



CDB SEMINAR

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Mount Sinai Hospital, Toronto, Canada

Wednesday, March 18, 2009

16:00~17:00 C1F CDB Auditorium

Regulation of Planar Cell Polarity by Smurf Ubiquitin Ligases

Summary

Regulation of the polarity of cells in the plane of the tissue is critical for morphogenesis. In vertebrates, disruption of planar cell polarity (PCP) causes misalignment of stereocilia in the neurosensory cells of the cochlea and interferes with convergence and extension (CE), causing neural tube defects. Noncanonical Wnt morphogens are key regulators of PCP, but the molecular mechanisms underlying PCP signalling remain unclear. Here we demonstrate that mutation of the ubiquitin ligases *Smurf1* and *Smurf2* in mice causes PCP defects that include CE and neural tube closure defects, misalignment of stereocilia and disruption in the hexagonal arrangement of cells in the inner ear. Smurfs interact specifically with phosphorylated Dishevelled 2 (Dvl2), which is a key component of noncanonical Wnt signalling and are recruited via Dvl2 to the polarity protein, Par6. Par6 also binds the PCP component Prickle 1 (Pk1), thereby mediating Smurf- and Dvl2-dependent Pk1 degradation. In *Smurf* mutants, the asymmetric subcellular localization of Pk1 in the cochlea hair cells and neuroepithelium is lost. Thus Smurf-dependent degradation of PCP components thus plays a critical role in establishing PCP and CE during embryogenesis.

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