IIT Bombay INSPIRE fellow explores how lipids play critical roles in infectious diseases

Recipient of the Inspire Faculty Award instituted by Department of Science and Technology, Govt. of India, Dr. Shobhna Kapoor from IIT Bombay is using biologically active lipid molecules as chemical biology tools to elucidate their biological disease-causing function.

Dr. Kapoor's group is interested to explore how lipids play critical roles in infectious diseases by intervening in cellular signaling, membrane trafficking, and protein function—all of which are intimately involved in host-pathogen interplay. Lipids are important components of living cells and are responsible for maintaining the integrity of our cell membrane, which allows nutrients and drugs to pass through the cell. These are commonly breached during infection and in diseases.

Lipids play a major role in altering cell membrane properties modulating lipid and protein diffusion and membrane organization. Thus, changes in membrane properties control the proper functioning of cells and are harnessed by pathogens for their survival and infection.

Dr. Kapoor's group works with lipids from Mycobacteria tuberculosis (Mtb), which synthesizes atypical lipids predisposed on its surface to interact with the human host membrane. Using Mtb lipids as tools, her group combines chemical synthesis, biophysics with cell biology to elucidate a direct correlation between human host lipid membrane modification and modulation of associated signaling pathways by these exogenous Mtb lipids.

They have recently shown that mycobacterial lipid insertion induces the re-modeling of the host plasma membrane and alters the host autophagy signaling pathway. Thus, their collective work is substantiating the host cell membrane insertion and modification of cellular immune processes as a well-accepted mode of action of virulent mycobacterial lipids. The mechanism of action of Mtb lipids on human host membrane and related cellular events represents a golden opportunity to deepen the understanding of the function of Mtb lipids in membrane-dictated bacterial survival, pathogenesis, and drug resistance.

Dr. Kapoor also investigates the role of Mtb lipids in drug-membrane interactions, underscored by the fact that lipids critically dictate the molecular interactions of drugs with membranes influencing drug diffusion, partitioning, and accumulation, thereby underpinning a lipid-composition specificity. Chemical differences between Mtb and mammalian lipid structures make this research work even more intriguing. Spurring selective passive drug diffusion is an obvious solution to combat growing antibiotic resistance with minimized toxicities. They have developed membrane scaffolds specific to mycobacterial outer (mycomembrane) and inner lipids and demonstrated them as 'cell-free' platforms for anti-tubercular drug interactions.

The outcome of their research has myriad implications in drug discovery, basic sciences, and biotechnological applications. First, the membrane lipid scaffolds envisioned are expected to serve as perfect platforms to quantitatively investigate antibiotic interactions with mycobacterial (causative agent of Tuberculosis) specific membranes, enabling cell-free high-throughput screening of compounds for future antibiotic design. Second, capturing the whole spectrum of interactions between the drug and lipid membranes rendered by incorporating the

natural mycobacterial lipid moieties would provide an insightful toolbox for shaping the effectiveness of already existing anti-TB drug molecules and foster development of new chemotypes. Third, the chemical, biological output of individual Mtb lipid molecules in host cells (studied using cell and molecular biology) would help the investigation of host cellular pathways rewired by pathogenic factors and elucidate possible therapeutic targets in Tuberculosis, which small molecules can hit. Her current work as an INSPIRE fellow got published in Scientific Reports, Biochimica et Biophysica Acta BBA Biomembranes, Biophysical Journal, which are peer-reviewed scientific journals of high repute.

Using the Inspire fellowship Dr. Kapoor will pursue further research for discovering novel approaches to tackle tubercular infections and antibiotic resistance-associated problems in general. This fellowship also helped her to conduct independent research, train students, and develop innovative thinking in her students.