The University of Queensland - IIT Delhi Academy of Research Joint PhD Project

PROJECT TITLE	**NEW APPROACHES TO DISCOVER ANTIBIOTICS FOR GRAM-NEGATIVE BACTERIA**
PROJECT CODE	**UQIDAR 00176**
PROJECT DESCRIPTION	There is desperate medical need for new antibiotics to target infections caused by multidrug-resistant (MDR) and extensively drug-resistant (XDR) bacteria, exacerbated by a lack of new drug candidates in the pharmaceutical pipeline. Gram-negative bacteria are particularly challenging to kill, as they have an additional protective membrane compared to Gram-positive bacteria. An aging population is particularly affected by antimicrobial resistance, as without effective antibiotics common infections and routine medical procedures (such as surgery and anticancer therapy) become deadly. An innovative initiative at UQ, the Community for Open Antimicrobial Drug Discovery (www.co-add.org) [1] has tested hundreds of thousands of crowd-sourced compounds over the past four years, collecting a unique set of antibacterial high-throughput screening data. This database is being used to construct predictive cheminformatics models that can identify and design compounds with the ability to penetrate and kill Gram-negative bacteria. This project will apply these predictive models (developed by associate UQ supervisor Zuegg) to 1) modify structures from the CO-ADD collection that have existing Gram-positive activity so they penetrate Gram-negative bacteria, and 2) virtually screen large commercial libraries to identify novel chemotypes with antibacterial activity, then use these to build a focused medicinal chemistry program. These activities will rely on the heterocyclic synthetic chemistry expertise of IIDT supervisor Nain, the antibiotic development expertise of UQ supervisor Blaskovich, and the cheminformatics experience of Zuegg. Synthetic chemistry activities will be primarily conducted at IIDT, with antibiotic characterization and molecular modelling at UQ. References: [1] Nature Reviews Drug Discovery 2015 14, 587-588
PROJECT OUTCOMES	This project will produce: 1) new chemical scaffolds with activity against Gram-negative bacteria 2) a medicinal chemistry program based on preparing a series of analogs around the most promising new scaffolds. Compounds will be assessed for antimicrobial activity and drug-like properties, with interesting compounds advanced into more comprehensive antibacterial testing, including in vivo mouse models. 3) validation and refinement of predictive computational models that can be used to assess the antimicrobial potential of new compounds
ADVISORY TEAM	**Dr Mark Blaskovich** http://researchers.uq.edu.au/researcher/1614 m.blaskovich@uq.edu.au Institute for Molecular Bioscience (IMB) The University of Queensland **Professor Nidhi Jain** http://chemistry.iitd.ac.in/faculty/jain.html njain@chemistry.iitd.ac.in Department of Chemistry Indian Institute of Technology Delhi
TYPE OF STUDENT	Applications are open to i/a students who meet eligibility criteria. note: i-students must have own scholarship to apply (CSIR, UCG-NET, etc)

DISCIPLINE BACKGROUND OF STUDENT	Ideally, this project requires students with a background in organic synthetic chemistry
IDEAL CANDIDATE	Essential capabilities: • competence in organic synthetic chemistry competence in purification and characterization of compounds Desirable capabilities: • medicinal chemistry microbiological assays molecular modelling machine learning Expected qualifications (courses, degrees, etc): • BSc in chemistry (synthetic) or related
APPLICATION PROCESS	Apply online by the due date: https://www.uqidar.org/students/how-to-apply/