REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Uncovering The Secrets Behind Cellular Polarization: Different Systems, Common Platform

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Seminar Room

One of the fundamental questions in biology is how cells are polarized. That is, how the cellular membranes are subcompartmentalized into distinct domains of specific composition and functions. It is now well accepted that underlying this phenomena are the secrets of regeneration and tissue engineering as well the means of revival from the pathological settings. However, the core or hub polarity molecules, their networks and mode/s of action are still not completely understood.

During my PhD research, I found that a vertebrate nervous system specific protein called GAP-43 associates with 'lipid rafts' that are dynamic assemblies of cholesterol, sphingolipids, phospholipids and certain proteins on the plasma membrane. This association is imperative for co-ordination of extrinsic signaling cues with the positioning of key structural module, the centrosome and its microtubules, responsible for polarized trafficking of domain specific cargo. This enables subcompartmentalization of cerebellar granule neuron into functional dendrites and an axon. A perturbation to this process causes defects in cerebellar development that is further manifested in severe motor co-ordination defects.

Given the role of lipid raft domains in cell polarity, I sought for the mechanistic insights into how components of these plasma membrane domains are continuously recycled and replenished from the intracellular machinery, that is, how raft transport carriers are formed. As a postdoctorate fellow, I found that an unconventionally secreted protein called Galectin-9 binds to the glycan headgroup of a glycosphingolipid leading to vectorial recycling of lipid raft associated cargo from the Golgi apparatus to the apical cell surface of a kidney epithelial cell. Depletion of Gal-9 or the glycosphingolipid caused similar defects in epithelial polarization and function. Together my work suggest that the biomembranes are common platforms for morphogenetic transformations associated with specific lipid-protein interaction domains leading to generation of tissue architecture, development of organs such as brain and kidney and in defining their function. On these lines, my independent work will focus on dissecting the role galectin-glycosphingolipid couples and lipid polymorphism in vertebrate nervous system development, pathogenicity and degeneration.