



Project Proposal for Ph.D.

Project Details	
Project Title	Targeting sulfur metabolism as an effective strategy for insights into mycobacterial survival and drug discovery
Project Summary	Mycobacteria represent one of the most successful zoonotic pathogens known to mankind. This research initiative focuses on exploring the sulfur metabolism pathway to gain deeper insights into mycobacterial survival mechanisms and use this knowledge to develop novel adjunct therapies. We have earlier shown that mycobacteria can produce H₂S which can stimulate mycobacterial growth and respiration during establishment of infection (1). We have also observed that H₂S production by host also increases substantially following infection (1). We also observed that the inhibition of H₂S in macrophages led to ~20-30% increase in nitric oxide (NO) production, that has a bacteriostatic function (2), and aids in infection control. Moreover, H₂S can regulate cell death processes, which mycobacteria manipulates to aid its dissemination. This data therefore supports for a major role for sulphur metabolism in the establishment and control of mycobacterial infections. Based on these findings and other evidence in literature, we propose to investigate the sulfur metabolism pathway of host and bacteria during mycobacterial infections. We will also evaluate how modulation of H₂S during infection can impact cell signaling, metabolism and cell death pathways to impact dissemination. This may lead to identification of survival strategies opted by mycobacteria; and identify and target specific genes within this pathway for drug discovery, utilizing chemical inhibitors. Thus, by unraveling the complexities of sulfur metabolism, we aspire to pave the way for the development of effective therapeutic interventions against bacterial infections. Considering the work at the interface of infection, gaseous signaling, drug discovery and cell biology, an inter-disciplinary expertise is needed. Dr Vikram Saini (AIIMS Delhi) has extensive expertise in H₂S biology, redox biology and access to clinical/animal cohort to study infections. Dr Parul Mehrotra (IIT Delhi) will provide expertise in cell biology specifically cell death mechanisms, and metabolomics. The scholarship of both the PIs is established through there publication record. Rigor and reproducibility will be ensured by repetitions, careful supervision and periodic joint meetings between AIIMS-IIT team. This inter-disciplinary expertise is critical for superior outcomes and ultimately identification of lead molecules for improved therapeutics.

Ph.D. Supervisors				
Role	Name of Faculty		Academic Unit in IITD/Institute/University	Email ID (Official)
Supervisor 1	Dr Vikram Saini		Associate Professor, Biotechnology, AIIMS New Delhi	vikramjind@gmail.com
Supervisor 2	Dr Parul Mehrotra		Assistant Professor, Kusuma School of Biological Sciences, IIT Delhi	pmehrotra@iitd.ac.in

Project requirements (Student qualifications, experience required, etc)

*The candidate will be shortlisted based on common shortlisting criteria decided by ScRC (SIRe)

- The student should have a Master’s degree with a minimum of 60% marks.
- The candidate should have GATE or NET qualified and should preferrably have prior experience in working with infection biology/gaseous biology.

Source of fellowship/funding
(CSIR/UGC/DBT/ICMR/ICAR/NEET-PG/DST-INSPIRE/IRD/FITT Project details, if any)

Institute fellowship/ Project fellowship

Role of Faculty Members involved:

Supervisor-1	Dr. Vikram Saini is a distinguished researcher with a proven track record in elucidating the intricate mechanisms of redox signaling involving gaseous molecules. Dr. Saini will provide mentorship and training in the area of H ₂ S biology, redox biology and access to clinical/animal cohort to study infections. Dr. Saini will provide fellowship, experimental expenses to support innovative projects. Through Dr Saini the candidate will have full access to Laboratory resources, A-BSL3/BSL3 access, and access to all core facilities of AIIMS.
Supervisor-2	Dr. Parul Mehrotra has contributed significantly in the area of immunometabolism and cell death pathways. Dr. Mehrotra's research has contributed significantly to the field of immunometabolic landscaping, shedding light on how cellular metabolism influences cell fate. As part of PhD program, students will have the opportunity to work closely with Dr. Mehrotra and contribute to cutting-edge research in metabolomics and cell death pathways. Candidate will also have access to resources at IIT Delhi/central facilities especially computational resources for drug discovery and experimental support through Dr Mehrotra. Both PIs will also compete for AIIMS- IIT Delhi joint funding opportunities.

REFERENCES

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