CDB SEMINAR

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16:00~17:00 A7F Conference Room

Atypical cadherin Fat4 governs planar cell polarity (PCP) in vertebrates

Summary

Tissue patterning and growth are two major aspects required for proper development of multi-cellular organisms. Both cellular actions need to proceed in a coordinated manner to constitute an entire body in which all type of cells are functionally organized. Drosophila fat is one of the genes that regulate both cellular actions in parallel during development. A pathway controlling tissue organization, known as the planar cell polarity (PCP) pathway, consists of the core PCP gene products, Frizzled, Dishevelled, Prickle, Van Gogh and Flamingo, and tissue-specific PCP effectors such as Inturned and Fuzzy. Core PCP elements and tissue specific effectors have been shown to be conserved from flies to mammals, and loss of vertebrate core PCP genes has been shown to lead to defects in convergent extension, cochlear hair cell orientation and neural tube closure. Recent studies have identified another group of Drosophila PCP elements, the atypical cadherins Fat (Ft) and Dachsous (Ds) and the transmembrane protein Four-jointed (Fj), which provide directional cue to individual cells so that the cell can recognize an axis orientation of the tissue. However, it has been unclear if the Ft/Ds/Fj cassette controls PCP in vertebrates. I will describe genetic studies that suggest that the mammalian ortholog of fat, Fat4, is an essential gene playing a key role in vertebrate planar cell polarity, and that it functions through the same signalling pathway as in Drosophila. I will also discuss some evidences that indicate that oriented cell division (OCD) is disrupted by loss of Fat4 signalling in the mouse. The loss of OCD leads to a loss of renal tubular elongation during kidney development, resulting in cystic disease. These studies demonstrate that OCD in the kidney is downstream readout of PCP signaling in the mouse and provide the first mammalian model of cystic kidney disease caused by defective PCP.

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