IMCB Invited Speaker

Speaker : **Prof. Ludger Johannes**
Head, Traffic, Signaling and Delivery Group,
Department of Cellular Compartmentalization and Dynamics,
UMR144 Curie/CNRS, Curie Institute, France

Date : 2 August 2012 (Thursday)

Time : 11:00AM - 12:00PM

Venue : Level 3, IMCB Seminar Room 3-46, Proteos, Biopolis

Host : Prof. Wanjin Hong

Seminar :

Mechanisms of membrane bending in clathrin-independent endocytosis of pathogens and signaling receptors

Several endocytic processes exist that do not require the activity of clathrin, and it has been a major question in cell biology to know how the plasma membrane is bent in these cases. Our recent studies have uncovered a novel mechanism through which nanodomain construction by glycosphingolipid-binding toxins (Shiga and cholera toxins) or polyoma viruses (SV40) induces membrane curvature changes and drives the formation of plasma membrane invaginations, leading to the endocytic uptake of these pathogens or pathogenic factors into cells (Nature 450, 670-675; NCB 12, 11-18). We could show that actin polymerization on Shiga toxin-induced endocytic tubules is sufficient to induce scission in a process that requires membrane reorganization and domain formation (Cell 140, 540-553). Our data suggests that tubule membranes are poised such that an appropriate inducer can cause lipid segregation, thereby generating domain boundary forces that trigger line tension-driven squeezing of the tubule membranes leading to scission. We could provide evidence that Shiga toxin-induced endocytic tubules are enriched in glycosphingolipid species that are not the direct toxin receptors (Traffic 11, 1519-1529). This lipid co-sorting mechanism is dominant over curvature-mediated lipid sorting, and to be efficient, theoretical arguments suggest that the tubule membrane compositions must be close to demixing. The possibility that this concept can be generalized opens exciting perspectives on how lipid repartitioning can be exploited for membrane mechanics (Cell 142, 507-510). We are now analyzing how cortical actin dynamics may contribute to glycosphingolipid clustering on active membranes, which may facilitate the nucleation of endocytic tubules. Another important aspect concerns the recruitment of machinery for targeting to and fusion with endosomes. Finally, we are studying cellular proteins that like the toxins use glycosphingolipids for endocytic membrane mechanics, thereby regulating the cell surface dynamics of various markers with critical roles in cellular processes such as cell migration.

About the Speaker :

Ludger Johannes is a Research Director (DR1) at INSERM. Since 2001, he is heading the Traffic, Signaling and Delivery Group in the Cell Biology Department (UMR144 CNRS) of the Curie Institute. His research aims at establishing fundamental concepts of endocytosis and intracellular trafficking. The Johannes group has made two major contributions in this context: the discovery of retrograde trafficking between the early endosome and the Golgi apparatus, and the demonstration that dynamic protein-induced glycosphingolipid clustering acts as a driving force for membrane invagination in clathrin-independent endocytosis. These studies have been published in high-ranking journals (Cell, Nature, Dev Cell, Nat Cell Biol, J Cell Biol). He also aims at exploiting these discoveries in fundamental membrane biology for the development of innovative cancer therapy strategies. His basic studies have allowed him to validate the B-subunit of Shiga toxin (STxB) as an "intracellular pilot" for the delivery of therapeutic compounds to precise intracellular locations of dendritic and tumor cells (7 patent families, 4 of which are delivered in the US, Europe and other countries). These findings are the basis for a translational research program on intracellular delivery that he coordinates at the Curie Institute. These findings are also exploited in collaboration with biotech companies, one of which he has founded in 2012 (STxB Pharma Technologies Inc).

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