SFB 1286 Quantitative Synaptology

UNIVERSITÄTSMEDIZIN GÖTTINGEN : UMG

"Role of forces in membrane dynamics and liver tissue morphogenesis"

Speaker

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Date and Time

Thursday, 2nd May 2024
12:15 pm

Location

Center for Biostructural Imaging of Neurodegeneration (BIN)
Von-Siebold-Straße 3a, 37075 Göttingen
Seminar Room

Abstract
Rab GTPases are key components for the biogenesis, transport and function of cellular membrane organelles. The specificity and directionality of membrane fusion is mediated by Rab GTPases and their effectors. Membrane tethering factors provide the first level of specificity in the recognition of a vesicle by its target compartment. The tether EEA1 is a long dimeric coiled-coil tether molecule which is recruited on the early endosome membrane. Upon binding Rab5 to its N-terminus, it undergoes a conformational change, from extended to a more flexible "collapsed" state, giving rise to an effective force. Rab5 and EEA1 effectively constitute a novel two-component molecular motor, cyclically converting the free energy of GTP binding and hydrolysis into mechanical work. We are now exploring the role of Rab GTPases and endocytic mechanisms in liver tissue organization and regeneration. In the liver, hepatocytes are uniquely polarized cells at the interface of sinusoidal endothelial and bile canaliculi networks that transport blood and bile, respectively. In contrast to simple epithelia, where the cells have a single apical surface facing the lumen of organs, hepatocytes exhibit a multipolar (biaxial) organization, i.e. have multiple apical and basal domains, and their apical surface grows anisotropically to create the narrow tubes of the bile canaliculi and their three-dimensional 3D organization. By studying bile canalicular network morphogenesis in hepatoblasts in vitro, we discovered that such anisotropic growth is due to the generation of apical protrusions along the tight junction belt that connect the opposed apical surfaces of hepatocytes. These protrusions form a pattern reminiscent of the bulkheads of boats, hence we termed them apical bulkheads. The apical bulkheads are under tension and, thus, are structural elements which can provide mechanical stability to the elongating bile canalicular lumen under inner pressure. The small GTPase Rab35 is required for the formation of apical bulkheads and bile canaliculi. Our recent results suggest ***the existence of a mechano-sensing and -transduction mechanism whereby mechanical alterations of bile canaliculi are sensed and regulate hepatocyte fate.***

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