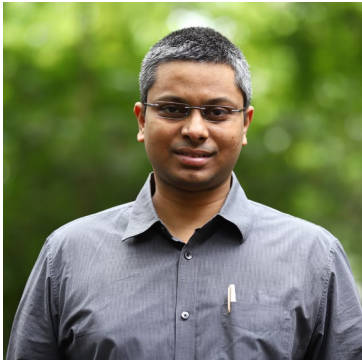


SEMINAR

Thurs, 18 Apr 2024 | 3 pm | DBS Conference Room 1

Hosted by Assist. Prof Hu Chunyi

Structural insights into antibacterial efflux through drug:proton antiporters



By Aravind Penmatsa

Indian Institute of Science, Bangalore, India

About the Speaker

Aravind Penmatsa is an Associate professor at the Molecular Biophysics Unit, Indian Institute of Science. His early training was in pharmaceutical sciences at Osmania university. He subsequently did a PhD at the Centre for Cellular and Molecular Biology, Hyderabad in structural biology and biophysics of ion-binding proteins. He did his postdoctoral research as an American Heart Association Fellow at the Vollum Institute, OHSU where he studied the mechanisms and pharmacology of neurotransmitter uptake system involved in dopamine transport in neurons. He returned to India and setup his lab at MBU, IISc in 2015 where his group studies the transport mechanisms of neurotransmitters like noradrenaline and GABA and their inhibition by pain and antiepileptic medications. His group also studies antiporters involved in multi-drug efflux and develops novel strategies for using antibodies to determine the structures of integral membrane transporters to study their mechanisms and functional roles. Aravind is a senior fellow of the DBT-Wellcome Trust India Alliance and an EMBO Global Investigator.

Superbugs like methicillin resistant *Staphylococcus aureus* employ integral membrane transporters that use proton gradients across the bacterial membrane to drive antibacterial efflux. A major transporter that belongs to this class referred to as QacA is a highly promiscuous antiporter that effluxes nearly 30 different cationic antibacterial compounds. Our studies on QacA revealed the role of protonation sites in aiding the recognition and transport of monovalent and divalent cationic compounds. Using a protonation site mutant that yielded homogenous sample we could resolve the structure of QacA through cryoEM and single domain camelid antibodies and through the use of simulations and models we could gain insights into the role of a unique hairpin loop that controls transport via formation of the extracellular gate during the transport cycle.