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Brief Profile

Sharmistha Banerjee received her Ph.D. in Biochemistry in 2005 from University of Hyderabad. She worked at Centre for DNA Fingerprinting and Diagnostics, Hyderabad, India, on TCA cycle enzymes of *Mycobacterium tuberculosis* and later continued her postdoctoral studies at the Laboratory of Transcriptional Biology on mechanisms of Rho-dependent termination in *E. coli.* She worked briefly at Molecular Cardiology Unit, Lerner Research Institute, The Cleveland Clinic, Cleveland, USA on role of integrins in prostate cancer metastasis.

Presently, as a Professor in the Department of Biochemistry, School of Life Sciences, she works on Mycobacterial adaptation and HIV cellular tropism, and teaches Immunology and Enzymology along with various topics on Infectious diseases and host pathogen interactions.

Honours and Awards:

- Member, The Society of Council of Scientific and Industrial Research), Ministry of Science and Technology, 2019-2022
- Chancellor's Award 2017, University of Hyderabad
- National Women Bioscientists Award (Young Category) 2016, from Department of Biotechnology, Govt. of India
- Prof BK Bachhawat International Travel Grant for Young Scientists 2018
- Innovative Young Biotechnologist Award (IYBA) 2011, *from* Department of Biotechnology, Govt. of India
- BioAsia Innovation Award 2008
- INSA Young Scientist Award 2005, from The Indian National Science Academy

Research Interests: Mycobacterial Biology and HIV Cell Tropism

The principal theme of the lab is to comprehend and decode the evolutionary conflicts between host and pathogens using two critical human pathogens as model systems, *Mycobacterium tuberculosis* (the tuberculosis [TB] causing bacilli) and Human Immunodeficiency Virus (HIV), which are not only major health hazards but have huge socioeconomic impact on our society. We are investigating metabolic rewiring as an adaptive response by *Mycobacterium tuberculosis* (*M.tb*) to intracellular microbicidal stresses and its cross-talk with host (macrophages) metabolism,

which orients host responses to aggressive clearance or persistence and dissemination of *M.tb* during mono-infection or during co-morbidities like HIV infection and dyslipidemia, identifying potential drug targets and biomarkers.

We are also focusing on pathophysiology of HIV, especially in the context of cell-specific regulation imposed on viral titers and infectivity dynamics, which defines rapid, latent or abortive propagation. The focus is on discovering cell-specific intrinsic antiviral mechanisms that can add new facets to our understanding of host innate immune mechanism against retroviruses.

The long-term objective of the lab is to translate the basic sciences know-how into intervention strategies in the form of new biomarkers, anti-retrovirals and anti-mycobacterials.

Publications:

