batch 2016	19.08.2021

INVITED TALKS/LECTURES/WEBINARS DELIVERED BY NII SCIENTISTS

S. No.	Scientist	Title	Organizer/Name of the Institute/College/ School/Organisation	Date
1.	Dr. P. Tailor	Ying and yang of dendritic cell diversity development	The Society for Integrative Biosciences	September 8th, 2021
2.	Dr. P. Tailor	Does the walker choose the path, or the path the walker? Dynamic mechanisms of cell fate decisions in dendritic cell differentiation	National Conference on Philosophy of Immunology in Health Sciences, NIT, Durgapur	September 18th, 2021
3.	Dr. P. Tailor	Transcriptional regulation of metabolic pathway in dendritic cell subsets	Annual Conference of the Indian Immunology Society, IICB, Kolkata	December 18th, 2021
4.	Dr. A.P. Singh	Malaria vaccines: Hurdles and Opportunities	Mehr Chand Mahajan, DAV College, Chandigarh	November 16th, 2021
5.	Dr. D. Sehgal	From infection to immunity	UGC-HRDC :Refresher course in Life Sciences and Biotechnology, Jawaharlal Nehru University, New Delhi	December 15th, 2021
6.	Dr. D. Sehgal	From pandemic to immunity	Zakir Husain College, Delhi University, New Delhi	March 15th, 2022
7.	Dr. R. Pal	Disorders of proliferation: Analysis of novel pathways and targets	School of Biosciences & Technology, Department of Integrative Biology, Vellore Institute of Technology, Vellore	December 6th, 2021
8.	Dr. S. Bhaskar	Journey of a whole bacteria candidate Vaccine	Chaiduar College, Ghopur, Assam	August 11th, 2021
9.	Dr. S. Basak	RNA viruses and NF-kappa B signaling: friends or foe	Central University of Punjab, Ghudda, Punjab	April 12th, 2021
10.	Dr. S. Basak	Intestinal inflammation gone awry!	Regional Centre for Biotechnology, Faridabad	July 2nd, 2021

11.	Dr. S. Basak	Intestinal inflammation and the NF-κB system	Frontiers in Biological Research: Challenges and Opportunities. Amity University, Kolkata	August 13th, 2021
12.	Dr. S. Basak	Intestinal inflammation gone awry!	IISER Tirupati	September 14th, 2021
13.	Dr. S. Basak	A RelB NF-κB-type-1 IFN signaling axis in antiviral vitamin D functions	Advances in Basic and Translational Research in Biology, Tezpur University	March 11th, 2022
14.	Dr. N. Gupta	Non-specific effects of vaccines	Indian Academy of Paediatrics National Conference-2022	March 20th, 2022
15.	Dr. N. Gupta	T-cell response to inactivated SARS-CoV-2 vaccine	Annual Conference of the Indian Immunology Society. Meeting of the Indian Immunology Society	December 19th, 2021
16.	Dr. N. Gupta	Cellular immune response in COVID-19: The T-cell story	Annual Conference of Society of Inflammation Research	November 21st, 2021
17.	Dr. N. Gupta	A dive into the immunology of COVID-19 vaccines	Manav Rachna International Institute, Faridabad	June 11th, 2021
18.	Dr. N. Gupta	A deep dive into the immunology of COVID-19 vaccines	Miranda House, University of Delhi	May 20th, 2021
19.	Dr. N. Gupta	Immunological memory to SARS-CoV-2	Indian Institute of Technology, Roorkee	April 29th, 2021
20.	Dr. N. Gupta	COVID-19 research at NII	Launching Ceremony of the BRICS Vaccine R&D Center and Workshop on Vaccine Cooperation	March 22nd, 2022
21.	Dr. V.S. Patil	Development of immunological memory: Lessons from multi-omics	St. Xavier's College, Mumbai	September 23rd, 2021
22.	Dr. V.S. Patil	Human $CD4^+$ T cell memory subsets in infectious diseases: Lessons from multi-omics analysis	Omics 2021, CSIR-CCMB, Hyderabad	October 21st-23rd 2021
23.	Dr. S. Singha	Nano-immunotherapy: An emerging platform for cancer treatment	Fergusson College, Pune	July 28th, 2021
24.	Dr. S. Singha	Application of nanoparticles in cancer immunotherapy	Amity University, Haryana	August 5th, 2021

25.	Dr. S. Singha	Nanomaterials for cancer immunotherapy	Centre of Advanced Study in Crystallography & Biophysics, University of Madras, Chennai	October 12th, 2021
26.	Dr. S. Singha	Nanoparticles for modulating immune responses	JNU, New Delhi	January 19th, 2022
27.	Dr. T. Majumdar	Riddle of herd immunity in SARS-CoV-2-induced viral terrorism: Science to Society	Government Degree College for Women, Anantnag, J & K	September 19th, 2021
28.	Dr. T. Majumdar	Immunological techniques and applications'	Bhaskaracharya College of Applied Sciences, University of Delhi	October 22nd, 2021
29.	Dr. T. Majumdar	Microbiome based nutritional therapy	Nanaji Deshmukh Veterinary Science University, Jabalpur, Madhya Pradesh	October 30th, 2021
30.	Dr. S. Gupta	Targeting neuronal insulin resistance by AdipoRon ameliorates disease burden in APP/PS1 mouse model of Alzheimer's disease	National Conference on Computational and Biochemical Drug Discovery, IIT-BHU, UP	September 11th-12th, 2021
31.	Dr. S. Gupta	Science Setu talk	Protein aggregation: From diseases to long-acting therapeutics	January 18th, 2022
32.	Dr. S. Gupta	Current pandemic situation and its future course	Samvad- IIT Delhi, Delhi	June 30th, 2021
33.	Dr. Apurba Kumar Sau	Understanding human guanylate binding proteins (GBPs) activity-mediated antiviral response	INDO-US Symposium on Molecular Virology. IIT Mandi	February 17th, 2022
34.	Dr. Debasisa Mohanty	Mining of NGS data on bacterial genomes & human microbiome for identification of novel small ORFs and secondary metabolites	Ashoka University, Sonipat, Haryana	March 3rd, 2022
35.	Dr. Debasisa Mohanty	Application of machine learning in protein structure prediction and drug discovery	DAV College, Chandigarh	February 24th, 2022
36.	Dr. Debasisa Mohanty	Brief overview of computational methods for prediction of biomolecular structure & function	Patna Women's College, Patna	February 15th, 2022

