CDB SEMINAR

Speaker: **Ichiro Yahara**

< Ina Institute, Medical & Biological Laboratories, Co. Ltd.>

Title:

"Mechanism of Antigen Cross-presentation by Dendritic Cells"

Date:	Monday, January 17
Time:	16:30 -17:30
Place:	7F Conference Room of Building A,CDB

Summary:

MHC class I molecules are expressed with short peptides generated from endogenous proteins on most nucleated cells and function as immunological self markers. Cancer or virally infected cells express cancer- or virus-specific antigenic peptides, respectively, associated with MHC class I as non-self markers. Cytotoxic T lymphocytes (CTL) attack cancer or virally infected cells by recognizing these non-self markers. CTL derive from naïve $CD8^+$ T cells upon appropriate stimulation. However, naïve $CD8^+$ T cells, though they express the same T cell receptor repertoire as that of CTL, are unable to respond to CTL-target cells and never differentiate into CTL. Dendritic cells (DC) function as the unique stimulator for naïve $CD8^+$ T cells by presenting cancer or viral antigens along with MHC class I molecules.

Uptake and processing of exogenous antigens have been well documented for presentation with MHC class II molecules to $CD4^+$ T cells by antigen presenting cells (APC) such as macrophages and DC. DC are additionally capable of processing and presenting exogenous antigens along with MHC class I to $CD8^+$ T cells, which is called antigen cross-presentation. Evidence has been accumulated for that the generation of antigenic peptides for cross-presentation is the ubiquitin-proteasome system- as well as TAP-dependent as is for presentation of endogenous antigens with MHC class I. This raised a fundamental question as to how exogenous antigens cross membrane barriers to encounter the ubiquitin-proteasome system.

To address this question, we employed as a model system a murine dendritic cell line DC2.4 capable of presenting exogenous antigens such as ovalbumin (OVA) with MHC class I. We demonstrate that exogenously added OVA is accumulated in the endoplasmic reticulum (ER) followed by retrograde transport to the cytoplasm through the Sec61 transporter complexes and that CHIP functions as an E3 ubiquitin-ligase for OVA degradation by proteasomes. This mechanism is essentially the same as that known as the ER-associated degradation (ERAD) in the quality control of secretary and membrane proteins.

Host: Shin-Ichi Nishikawa <Stem Cell Biology, CDB>

E-mail: nishikawa@cdb.riken.jp Tel: 078-306-1893 (ext:5301) RIKEN Center for developmental Biology http://www.cdb.riken.go.jp/