CDB SEMINAR

Speaker: **Hajime Ogino**

< Department of Biology, University of Virginia >

Title: **"From lens induction to functional genomics in *Xenopus*"**

Date:	**Tuesday, December 13**
Time:	**16:00 -17:30**
Place:	**1F Auditorium of Building C,CDB**

Summary:

Remarkable progress in comparative analysis of genome sequences has highlighted the existence of a large number of conserved non-coding elements (CNEs) in vertebrate genomes. Since many of these appear to be cis-regulatory elements (enhancers and silencers) associated with developmental regulation, functional characterization of these CNEs becomes an important task for untangling gene regulatory networks in development. In this study, we undertake an enhancer analysis of a gene involved in lens formation, *Lens1/FoxE3*, presenting a high-resolution analysis of CNEs using *Xenopus* genomic sequence and studying their function using the efficient *Xenopus* transgenic system, a combination which is very useful for revealing upstream regulatory pathways. Prediction of functional CNEs by sequence comparison of the human and mouse *Lens1/FoxE3* locus is difficult because sequence conservation is generally so high due to their close evolutionary distance. However, comparative sequence analysis of the mammalian and *Xenopus Lens1/FoxE3* locus led to identification of only one CNE, which matched the enhancer region identified by a classic deletion analysis. Furthermore, phylogenetic footprinting analysis with the *Xenopus* sequence resolved this CNE into discontinuous stretches of short conserved sequences, each 6-11 bases long, many of which match known transcription factor binding motifs. A series of detailed mutation analyses of these conserved motifs in transgenic *Xenopus* embryos revealed involvement of Notch signaling in the early steps of lens induction. To further refine the *Xenopus* system as a tool for CNE studies, we also developed (1) a rapid strategy for surveying enhancer activity of CNEs without having to clone enhancers, and (2) a new high-throughput transgenesis method using meganuclease *I-SceI* for the fast-breeding frog, *Xenopus tropicalis*. The combination of these new techniques results in a rapid pipeline for systematic analysis of CNEs and generation of transgenic CNE reporter lines.

Host: **Yoshiko Takahashi** **<Body Patterning,CDB>**

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