37.	Dr. Debasisa Mohanty	Machine learning-based method for the design of inhibitors of protein-protein interaction	Dr. B.R. Ambedkar Center for Biomedical Research (ACBR), Delhi University, Delhi	December 22nd, 2021
38.	Dr. Debasisa Mohanty	*In silico* approaches for design of Protein-Protein Interaction inhibitors as novel antiviral molecules for SARS-CoV-2	Indraprastha Institute of Information Technology Delhi (IIIT Delhi), Delhi	October 17th, 2021
39.	Dr. Debasisa Mohanty	Panel discussion on "Exascale Computing"	CDAC Technology Conclave 2021, CDAC, Pune	July 28th, 2021
40.	Dr. Debasisa Mohanty	Machine learning based method for prediction of small molecule modulators of protein-protein interactions	Netaji Subhas Institute of Technology (NSUT), Delhi	July 7th, 2021
41.	Dr. Srinivasa-Gopalan Sampathkumar	How to engineer and inhibit glycans in living animals using monosaccharide analogues? - Tips for carbohydrate chemists who aspire to tackle the complexities of glycobiology	Indian Carbohydrates E-Meetings (ICarE), Mumbai, Kolkata, New Delhi	June 30th, 2021
42.	Dr. G Senthil Kumar	Understanding the activation and regulation of mitogen activated protein kinase p38 usingsolution NMR Spectroscopy	NMRS 2022 meeting, IIT Gandhinagar, Gandhinagar	March 6th-9th, 2022
43.	Dr. G Senthil Kumar	Protein structure and function	Sri Venkateswara College, New Delhi	July 26th, 2021
44.	Dr. Anil Suri	Reproductive health for all - Sustainable development goal 3 for non-communicable disease	International Conference on Reproductive Healthcare & Annual meeting of the Indian Society for the Study of Reproduction and Fertility.	February 11th-13th, 2022
45.	Dr. Anil Suri	Newer strategies and innovative approaches for cancer treatment	National Academy of Sciences, India (NASI) Rajasthan	January 29th, 2022
46.	Dr. Arnab Mukhopadhyay	Adaptive capacity to dietary Vitamin B12 levels in *C. elegans* is maintained by a gene-diet interaction	*C. elegans* PI meeting, MRDG, IISc Bangalore	April 3rd, 2021

47.	Dr. Arnab Mukhopadhyay	Diet gene interactions in longevity assurance	IISER, Trivandrum	April 9th, 2021
48.	Dr. Arnab Mukhopadhyay	Regulatory mechanisms of longevity assurance: linking metabolism to gene expression	Bio Next 2021: Frontiers in Modern Biology, Adamas University, Kolkata	April 24th, 2021
49.	Dr. Arnab Mukhopadhyay	Biosafety regulations	Jawaharlal Nehru University, New Delhi	April 28th, 2021
50.	Dr. Arnab Mukhopadhyay	RNAi as a tool in developmental biology	Maharani Lakshmi Ammanni College for Women Autonomous, MLACW (mLAC) , Bengaluru	June 3rd, 2021
51.	Dr. Arnab Mukhopadhyay	Learning secrets of longevity from a humble nematode	Maitreyi College, New Delhi	July 30th, 2021
52.	Dr. Arnab Mukhopadhyay	Mechanisms of aging and ways to delay it	IIT Mandi, Mandi	October 6th, 2021
53.	Dr. Arnab Mukhopadhyay	Gene-diet interactions that maintain optimal life span: lessons learnt from a tiny nematode	IISER Tirupati, Tirupati	March 1st, 2022
54.	Dr. Sagar Sengupta	DNA Damage Sensitive MicroRNAs: a sensitive tool for detection of early-stage colon cancer)	IISER Bhopal, Bhopal	October 1st, 2021
55.	Dr. Sagar Sengupta	Understanding the basics of cancer biology and a recent effort towards the detection of colon cancer)	Bhaskaracharya College of Applied Science, Delhi	November 9th, 2021
56.	Dr. Sagar Sengupta	Trying to reach the bed from the bench: The gap remains	Shiv Nadar University, Delhi-NCR	December 18th, 2021
57.	Dr. Sagar Sengupta	DNA Damage Sensitive MicroRNAs: A sensitive tool for detection of early stage colon cancer	Annual Meeting of the Indian Association of Cancer Research, International Amity Institute of Molecular Medicine & amp; Stem Cell Research (AIMMSCR), Amity University, Noida	March 2nd-5th, 2022
58.	Dr. Sanjeev Das	Deciphering the role of PRAMEF2, a novel cancer testis antigen, in tumorigenesis	Annual Convention of the Indian Association for Cancer Research, Amity University, Noida	March 5th, 2022

