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

Title of Project : The mechanisms of development and differentiation in Valpha14 NKT cells

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Research Area : Medicine, dentistry, and pharmacy
Keyword : Valpha14 NKT cells, Cloned mouse, early development, precursor NKT cell, NKT specific GFP mouse

【Purpose and Background of the Research】

We have identified NKT cells characterized by the expression of invariant Va14Ja18 and by mediating protective and regulatory responses. However, it remains unclear whether NKT cells are different lineages from T cells. Here, we identify genes for lineage commitment and functions, and establish technology to develop artificial NKT cells with desired function.

【Research Methods】

1) Identification of genes responsible for lineage commitment and function of NKT cells: The precursor NKT cells we identified do not express Va14Ja18 on the surface, while express in the cytoplasm. By using these precursor cells, we identify genes for lineage commitment and function at a single cell level. For this purpose, we isolate precursor NKT cells by single cell sorting followed by high-throughput qPCR to identify specific genes for precursor NKT cells and NKT cells. These genes will be analyzed by transfection of shRNA in the lenti-virus vector into iPS to investigate generation of NKT cells in vitro or knock-out mice.

2) Gene expression profiles and Epigenetic analysis: By using subsets of NKT cells with different functions, we are analyzing mRNA expression profiles by CAGE. We carry out epigenetic analysis by characterizing chromatin with ChIP-Chip analysis to understand the mechanisms of gene regulation of NKT cell function.

3) Generation of artificial NKT cells: Based on the genetic and epigenetic profiles of NKT cell subsets, precursor NKT cells will be introduced gene sets related to specific functions to obtain a subset of artificial NKT cells with desired function.

【Expected Research Achievements and Scientific Significance】

Identify genes for NKT cell lineage commitment and functions to investigate whether NKT cells are different lineage from conventional T cells. Investigate gene and epigenetic profiles of NKT cells with different differentiation stages to evaluate the relationship between gene sets and their functions. Establish a method to generate artificial NKT cells with desired functions by the transfer of sets of genes identified above.

【Publications Relevant to the Project】

- Watarai H, Rybouchkin A, Nagata Y, Hongo N, Sakata S, Sekine E, Dashtsoodol N, Tashiro T, Fujii S, Shimizu K, Mori K, Kawamoto H, Koseki H, **Taniguchi M**. Generation of functional NKT cells in vitro from embryonic stem cells bearing rearranged invariant Va14-Ja18 TCR gene. ***Blood*** 115, 230-237, 2010.
- Watarai H, Fujii SI, Yamada D, Rybouchkin A, Sakata S, Nagata Y, Iida-Kobayashi M, Sekine-Kondo E, Shimizu K, Shozaki Y, Sharif J, Matsuda M, Mochiduki S, Hasegawa T, Kitahara G, Endo TA, Toyoda T, Ohara O, Harigaya KI, Koseki H, **Taniguchi M.** Murine induced pluripotent stem cells can be derived from and differentiate into natural killer T cells. ***J Clin Invest.*** 120: 2610-2618, 2010

【Term of Project】 FY2011-2015

【Budget Allocation】 82,600 Thousand Yen

【Homepage Address and Other Contact Information】

http://web.rcai.riken.jp/en/labo/regulation/index.html