



CDB SEMINAR

Speaker: Yehudit Bergman

**<Department of Experimental Medicine,
Hebrew University Medical School>**

**Title: “Oct 3/4 is a key player in early normal
development and germ cell neoplasia”**

Date:	Friday, October 21
Time:	16:00 - 17:00
Place:	1F Auditorium of Building C, CDB

Summary

Oct-3/4 is a POU domain homeobox gene expressed during gametogenesis and in early embryonic cells, where it has been shown to be important for maintaining pluripotency. We show that Oct-3/4 is expressed in all human testicular germ cell tumors (GCTs) tested, even in the early premalignant component. We demonstrate that Oct-3/4 dictates ES cells' oncogenic potential in a dose-dependent manner; high levels increase the malignant potential of ES cell-derived tumors while Oct-3/4 inactivation induces regression of the malignant component. Oct-3/4 expression in a heterologous cell system transforms non-tumorigenic cells and endows tumorigenicity in nude mice, suggesting that Oct-3/4 plays a critical role in the genesis of these tumors.

Following implantation, Oct-3/4 undergoes a multi-step program of inactivation. We demonstrate that this process is carried out in three stages, which include acute transcriptional repression (by transcription factors), heterochromatinization through the methylation of histones together with concomitant binding of the chromodomain protein, HP1, and finally, *de novo* methylation of the promoter. We have shown that repression of Oct-3/4 gene both *in vivo* and in differentiating ES cells is accompanied by histone H3 methylation at lysine 9 and heterochromatinization through the binding of HP1. Our genetic studies demonstrate that this process is carried out by the histone methylase G9a, which is absolutely required for subsequent DNA methylation of the Oct-3/4 promoter by the *de novo* methylases Dnmt3a and 3b. Genetic studies show that these epigenetic changes actually play an important role by inhibiting Oct-3/4 re-expression, thereby preventing reprogramming.

Host : Hitoshi Niwa <Pluripotent Cell Studies, CDB>
E-mail: niwa@cdb.riken.jp Tel: 078-306-1930(ext. 1461)
RIKEN Center for Developmental Biology <http://www.cdb.riken.go.jp/>