CDB SEMINAR

Speaker: Nobuaki Kudo

< IMP at Vienna Biocenter, Vienna, Austria >

Title: "PROTEOLYTIC CLEAVAGE OF MEIOTIC COHESIN REC8 BY SEPARASE IS REQUIRED FOR MURINE SPERMATOGENESIS"

Date: Wednesday, December 3
Time: 16:00 P.M.～17:00 P.M.
Place: 7th floor Conference Room of Building A, CDB

Summary:

During mitotic cell cycle, sister chromatids generated by DNA replication are held together by the cohesin complex until metaphase. At the onset of anaphase, separase that is a protease under the control of the anaphase promoting complex (APC/c) is activated and cleaves Scc1 subunit of cohesin, then sisters start to segregate to each pole by the pulling force of spindles. In meiosis, cohesin complexes that contain some compatible subunits are responsible for sister chromatid cohesion. Remarkably, Rec8 is a meiosis specific subunit that is homologous to Scc1 and it consists of the meiotic cohesin complex by replacing mitotic subunit Scc1. The meiotic cohesin complex localizes all along the chromosome axes in meiotic prophase from S-phase till metaphase I, but at the onset of anaphase I it is removed from the arm regions of chromosomes and remains only at the centromeres. After anaphase II, it is not detectable on chromosomes any more. In budding yeast, it was shown that the arm region specific release of cohesin is dependent on Rec8 cleavage by separase and that allows separation of homologous chromosomes in meiosis I. However, in vertebrates, whether homolog segregation in meiosis I is also accomplished by the same mechanism as yeast is still questionable. Because, 1) In mammalian mitosis, cohesin at chromosome arm regions is released by a Scc1 cleavage independent manner from prophase to metaphase. That indicates higher eukaryotic cells have a mechanism to remove arm cohesin without cleaving it. 2) In *Xenopus* oogenesis, inactivation of APC/c did not inhibit meiosis I. With those two reasons, our question is whether homolog segregation in mammalian meiosis I requires cleavage of Rec8 or not. We identified separase cleavage sites on mouse Rec8 by *in vitro* experiments. Then we generated transgenic mice that express a non-cleavable mutant of Rec8 from a recombinant bacterial artificial chromosome by a conditional manner utilizing Cre-loxP recombination system. Spermatogenesis of the transgenic mouse was severely impaired. We think that detailed analyses allow us to demonstrate which stage of spermatogenesis requires Rec8 cleavage by separase.

Host: Mitinori Saitou Mammalian Germ Cell Biology,CDB

E-mail: saitou@cdb.riken.jp Tel: 078-306-3376

RIKEN Center for developmental Biology http://www.cdb.riken.go.jp/