



# CDB SEMINAR

**Speaker: Taku Naito**

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**Title: “Role of chromatin remodeler Mi-2 $\beta$  in T cell development and CD4 gene regulation”**

<b>Date:</b>	<b>Monday, December 13</b>
<b>Time:</b>	<b>15:00 P.M. - 16:30 P.M.</b>
<b>Place:</b>	<b>7F Conference Room of Building A</b>

## Summary:

Changes in chromatin structure are fundamental to gene regulation, and accompany to every developmental step. There are groups of enzymes that can change the chromatin structure through covalent modification of histones or through changing histone-DNA contact (chromatin remodeling). Chromatin remodeler Mi-2 $\beta$  is known to interact with histone deacetylase (HDAC) 1/2 to form NuRD (Nucleosome Remodeling and Histone Deacetylation) complex, suggesting that it can mediate structural changes of chromatin through two different means. Mi-2 $\beta$  is highly expressed in thymus and interacts with transcription factor Ikaros, which is essential for normal T cell development. Thus it is predicted that Mi-2 $\beta$  plays an important role during T cell ontogeny. To elucidate the *in vivo* role of Mi-2 $\beta$ , we created a conditional Mi-2 $\beta$  knockout mouse and examined the effect of its deletion on T cell development. Mi-2 $\beta$  deletion in thymus resulted in greatly reduced T cell number, which is partly accounted by a temporal developmental block in immature thymocytes. In addition, mature T cells lacking Mi-2 $\beta$  showed reduced proliferative response upon T cell receptor mediated activation. Thymus profile was also greatly altered, largely due to deregulated CD4 expression. At the molecular level, we found that Mi-2 $\beta$  directly regulates *CD4* gene expression in developing T cells. Mi-2 $\beta$  coordinately regulates both the *CD4* enhancer and silencer activity through its cooperation with different histone acetyltransferases. These regulations were suggested to take place outside the NuRD complex. Our results indicate that Mi-2 $\beta$  is necessary for normal T cell development as well as mature T cell function and shed new light on its molecular action outside the conventional NuRD complex.

## References:

Naito T *et al.*, “The chromatin remodeler Mi-2 $\beta$  is required for CD4 expression and T cell development”; **Immunity** 2004 Jun;20(6):719-33.

Harker N *et al.* “The CD8alpha gene locus is regulated by the Ikaros family of proteins”; **Mol Cell.** 2002 Dec;10(6):1403-15.

**Host: Jun-ichi Nakayama** <Chromatin Dynamics, CDB>

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