Indian Institute of Science
Centre for BioSystems Science and Engineering

BSSE Annual Work Presentation

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Biological Sciences Building

Understanding the correlation between protein conformational states and membrane dynamics due to attack by pore forming

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ABSTRACT

Pore forming toxins (PFTs) are a class of proteins implicated in a wide range of virulent bacterial infections and diseases. These toxins bind to target membranes and subsequently oligomerize to form functional pores that eventually lead to cell lysis. While the protein undergoes large conformational changes on the bilayer, the connection between intermediate oligomeric states and lipid reorganization during pore formation is largely unexplored. Cholesterol dependent cytolysins (CDCs) are a sub-class of PFTs widely implicated in food poisoning and other related infections. Using a proto-typical CDC listeriolysin O (LLO), we provide a microscopic connection between pore formation, lipid dynamics and leakage kinetics by using a combination of Förster resonance energy transfer (FRET) and fluorescence correlation spectroscopy (FCS) measurements on single giant unilamellar vesicles (GUVs). Upon exposure to LLO two distinct populations of GUVs with widely different leakage kinetics emerge. We attribute these differences to the existence of oligomeric intermediates, sampling various membrane bound conformational states of the protein, and their intimate coupling to lipid rearrangement and dynamics. The change in the lipid dynamics was observed to vary with concentration of the toxin on the membrane. Underlying mechanism of this difference is being elucidated with the help of structural insights from FRET based technique. Our study establishes a microscopic connection between membrane binding, conformational changes and their influence on lipid reorganization during PFT mediated cell lysis. Additionally, our study provides novel insights into membrane mediated protein interactions.