CDB SEMINAR


# Hiroyuki Kishimoto

Research Institute of Molecular Pathology (I.M.P.), Vienna, Austria


Thursday, March 12, 2009

13:30~15:00 A7F CDB Seminar Room

## Regulation of *Xist* function in X chromosome inactivation


**Summary**

*Xist* is the trigger for X inactivation in female mammals. The long non-coding *Xist* RNA localizes along one of the two female X chromosomes and initiates chromosome-wide silencing in the early embryo. It has been reported that epigenetic modifications such as methylations and hypoacethylation of histones, histone variants and methylation of DNA are involved in the chromosome wide silencing. However what is directly interacting with *Xist* and what is essential for silencing is still unknown.

In differentiated cells, *Xist* is dispensable for the maintenance of the inactive X, and it was believed that *Xist* function for initiation of silencing is limited to early embryonic cells (Wutz *et.al.*). However, our group found that forced expression of *Xist* in male mice carrying an inducible allele triggers X inactivation in immature hematopoietic cells in specific developmental stages in each cell lineages. Silencing of X-linked genes results in cell loss and causes a lethal multi-lineage anaemia. Hematopoietic stem cells as well as somatic cells are not responsive to *Xist* expression (Savarese *et.al.*). This provoked the idea that a certain nuclear status, which underlies the competence of *Xist* to initiate silencing, could be a general hallmark of certain developmental stages in adult stem cell systems.

To address this question we studied the hair follicle stem cell system. We observed that *Xist* induction impaired the hair cycle in adult male mice, in which lethal anaemia was prevented by bone marrow transplantation. Additionally, induction of *Xist* expression starting in late embryogenesis resulted in baldness. Histological analysis of the skin revealed an altered morphology of the hair follicle, possibly resulting from Apoptosis caused by *Xist* expression. Our data suggest that cells in the hair follicle can respond to *Xist* expression and established X inactivation similar to the hematopoietic system. Future experiments aim to identify the specific cell type and the underlying mechanism of *Xist* action in the hair follicle. We expect to gain insight into the mechanism of *Xist* function and adult stem cell differentiation.



**Ref.) Wutz, *et.al.* Mol Cell. 5: 695-705 (2000).**

**Savarese, *et.al.* Mol Cell Biol. 26: 7167-77 (2006).**



**Host:**
**Hitoshi Niwa**
Pluripotent Cell Studies, CDB
niwa@cdb.riken.jp
Tel:078-306-1930 (ext:1461)