- Vadankula GR, Rizvi A, Ali H, Khunjamayum R, Eedara VVR, Nema V, Ningthoujam DS, Suresh Babu K, Shetty PR, Mande SC, Banerjee S* (2025) Secondary Metabolites from a New Antibiotic-Producing Endophytic Streptomyces Isolate Inhibited Pathogenic and Multidrug-Resistant Mycobacterium tuberculosis Strains. *Trop. Med. Infect. Dis.* 2025, 10(5), 117; https://doi.org/10.3390/tropicalmed10050117
- 2. Rangaraj S*, Agarwal A*, **Banerjee S* (2025)** Bird's Eye View on Mycobacterium tuberculosis-HIV Coinfection: Understanding the Molecular Synergism, Challenges, and New Approaches to Therapeutics. ACS Infect Dis, 2025 Apr 14.doi: 10.1021/acsinfecdis.4c00870. *#equal contribution.
- 3. Mohareer K*, Medikonda J, Yandrapally S, Agarwal A, **Banerjee S* (2025)** Monitoring the mitochondrial localization of mycobacterial proteins. Methods in Cell Biology, Academic Press, ISSN 0091-679X, https://doi.org/10.1016/bs.mcb.2024.10.018.
- Medikonda J, Wankar N, Asalla S, Raja SO, Yandrapally S, Jindal H, Agarwal A, Pant C, Kalivendi SV, Dubey HK, Mohareer K, Gulyani A, Banerjee S* (2024) Rv0547c, a functional oxidoreductase, supports Mycobacterium tuberculosis persistence by reprogramming host mitochondrial fatty acid metabolism. Mitochondrion, https://doi.org/10.1016/j.mito.2024.101931.
- Vadankula GR, Nilkanth VV, Rizvi A, Yandrapally S, Agarwal A, Chirra H, Biswas R, Arifuddin M*, Nema V, Mallika A, Mande SC, Banerjee S* (2024) Confronting Tuberculosis: A Synthetic Quinoline-Isonicotinic Acid Hydrazide Hybrid Compound as a Potent Lead Molecule Against Mycobacterium tuberculosis. ACS Infect. Dis. 2024, 10, 6, 2288–2302; https://doi.org/10.1021/acsinfecdis.4c00277
- Kumaraswami C, Yandrapally S, Faiz W, Kispotta CR, Sarkar S, Mishra K, Banerjee S*(2024) The nuclear pore protein NUP98 impedes LTR-driven basal gene expression of HIV-1, viral propagation, and infectivity. Front Immunol. 2024 Feb 21:15:1330738.; doi: 10.3389/fimmu.2024.1330738.
- Yandrapally S, Sarkar S, Banerjee S (2023). HIV-1 Tat commandeers nuclear export of Rev-viral RNA complex by controlling hnRNPA2-mediated splicing. *Journal of Virology*, J Virol2023 Oct 31:e0104423, doi: 10.1128/jvi.01044-23.
- 8. Yandrapally S, Agarwal A[‡], Chatterjee A[‡], Sarkar S[§], Mohareer K[§], **Banerjee S* (2023).** Mycobacterium tuberculosis EspR modulates Th1-Th2 shift by transcriptionally regulating IL-4, steering increased mycobacterial persistence and HIV propagation during coinfection. *Front. Immunol.*, Vol 14, https://doi.org/10.3389/fimmu.2023.1276817
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- 10. Mohareer K* and **Banerjee S*** (2023) Mycobacterial infection and host mitochondrial activity. *International Review of Cell and Molecular Biology*. https://doi.org/10.1016/bs.ircmb.2023.01.007

