



Project Proposal for Ph.D.

Project Details (The research problem must clearly indicate the need for an interdisciplinary approach)

Project Title	Resolution-competent antimicrobial myeloid states in BCG-induced trained immunity: a single-cell, functional and in vivo investigation in tuberculosis
Project Summary (Minimum 500 and maximum 2000 characters)	BCG is the only licensed vaccine against tuberculosis, and its mechanism remains unclear. BCG's protection is heterologous: it lowers all-cause infant mortality beyond what TB prevention explains, guards against unrelated respiratory and viral infections, and treats bladder cancer. The trained immunity is credited for driving this protection rather than antigen specific memory. Training is mostly measured as amplified pro-inflammatory output on restimulation. However, BCG lowers systemic inflammatory tone while protecting in broader side, which cannot be explained in one axis. Chakraborty et al. showed alveolar macrophages trained with LPS acquire greater efferocytic capacity through KLF4-driven MERTK upregulation and limit lung injury, so resolution-competent training exists. Whether BCG could generate this is untested, and its role against an intracellular pathogen is open. In TB, efferocytosis is both an antibacterial mechanism and a route for Mtb dissemination. This project asks whether BCG produces a myeloid state that is both antibacterial and pro-resolving, and where that capacity comes from: the bone marrow, the alveolar niche, or replacement of resident macrophages by recruited monocytes. It requires computational modelling of cell states from large single-cell datasets, controlled cellular immunology at the bench, and in vivo infection biology under BSL-3 containment, with functional data returning to constrain the models. The three broad research objectives are: 1- To search published BCG and Mtb single-cell datasets for a myeloid programme combining antimicrobial and resolving capacity and relate it to cell ontogeny. 2- To test whether the resting environment decides acquisition of this state in human macrophages trained with BCG. 3- To determine whether the state forms in vivo during Mtb infection, whether it depends on the origin of lung myeloid cells, and whether it improves bacterial control without immunopathology.

Ph.D. Supervisors* (Supervisor 1 and Supervisor 2 cannot be from the same department of IITD)				
Role	Name of Faculty	Date of Superannuation [§] (DD/MM/YYYY)	Academic Unit in IITD/Institute/University	Email ID (Official) & Contact Number
Supervisor 1*	Parul Mehrotra	31 December 2051	KSBS, IITD	pmehrotra@iitd.ac.in
Supervisor 2	Dhiraj Kumar	31 March 2040	ICGEB, New Delhi	dhiraj@icgeb.res.in

*Supervisor 1 must be from IIT, Delhi.

+All cells in this table are mandatory fields that need to be filled by faculty for consideration of proposal.

§The date of superannuation of supervisors should be at least three years from the date of registration of selected candidates.

Project requirements (Student qualifications, experience required, etc)

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

- Master's degree in Life Sciences, Biotechnology, Immunology, Computational Biology, Bioengineering or an allied discipline.
- Working knowledge of single-cell transcriptomic analysis (R/Python; Seurat or Scanpy) and of standard statistical analysis.

- Hands-on experience in mammalian cell culture, primary macrophage isolation and flow cytometry.
- Prior exposure to BSL-2/BSL-3 microbiological practice is mandatory.

Source of fellowship/funding and project number (CSIR/UGC/DBT/ICMR/ICAR/NEET-PG/DST-INSPIRE/IRD/FITT Project details, if any)
Project Funding (DBT) : BT/PR50983/MED/29/1650/2023

Role of Faculty Members involved:	
Supervisor-1	This proposal sits at the intersection of two fields that are rarely studied together efferocytosis+resolution biology (Experiese of the PI) and intracellular Mtb host-cell biology under containment (Expertiese of co-PI). The PI brings direct expertise in efferocytosis biology and its pharmacological manipulation. She will lead Aim 2 and guide the resolution arm throughout: the human macrophage training system under different niche conditions, all efferocytosis readouts (binding versus internalisation, continued uptake, surface and soluble MERTK), and the KLF4/MERTK perturbation and chromatin work. She defines the resolution module in Aim 1 and co-leads the <i>in vivo</i> resolution and immunopathology endpoints in Aim 3, including the conditional <i>Mertk/Klf4</i> and fate-reporter arms.
Supervisor-2	Dr. Kumar leads the Cellular Immunology group at ICGEB, working on host–pathogen interactions in <i>M. tuberculosis</i> infection, with established strengths in phagocyte cell biology, high-throughput experimentation and computational biology. He will lead Aims 1 and 3 and guide the antimicrobial arm and all containment work: dataset integration, regulon and trajectory analysis in Aim 1, and in Aim 3 the BSL-3 aerosol challenge, bacterial burden, chimera and adoptive-transfer arms, and sorting for single-cell sequencing. He will co-lead the bacterial handling readouts in Aim 2 and will host the virulent-Mtb components.

Note :-

1. Approval from the respective DRC/CRC/ScRC of your Department/Centre/School will be required for using the "Full-time Institute Assistantship (Category-wise) (FIA)" for selecting the students in SRe.
2. Declaration:- Faculty members, please ensure that you have at least 3 years of service left before superannuation along with adequate sitting space & lab facilities for the SRe student.
3. PI/s are also encouraged to submit joint proposals with AIIMS, NII, JNU and institutes with which IITD has an existing MoU. If the Co-PI (Supervisor 2) is from outside IITD, kindly share his/her detailed CV.
4. If a research scholar is to be considered for selection under the project fellowship, then the project should have a minimum of two-year duration remaining.
5. A candidate applying with a valid JRF/INSPIRE/any national level fellowship should have at least two-year validity from the date of joining the Ph.D. program.
6. The third supervisor’s name (if required) can be added only after the formation of Student Research Committee (SRC) subject to a strong recommendation of SRC and subsequent approval from the competent authority.
7. If institute fellowship is being sought then the DRC approval of the parent departments of both supervisors is required at the time of selection.