BDR SEMINAR in Kobe

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16:00-17:00, 7F Seminar Room, DB Building A

Conserved Map7/7D1/Ens proteins coordinate microtubule remodeling and Wnt/PCP signaling for cell polarity formation

Summary

Tissue morphogenesis requires the establishment and maintenance of cell polarity that involves microtubule (MT) remodeling. MT remodeling is often promoted by β-catenin-independent Wnt/PCP signaling. This signaling and microtubule remodeling are regulated interdependently, by an unknown mechanism. Here we show that the paralogous microtubule-associated proteins Map7 and Map7D1 (Map7/7D1) participate in a feedback loop between one of Wnt/PCP signaling pathways, Wnt5a signaling and MT remodeling (named MT-Wnt/PCP network) through a direct interaction with Dishevelled in HeLa cells. Map7/7D1 direct the cortical localization of Dishevelled (Dvl), and facilitate the cortical targeting of MT plus-ends in response to Wnt5a signaling. Wnt5a signaling also promotes Map7/7D1 movement toward MT plus-ends, and depletion of the Kinesin-1 member Kif5b abolishes the Map7/7D1 dynamics and Dvl localization. Furthermore, Dvl stabilizes Map7/7D1. Intriguingly, Map7/7D1 and its *Drosophila* ortholog, Ensconsin (Ens) show planar-polarized distribution in both mouse and fly epithelia, and Ens influences proper localization of *Drosophila* Dvl, Dsh in pupal wing cells. These results suggest that the role of Map7/7D1/Ens in Dvl/Dsh localization is evolutionarily conserved.

As a methodological highlight, we adapted a state-of-the-art CRISPR-Cas9-mediated genome editing technology to generate knock-in HeLa cells and fly strains. As the overexpression of Map7/7D1/Ens proteins is reported to induce aberrant MT bundling, this strategy allowed us to reliably analyze behaviors of endogenous Map7 proteins in cells and tissues.

Based on the above results, to understand the roles of MT-Wnt/PCP network regulators, Map7/7D1 for mammalian tissue morphogenesis, we are now analyzing *MAP7D1* knock-out mice. Involvement of Map7D1 in mammalian tissue morphogenesis will be discussed in the seminar.

[Reference]

EMBO Rep. 19: e45471, 2018.; ***Cancer Res.*** 73: 4362-4371, 2013.; ***J. Cell Sci.*** 125: 4822-4832, 2012.; ***EMBO J.*** 29: 3470-3483, 2010.

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