G-4

Mechanisms of Fringe/Notch Signaling in Animal Development

Jaeseob Kim
Institute of Molecular Biology and Genetics, Seoul National University,
Seoul 151-742, Korea

Fringe (Fng), which has been proposed as a secreted signaling molecule, plays important roles in animal development. It determines the dorsoventral (D/V) boundaries of the developing wing and eye in *Drosophila1*. It is also involved in the formation of the apical ectodermal ridge in chicken limb buds and the segmentation of somites in mice. In the developing *Drosophila* wing and chicken limb, the juxtaposition of Fng-expressing dorsal cells and ventral cells not expressing Fng activates the dorsal boundary cells to induce Serrate (Ser), a ligand of the Notch (N) receptor. The Ser signal is then received by the N in the ventral boundary cells, and transduced via Suppressor of Hairless [Su(H)] protein to activate the D/V boundary specific genes including a putative ventral signal, which is probably Delta (Dl) in Drosophila. The Dl produced by the ventral boundary cells then signals back to the dorsal boundary cells and activates N to induce the D/V boundary specific genes in the dorsal boundary cells. The clonal analysis data of Su(H) and the data showing that Dl can induce Ser in the Fng-expressing dorsal cells suggest that this D/V signaling cascade is a circular process. Based on ectopic expression experiments of Fng, Ser, and Dl, it has been proposed that the Fng in the dorsal cells induces Ser and inhibits Ser-N signaling while it potentiates Dl-N signaling. However, the molecular mechanisms how Fng-expressing cells recognize the neighboring cells not expressing Fng and how Fng induces Ser and modulates the susceptibility of N to two different ligands are largely unknown. In order to understand these questions, identification of Fng receptor or partner molecule is critical. In this talk, the molecular identity of the Fng partner molecule will be discussed.