



Project Proposal for Ph.D.

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

Project Title	Implications of deregulated MUC4 gene expression on the risk stratification and clinical outcome in B-cell acute lymphoblastic leukemia
Project Summary (Minimum 500 and maximum 2000 characters)	B cell acute lymphoblastic leukemia is characterized by the proliferation of immature pre-B cell-like leukemic blasts that carry one or more genetic lesions such as translocations (example BCR:ABL1), aneuploidies and gene deletions (example deletion of IKZF1, TP53). Therapy refractory B-ALL remains a challenge in the clinics despite the introduction of advanced therapy such as anti-CD19 monoclonal antibody. Moreover, such therapeutic approaches are beyond the economic reach of the average Indian household. Therefore, advancement of risk stratification and finding cost effective therapeutics is required for better management of B-ALL in the clinics. Previously, we employed RNA sequencing in a cohort of 56 B-ALL patients in our clinic and observed a specific upregulation of MUC4 (a cell surface mucin) in patients with IKZF1 deletion. Interestingly, we have shown that deletion of IKZF1 is linked to poor prognosis in Indian patients. Therefore, we asked the following questions: 1. Is the high expression of MUC4 linked to the genetic background of the patients – BCR:ABL1, IKZF1 deletion, TP53 deletion etc. 2. At the molecular level, do all B-ALL blasts express MUC4 on the cell surface and is the surface MUC4 linked to proliferation and survival mechanisms of leukemic blasts. 3. Is MUC4 expression linked to the overall survival (OS) and event free survival (EFS) of the patients. To address these questions, we will recruit B-ALL patients and perform RNA sequencing and NGS to analyze the background mutations and MUC4 expression. We will use flow cytometry to analyze the expression of surface MUC4 on the blasts. We will follow up the patients in our clinic to analyze their OS and EFS. Finally, we will use a co-culture system of stromal cell line with isolated B-ALL blasts and a cell line model of B-ALL to study the effects of surface MUC4 on survival signaling.

Ph.D. Supervisors*
(Supervisor 1 and Supervisor 2 cannot be from the same department of IITD)

Role	Name of Faculty	Academic Unit in IITD/Institute/University	Email ID (Official)
Supervisor 1*	Dr. Anita Roy	Kusuma School of Biological Sciences, IIT Delhi	anita.roy@bioschool.iitd.ac.in
Supervisor 2	Dr. Sanjeev K. Gupta	Laboratory Oncology, Dr.B.R.A. IRCH, AIIMS New Delhi	drskgupta1@gmail.com

*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)

- Candidate must have a BE/BTech/MSc/MTech or their equivalent degree in any area of **life sciences** with a first class in the last qualifying examination. Candidates with MBBS/MD will also be considered.
- Candidates must have a valid JRF from CSIR/UGC/DBT/ICMR/DST or equivalent organizations.
- Candidates are expected to maintain B cell lines in culture and should have knowledge of routine biochemistry methodologies such as PCR, SDS PAGE, western blotting etc
- Knowledge at least one of the following will be preferred: CRISPR-Cas9 knockout, flow cytometry, RNA sequencing and data analysis

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

Candidates with his own fellowship/CSIR/UGC/DBT/ICMR/DST or equivalent organizations

Role of Faculty Members involved:

Supervisor-1	Supervision of the generation of knock-out cell line models, routine biochemistry and flow cytometric analysis of the clones, identifying the effects of MUC4 and its signaling pathway in B cells
Supervisor-2	Supervision of clinical data generation and management including survival, patient samples collection, patient characterization, RNA sequencing and bioinformatic analysis

- 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 DRC approval of the parent department of Supervisor 1 is required at the time of selection.**