CDB SEMINAR

Makoto Sato

Laboratory of Morphogenesis, Institute of Molecular and Cellular Biosciences, University of Tokyo

Thursday, September 28

16:00~17:00 C1F CDB Auditorium

DWnt4 regulates the dorsoventral specificity of retinal projections in the *Drosophila* visual system

Summary

Precise topographic mapping of photoreceptor neurons to their targets in the brain, 'retinotopic mapping,' is necessary for the correct interpretation of visual information received in the retina. In *Drosophila*, photoreceptor cells retinotopically send their axons to the first optic ganglion, the lamina. Although mechanisms that control retinotopic mapping have been extensively studied in vertebrate systems, the genetic mechanisms regulating retinotopy have not been documented in flies.

The homeobox genes of the *iroquois* complex are expressed in the dorsal half of the retina and specify the dorsal identity. Our finding that *iroquois* mutant dorsal axons misprojected to the ventral lamina suggests *iroquois* are the dorsal cues for the retina.
We subsequently showed that *DWnt4*, a secreted protein of the Wnt family, is the ventral cue for the lamina. *DWnt4* is normally expressed in the ventral half of the lamina and *DWnt4* protein was found along the ventral retinal axons, suggesting its involvement in retinal axon guidance. Indeed, ventral retinal axons misprojected to the dorsal lamina in *DWnt4* mutant backgrounds. Ventral axons were attracted by the ectopic source of *DWnt4*. *Dfrizzled2* and *dishevelled*, respectively, encode a receptor and a signaling molecule required for Wnt signaling. Mutations in both genes and inhibition of non-canonical Wnt signaling in the retina resulted in *DWnt4*-like phenotype, suggesting direct roles of *DWnt4* and non-canonical Wnt signaling for retinal axon guidance.
Interestingly, *iroquois* mutant dorsal axons accumulated ectopic *DWnt4* and misprojected to the ventral lamina, perhaps because dorsal axons were attracted by *DWnt4* in the absence of *iroquois*. Since the phenotype was suppressed in *iroquois Dfrizzled2* double mutant backgrounds, *iroquois* may attenuate the competence of Dfrizzled2 to respond to *DWnt4.*

In vertebrates, Eph/Ephrin family proteins play key roles in the retinotopic mapping. Similarly, genes other than *iroquois* and *DWnt4* must be involved in the retinotopy of flies. Recently, it has been reported that Wnt3 regulates the retinotopy along the dorsoventral axis in concert with Eph/Ephrin in vertebrates. It will be interesting to see if the molecular mechanisms underlying retinotopy are conserved in vertebrates and invertebrates.

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