59.	Dr. G. Aneeshkumar Arimbasseri	Nutritional strategies to address metabolic dysfunctions	iCEN-24 : CSIR	June 16th, 2022
60.	Dr. G. Aneeshkumar Arimbasseri	Lack of vitamin D leads to defective carbohydrate utilization in skeletal muscles	Yenepoya University, Mangalore	December 21st, 2021
61.	Dr. Devram Sampat Ghorpade	Organ-specific therapeutic approach to combat modern-day metabolic diseases	Vellore Institute of Technology, Vellore	October 7th, 2021
62.	Dr. Anil Kumar	Intellectual property rights	Refresher course in physical sciences & nano sciences, HRDC JNU, New Delhi	January 14th, 2022
63.	Dr. Anil Kumar	Gut microbiota- derived metabolites as potential biomarkers in different diseases	National Conference on Microbiome: The Story Untold! VPM's BN Bandodkar College of Science, Thane, Maharashtra	January 7th, 2022
64.	Dr. Anil Kumar	Gut microbiota- derived metabolites as potential biomarkers	ECS-JNU Student's Chapter, JNU, New Delhi	January 13th, 2022
65.	Dr. Anil Kumar	Intellectual property rights and their relevance to science and society	Mata Gujri College, Fatehgarh Sahib, Punjab	October 29th, 2021
66.	Dr. Anil Kumar	Intellectual property rights and their relevance to science and society	Dyal Singh College, New Delhi	August 5th, 2021
67.	Dr. Anil Kumar	Virtual tour of NII and understanding about immuno-biotech aspects	Maitreyi College, University of Delhi, Delhi	March 9th, 2022

INFRASTRUCTURE

Equipment

While individual laboratories are very well-equipped, some high-end equipment is also placed in central instrumentation facilities. Examples of equipment being frequently employed include mass spectrometers, an NMR spectrometer, confocal microscopes, an atomic force microscope, scanning and transmission electron microscopes, high-throughput DNA sequencers, flow cytometers, a dual wavelength X-ray generator, a whole-body imaging system, a CD spectroscope, a surface plasmon resonance system and an amino acid sequencer.

BSL-III Facility

There are three Biosafety Level III facilities at NII which individually cater to experiments involving *Mycobacterium tuberculosis, Streptococcus pneumonia* and HIV.

Small Animal Facility

The Small Animal Facility of the Institute is dedicated to ensuring the humane care and breeding of experimental animals used in approved research and to provide defined strains of mice and rats to the scientific community. At present, the small animal facility houses 113 mouse strains, 5 rat strains and 1 stock of rabbits.

The breeding of all defined strains is maintained in a three-tier system i.e., the Foundation Stock (FS), Pedigreed Expansion Stock (PES), and Production Stock (PS). Breeding of genetically modified mice strains are bred either by homozygous mutant (-/-) x homozygous mutant (-/-), by heterozygous mutant (-/+) x homozygous mutant (-/-), or by heterozygous mutant (-/+) x heterozygous mutant (-/+) mating strategies.

Defined breeding protocols and careful management and husbandry procedures are followed to safeguard the purity of each inbred strain. New breeders are employed to minimize genetic drift and inbreeding depression. Also, genetic monitoring is carried out of foundation, expansion and production stocks (employing a few microsatellite markers) to ensure genetic purity. The facility also gets support from various principal investigators in the genotyping of a few transgenic and knockout mice strains to confirm the presence or absence selected gene/s of interest.

The health monitoring program includes regular screening of pathogens using sentinels that includes murine hepatitis virus, parvovirus, norovirus and pneumonia virus as well as mycoplasma and Sendai virus using ELISA and PCR. Bacterial pathogens such as *Pseudomonas aeroginosa, Streptobacillus moniliformis, Bordetella, Bronchiseptica, Citrobacter rodentitium, Pasteurella pneumotropica, Staphylococci* and *E. coli* are also screened for using culture, biochemical and PCR methods. Fecal samples are randomly selected to check for the presence of syphacia and aspicularis endoparasites by the sedimentation method. Also, periodic FACS analyses is done on immunodeficient mice to assess "leakiness".

Standard quality control protocols are implemented in the facility to reduce chances of transmission of infection between cages, which include careful handling of animals, automated washing procedures, use of sterilized corn cob bedding and autoclaved cages, and acidification of water. The breeding and experimental colonies are maintained in a barrier system with individually-ventilated cages. Prompt action is taken by the veterinarian, based on clinical signs and necropsy/ autopsy of the diseased /deceased animals. A preventive and recommended

schedule of medication is strictly followed to prevent infections.

Primate Research Centre

The National Institute of Immunology has a separate and dedicated Primate Research Centre. Clearance of the research proposals by CPCSEA after primary clearance from the Institutional Animal Ethics Committee is a necessary requirement for animal use.

Macaques are bred and maintained, and animals of defined age and parentage are employed for approved basic, pre-clinical, and toxicological research. Group mating protocols are followed under the breeding program. The Institute has large open pens, which are used for group mating under semi-natural conditions, where food and water is provided ad libitum. Infants are weaned at the age of six to twelve months (depending on the season and the weight of infants) after which they are transferred to open enclosures/semi-natural housing which aids in the development of bones and muscles, improves coordination, and boosts overall growth. Monkeys are housed in independent cages when they attain puberty. To prevent cross-cage contamination or infection, procedures promoting hygiene are strictly followed as routine practice. Primates are regularly screened for simian herpes virus and simian hepatitis virus by ELISA; PPD is employed to diagnose tuberculosis. Sick animals are immediately isolated and appropriate treatments initiated. Primates are provided with standardized pellet feed as per recommendations. In addition, bread, soaked bengal gram, vegetables, and/or fruits are also provided daily, as are periodic vitamin and calcium supplements.

