CDB SEMINAR

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Wednesday, September 20

16:00~17:00 C1F CDB Auditorium

Cell fate specification by polarity determinants

Summary

In embryonic development, patterning decisions commonly depend on cascades of transcriptional factors that mediate spatial and temporal regulation of gene expression. Additionally, cell polarity has been proposed to influence cell fates by affecting asymmetric cell division and localization of cell fate determinants, however, direct evidence for this process in vertebrate embryos has been limiting.

Partitioning-defective 1 (PAR-1), lethal giant larvae (Lgl) and atypical protein kinase C (aPKC) are involved in the establishment of cell polarity in many species from yeast to humans. In gain-and loss-of function experiments, we show that PAR-1 and Lgl regulate fates of ectoderm cells according to their position along the apical-basal axis. During neurogenesis, PAR-1 functions as a molecular substrate of aPKC, since PAR-1 that is insensitive to aPKC-mediated phosphorylation caused an increase in the number of primary neurons in the sensorial layer of *Xenopus* ectoderm. By contrast, aPKC mislocalized PAR-1 and suppressed neurogenic fate while promoting superficial layer differentiation. We also find that the same polarity determinants regulate cell fate in both neural and non-neural ectoderm. These findings suggest that aPKC and PAR-1 function sequentially in a conserved molecular pathway that links apical-basal cell polarity to cell fate determination. The observed patterning mechanism does not depend on tissue type and may operate in a wide range of epithelial tissues in many species.

Speaker Profile

Professor Sokol was a graduate student in Doug Melton lab. At that time, he identified a factor called PIF that induces mesoderm in *Xenopus.* PIF turn out to be same as activin. Since then, he has been working on roles of Wnt signaling in axis specification in *Xenpous.* His work on the Disevelled protein showed that Wnt signaling controls morphogenetic movements during gastrulation in vertebrates. He recently discovered a novel function of Dishevelled in the regulation of apical-basal polarity by association with LGL (lethal giant larvae).

<Selected Publications>

Sokol S, Wong GG, Melton DA. (1990) A mouse macrophage factor induces head structures and organizes a body axis in *Xenopus*. **Science.** 249, 561-564.

Sokol, S.Y. (1996). Analysis of Dishevelled signalling pathways during *Xenopus* development. **Curr. Biol.** 6, 1456-1467.

Gloy J, Hikasa H, Sokol S. Y. (2002). Frodo interacts with Dishevelled to transduce Wnt signals. **Nature Cell Biol.**, 4, 351-357.

Dollar, G., Weber, U., Mlodzik, M., and Sokol, S. Y. (2005). Regulation of Lethal giant larvae by Dishevelled. **Nature** 437, 1376-1380.

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