

Department of Biological Sciences

VISITOR'S TALK

*Speaker: Dr. Jeet Kalia, PhD*

*Assistant Professor & Wellcome-DBT Intermediate Fellow, IISER Pune*

*Date/Time: Monday, November 6<sup>th</sup>, 2017 at 11:00 am*

*Venue: L8, LHC*

**Title:** Membrane protein-lipid interfaces: Discovery and significance

Membrane proteins are surrounded by thousands of different kinds of lipids within cellular membranes. Historically, these lipids have been considered as mere spectators that passively anchor membrane proteins as they orchestrate vital cellular functions. This classical paradigm, however, has been strongly challenged recently by both structural and mass spectrometry-based studies that have revealed intimate lipid-protein interactions, suggesting that lipids actively regulate membrane protein function. Molecular-level insights into how such interactions influence protein function are lacking. In my talk, I shall describe two approaches that we are pursuing to address this question. One of our approaches leverages electrophysiological techniques that enable detailed mechanistic investigations of ion channel membrane proteins in cells. By performing such studies on the mammalian TRPV1 ion channel, we have demonstrated the critical role of the membrane in channel activation by the double-knot spider toxin, a unique bi-lobed peptide produced by the Chinese bird spider. Our second approach employs a chemical biology-based strategy that involves metabolic labeling of lipids with synthetic lipid precursor analogs. We have been successful in labeling choline lipids in mammalian cells with synthetic choline analogs containing biorthogonal handles that have enabled us to devise a chemoproteomic approach for mapping the entire choline lipid-interacting proteome of these cells. Furthermore, by performing electrophysiological studies on ion channels expressed in cells harboring these “lipid mutants”, we hope to elucidate the role of these lipids in channel function. Taken together, we believe that our interdisciplinary approach that combines electrophysiology, lipidomics and synthetic chemistry will provide significant insights into the roles of lipids in membrane protein function.