Staff at PRC undergo annual preventative health check-ups. All surgeries, treatment of injuries, and application of medicationare performed by a registered veterinarian. Experienced staff assist in procedures like surgery, immunization, blood sampling and biopsy. Staff make sure that all the procedures involved in animal handling are pain-free with minimum stress to the animal. A constant effort is made to keep the animals in a comfortable zone and stress-free environment as per the available guidelines. There are seventeen open enclosures with swings and shelters; monkeys are frequently rotated through these enclosures for rehabilitation or to provide and environment where they can socialize. Attempts are made to keep animals in open enclosures, depending on the climatic conditions.

A research laboratory situated at the Centre provides basic services to investigators, including the primary processing of biological samples.

SUPPORTING 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 for formulating policies and ensuring their effective implementation. Other key areas included handling of all service matters and recruitments, coordinating career development initiatives, arranging for foreign visits of scientists for training, conferences or bilateral exchange. The division also carries out functions related to staff welfare, the dispensation of post-retirement benefits, as well as the submission of periodic reports to the ministry, and prepares responses to parliament questions. To bolster capabilities and enhance productivity, the Institute periodically sponsors administrative and technical staff for training at recognized training institutes.

The Institute's "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, management of fund utilization, receipt and disbursement of all payments, internal auditing, getting accounts audited by statutory and CAG auditors, sending reports to funding agencies, and recovery and remittance of TDS from salary and contractors, filing an institutional income tax return, obtaining required exemptions from the Income Tax Department, maintaining bank accounts, management of trust for CPF, Gratuity Fund and recovery and remittance of subscriptions of NPS.

Stores and Purchase Department

The Stores & Purchase Department deals with the procurement of chemicals, consumables, glassware, plastic ware equipment, and other items which are used in the research laboratories. Purchase Committees evaluate critical aspects of purchase before an order is placed. Such Purchase Committees comprise of 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 purchases till the payment is made. Close rapport with the other departments is maintained to mitigate any bottle-necks that may arise during the process.

Engineering, Maintenance and Instrumentation Services

The Engineering Department has been entrusted with all engineering activities involving maintenance, routine services and capital works. Systems are continuously upgraded to enable use of the latest technologies. Major activities undertaken during the reporting year are outlined here.

- An ABSL-3 for non-human primates is being established. The project is being carried out on a turnkey basis, including comprehensive operations and maintenance for a period of 5 years.
- The rain water harvesting and drainage system is being up-graded and connected with the existing dug well.

- Damaged grit plaster is continuously repaired, restoring external aesthetics of the building.
- New laboratories and offices spaces are being created and functionalized.
- Staff quarters are being constructed at Sector-5 Dwarka through the Central Public Works Division.
- BSL-3 facilities are being up-graded.
- Supply, installation, testing and commissioning of a100 Kwp rooftop grid sharing solar system is underway.
- Up-gradation of the BMS system is on-going.

Library and Documentation Services

The Library and Documentation Department is a service-oriented supportive unit which works as an information repository and dissemination centre. It provides information support to the scientific 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 (both online and print) for the subscription of journals, 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 also 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, reports on institutional workshops, and submitting documentation for the Scientific Industrial Research Organization registration.

Information on subscriptions, new procurements and publications is regularly updated on the NII website. The library maintains a searchable Institutional Digital Repository, (IDR) containing full texts of articles published from NII from the year 2008. The library also conducts an induction programme for newcomers, as well as holds workshops on various subjects such as the use of software for the detection of plagiarism and use of Scopus software.

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. Twenty-six new books have been added to the library collection over the past year. The library participates in organizing institutional lectures such as the Foundation Day Lecture, and the National Science Day Lecture.

Academic and Training Services

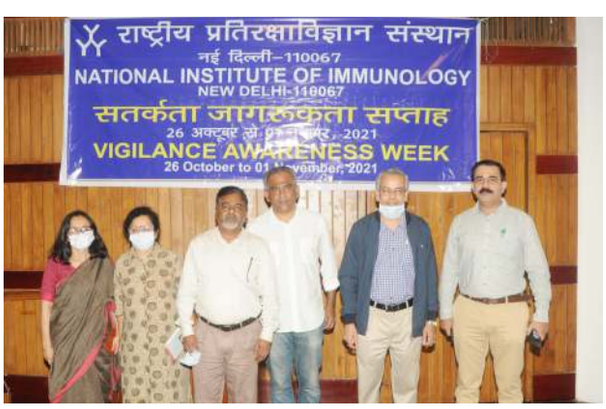
The activities of the Academic & Training Department are divided into three major categories: Student affairs, in-house training, and training at other institutions. The department has been involved in Ph.D. admissions and pre-Ph.D. registration courses, the scheduling of doctoral committee meetings, and also coordinates disbursal of fellowship to scholars. It also helps organize meetings of the institute's Academic Committee. The Institute takes in scientists who have been awarded independent fellowships from the following institutions who then work under 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. The institute also hosts eligible individuals holding the Ramalingaswami Re-entry Fellowship.

The Institute imparts short-term training to the post-graduate students sponsored by the Indian Academy of Science, Bangalore, six-month project work. Under-graduate students belonging to different colleges also receive training under the Science Setu Programme. The department has also been involved in arranging the participation of scientific, technical, and administrative

officials of the Institute in various training courses.

Vigilance Cell

The Institute has a Vigilance Cell headed by a scientist nominated as part-time Chief Vigilance Officer (CVO) by the Central Vigilance Commission (CVC). The CVO and 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, if properly conceived and executed, can aid in reducing improper conduct and practice. The institute 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 members employed in areas prone to corruption are periodically re-assigned to other 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, such institutional committees are reconstituted. The cell has been rendering periodical reports to the administration and the CVC.



