RIBS • CADM Seminar

Date: October 9 **日時：10月9日(火)**

Time: 11:00 –12：00 **午前11-12時**

Place: Research Institute for Biomedical Science, Tokyo University of Science, Conference Room, 2rd Floor.

A human immune system (HIS) mouse model for vaccine/adjuvant research

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2018年度東京理科大学 外国人招へい教員プログラム

We have recently generated human immune system (HIS) mice that can mount functional human CD8+ T cells, called HIS-CD8 mice. These HIS-CD8 mice were made by transducing immunodeficient NSG mice with human genes encoding HLA class-I (HLA-A2 fused to human β2-microglobulin) and selected human cytokines (IL-3, IL-15, and GM-CSF), using a cutting-edge adeno-associated virus serotype 9 (AAV9)-based gene transfer technology. They were then irradiated sub-lethally and engrafted with HLA-A2-matched human hematopoietic stem cells (HSCs). More than 85% of PBMCs in these HIS-CD8 mice consist of human CD45+ leukocytes. Upon immunization with a human malaria vaccine expressing Plasmodium falciparum circumsporozoite protein (PfCSP), HIS-CD8 mice induce not only a high level of PfCSP-specific, A2-restricted human CD8+ T-cell response, but also a protective anti-malaria immunity against transgenic rodent P. yoelii parasites, expressing PfCSP (PfCSP/Py). This malaria-specific human T-cell response was significantly enhanced when a CD1d-binding invariant natural killer T-cell stimulatory glycolipid, 7DW8-5, was co-administered as an adjuvant. More recently, we have successfully generated HIS-CD4/B mice, in which both human CD4+ T cells and B cells are functional, by transducing HLA-class II and human cytokine genes via AAV9 vector. Thus, these HIS-CD4/B mice were able to produce neutralizing human antibodies and ultimately protected against challenge with the PfCSP/Py parasites. We believe that our HIS-CD8 and HIS-CD4/B mouse models may become a useful tool to swiftly evaluate the immunogenicity and efficacy of various human vaccine/adjuvant candidates in a pre-clinical setting.

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