Indian Institute of Science

Centre for BioSystems Science and Engineering

SEMINAR

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MRDG Seminar Hall

Nanomachines to Nanoclusters: From Sensors to regulators of Mitochondrial Cristae

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The eukaryotic cell consists of several nanoscale materials that carry out very precise functions. One of such nanomaterials is DNA. The remarkable specificity and predictable affinities of base-pairing have led to the use of DNA as a building block to create different structures at the nanoscale. This field has created a variety of DNA based nanomachines of exquisite complexity which undergo controlled molecular motions. My initial studies were based on design and application of an autonomous DNA nanomachine as a pH sensor inside living cells. These nanomachines were further targeted to different cellular organelles using a molecular technique involving a recombinant antibody (single chain variable fragment or scFv) as an artificial adapter. scFv and other recombinant antibodies (e.g. VHH only nanobodies) are another type of nanoscale materials which are extensively used to report various cellular signaling events. Extending my interest in nanosensors and recombinant antibodies, I developed a small and highly specific Quantum Dot conjugated nanoprobe functionalized with a nanobody against the green fluorescent protein. This QD-nanobody conjugate was further used to explore the diffusion of adhesion molecules on growth cones and neurotransmitter receptors at synapses. Our data reveal that this smaller probe can easily access both excitatory and inhibitory synapses and measure neurotransmitter receptor dynamics in hippocampal cultures as well as in ex vivo rat brain slices. These nanobodies are proteins and proteins are known to interact with each other to form nanodomains on the surface of an organelle. My studies demonstrated Miro or Mitochondrial Rho GTPase is one such protein that dimerizes and form nanoscale clusters along the outer mitochondrial membrane. These dimeric Miro proteins are found associated with the Mitochondrial Inner Membrane Organizing System (MINOS). We further demonstrated that Miro proteins are required for normal mitochondrial cristae morphology and endoplasmic reticulum structure as genetic knockout of both Miro1 and Miro2 resulted in the loss of cristae architectures and decreased ER-mitochondria contacts (ERMCS). This nanoscale organization, association with the MINOS complex and ER-mitochondria junctions confirmed novel macromolecular complex formation by Miro proteins on the mitochondrial membrane with additional roles besides organelle trafficking.

Souvik is an organic chemist, who graduated from Dr. Yamuna Krishnan's Lab at NCBS, TIFR, Bangalore. His Ph.D. was based on developing novel DNA based pH sensors and their application in cells. Then I moved to university college London after obtaining EMBO fellowship in the lab of Josef Kittler, where I worked on mitochondrial transport adaptor Miro and its structural organisation and functional interactions at the outer mitochondrial membrane. I am currently working at TIFR as part of re-entry phase under Marie curie fellowship