Project Title:	**Biophysical characterization of mycobacterial membranes: Towards understanding membrane-centric host-pathogen interactions and for drug screening applications**	
Project Number	**IMURA1017**	
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Research Clusters:

Highlight which of the Academy's CLUSTERS this project will address? *(Please nominate JUST **one.** For more information, see www.iitbmonash.org)*	
1	*Material Science/Engineering (including Nano, Metallurgy)*
2	*Energy, Green Chem, Chemistry, Catalysis, Reaction Eng*
3	*Math, CFD, Modelling, Manufacturing*
4	*CSE, IT, Optimisation, Data, Sensors, Systems, Signal Processing, Control*
5	*Earth Sciences and Civil Engineering (Geo, Water, Climate)*
6	*Bio, Stem Cells, Bio Chem, Pharma, Food*
7	*Semi-Conductors, Optics, Photonics, Networks, Telecomm, Power Eng*
8	*HSS, Design, Management*

Research Themes:

Highlight which of the Academy's Theme(s) this project will address? *(Feel free to nominate more than one. For more information, see www.iitbmonash.org)*	
1	*Advanced computational engineering, simulation and manufacture*
2	*Infrastructure Engineering*
3	*Clean Energy*
4	*Water*
5	Nanotechnology
6	*Biotechnology and Stem Cell Research*
7	*Humanities and social sciences*
8	Design

The research problem

Biophysical membrane properties are known to be critical players for membrane-associated physiological processes. The basic structure element of biological membranes is a lamellar bilayer matrix, though other non-lamellar structures such as inverse cubic or hexagonal lipid structures are also of biological relevance. Numerous factors determine the particular lipid phase structure such as type of lipids, lipid chain length, head to tail area ratio, chain conformation, degree of unsaturation, head group charge and area, solvent properties, pH, temperature and pressure. Importantly during infection, host and drug interactions, and genetic regulation, mycobacteria respond by broadly remodeling their cell membrane. From the membrane biophysics perspective, these remodeling, most likely involves rearrangement of lipids where various local transient non-lamellar and static cubic lipid structures are involved, associated with fluctuations in curvature and bending elasticity. This application seeks to answer basic questions pertaining to membrane biophysics of mycobacteria cell wall lipids in terms of their structure, conformation and possible lipid phases in near native environment and lipid-composition complexity in bacterial context and upon host contact.

Project aims

Work from our lab and others have shown that mycobacterial inner and outer lipid membrane layers in mycobacterium smegmatis (*Msm*) are composed of mutually exclusive lipids, and lipid dictated spatially resolved domain organization and associated properties (e.g. order, fluidity and conformation). In this work going forward, we are proposing to (a) investigate the structural and thermodynamic aspects of mycobacterial lipids as encountered under physiological conditions within the bacterial envelope and (b) to query membrane structural modulations induced by the intercalation of mycobacterial into the host cell membrane, both in vitro and in vivo using under ambient conditions. We will also supplement the experiments with MD simulations.

Expected outcomes

Highlight the expected outcomes of the project

1. In-depth characterization of mycobacterial lipids within bacteria and host context
2. Development of lipid platforms for effective and quick screening of anti-Tb drugs for unspecific membrane toxicity, obviating the complexity of *in vivo* systems.

How will the project address the Goals of the above Themes?

Compared to simple membrane systems made form a few synthetic lipids, biomimetic liposomal model systems comprising of mycobacterial lipids represent an improved novel model of natural mycobacterial cell membrane, for drug-membrane interactions in tuberculosis research. In depth characterization of mycobacterial–specific membranes and detailed understanding of biophysical interaction between them and anti-tubercular drugs would permit leveraging the relationship between affinity and specificity; wherein the gained findings could be applied for rational design of novel compounds which may be weak inhibitors of the target but may concentrate specifically in the mycobacterial membranes driving inhibition. Further, understanding the spectrum of lipid phases induced by mycobacterial lipids would enrich our understanding on how the bacteria modulates host membrane-associated responses during infection to aid survival.

Capabilities and Degrees Required

Masters in Chemistry (Physical or Organic), Physics, or Biophysics. Basic knowledge of Biophysical Methods such as Fluorescence spectroscopy, microscopy, working with membranes and lipids, and chromatographic separation methods. Having experience in handling bacterial and mammalian culture would be advantageous. Proficient in written and spoken English.

Potential Collaborators

NA

Select up to **(4)** keywords from the Academy's approved keyword list **(available at http://www.iitbmonash.org/becoming-a-research-supervisor/)** relating to this project to make it easier for the students to apply.

BioScience, Bio Chemistry, Drug-Membrane interactions, Novel Functional Materials, Nanotechnology,