Regulatory factors (lipids and proteins) of membrane fusion in neuritogenesis

Date : 17/03/2009

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Subjects / Tools-Methodologies
1. In vitro reconstitution / Protein purification and labeling
2. Membrane protein dynamics / Confocal and PALM microscopy
3. Membrane fusion / FRET-based lipid mixing

Summary of lab's interests

The aim of our team is to understand the molecular and cellular mechanisms of membrane trafficking and cell-cell adhesion in neuronal and epithelial morphogenesis. We are particularly focused on tetanus neurotoxin-sensitive and insensitive exocytosis in axonal outgrowth and epithelial cell migration. We study the function of the vesicular SNARE proteins cellubrevin, synaptobrevin, and TI-VAMP, and two cell-cell adhesion molecules: vezatin and L1-CAM.
We use classical techniques of cellular and molecular biology with special emphasis on live cell imaging and proteomics, as well as biophysical approaches to study membrane interaction and fusion in vitro. Our models include mutant mice, cultured neurons and epithelial cells, and neuronal explants in 3D gels.

Summary of project

Membrane fusion is central to many areas of cell physiology, including neuritogenesis, synaptic transmission, viral infection, and mitochondrial dynamics. The fusion of biological membranes uses complex molecular machineries, orchestrated by specialized proteins, and regulated by various factors (lipids or proteins) which facilitate fusion and ensure that fusion occurs at the right time and place. All intracellular membrane fusion events, except those involving mitochondria, are orchestrated by proteins from the SNARE family; the best described being those involved in neurotransmission. With this proposal, we want to extend our current biophysical understanding of SNARE fusion machineries by studying the core molecular mechanisms and the regulatory factors of SNARE proteins involved in neuritogenesis. We will reconstitute SNARE proteins into various artificial lipidic platforms (small, large, or giant liposomes), and use some biophysical assays (measuring membrane protein distribution and mobility, membrane adhesion and fusion events, etc.) to gain insight into how these proteins execute fusion. These experiments will be performed in the absence or the presence of various known in vivo regulators with unknown molecular mechanisms.