- 11. Sarkar S, Balakrishnan K, Chintala K, Mohareer K, Luedde T, Jaguva Vasudevan AA, Münk C and Banerjee S* (2022). Tough Way In, Tough Way Out: The Complex Interplay of Host and Viral Factors in Nucleocytoplasmic Trafficking during HIV-1 Infection. Viruses 2022, 14, 2503. https://doi.org/10.3390/v14112503 (9th Nov 2022)
- 12. Balakrishnan K, Munusami P, Mohareer K, Priyakumar UD, Banerjee A, Luedde T, Mande SC, Münk C*, **Banerjee S* (2022)**. Staufen-2 functions as a cofactor for enhanced Revmediated nucleocytoplasmic trafficking of HIV-1 genomic RNA via the CRM1 pathway. *The FEBS J, 289 (21): 6731-6751; doi.org/10.1111/febs.16546*
- 13. Conde R, Laires R, Gonçalves, LG, Rizvi A, Barroso C, Villar M, Macedo R, Simões MJ, Gaddam S, Lamosa P, Puchades-Carrasco L, Pineda-Lucena A, Patel AB, Mande SC, Banerjee S, Matzapetakis M, Coelho AV (2022). Discovery of serum biomarkers for diagnosis of tuberculosis by NMR metabolomics including cross-validation with a second cohort. Biomedical J. 2022, 45: 654-664. https://doi.org/10.1016/j.bj.2021.07.006 Aug 2022
- 14. Yenuganti VR*, Afroz S, Khan RA, Bharadwaj C, Nabariya DK, Nayak N, Subbiah M, Chinthala K, **Banerjee S**, Reddanna P, Khan N* **(2022).** Milk exosomes elicits a potent anti-viral activity against Dengue virus. *J Nanobiotech* https://doi.org/10.1186/s12951-022-01496-5 jul 2022
- 15. Kanaparthi KJ, Afroz S, Minhas G, Moitra A, Khan RA, Medikonda J, Naz S, Cholleti NS, Banerjee S, Khan N (2022). Immunogenic profiling of Mycobacterium tuberculosis DosR protein Rv0569 reveals its ability to switch on Th1 based immunity. *Immunol Lett, 242; 27-36.*
- 16. Nehvi IB, Quadir N, Khubaib M, Sheikh JA, Shariq M, Mohareer K, **Banerjee S**, Rahman SA, Ehtesham NZ, Hasnain SE **(2022)**. ArgD of Mycobacterium tuberculosis is a functional N-acetylornithine aminotransferase with moonlighting function as an effective immune modulator. *Int J Med Microbiol.* 312 (1):151544. doi: 10.1016/j.ijmm.2021.151544.
- 17. Balakrishnan, K.; Vasudevan, A.A.J.; Mohareer, K.; Luedde, T.; Münk, C*.; Banerjee, S* (2021). Encapsidation of Staufen-2 Enhances Infectivity of HIV-1. *Viruses 2021, 13, 2459. https://doi.org/10.3390/v13122459*
- 18. Chintala K, Mohareer K, Banerjee S*. (2021). Dodging the host Interferon-Stimulated Gene mediated innate immunity by HIV-1: a brief update on intrinsic mechanisms and counter-mechanisms. *Frontiers in Immunology, 2021 Jul 29;12:716927. DOI: 10.3389/fimmu.2021.716927.*
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- Vasudevan AAJ¹, Balakrishnan K¹, Gertzen CGW, Borvető F, Zhang Z, Sangwiman A, Held U, Küstermann C, Banerjee S, Schumann GG, Häussinger D, Bravo IG, Gohlke H, Münk C. (1 contributed equally) (2020). Loop 1 of APOBEC3C regulates its antiviral activity against HIV-1. *J Mol Biol.* doi: 10.1016/j.jmb.2020.10.014; Nov 20;432(23):6200-6227.
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- 29. Asalla S, Mohareer K, **Banerjee S**. (2017) Small molecule mediated restoration of mitochondrial function augments anti-mycobacterial activity of human macrophages subjected to cholesterol induced asymptomatic dyslipidemia. *Front. Cell. Infect. Microbiol*. 2017; 7: 439 doi: 10.3389/fcimb.2017.00439
- 30. Balakrishnan K, Mohareer K, **Banerjee S.** (2017) Mycobacterium tuberculosis Rv1474c is a TetR-like transcriptional repressor that regulates aconitase, an essential enzyme and RNA-binding protein, in an iron-responsive manner. *Tuberculosis (Edinb)*. 103: 71–82
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- 32. Reddy ER, Yaseen AM, Rizvi A, Deora GS, **Banerjee S**, Sevilimedu A, Rajadurai M. (2017) Antibacterial Nanoparticles Based on Fluorescent 3-Substituted Uridine Analogue *Chemistry Select* 2017, 2, 557 –561
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- 34. Vemula MH, Ganji R, Sivangala R, Jakkala K, Gaddam S, Penmetsa S, **Banerjee S**. (2016). Mycobacterium tuberculosis Zinc Metalloprotease-1 Elicits Tuberculosis-Specific Humoral Immune Response Independent of Mycobacterial Load in Pulmonary and Extra-Pulmonary Tuberculosis Patients. *Front Microbiol. 7: 418.*
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- 40. Banerjee A, Benjamin R, Balakrishnan K, Ghosh P and **Banerjee S*** (2014) Human protein Staufen-2 promotes HIV-1 proliferation by positively regulating RNA export activity of viral protein Rev. *Retrovirology* 11:18.

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- 43. Benjamin R, Banerjee A, Sunder SR, Gaddam S, Valluri VL and **Banerjee S** (2013) Discordance in CD4+T-Cell Levels and Viral Loads with Co-Occurrence of Elevated Peripheral TNF-α and IL-4 in Newly Diagnosed HIV-TB Co-Infected Cases. *PLoS ONE* 8(8): e70250. doi:10.1371/journal.pone.0070250
- 44. Banerjee A, Benjamin R, **Banerjee S** (2013). Impact of viral factors on subcellular distribution and RNA export activity of HIV-1 rev in astrocytes 1321N1. *PLoS One.* 2013 Sep 4;8(9):e72905. doi: 10.1371/journal.pone.0072905.
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- 47. **Banerjee S**, Farhana A, Ehtesham NZ, Hasnain SE. Iron acquisition, assimilation and regulation in mycobacteria. (2011) *Infection, Genetics and Evolution* 11: 825–838.
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Book Chapters:

