CDB SEMINAR

Kenzi Oshima

Laboratory of Molecular Bioregulation, Graduate School of Bioagricultural Sciences, Nagoya University

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15:30~16:30 A7F Seminar Room <Time revised>

Multifaceted analysis of the *Drosophila* epithelial barrier junction, the septate junction

Summary

The formation of an intercellular junction in a specific membrane domain is an elaborate process that is dependent on the regulated synthesis, assembly and membrane targeting of constituting components. The invertebrate septate junction (SJ) appears molecularly and structurally similar to the vertebrate paranodal septate junction, and not only provides a paracellular diffusion barrier but also maintains cell polarity. Although previous studies have found more than fifteen SJ associated proteins, the mechanism by which they assemble into a highly ordered multiprotein complex and their exact functions are still unclear. Here I will present the results of a genetic screen for SJ components and regulators in *Drosophila* and an analysis of SJ dynamics in living tissues. Genome wide screening disclosed four novel SJ mutants in which proper localization of the SJ proteins was disrupted. Three of these genes encode small GPI-anchored Ly6-like proteins required for septa formation and barrier function. Two non-redundant Ly6-like proteins, Crooked (Crok) and Coiled (Cold), were detected in intracellular puncta and acted tissue-autonomously. *crok* and *cold* mutants accumulated Neurexin IV, a core SJ component, in endocytic vesicles, suggesting their cooperation in the assembly of SJ components in intracellular compartments. To understand how the SJ assembly is regulated *in vivo*, I used fluorescence recovery after photobleaching (FRAP) and found that most SJ-associated proteins examined in this study displayed similar, extremely immobile kinetics. Loss of any of these components resulted in dramatically increased mobility of all others, suggesting that they form a single, highly interdependent core complex. Immobilization of SJ core components coincided with formation of the morphological SJ. Loss of the tumor suppressor protein Discs large, which is associated with the SJ, affected localization of SJ core components, but did not affect their mobility. These results indicate that formation of a stable SJ core complex is separable from its proper subcellular localization, and provide new insights into the complex processes that regulate epithelial polarity and assembly of the SJ.

Host:
Shigeo Hayashi
Morphogenetic Signaling, CDB
shayashi@cdb.riken.jp
Tel:078-306-3185 (ext:1523)