Vigilance Officer Shri. T. P. Sharma (under Secretary from CVC) with Dr. A.K Sau (CVC, NII) Dr. P. Sharma (Director, NII) Dr. D. K Vashist (Senior Manager), Ms. Anju Sarkar (Manager), Ms. Daisy Sapra (Sec. Officer) at a lecture delivered by Sri. T. P . Sharma

Vigilance Awareness Week' was observed by the Institute from October 26th to November 1st, 2021. A banner announcing the observance of the Vigilance Awareness Week was put up at the main entrance of the Institute. Placards bearing slogans against corruption were displayed on the premises. A pledge to fight corruption was taken by the NII community on October 26th, 2021; members of the community also took an Integrity Pledge on the CVC website. An essay-writing competition was organized online on November 1st, 2021 on the theme "Independent Indian @75: Self Reliance with Integrity".

The report on an indicative List of areas/activities which are to be taken up in campaign mode as part of Vigilance Awareness Week 2021 strictly adhered to extant Covid -19 prevention guidelines at all locations and economic measures as per the Ministry of Finance.

Computer Centre

The Computer Centre has been providing all information technology-related support to the institute, which involves managing switches and Wi-Fi controllers 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. Computer Center staff facilitates day-to-day troubleshooting, maintenance and anti-virus support of about 850 PCs and other peripheral devices. In addition, the Computer Center also provides specialized services like management of HPC clusters, managing floating licenses for access to bioinformatics software over LAN and IT support for developing in-house software for Pay Roll, an online complaint logging system and creation of email accounts. The center also helps in the organization and conduct of virtual meetings and lectures.

NOTABLE ACTIVITIES

Academic Courses, Training Programmes and Interaction with Other Academic Institutes

The Institute imparts long-term residential training leading to a Ph.D. degree by Jawaharlal Nehru University, New Delhi. From a large number of applicants from across the country, 30-35 scholars are admitted to this programme (after an examination and interviews) every year.

The Ph.D. Programme of the Institute was launched in the academic year 1986-87. So far, 529 students have been awarded the Ph.D. degree, including 19 who obtained the degree in the academic year 2021-22 (Annexure-II).

As also outlined above, the institute also welcomes undergraduate and postgraduate students from various universities/institutions for short-term project work.

Publications

Eighty-three research papers were published this year. Of these publications, seventy-five were published in journals as peer-reviewed research papers and the remaining as reviews/proceedings. Details of these papers are available in Annexure-I.

Patents

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

Lectures Delivered on Invitation/ Papers Presented

Scientists of the Institute continued to deliver lectures including 'Keynote / Inaugural Addresses' and 'Serial Lectures' at various institutions, conferences, symposia, workshops and training programmes in India and abroad.

Lectures/seminars by Visiting Scientists/Guest Investigators

The institute continued to receive visiting scientists and guest investigators from all over the world. Twenty- six seminars were organized in various areas of interest. 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, 2021. 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

With the aim of promoting national integration and communal harmony among peoples of all religions, languages and regions, "Sadhbhavna Diwas" was observed on 20th August, 2021, the birth anniversary of Late Shri Rajiv Gandhi. 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 was observed on October 31st, 2021, the birth anniversary of Late Shri Sardar Vallabhbhai Patel. 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 August 15th, 2021. The event was marked by a message from the Director, followed by the singing of the National Anthem by the students and children of the staff of the Institute.

The Director hoisting the flag on Independence Day

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 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:

1. To promote Hindi as an official language in official work, a Hindi Pakhwara (Hindi Fortnight) was celebrated in the Institute with great zeal from September 1st-14th, 2021. During this period, various Hindi competitions such as Hindi Sulekh (Hindi writing), Hindi Nibandh (Hindi essay) and Hindi Tippadevam Praroop (Hindi noting and drafting) were organized, in which a large number of faculty members, staff members and students participated. Hindi Diwas (Hindi Day) was celebrated on September 14th, 2021 at the culmination of Hindi Pakhwara.
2. In order to reduce hesitation while doing official work in Hindi, the Institute organized quarterly Hindi workshops/lectures for employees during the year.
3. The Institute has implemented the Government of India incentive scheme of 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.
4. The fifth edition of in-house magazine "JAIPRATIRAKSHA DARPAN" in Hindi will be published shortly.

RTI ANNUAL RETURN INFORMATION SYSTEM

Report on Receipt and Monthly Disposal of RTI Cases (2021-2022)

S. No	Year	Month	Opening balance	Receipt	Disposed	Closing Balance
1	2021	April	398	3	0	401
2	2021	May	401	2	4	403
3	2021	June	403	4	2	407
4	2021	July	407	7	4	414
5	2021	August	414	3	7	416
6	2021	Sept	416	5	2	422
7	2021	Oct	422	2	6	424
8	2021	Nov	424	2	2	426
9	2021	Dec	426	1	1	427
10	2022	Jan	427	0	0	427
11	2022	Feb	427	2	2	429
12	2022	March	429	4	4	433
	Total			35	34	

Total RTI cases disposed off as on March 31st, 2022 = 433

RTI ANNUAL RETURN INFORMATION SYSTEM (2021 -2022)

ANNUAL RETURN FORM
Year 2021 (up to March 2022)
Insert Mode (New Return)

	Opening balance as on 1-04-2021	Received during the Year 2021-2022 (including cases transferred to another Public Authority)	No. of cases transferred to another Public Authority	Decisions were request/appeals rejects/appeals rejected	Decision were requests/appeals accepted
Request	0	35	0	6	29
First Appeal	0	6	0	3	3

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
									2				4

Amount Charges Collected (in Rs)		
Registration Fee Amount	Additional Fee & Any other charges	Penalties Amount
20	-	-

Last date of uploading the pro-active disclosures on the website of PA	http://www.nii.res.in/others/right-information on 28-06-2021

ORGANIZATIONS

COMMITTEES OF THE INSTITUTE

(As on 31.03.2022)

NII SOCIETY

Dr. Jitendra Singh
President, NII Society
Hon'ble Minister of State (Independent Charge)
Science & technology and Earth Sciences

