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NEK3-mediated serine 105 phosphorylation of *SNAP29* modulates its membrane association and SNARE fusion dependent processes

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Intracellular membrane fusion depends on the presence of specific mediators, the vesicle (v-) and the target (t-) SNAREs (Soluble N-ethylmaleimide-sensitive factor, NSF, attachment protein SNAP receptors), which interaction brings apposing membranes to proximity and initiates their fusion. The v-SNAREs consist of vesicle-associated membrane proteins (VAMP) whereas t-SNAREs include a syntaxin and a synaptosomal-associated protein (SNAP). *SNAP29* is involved in multiple fusion events during intracellular transport and therefore affects structure of organelles such as the Golgi apparatus and the focal adhesions. Mutations in *SNAP29* gene lead to Cerebral Dysgenesis, Neuropathy, Ichthyosis, and palmoplantar Keratoderma (CEDNIK) syndrome. In the present study, we show that NEK3 (NIMA-never in mitosis gene A-related kinase 3)- mediated serine 105 (S105) phosphorylation of *SNAP29* directs its membrane association, without which cells present defective focal adhesion formation, impaired Golgi structure and attenuated cellular recycling. Wildtype *SNAP29*, in contrast to a phosphorylation-defective serine 105 to alanine (S105A) *SNAP29* mutant, partially rescued the abnormal morphology of CEDNIK patient-derived fibroblasts. Our results highlight the importance of S105 phosphorylation of *SNAP29*, mediated by NEK3, for its membrane localization and therefore, for membrane fusion dependent processes. In this seminar, I will characterize the molecular aspects of the rare genetic syndrome denominated CEDNIK and I will discuss the post-translational modification of *SNAP29* and its biological significance.

Biography

Debora Rapaport works on Genetics and Molecular Cell Biology. She works at the lab of Prof. Mia Horowitz which focuses on genetic disorders and their association with intracellular trafficking. The methodologies we utilize in the lab are based on molecular cell biology, RNAi, knockout mice models and confocal microscopy as a tool to identify diverse cellular phenotypes related with intracellular trafficking.

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