Informal Seminar Supported by Laboratory for Early Embryogenesis

Kiyo Sakagami

Jules Stein Eye Institute and Molecular Biology Institute
University of California, Los Angeles, CA, USA

Thursday, January 10
13:00 ～ 14:00 C1F Auditorium

Regulation of Cell Cycle and Cell Fate by Hedgehog Signals during Mouse Retinal Development

Summary

The mature vertebrate neural retina consists of six major types of neuronal and glial cells and is an excellent system for studying neuronal differentiation. Accumulating evidence indicates that proliferation and cell fate specification of neural progenitor cells are regulated by both cell-intrinsic factors and cell-extrinsic cues. Among the known growth factors, the Hedgehog family of molecules has been shown to regulate neural tissue patterning, cell proliferation, laminar organization, and neuronal differentiation in the vertebrate retina. Previously, we have reported that Shh secreted by differentiated neurons negatively regulates retinal ganglion cell (RGC) genesis behind the neurogenic wave front in the developing chicken retina. We provide further evidence that in cultured mouse retinal cells recombinant Shh-N similar suppresses RGC differentiation. To further elucidate the functions of Hh signaling in the developing mammalian retina, we have performed conditionally deletion of the Hh signaling component Smoothened (Smo) using Cre/LoxP recombination. Our analyses show that Hh signaling is critical in proliferating retinal progenitor cells prior to their withdrawal from the final mitotic cell cycle. Early deletion of Smo results in an increased RGC and photoreceptor cell production, which is accompanied by altered expression of key bHLH proneural genes. We also show that Smo ablation disrupts cell cycle regulator CyclinD1 and leads to abnormal cell cycle progression through G1 to S transition. These results indicate that Hh signaling is important for RGC and photoreceptor cell fate specification and is required for progenitor cells to maintain the cell cycle. These molecular genetic analyses thus reveal specific functions and the critical timing of Hedgehog signaling for neuronal differentiation and cell proliferation in the mammalian retina.

Host:
Guojun Sheng
Early Embryogenesis, CDB
sheng@cdb.riken.jp
Tel: 078-306-3132 (ext: 4201)