Tata Institute of Fundamental Research
Survey No. 36/P, Gopanpally Village, Serilingampally, Ranga Reddy Dist., Hyderabad – 500 046

Colloquium

Regulatory mechanisms in membrane fission and their relevance to physiology

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Membrane fission, or the splitting of a membrane compartment, is a central theme in biology that manifests during cell and organelle division, maintenance of organelle quality and transport of lipids and proteins across membrane compartments. Fission requires the local application of forces to bend and constrict tubular membranes. The large GTPase dynamins are the best-known catalysts of membrane fission. From a functional design standpoint, dynamins are self-sufficient in membrane fission, relying on their ability to spontaneously polymerise into helical scaffolds, which in turn stimulates their GTPase activity. Stimulated GTP hydrolysis causes the scaffold to constrict and cause fission. But this self-sufficiency prompts an evaluation of how fission is regulated. Using templates that mimic organelles in lipid composition and topology, we have analysed mechanisms that regulate the dynamin-catalysed fission process. Our recent work unravels novel intrinsic and extrinsic regulatory mechanisms. The intrinsic mechanism relies on the insertion of unstructured loops in dynamin into the membrane and sensing membrane packing defects, which in turn controls the throughput of the fission reaction. The extrinsic mechanism arises from the ability of dynamin-recruiting proteins to compete with dynamin for binding lipids. In the case of mitochondrial dynamins, the intrinsic mechanism functions in an organelle quality control axis. In the case of endocytic dynamins, disruption of the intrinsic or the extrinsic regulatory mechanisms is linked to neuropathies and myopathies. Together, these results highlight regulatory mechanisms in membrane fission and their relevance to physiology.

Wednesday, Dec 13th 2023

11:30 AM (Tea / Coffee 11.15 AM)

Auditorium, TIFR-H