Sh. Satyendar Jain
Health Minister
Delhi Government

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

Prof. Balram Bhargava
Secretary
Department of Health Research (DHR)
Govt. of India, New Delhi

Dr. Shekhar C. Mande
Secretary
Department of Scientific &
Industrial Research (DSIR)
Govt. of India, New Delhi

Sh. Bhupinder S. Bhalla,
Principal Secretary
Health & Family Welfare
Delhi Government

Sh. Vishvajit Sahay
Financial Adviser
Department of Biotechnology
Ministry of Science & Technology
Govt of India, New Delhi

Sh. Chaitanya Murti
Joint Secretary (Admin)
Department of Biotechnology
Ministry of Science & Technology
Govt of India, New Delhi

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

Prof. Y. K. Gupta
President
AIIMS,
Bhopal, MP

Prof. M. Jagadesh Kumar
Chairman
UGC, New Delhi

Dr. Rajesh Jain
Managing Director
Panacea Biotech, New Delhi

Prof. G. Padmanaban
Former Director
IISc, Bengaluru

Dr. Subeer S. Majumdar
Distinguished Scientist,
NIAB and Former Director (NIAB)
Hyderabad

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

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'
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Ministry of Science & Technology
Government of India
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Director, RMLIMS
Professor, Department of Hematology
Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGI)
Lucknow

Dr. Anurag Agrawal
Director
CSIR-Institute of Genomics
and Integrative Biology (CSIR-IGIB)
New Delhi

Dr. Manoj Kumar Bhat
Director
National Centre for Cell Science (NCCS)
Pune

Prof. Minakshi Bhardwaj
Professor of Pathology,
RML Hospital and ABVIMS
New Delhi

Dr. Kakali Dey Dasgupta
Nodal Officer of NII
Scientist-E
Department of Biotechnology
Ministry of Science & Technology
Govt. of India, New Delhi

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

Dr. Debasisa Mohanty
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. RV Hosur
(Chairman)
Tata Institute of Fundamental Research
Mumbai - 400005

Prof. Amita Aggarwal
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow - 226014

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Ashoka University
Sonepat- 131029

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Tata Memorial Centre
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Irvine
USA

Dr. Suchita Ninawe
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Department of Bioechnology
Government of India

Prof. Soniya Nityanand
RMLIMS, Lucknow and
Sanjay Gandhi Postgraduate Institute of Medical Sciences
Lucknow - 226014

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Berhampur
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Punjab - 140306

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Bengaluru - 560012

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Kanpur - 208016

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National Centre for Biological Sciences
Bangalore - 560065

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University of Delhi
Delhi - 110007

Dr. Mohan Wani
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Pune - 411007

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Financial Adviser
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Dr. Suchita Ninawe
Scientist 'G
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New Delhi

Dr. Monica Singhania
Professor
Faculty of Management Studies,
University of Delhi
New Delhi

Sh Sanjay Gupta
Former President
Institute of Cost Accounts of India,
New Delhi

Dr. Pushakr Sharma
Director (Additional Charge)
National Institute of Immunology
New Delhi

Dr. D.K Vashist
Senior Manager
National Institute of Immunology
New Delhi

Sh. Pradeep Chawla
Finance & Accounts Officer
National Institute of Immunology
New Delhi

BUILDING COMMITTEE

Shri Ashwani Nagar
(Chairperson)
Retired Principal General Manager & Head of Civil Engineering Division of Department of Telecom

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

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

Director, NII
Member (Ex-Officio)
Ex-officio Director
National Institute of Immunology
Aruna Asaf Ali Marg
New Delhi

Sh. M.K. Gupta
Ex. Engineer-in- charge (Civil), IUAC
New Delhi

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

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

ACADEMIC COMMITTEE

Dr. Pushkar Sharma
Chairperson
Director (Additional Charge)
National Institute of Immunology
Aruna Asaf Ali Marg
New Delhi

Prof. Subrata Sinha
Professor & Head
Department of Biochemistry
All India Institute of Medical Sciences
New Delhi

Prof. Yogendra Singh
Department of Zoology
University of Delhi

Prof. Ajay Kumar Saxena
School of Life Sciences
J.N.U. New Delhi

Prof. B. R Panda
School of Biotechnology
J.N.U. New Delhi

Prof. Satish Chandra Garkoti
Rector-II
Jawaharlal Nehru University
New Delhi

Dr. Sanjeev Das
Staff Scientist
National Institute of Immunology
Aruna Asaf Ali Marg
New Delhi

Dr. Monica Sundd
Staff Scientist
National Institute of Immunology
Aruna Asaf Ali Marg
New Delhi

Dr. Debasisa Mohanty
Academic/Student Affairs
Staff Scientist
National Institute of Immunology
Aruna Asaf Ali Marg
New Delhi

INSTITUTIONAL ANIMAL ETHICS COMMITTEE

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

Dr. Bal Gangadhar Roy
(CPCSEA Main Nominee)
EFA, Institute of Nuclear Medicine &
Applied Sciences (INMAS)
Delhi

Dr. Jyoti Yadav
(CPCSEA Link Nominee)
CSIR- Institute of Genomics and Integrative
Biology
Mall Road, Delhi

Dr. Poonam Vishwakarma
(CPCSEA nominated Member)
Veterinarian, Biosafety Support Unit
New Delhi

Sh. Amit Kamboj
(CPCSEA nominated Member)
MSS – Control Medical Service Society
New Delhi

Dr. Madhulika Srivastava
Staff Scientist
National Institute of Immunology
New Delhi

Dr. P Nagarajan
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

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. Prafullakumanr B Tailor
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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. Sandeep Mathur
All India Institute of Medical Sciences
New Delhi

