School of Life Sciences

Seminar Series

No. 2019-28

Wed., **20 November**, 4:45pm

Jukhyun Bio Auditorium(RM.121)

English

Regulation of active / quiescent neural stem cells by Notch signaling

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Host | Prof. Mi-Ryoung Song

광주과학기술원 생명과학부

Gwangju Institute of Science and Technology School of Life Sciences

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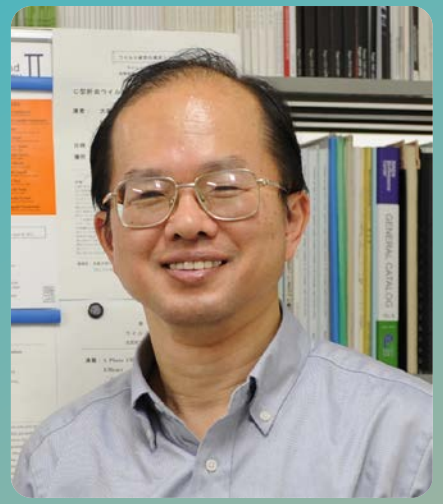

Short Biography

Ryoichiro Kageyama received his M.D. in 1982 from Kyoto University and his Ph.D. in 1986 from the same institution for his work on the structural characterization and transcriptional control of the renin-angiotensin-kinin system. After spending 3.5 years as a postdoctoral fellow at the National Cancer Institute in the United States, he returned to Japan and was appointed Assistant Professor in 1989 and Associate Professor in 1991 in the Faculty of Medicine of Kyoto University. There, he began the research of bHLH genes, such as Hes1 and Math1, and analyzed their roles in neural development. He then moved to Kyoto University's Institute for Virus Research (now, Institute for Frontier Life and Medical Sciences) to assume a full professorship in 1997, continuing his study on the roles of bHLH genes in neural development. In April 2006, he was appointed Director of the same institute (until March 2010). From February 2013 (until March 2019), he was appointed Deputy Director of Institute for Integrated Cell-Material Sciences, Kyoto University.

Ryoichiro Kageyama, M.D./Ph.D.

Abstract

Somatic stem/progenitor cells are active in embryonic tissues but quiescent in many adult tissues. Notch signaling is known to regulate both active and quiescent neural stem cells, but its detailed mechanism of how Notch signaling regulates both remains to be analyzed. In active neural stem cells, expression of the Notch effector Hes1 oscillates by negative feedback, which drives cyclic expression of the proneural gene Ascl1. While sustained expression of Ascl1 induces neuronal differentiation, oscillatory expression of Ascl1 activates proliferation of neural stem cells, suggesting that oscillations are important for active neural stem cells. When Hes1 oscillations are dampened, proliferation of neural stem cells is impaired, which causes microcephaly. Furthermore, in quiescent neural stem cells in the adult brain Hes1 levels are oscillatory, but the peaks and troughs are higher than those in active neural stem cells, causing Ascl1 expression to be continuously suppressed. Inactivation of Hes1 and its related genes up-regulates Ascl1 expression and increases neurogenesis. This causes rapid depletion of neural stem cells and premature termination of neurogenesis. Conversely, sustained Hes1 expression represses Ascl1, inhibits neurogenesis, and maintains quiescent neural stem cells. By contrast, induction of Ascl1 oscillations activates neural stem cells and increases neurogenesis in the adult brain. Thus, Ascl1 oscillations, which normally depend on Hes1 oscillations, regulate the active state, while high Hes1 expression and resultant Ascl1 suppression promote quiescence in neural stem cells.