CDB SEMINAR

Speaker: Patricia Labosky

< Department of Cell and Developmental Biology,
University of Pennsylvania, Philadelphia, USA>

Title: "Regulation of multipotent cell lineages in the mammalian embryo"

Date: Wednesday, January 21
Time: 16:00 P.M.~17:00 P.M.
Place: 6th floor Conference Room of Building C, CDB

Summary :

Pluripotent or multipotent stem cells have the unique properties of self renewal and multipotency. These stem cells hold the prospect for novel treatments of disease either by cellular transplantation or testing of new drug therapies. Critical to development of these technologies is a thorough understanding of the genetic regulation of stem cell fate. Here we report that *Foxd3*, a member of the family of forkhead or winged helix transcriptional regulators, is required for maintenance of both pluripotent embryonic stem (ES) cells and multipotent extraembryonic trophoblast stem (TS) cells. *Foxd3* (originally called *Genesis* or *Hfh2*) is expressed in several regions of the mouse embryo able to give rise to multipotent stem cells in vitro. Transcripts are abundant in undifferentiated murine ES and TS cells and expression is extinguished as these cells differentiate. FOXD3 expression is also a characteristic of human ES cells suggesting a conserved role for this gene in stem cells in mammals. *Foxd3*$^{-/-}$ embryos die shortly after implantation with a loss of pluripotent epiblast cells and expansion of proximal extraembryonic tissues. It has not been possible to establish *Foxd3*$^{-/-}$ ES cell lines or generate *Foxd3*$^{-/-}$ teratocarcinomas, indicating the requirement for *Foxd3* in establishing multiple pluripotent cell types. In the extraembryonic tissue *Foxd3* expression is detected in scattered cells at the edge of the ectoplacental plate and in the placenta. Despite the expansion of the extraembryonic tissue in the *Foxd3*$^{-/-}$ embryos, trophoblast stem (TS) cell lines are not generated from *Foxd3*$^{-/-}$ blastocysts or 6.5 days p.c. embryos. These results establish *Foxd3* as a factor required for the establishment and/or maintenance of multiple multipotent lineages in the mammalian embryo. The role of *Foxd3* in the neural crest stem cells will be also presented.

References:
Labosky, P.A. and Kaestner, K. (1998). The winged helix transcription factor Hfh2 is expressed in neural crest and spinal cord during mouse development. Mech. of Dev. 78, 185-190.
Hanna, L.A., Foreman, R.K., Tarasenko, I.A., Kessler, D.S. and P.A. Labosky. (2002). Requirement for Foxd3 in establishing pluripotent stem cells of the early mouse embryo. Genes and Development 16, 2650-2661.

Host **Hiroshi Sasaki** **Embryonic Induction,CDB**
E-mail sasaki@cdb.riken.jp Tel:078-306-0102
RIKEN Center for developmental Biology http://www.cdb.riken.go.jp/