Dr. Shinjini Bhatnagar
Translational Health Science &
Technology Institute
Faridabad

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

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

Mr. 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 31.03.2022)

SCIENTIFIC STAFF

Core & Infrastructure Scientists

Dr. Pushkar Sharma, Staff Scientist-VII & Director (Additional Charge)

Dr. Debasisa Mohanty, Staff Scientist-VII

Dr. Madhulika Srivastava, Staff Scientist-VII

Dr. Vinay K. Nandicoori, Staff Scientist-VII (On Deputation)

Dr. Sagar Sengupta, Staff Scientist-VII

Dr. Sangeeta Bhaskar, Staff Scientist-VII

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. Anil Kumar, Staff Scientist-IV

Dr. Devram Ghorpade, Staff Scientist-IV

Dr. Santiswarup Singha, Staff Scientist-IV

Dr. Tanmay Majumdar, Staff Scientist-IV

Dr. Senthil Kumar, Staff Scientist-IV

Dr. Ankita Varshney, Staff Scientist-III

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Dr. Rahul Pal

Professor of Eminence

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Dr Archana Pant

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Mr. Amir Khan

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TARE Fellowship
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Research Associate II
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Dr. Monika Chauhan
Dr. Manju Kashyap

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Ms. Deepa Kale
Ms. Ridhi Sharma
Sh. Pradeep Ganguly
Sh. Biplab Singha
Ms. Priya Gupta
Sh. Rahul Singh Rawat
Sh. Uday Aditya Sarkar
Dr. Syed Yusuf Mian
Ms. Kritee Mehdiratta
Sh. Shams Tabrez
Dr. Richa Pahuja
Ms. Charu Garg
Ms. Shilpa Sachan
Sh. Somdeb Chattopadhyay
Sh. Rajesh Vikkurthi
Ms. Arushi Goel

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Ms. Pooja
Ms. Debalina Chatterjee
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Mr. Amir Khan
Ms. Anam Ashraf
Ms. Anurag Kalia
Ms. Ayushi Jain
Mr. Bhushan Dilip Dhamale
Ms. Gagandeep Kaur
Ms. Garima
Mr. Gautam Chandra Sarkar
Ms. Hema Sori
Mr. Irshad
Mr. Lalit Pal
Ms. Monika Chauhan
Ms. Monika Yadav
Ms. Prakriti Sinha
Ms. Sowmiya Gupta
Ms. Yashika Ratra
Ms. Annesa Das
Ms. Anam Tasneem
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Ms. Tripti Nair
Mr. Uday Adity Sarkar
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Ms. Nilakhe Aishwarya Shirkant
Mr. Abhiraj R
Mr. Aftab Mohammed
Ms. Ankita Pal
Ms. Antara Mondal
Mr. Biswajit Ghosh
Ms. Chandrima Bharadwaj
Mr. Chem Chongtham
Ms. Deepsikha Kar
Ms. Anjali Kalia
Ms. Sivani Karalia
Ms. Komal
Mr. Mohit Yadav
Mr. Naveen Kumar
Ms. Priyadarshini Sanyal
Ms. Rashmi Sanjay Bhosale
Mr. Raunak Kar
Ms. Rimpy Arun
Ms. Sabnam Sahin Rahman
Ms. Sapna Pal
Ms. Shabnam
Ms. Shreya Bhattacharya
Mr. Someshwar Natha Jha
Mr. Soumya Banerjee
Ms. Yogita Kapoor
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
Mr. MD Azad
Ms. Pratiksha Shome
Ms. Rashi Mittal
Ms. Savita
Ms. Shaika 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

TECHNICAL STAFF

Senior Technical Officers
Sh. Ajay Kumar
Ms. Sweety Batra
Ms. Rekha Rani
Ms. Sushma Nagpal
Ms. Archana Ranjan
Dr. Neerja Wadhwa

Technical Officers II
Ms. Neetu Kunj
Sh. Ranbir Singh
Sh. Md Aslam
Sh. Ashok Kumar
Sh. Dayanand
Sh. Ram Bodh
Sh. Rajit Ram
Sh. Kevlanand
Sh. Inderjit Singh
Sh. Chanderdeep Roy
Sh. Sunder Singh Bisht
Sh. Dharamvir 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

Technical Officers I
Sh. Ravi Ranjan Kumar
(S/o Sh.Vijay Kumar)
Sh. Ravi Ranjan Kumar
(S/o Sh Shivajee Prasad)
Sh. Ankit Sharma
Sh. Sudipta Das
Sh. Pankaj Kumar Mahto
Sh. Vimlesh Singh
Ms. Sarojini Minj
Sh. T. Khaling
Sh. Raghav Ram

Technicians I
Sh. Raj Kr. Pedipaga
Sh. Ajay Bansal
Sh. Vijendra Kumar
Sh. Nand Lal Arya
Sh. Rakesh Kumar
Sh. Kiran Pal
Sh. Babu Lal Meena
Sh. Birender Roy
Sh. Puran Singh
Sh. Shahnawaj Haider
Sh. Rajesh K. Meena
Sh. Anand Prakash Toppo

Technicians II
Sh. Vineet Singh
Sh. Naresh Kumar
Sh. Pankaj Kumar
Sh. Surender Singh Rawat
Sh. Sonu Gupta
Sh. Arun Lal

Skilled Work Assistants
Sh. Raj Kumar
Sh. Vijay Pal
Sh. Bhan Singh
Sh. Ram Chander
Sh. Chatter Singh
Sh. Amarnath Prasad
Sh. Jawahar Singh
Sh. Rakesh Kumar II
Sh. Hemant
Ms. Monika
Sh. Himanshu Kumar

