CDB SEMINAR

Philip A. Beachy

Institute for Stem Cell Biology and Regenerative Medicine
Stanford University School of Medicine, Howard Hughes Medical Institute

Tuesday, November 20, 2007
14:30~15:30 C1F Auditorium

Hedgehog signaling in development and disease

Summary

Cellular differentiation and proliferation responses elicited by the Hedgehog (Hh) family of secreted signaling proteins play an important role in the growth and patterning of multicellular embryos. The tissue distribution of the Hh signal and its receptor-mediated responses are both influenced by autoprocessing and lipid modification reactions that produce a signaling peptide dually modified at its N- and C-termini by palmitoyl and cholesteryl adducts, respectively. Pathway activation is triggered by stoichiometric binding of the mature Hh ligand to Patched (Ptc), an apparent transmembrane transporter that in the absence of Hh acts catalytically to suppress activity of the seven transmembrane protein Smoothened (Smo). Inactivation of Ptc by binding to Hh permits activation of Smo, which in turn results in activation of latent cytoplasmic transcription factors, the Ci protein in Drosophila and the homologous Gli proteins in mammals.

Recent studies point to regulation of tissue stem and progenitor cell physiology as a normal postembryonic role for activity of the Hh signaling pathway. Inappropriate pathway activity thus appears to play a critical role in growth of certain cancers whereas inadequate activity can contribute to defects in tissue homeostasis and postembryonic development. I will discuss pharmacological manipulation of pathway activity in both types of disorders. I will also discuss my laboratory's recent work on the role of the novel receptor component Ihog, which appears to collaborate with Ptc in binding of the Hh ligand.

This seminar will be carried out right after Dr. Howard Lipshitz's lecture beginning at 13:30 in the same venue.

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