



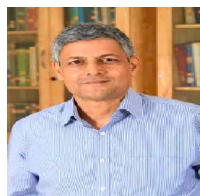
# INSTITUTE COLLOQUIUM (THROUGH WEBINAR)

30<sup>th</sup> APRIL '2021  
4.00 PM (IST)

## ➤ TITLE OF THE TALK ::

**Unravelling Membrane- Protein Intermediates and Lipid Modulation by Pore Forming Toxins**

## ➤ SPEAKER ::



**Prof. K. Ganapathy Ayappa, Indian Institute of Science**

➤ **ABSTRACT** :: Protein-membrane interactions play an important role in our understanding of diverse phenomena ranging from membrane-assisted protein aggregation, oligomerization and folding. Pore-forming toxins (PFTs) are the primary vehicle for infection by several strains of virulent bacteria and are responsible for over 40 % of bacterial infections. With the rise in antimicrobial resistance a molecular understanding of the infection pathways could open up novel treatment strategies. PFTs expressed in a water-soluble form (monomers) bind to the target membrane and self assemble to form multimeric transmembrane pore complexes. In this talk, I will summarize our ongoing work on determining oligomerization pathways and intermediates, as well as monitoring lipid modulation and disruption during pore formation. Using a combination of molecular dynamics simulations at atomistic and coarse grained levels of description and experiments on supported bilayer and vesicle platforms we unravel the process of pore formation of both bacterial  $\alpha$  and  $\beta$ -PFTs. We show that transmembrane oligomeric intermediates or “arcs” form stable proteolipid complexes consisting of protein arcs with toroidal lipids lining the free edges. Spontaneous lipid evacuation occurs on the time scale of tens of nanoseconds, suggesting that transmembrane arcs rapidly stabilize to form functional water channels capable of leakage and lysis. Kinetic models of calcein leakage experiments on small unilamellar vesicles reveal that arcs do indeed play an important role. We connect membrane insertion and ensuing conformational changes with recent single molecule and vesicle leakage data and discuss the vital role played by cholesterol during the pore forming pathway.

WEBINAR LINK

YOUTUBE LINK

**S.N. BOSE NATIONAL CENTRE FOR BASIC SCIENCE**

( an Autonomous Research establishment under DST. GOI )

Block-JD, Sector-III, Salt Lake, Kolkata-700 106

For more visit : [www.bose.res.in](http://www.bose.res.in)