

**Establishment of autoimmune disease therapies based on the elucidation of target genes**

**Koji Yasutomo**

(The University of Tokushima, Graduate School Institute of Health Biosciences, Professor)

**【Outline of survey】**

Most of the genes involved in autoimmune diseases remain unclear despite a variety of basic immunological and genetic studies. It is crucial to clarify the complex regulatory mechanisms that maintain the homeostasis of the immune system as well as acquire immune tolerance in order to establish therapeutic systems to treat autoimmune diseases. We plan to identify crucial genes that cause autoimmune diseases by genome wide screens in this study. In addition, we plan to clarify the roles of Notch signaling that is associated with T cell-mediated autoimmunity.

**【Expected results】**

The discovery of target genes that play key role in the etiology of autoimmune diseases would help establish targeted therapies to treat autoimmune diseases. Furthermore, such studies might help identify a novel regulatory mechanism to control immune homeostasis. Dissecting the specific roles of Notch in the immune system or elucidating the relationship between Notch and other regulatory systems would contribute not only to a better understanding of complex immune networks but also provide a new approach to modulate the immune systems.

**【References by the principal investigator】**

- (1) Kijima M, et al. Dendritic cell-mediated NK cell activation is controlled by Jagged2-Notch interaction. Proc Natl Acad Sci USA 105: 7010-7015 (2008)
- (2) Maekawa Y, et al. Delta1-Notch3 interactions bias the functional differentiation of activated CD4+ T-cells. Immunity 19:549-59 (2003).
- (3) Yasutomo K, et al. Mutation of DNASE1 in people with systemic lupus erythematosus. Nat Genet. 28:313-4 (2001)
- (4) Yasutomo K, et al. The duration of antigen receptor signalling determines CD4+ versus CD8+ T-cell lineage fate. Nature.404:506-10 (2000)

**【 Term of project 】 FY2008 — 2012**

**【Budget allocation】**

**81,200,000 yen** (direct cost)

**【Homepage address】**

<http://immunology.hosp.med.tokushima-u.ac.jp/immunology/system/top/index.php>