CDB SEMINAR

Speaker: Alexander D. Bershadsky

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Title: "Aspects of Cross-Talk between Cadherin-Mediated Cell Adhesion and the Cytoskeleton"

Date:	Monday, May 24
Time:	14:30 -15:30
Place:	7th floor Conference Room of Building A,CDB

Summary:

The armadillo family protein, p120 catenin (p120) binds juxtamembrane domains of classical cadherins and localizes to cell-cell junctions. Upon overexpression, it enhances the activity of the Rho family GTPases Rac and Cdc42 and augments cell motility. Recently, we found p120 in the actin-enriched structures lamellipodia, ruffles, and 'tails' associated with moving endocytotic vesicles. Co-immunoprecipitation revealed the association of p120 with another component of these structures, cortactin.

Downregulation of p120 by siRNA not only destabilized cadherin junctions, but also disorganized lamellipodial activity, resulting in inhibition of cell spreading and migration. Finally, intracellular vesicle velocity increased upon p120 overexpression and decreased upon its downregulation.

Thus, in addition to its function at cell-cell junctions, p120 appears to be a potent regulator of actin polymerization-driven cell motility. We propose that p120 may couple the formation and disruption of cadherin-mediated contacts with the regulation of cell migration. Formation of cadherin-mediated cell-cell junctions was also shown to affect microtubule dynamics, protecting microtubule minus-ends from depolymerization in centrosome-free cytoplasts. To elucidate the functions of cadherin-catenin complex components in this signaling pathway, we prepared chimeric constructs, in which the N-terminal ends of beta-catenin, p120 catenin and alpha-catenin were fused with the extracellular/transmembrane portion of the alpha subunit of the interleukin-2 receptor (IL2R) serving as a plasma membrane anchor. We show that membrane targeting of alpha-catenin significantly increased the microtubule polymerization level in centrosome-free cytoplasts, while both membrane-targeted and non-targeted beta-catenin or p120 were ineffective in this system. Possible mechanisms of alpha-catenin-mediated alterations in microtubule dynamics will be discussed.

Host: Masatoshi Takeichi Cell Adhesion/Tissue Patterning ,CDB
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