CDB SEMINAR

Speaker: Hisato Kondoh
Graduate School of Frontier Biosciences
Osaka University

Title: " Genesis of the neural primordia and their regional diversities through regulation of *Sox2* "

Date: Tuesday, November 18

Time: 16:00 P.M.～17:00 P.M.

Place: 7th floor Conference Room of Building A, CDB

Summary

Expression of the transcription factor SOX2 marks the neural primordia at various stages of the CNS development, and regulation and action of SOX2 in the neural tissues is a central issue of neural development. In the early embryonic CNS *Sox2* expression appears uniform, but it is actually pieced together by five separate enhancers with distinct regional specificities, including enhancer N-1 activated by the neural induction signal emanating from the organizer (1). Following initiation of the *Sox2* expression by enhancer N-1, the expression is maintained by the action of remaining enhancers covering different domains of the CNS. Minimal and essential DNA sequence for the activity of enhancer N-1 is narrowed down to 60 base pairs where several transcription factors bind. SOX2 participates in a number of developmental processes as a determinant of cell type, but by itself it does not have much function. It interacts with distinct partner transcription factors to regulate different sets of genes and directs differentiation of a variety of cells (2). In the ES cells SOX2 cooperates with Oct3/4 to maintain its characteristics, while in lens development SOX2 chooses Pax6 as its partner in activating the lens-specific genetic cascades (3).

In the neural primordia of the embryo, the SOX2 protein interacts with Class III POU transcription factors and these synergistically activate the group of genes that characterize the neural primordia (4). Analogous interactions of the transcription factors presumably occur in the neural stem cells of later development. This SOX-POU interaction is the basic mechanism at the transcriptional level to derive the neural primordia. The CNS is divided into several functionally and morphologically distinct domains, and this division stems from the regional diversity of the neural primordia, a diversity partly caused by regional heterogeneity of the signals emitted by neighboring tissues and converging to the early neural plate (5). The distinct neural enhancers of *Sox2* must respond to the local signals varying along the antero-posterior axis of the embryo, and the same signals are presumably responsible for generating the diversity of the neural primordia. Thus, the mechanism of activation of the region-specific neural enhancers of the *Sox2* gene should provide a clue to differentiation of the CNS domains.

(1) Uchikawa M, Ishida Y, Takemoto T, Kamachi Y, and Kondoh, H. (2003) Dev. Cell 4, 509-519.
(2) Kamachi Y, Uchikawa M, Kondoh H. (2000) Trends Genet. 6, 182-187.
(3) Kamachi Y, Uchikawa M, Tanouchi A, Sekido R, Kondoh H. (2001) Genes Dev. 15, 1272-1286.
(4) Tanaka S, Kamachi Y, Tanouchi, A, Hamada H, Jing N, and Kondoh H. Submitted.
(5) Muhr J, Graziano E, Wilson S, Jessell TM, and Edlund T. (1999). Neuron 23, 689-702.

Contact: Shigeo Hayashi /Morphogenetic Signaling, CDB e-mail: shayashi@cdb.riken.go.jp
Tel: 078-306-3185; RIKEN Center for Developmental Biology, http://www.cdb.riken.go.jp/