

**Establishment of a IL-1-related gene manipulated mouse library
to understand diseases from a systems biological view point**

Yoichiro Iwakura

(The University of Tokyo, The Institute of Medical Science, Professor)

【Outline of survey】

Cytokines are messenger molecules that are secreted by various cells and transfer information among cells. They are good therapeutic targets, because they play important roles in maintaining homeostasis of the body as well as in the development of various diseases. Because many genes are involved in the development of these diseases, systematic approaches are required to understand the molecular pathogenesis. In this study, we are planning to generate gene manipulated mice related to IL-1 to elucidate functions of these genes in a living animal, because IL-1 plays a central role in the immuno-neuro-endocrine system and is involved in various diseases such as infectious diseases, immune disorders, diabetes and stress responses. We are also planning to distribute these mice to promote researches in these fields.

【Expected results】

By generating gene manipulated mice systematically, not only we can analyze the roles of a particular gene in the development of diseases, but also we can analyze the relationship among genes. This kind of knowledge should allow us a system biological approach to develop a novel therapeutics to many immunological, neurological, and endocrinological diseases. We are also pretty confident about the usefulness of these gene manipulated mice in the researches in the related fields.

【References by the principal investigator】

- Fjikado, N, Saijo, S, Yonezawa, T, Shimamori, K, Ishii, A, Sugai, S, Kotaki, H, Sudo, K, Nose, M, and Iwakura, Y. DCIR deficiency causes development of autoimmune diseases in mice due to excess expansion of dendritic cells. *Nature Med.*, **14**, 176-180, (2008)
- Saijo, S., Fujikado, N., Furuta, T., Chung, S., Kotaki, H., Seki, K., Sudo, K., Akira, S., Adachi, Y., Ohno, N., Kinjo, T., Nakamura, K., Kawakami, K., and Iwakura, Y. Dectin-1 is required for host defense against *Pneumocystis carinii* but not against *Candida albicans*. *Nature Immunol.*, **8**, 39-46 (2007).
- Ishigame, H., Nakajima, A., Saijo, S., Komiyama, Y., Mastuki, T., Nakae, S., Horai, R., Kakuta, S., and Iwakura, Y. The role of TNF α and IL-17 in the development of excess IL-1 signaling-induced inflammatory diseases in IL-1 receptor antagonist-deficient mice. *Ernst Schering Res. Found. Workshop*, **56**, 129-153 (2006)
- Iwakura, Y., and Ishigame, H. The IL-23/IL-17 axis in inflammation. *J. Clin. Invest.*, **116**, 1218-1222 (2006).

【Term of project】 FY2008– 2011

【Budget allocation】

78,100,000 yen (direct cost)

【Homepage address】

http://www.ims.u-tokyo.ac.jp/cem_dcb/index.html