- Mohareer K, Medikonda J, Yandrapally S, Agarwal A Gulyani A, Banerjee S. (2024) Monitoring the mitochondrial localization of mycobacterial proteins in *Methods in Cell Biology*, Academic Press, ISSN 0091-679X, DOI: <u>10.1016/bs.mcb.2024.10.018</u>.
- Mohareer K and Banerjee S* (2021) Zmp1 peptidase ({Mycobacterium}-type), Rawlings -Vol. 1 - Handbook of Proteolytic Enzymes, 4e: Metallopeptidases, Elsevier (In press); Editors: Neil Rawlings, David Auld; Paperback ISBN: 9780128235874
- 3. Mohareer K, **Banerjee S** and Hasnain SE (2013). Recombinant DNA technology in Eukaryotic gene expression system. (In: Textbook of Biochemistry, Biotechnology, Allied & Molecular Medicine (Editor: G.P. Talwar), Prentice Hall of India, 2013
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- 5. **Banerjee S**, Mohareer K, Hasnain SE. (2010) Molecular diagnostics of MDR and XDR TB. publishers: Ranbaxy Science Foundations. P:73-87.
- 6. **Banerjee S**, Siddiqi N, Hasnain SE (2009). Drug resistance tuberculosis. In Tuberculosis (2nd Edition), Edited by Sharma SK and Alladi Mohan

Ongoing themes in the lab with some relevant publications

Basic Biology Components

Stress adaptation and quorum sensing in mycobacteria

Deciphering adaptive metabolic and regulatory networks of *Mycobacterium tuberculosis* in response to infection and related stresses through proteomics and metabolomics; identification and validation of critical enzymes as potential targets and screening small molecule inhibitors against these targets for anti-mycobacterial activity.

- Mohareer K*, Medikonda J, Yandrapally S, Agarwal A, Banerjee S* (2024) Monitoring the mitochondrial localization of mycobacterial proteins. Methods in Cell Biology, Academic Press, ISSN 0091-679X, https://doi.org/10.1016/bs.mcb.2024.10.018.
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- Rizvi A, Shankar A, Chatterjee A, More TH, Bose T, Dutta A, Balakrishnan K, Madugulla L, Rapole S, Mande SS*, Banerjee S*, Mande SC* (2019). Rewiring of Metabolic Network in Mycobacterium tuberculosis During Adaptation to Different Stresses. Front Microbiol. 29;10:2417. doi: 10.3389/fmicb.2019.02417.
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 Mycobacterium tuberculosis Zinc Metalloprotease-1 assists mycobacterial dissemination in Zebrafish. Front Microbiol. 7: 1347

Cell-specific regulation of HIV and cellular tropism

Although chronic stages of HIV-1 disease witness infection of a wide range of cells, it propagates unrestrainedly in a few cell types (such as T-cells), while some cells limit viral propagation, serving as reservoirs (such as astrocytes). This points to distinct anti-viral strategies by 'HIV-1 propagation-limiting' cells. The impact of cell-specific microenvironments and cellular events modulating these dynamics and infectivity are poorly understood in the field. We aim to understand the fundamentals of HIV restriction systematically in HIV-propagation-limiting cells to address some of these questions, focusing on nucleocytoplasmic transport of viral factors and packaging of host cargoes in viruses emerging from different producer cells.

- Kumaraswami C, Yandrapally S, Faiz W, Kispotta CR, Sarkar S, Mishra K, Banerjee S* (2024) The nuclear pore protein NUP98 impedes LTR-driven basal gene expression of HIV-1, viral propagation, and infectivity. Front Immunol. 2024 Feb 21:15:1330738.; doi: 10.3389/fimmu.2024.1330738.
- Yandrapally S, Sarkar S, Banerjee S (2023). HIV-1 Tat commandeers nuclear export of Rev-viral RNA complex by controlling hnRNPA2-mediated splicing. *Journal of Virology*, J Virol2023 Oct 31:e0104423, doi: 10.1128/ivi.01044-23.
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Co-infection Biology: Mycobacterial factors influencing HIV propagation

System-wide studies to identify the concurrent perturbations in the proteomes of both host cell and intracellular mycobacteria during HIV co-infection and deciphering the underlying molecular mechanisms, focusing on mycobacterial factors affecting HIV propagation, either directly or via altering host microenvironment.

