REGIONAL CENTRE FOR BIOTECHNOLOGY
Seminar series

Multiple Roles of an Arf-like Small G-Protein, Arl8b, at the Lysosomes

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Board Room

Lysosomes are dynamic organelles whose functions are essential for maintaining general cellular homeostasis. They receive and degrade macromolecules from the endocytic, autophagic and phagocytic membrane-trafficking pathways. Moreover, lysosomes are the key cellular compartments where antigen presenting molecules including CD1 and MHC class II intersect with, and bind microbial antigens for presentation to T cells. While a number of molecules that drive the steps involved in vesicular trafficking have been described, only a few have been implicated in regulating lysosomal traffic. To identify molecular mediators of CD1 trafficking to and from the lysosomes, we assembled a library of short hairpin RNAs targeting members of the endocytic regulatory protein families and used it to screen for loss of CD1 antigen presenting function. Our screen identified Arl8b, a member of the Arf-like family of GTP-binding proteins as a strong mediator of lysosome-dependent antigen presentation. Here, I will discuss our recent findings highlighting the function of Arl8b in regulating trafficking towards lysosomes as well as in motility of lysosomes. Furthermore, a crucial role of Arl8b in phagosome-lysosome fusion will be discussed in relation to efficient microbial killing. As a part of the future studies, we propose to identify novel effectors of Arl8b that mediate its downstream function in endocytic trafficking and in phago-lysosome fusion. Additionally, we will investigate the role of Arl8b in secretion of lysosome-related organelles. Findings from these studies will have important implications for a variety of cellular and immunological functions of lysosomes, and lysosomes-related diseases.