Seminar

# 大学院セミナー（免疫識別学）

## Human natural killer cell function *in vitro* and *in vivo*


**Bo Dupont, M.D., D.Sc.**

(Professor of Immunology, Memorial Sloan-Kettering Cancer Center)


**Date: March 31 (Thur), 2011.　17:30〜18:30**

**Place: New Med. Edu. & Lib. Bldg., 3rd Floor, Lecture room-2**

## ヒトＮＫ細胞の in vitro および in vivo における機能解析


**講師：Bo Dupont 教授 (Memorial Sloan-Kettering Cancer Center)**


**日時：平成２３年３月３１日（木）17:30 〜18:30，会場：図書講義棟・３階 第２講義室**


**Abstract**

Natural Killer (NK) cells provide resistance to virus infections and play important roles in immuno-surveillance of certain tumors. Most of current knowledge addressing the role of NK cells in immune responses have been obtained from studies of genetically modified mice. There are, however, many differences in cell surface receptor expression and gene expression between human and mouse dendritic cells (DC) and NK cells, possibly resulting in differences in their function. We have therefore investigated the *in vitro* function of autologous human DCs and NK cells in response to Toll-like Receptor stimulation. Specifically, we wished to determine, if TLRs expressed by NK cells play a role in interferon-γ (IFN-γ) production by NK cells. Our studies demonstrate that IFN-γ production by human NK cells following stimulation with the TLR3 ligand poly(I:C) requires a direct stimulation of TLR3 in the NK cells. We demonstrate that Poly(I:C) activation of NK cells is a two-step process, where Poly I:C initially activate mDC production of IL-18 and IFN-alpha followed by IL-18, IFN-alpha and poly(I:C) stimulation of NK cells. Regulation of cytokine receptor expression and acidification of endosomal compartments in NK cells are required for the response.

In order to study DC-NK interactions *in vivo* in a small animal model, we have developed a mouse model with human NK cells and DCs. The mouse host is NOD; Rag-/-; Cγ-/-; Tg HLA-B*2705(Bw4). This immunocompromized mouse has no murine T or B cells due to the Rag-/-, and no murine NK cells because of Cγ-/-. The HLA-Bw4 allele was introduced as a transgene in order to educate the human NK cells on an HLA class I background. Human umbilical cord blood (UBC) CD34 cells with known HLA class I and KIR genotypes were transferred into the mice and NK cells developed during 7-8 weeks. NK cell growth was supported by human IL-15 provided by trans-presentation. Human DCs, monocytes and B cells also developed in these mice. The developing NK cells are mature, with normal NK receptor expression and function. These human NK cells are capable of eliminating human myeloid tumor cells *in vivo*.


**大学院学生の皆様方へ**：本セミナーの受講をもって、下記の大学院(修士および博士課程)の３科目のうちいずれか１つについて、１回受講したものと見なします。
会場で受講証明に必要事項を記載して、会場に設置してある箱に投函してください。

**● 医学・生命科学セミナー，● B3 造血免疫制御学理論(西村担当分)，**
**● 移植免疫学特論（発生・再生コース科目)(西村担当分)**


連絡先：免疫識別学分野　西村泰治　内線：5310（教授室)、5313（秘書室) e-mail：mxnishim@gpo.kumamoto-u.ac.jp