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Translational Biology Components

New drug targets and lead molecules against TB & HIV

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Biomarker for extrapulmonary and latent TB

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MOLECULAR PATHOGENESIS LABORATORY RESEARCH SCHOLARS

Govinda Raju Vadankula (PhD scholar): govindraj.vadankula @gmail.com



In the quest for new anti-mycobacterials, my research objectives focus on identifying inhibitors against *M.tb*, the bacillus that causes Tuberculosis. This research has led to the identification of several inhibitor molecules that primarily target pathogenic mycobacteria. The approaches used, including isolating secondary metabolites from natural products and synthesis, screening, and validating new molecules through untargeted and targeted screening against M.tb- shikimate kinase, have yielded promising results. The potential of these findings could revolutionize Tuberculosis treatment, particularly in overcoming the challenge of Multidrug-resistant TB, which is a cause for hope and optimism in microbiology and pharmacology.

Sriram Yandrapally (PhD awarded): sriramyendrapelly@gmail.com



Insights into cellular proteins and pathways affecting nucleocytoplasmic transport of HIV-1 factors and propagation: During my PhD, I aimed to understand the dynamics of the intra-host molecular evolution of viruses, which depend on the complexity of the host microenvironment while propagating through different cell types. During this tenure, I have advanced two research ideas. 1. Crosstalk between HIV-1 factors and host splicing machinery, and 2. Encapsidation of host factors and its impact on virus phenotypes and infectivity. Currently, I am moving to Yale University as a postdoctoral Associate, where I would be generating HIV resistant CD4+T lymphocytes and *in vivo* CARs against HIV.

Omkar Zade (PhD scholar): omkarzade02@gmail.com



research aims to explore *M.tb* protein, Zmp1, as а diagnostic for pulmonary and extra-pulmonary tuberculosis (EPTB) and its potential as a vaccine adjuvant. The diagnosis of EPTB is often challenging due to its non-specific symptoms and could benefit from a reliable biomarker like Zmp1, that would allow early detection and treatment. Additionally, incorporating Zmp1 as an adjuvant in existing TB vaccines could potentially boost immune responses, improving the efficacy of existing vaccines. This dual potential of Zmp1 could revolutionize TB management, offering more accurate diagnostics and robust preventive measures, ultimately contributing to the global efforts in combating this persistent infectious disease.

Nandini Wankar Vijay (PhD scholar): wankarnandini@gmail.com



The metabolite measurements coupled with metabolic network models and flux analysis indicated increased flux of L-asparagine and increased ammonia release under acidic stress when correlated with a decrease in Urease activity at early time points. We hypothesized that high levels of released ammonia as an early response to acidic stress may be due to increased flux through L-asparaginase rather than Urease, making it a potential target for novel tuberculosis therapies. Studying the metabolic knockout of Mtb L-asparaginase under infection conditions would lead us to understand the metabolic rewiring of Mycobacteria and how it influences the host immune response to establish the infection.

Anushka Agarwal (PhD scholar): anukartik70@gmail.com



The GABA SAGA: I am trying to understand the role of γ -aminobutyric acid (GABA), a metabolite produced by *M.tb* during infection, in host immuno-modulations. We hypothesize that mycobacteria produce GABA to adapt to stress conditions, particularly acidic stress within the phagolysosomes. Since GABA is a conserved metabolite between mycobacteria and humans, wherein it is known to have immunomodulatory functions, we also expect that GABA produced by Mtb can be sensed by the host system, which may alter the metabolism of the host cells. We are interested in

understanding whether such GABA-induced metabolic alterations in host can alter either macrophage phenotype or immune responses against *Mtb*. If yes, whether GABA would function as an anti-*Mtb* or pro-*Mtb* metabolite during infection?