ACADEMIC CELL

Administrative Officer
Sh. Madan Mohan

Section Officer
Ms. Sanju Bisht

Skilled Work Assistant
Ms. Rupinder Kaur

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Sh. M.S.V.V.S. Rao
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
Sh. Harendra Singh

Senior Technical Officer
Sh. Mukesh Chander

Assistant Engineers
Sh. Amarnath Sah
Sh. Sooraj Prakash
Sh. Rambir Singh
Sh. R.K. Bharadwaj
Sh. R.K. Sharma
Sh. Yogesh Kr. Tripathi
Sh. Iswari Prasad Sharma
Sh. Vinod Kumar Panchal
Sh. Mahabeer Singh Panwar

Technical Officer I
Sh. Sharwan Kumar

Management Assistant
Sh. Mohan S Negi

Technicians I
Sh. Akshyay Kumar Behra
Sh. Pramod Yadav
Sh Amarnath Gope
Sh. Sanish Kumar

Technicians 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

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Ms. Meenakshi
Sh. Ranjiv Mahajan

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Sh. Phunglianpau

Technical Officer I
Sh. Satish K Sharma

Technician I
Sh. Babu Lal

PRIMATE RESEARCH CENTRE

Senior Technical Officer (Vet)
Dr. Surender Singh

Senior Technical Officer
Sh. H. S. Sarna

Technical Officers II
Sh. Rajesh Kumar
Sh. J.P. Bhardwaj

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

SMALL ANIMAL FACILITY

Technical Officers II
Sh. Sadhu Ram
Sh. Surender Singh
Sh. Shailendra K. Arindkar
Sh. Mohan K Mandal
Sh. Dinesh CPS Negi
Sh. Kapoor Chand

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

Skilled Work Assistants
Sh. Kuldeep Kumar
Sh. Nand Kishore
Sh. Prem Chand
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

Section Officers
Ms. Sheela Satija
Ms. Daisy Sapra
Sh. Mahender Pal Singh

Management Assistants
Sh. Sant Lal
Sh. Siddharth Sharma
Ms. Neha
Sh. Sandeep Patil
Sh. Deepak Yadav
Sh. Virender Singh Kandoria

Junior Translator
Ms. Nisha

Junior Assistants
Sh. Alam Singh
Sh. Darwan Singh

Junior Assistant II
Sh. Atyush Kumar

Drivers
Sh. Madan Lal
Sh. Mahender Singh
Sh. Satyabir Singh
Sh. Suti Prakash

Skilled Work Assistants
Sh. Dinesh Singh
Sh. Nand Lal Malakar
Sh. Ajay Kumar
Sh. Rajeev Kumar
Ms. Usha

FINANCE & ACCOUNTS

Finance & Accounts Officer
Sh. Pradeep Chawla

Section Officers
Sh. Rakesh Satija
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

Management Assistants
Sh. Dharambir
Sh. Ramswaroop Meena

Junior Assistant I
Sh. Debarshi Deb

Skilled Work Assistant
Sh. Balraj

PATENT CELL
Dr. Anil Kumar

Management Assistant
Sh. Om Prakash

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

Anirban Molla, Tanya Jain and Phunglianpau

A PAGE FROM HISTORY

Dr. Manju Sharma (Secretary, DBT) inaugurating the Experimental Animal Wing on 6th October, 2002. Dr. Sandip Basu (Director, NII) and Mr. B Bose (Senior Manager, NII) were also present.

NII COLLABORATIONS

NII National Collaborations

1	**Aligarh**	AMU, Aligarh
2	**Ajmer**	Central University of Rajasthan, Ajmer
3	**Bangalore**	IISc, NCBS, JNCASR, IOB
4	**Bhubaneshwar**	ILS, RMRC
5	**Chennai**	Cancer Institute (WIA)
6	**Dehradun**	Government Doon Medical College
7	**Dibrugarh**	RMRC, Dibrugarh, Assam
8	**Faridabad**	THSTI, RCB, ESIC Medical College & Hospital
9	**Gandhinagar**	IIT Gandhinagar
10	**Gurugram**	Amity University, Gurugram
11	**Hyderabad**	CCMB, NIAB
12	**Indore**	RRCAT, Indore

13	**Jaipur**	MGH, SRCC
14	**Kolkata**	Bose Institute, Kolkata
15	**Mumbai**	TIFR
16	**New Delhi**	NIP, AIIMS, NIMR-ICMR, DU, JNU, IITD, ICGEB, VMMC/Safdarjung Hospital, ILBS, CSIR-IGIB, Dr Shroff Charity Eye Hospital, RML Hospital, JMI, NPL, VIMHANS, IRCH, NCI-AIIMS
17	**Pilani**	BITS-Pilani
18	**Puducherry**	JIPMER
19	**Pune**	CSIR-NCL, IISER
20	**Roorkee**	IIT-Roorkee
21	**Ropar**	IIT-Ropar
22	**Varanasi**	IIT-BHU

NII International Collaborations

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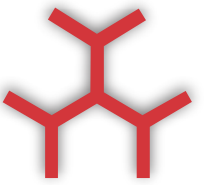
4	Karl Pfeifer (National Institutes of Health, Bethesda, USA)
5	Sriram Neelamegham (State University of New York, Buffalo, USA)
6	Abhyudai Singh (Universty of Delaware, USA)

7	Ilpo Huhtaniemi (Imperial College, London)
8	Alain Townsend (MRC, Oxford, United Kingdom)
9	Patrick Legembre (Universite de Rennes, France)
10	Etienne Joly (IPSB, Toulouse, France)
11	Cyrille Botte (IAB, University of Grenoble, Grenoble, France)
12	Subhra K. Biswas & Dilip Kumar (SIgN, A*STAR, Singapore)
13	Christian Doerig (RMIT University, Melbourne, Australia)



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