Indian Institute of Technology Delhi

School of Interdisciplinary Research (SIRe)

SIRe Project Number

2022-01-22

(will be assigned by SIRe)

PhD Project

Project Details	
Project Title	**Identification of novel drug targets and development of new drugs for tuberculosis**
Project Summary	In the past two decades, the pivotal role of small non-coding RNA (sRNA) in the regulation of multiple physiologic processes in bacteria, including pathogenesis, has been unfolding. This is especially true in gram negative bacteria, where, in addition to sRNA characterization, chaperons facilitating the sRNA-mRNA interactions were discovered and their role investigated. Less in known of the roles and mechanisms of activity of sRNA in gram-positive bacteria. In mycobacteria, including such important pathogens as *M. tuberculosis*, and others, no specific role in pathogenesis was assigned to sRNA molecules–despite the proven existence of hundreds of sRNA-encoding regions in various mycobacterial genomes. Still, the roles of *Mycobacterium tuberculosis* regulatory RNAs and the proteins that facilitate their functions remain elusive. In spite of significant endeavors in both drug discovery and vaccine development, tuberculosis, caused by *M. tuberculosis*, remains a global threat to human health. *M. tuberculosis* is contemplated as one of the most successful pathogens for causing tuberculosis in human. It is the predominant causative agent for death than any other microorganism. *M. tuberculosis* depends on the ability to adjust to stresses encountered in a range of host environments, adjustments that require significant changes in gene expression. Hence, understanding of sRNA-regulation in *M. tuberculosis* will help find an alternate pathway for disease control. The emergence of antibiotic resistance mechanisms among bacterial pathogens increases the demand for novel treatment strategies. Current drug treatment for TB is targeted primarily against proteins and a complex lengthy process often with severe side effects, especially for patients with multidrug and extensively drug resistant TB. Thus, manipulating the functions of sRNAs, which regulate the pathogenesis of *M. tuberculosis*, will open a new horizon of TB control in human. Objectives: 1. Identification of stress responsive small RNAs (sRNAs) in *Mycobacterium tuberculosis* through RNA-seq experiments and bioinformatics analysis. Stress conditions will be selected to mimic the infection condition. Small RNAs, if found to promote mycobacterium survival under stress, will be selected for this study. 2. To investigate the mechanism how selected sRNAs facilitate mycobacterium survival under stress. 3. *In silico* studies to design small molecules/ peptides against selected sRNAs. Investigation of the effect of those small molecules/peptides on *M. tuberculosis*.

PhD Supervisors			
Role	**Faculty**	**Academic Unit in IITD**	**Email ID**
Supervisor 1	Dr. Gaurav Goel	Department of Chemical Engineering	goelg@chemical.iitd.ac.in
Supervisor 2	Dr. Tanmay Dutta	Department of Chemistry	dtanmay@chemistry.iitd.ac.in

Project requirements (Student qualifications, experience required, etc)

- MSc Chemistry, Biochemistry, Biotechnology or any branch of Life Sciences, B. Tech. / M. Tech. In Chemical Engineering or Biochemical Engineering or related areas
- Student should have prior training in some of these aspects: Structural Bioinformatics, Molecular Thermodynamics,
- Valid GATE score

Source of funding (IRD/FITT Project details, if any)

Institute Slot (Valid GATE Score), Own fellowship (JRF of UGC/CSIR/ICMR/DBT or DST-Inspire)

Role of Faculty Members involved:

Dr. Gaurav Goel's Laboratory will be carrying out *in silico* studies to elucidate molecular details of protein-RNA interactions identified for disease progression, design small molecule/ peptide based drugs against *M. tuberculosis*.

Dr. Tanmay Dutta's laboratory will be carrying out the experiment related to identification and validation of small RNAs under stress conditions. His lab will also try to understand the mechanism of those sRNAs under stresses.