Siranjeevi Rangaraj (PhD scholar): siranjeeviharan12@gmail.com



I am working on *M.tb*-HIV coinfection biology. *M.tb* and HIV is a paradigm of syndemic. During the HIV-TB coinfection, *M.tb* increases the HIV viral titer and the switch between R5 to X4 viral tropism; on the other hand, HIV delays the *M.tb* clearance by inhibiting phagosome maturation. The *M.tb* molecular players responsible for the syndemic are yet to be explored. My larger aim would be to find the *M.tb* factors responsible for the positive impact on HIV during the coinfection state.

Satarupa Sarkar (PhD scholar): satarupasarkar658@gmail.com



My research quest involves the understanding of new host protein-pathogen interactions that are decisive in shaping HIV population dynamics and infectivity. Though HIV hampers various steps of the host to establish its life cycle, I am particularly interested in the nucleo-cytoplasmic transport of viral proteins and RNA. I am also looking at chaperones which may be useful in HIV protein folding and maturation after budding from the infected cell. These findings may be useful towards host guided therapy for the control of HIV disease progression.

Harish Kumar Dubey (PhD scholar): harishkd1989@gmail.com



My research focuses on the transcriptional regulation of PE/PPE genes that contribute 10% of the coding capacity of the *Mtb* genome and are established virulence factors. Earlier *insilico* analyses in the lab reveal that a set of *PE/PPE* are co-regulated with transcription factors (TFs)

in different stress conditions. The main aim of my study is to understand the regulations of these *PE/PPE* genes by the co-regulated TFs upon their overexpression and KO strains. TFs knockouts of *Mtb* have not been explored as potential vaccines. We expect that the attenuation will be severe and since the organism is *Mtb* itself, the immunological properties of the same may be better than the available *M. bovis* BCG vaccine.

Post Doctoral Fellows

Dr. Krishnaveni Mohareer (Project Scientist): krishnaveni.mohareer@gmail.com



I am interested in varied aspects of cell-cell communication in mycobacteria. We are exploring *insilico* analyses and metabolomics-based approaches in identifying various molecules that could play a role in cell-cell communication that potentially would lead to a variety of mycobacterial stress responses including biofilm formation, activation of drug resistance, and virulent gene expression. We are particularly interested in the LuxR gene family, which are known to monitor the extracellular environment as a two-component system that results in specific phenotypes *via* potential cell-cell communication.

Dr. Saima Naz (DHR-Women Scientist): saimanaz169@gmail.com



Dexosomes engineering for TB vaccine development: Engineering dendritic cell-derived exosomes (Dexosomes) represents a promising avenue for tuberculosis vaccine development. Dexosomes are nanosized vesicles that play a crucial role in antigen delivery and immune modulation. Consequently, loading Dexosomes with specific *M.tb* antigens can effectively present antigens to the immune system, eliciting robust antigen-specific CD4+ and CD8+ T cell responses. We have employed this strategy to leverage the natural antigen-presenting capabilities of Dexosomes, enhancing their potential as adjuvants and antigen delivery systems. Biocompatibility, low immunogenicity, and stability of exosomes further support their utilization as natural nanocarriers for vaccine antigen delivery. We have demonstrated that dexosomes carrying *M.tb* antigens can significantly induce robust immunity, underscoring their potential in TB vaccine development.

Lab alumni

Name	Year of PhD awarded	Position	Present affiliation
Sriram Yandrapally	2024	Post Doctoral Associate	Yale University, New Haven, Connecticut, USA
Jayashankar Medikonda	2024	Assistant Manager	Aurovaccines, Hyderabad, India
Kumaraswami Chintala	2024	Post Doctoral Fellow	Temple University, Philadelphia, USA
Kannan Balakrishnan	2022	Post Doctoral Fellow	Cleveland clinic, Florida, USA
Arshad Rizvi	2019	Post Doctoral Fellow	Emory University, Atlanta, USA
Iqra Bashir Nehvi	2019	Research Associate	University of Kashmir
Suman Asalla	2018	Post Doctoral Fellow	Ohio State University, Ohio, USA
Harika Vemula	2017	Research Associate	CDFD, Hyderabad
Rakesh Ganji	2016	Postdoctoral Scholar	Graduate School of Biomedical Sciences, Tufts University, Boston, USA
Ronald Benzamin	2014	Assistant Researcher	University of California, San Francisco, USA
Atoshi Banerjee	2014	Research Analyst	University of Nevada, Las Vegas, USA

Other Project Staff and interns:

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