Indian Institute of Technology Delhi

School of Interdisciplinary Research (SIRe)

# Project Proposal for Ph.D.

SIRe Project Number

**2025-02-08**

(will be assigned by SIRe)

| **Project Details** (The research problem must clearly indicate the need for an interdisciplinary approach) | |
|---|---|
| **Project Title** | Preclinical Assessment of a novel tyrosine kinase inhibitor as a Therapeutic Agent for Non-Small Cell Lung Cancer |
| **Project Summary**<br><br>(Minimum 500 and maximum 2000 characters) | Non-small cell lung cancers (NSCLCs) account for 85% of lung cancer cases, and alterations in the EGFR kinase domain at exons 19 to 21 are one of the primary causes of NSCLCs. EGFR-targeted therapy with several EGFR Tyrosine kinase inhibitors (TKIs) is currently used to treat NSCLC patients whose tumors have specific mutations in the EGFR gene. While these TKIs have shown promising results in improving patient outcomes, several challenges and limitations are still associated with this treatment method. One of the main challenges is the development of resistance to the existing EGFR TKI. Various mechanisms, including the emergence of new EGFR mutations, activation of alternative signaling pathways, and changes in the tumor microenvironment, can cause this resistance. To address the issue of resistance and improve patient outcomes, Dr. Krishna's lab at AIIMS and Dr. Shivaji's la at IIT-Delhi have designed and synthesized a new TKI called KKI04. This molecule is specifically developed to target the T790M/L858R mutation. KKI04 has demonstrated superior inhibition activity at both the molecular and cellular levels compared to existing drugs. Several KKI04 analogues have also been designed, and their potency is currently being validated through in vitro assays.<br><br>Project objectives:<br><br>1. Conduct efficiency studies of the newly designed EGFR kinase inhibitors against EGFR kinase and NSCLC cell lines.<br>2. Perform Pharmacokinetics and Pharmacodynamics studies of the KKI04 molecule on mice models.<br>3. Evaluate the efficacy of KKI04 in comparison to the standard drug, osimertinib, against EGFR-positive cancers (NSCLC) and its downstream signaling pathways using a mice xenograft model.<br><br>Pharmacokinetics and antitumor studies on mice models will provide the necessary data to establish the use of these molecules before they can proceed to clinical trials. |

**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*** | Shivajirao L. Gholap | Chemistry, IIT-Delhi | slgholap@chemistry.iitd.ac.in |
| **Supervisor 2** | Krishna K Inampudi | AIIMS,<br>Department of Biophysics | krishna.inampudi@aiims.edu |

*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 Master's degree (or equivalent) in chemistry, Biochemistry, Biotechnology, Biophysics, or a related field.

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| Hands-on experience in molecular biology techniques, cell culture, flow cytometry, and mass spectrometry will be helpful. Preference will be given to candidates who have experience in animal handling and cancer xenograft mice models. |

| **Source of fellowship/funding and project number**<br>(CSIR/UGC/DBT/ICMR/ICAR/NEET-PG/DST-INSPIRE/IRD/FITT Project details, if any) |
|---|
| ICMR Fellowship<br>Project ID: IIRP-2023-1172/F1 (Project approved from 2024-2027) |

| **Role of Faculty Members involved:** | |
|---|---|
| **Supervisor-1** | Dr. Shivaji's lab has synthesized and patented several Tyrosine Kinase Inhibitors (TKIs). As part of this collaboration, his lab will develop more TKI molecules specifically targeting the EGFR kinase and will be responsible for their synthesis. |
| **Supervisor-2** | The lab of Dr. Krishna has successfully developed Tyrosine Kinase Inhibitors (TKIs) that target the EGFR kinase. As part of this collaboration, his lab will provide access to the AIIMS animal house facility for the required mice studies. Dr. Krishna will also oversee the pharmacokinetic (PK) / pharmacodynamic (PD) studies for the newly synthesized TKI molecules. |

**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 SIRe.**
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 SIRe 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.**