【Grant-in-Aid for Scientific Research(S)】
Biological Sciences (Medicine, dentistry, and pharmacy I)

Title of Project : Analyses of transcription factors networks that govern T lymphocyte development

Ichiro Taniuchi
(RIKEN RCAI, Laboratory for transcriptional regulation, Team leader)

Research Area : Immunology
Keyword : T lymphocyte development

【Purpose and Background of the Research】

T lymphocytes play important roles during immune responses not only as effector cells but also as immune regulatory cells. T lymphocyte pools are composed of several subsets with distinct functions. It has been shown that imbalance in differentiation of these T cell subsets or dysfunction of T cell subsets is causatively related with human immunological disorders such as allergy and autoimmune disease. In order to develop new technology that can be applied to control above immunological disorders, it is, therefore, important to understand how differentiation of these T cell subsets are regulated. Given that developmental programs are mainly controlled by gene regulations in which interaction with transcription factors is central, understanding of T lymphocyte development requires elucidation of transcription factor networks.

【Research Methods】

By using genetic engineering technique in mouse and bio-informatics approaches, which are combined with conventional molecular and biochemical methods, I will try to identify master transcription factor for each T lymphocyte subset. Sequentially I will characterize upstream pathway that regulate expression of master transcription factor and will identify downstream target genes of master transcription factor. In particular, I will focus on a transcriptional regulation of helper versus cytotoxic lineage decision by DP thymocytes, and reveal how ThPOK, a master transcription factor for helper lineage, is regulated. In addition, I will study how differentiation of T helper cell subset in the peripheral lymphoid organs upon encountering with antigen are regulated

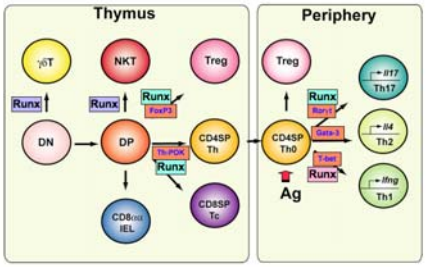

Fig.1.Transcription factors during T lymphocyte development.

【Expected Research Achievements and Scientific Significance】

An understanding of developmental programs regulating differentiation of T lymphocyte subsets would provide a novel technological base that could be applied to develop new therapeutic approach for controlling immunological disorders in human.

【Publications Relevant to the Project】

- Setoguchi R. et al. Repression of the transcription factor ThPOK by Runx Complexes in cytotoxic T cell development. ***Science*** 319:816, 2008.
- Muroi S. et al. Cascading suppression of transcriptional silencers by ThPOK seals helper T cell fate. ***Nat. Immunol.*** 9:1113, 2008.
- Collins A. et al. RUNX proteins in transcription factor networks that regulate T-cell lineage choice. ***Nat. Rev. Immunol.*** 9:106, 2009.

【Term of Project】 FY2009 - 2013

【Budget Allocation】 159,500 Thousand Yen

【 Homepage Address and Other Contact Information】

http://web.rcai.riken.jp/en/labo/regu/
taniuchi@rcai.riken.jp