

The mechanisms of development and differentiation in Valpha14 NKT cells

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【Outline of survey】

The NKT cell that we identified is an important cell that bridges the innate and acquired systems (Taniguchi et al. *Annual Review Immunol* 2003). Especially, NKT cells mediate two important functional activities, such as protective immunity and regulatory function. In the protective immune responses, NKT cells play important roles of protection against infection of bacteria, fungi, parasites, and viruses. It is also important for tumor immune responses in which NKT cells mediate adjuvant effects through IFN γ production to activate various immune cells, such as natural killer cells, neutrophils, and macrophages in the innate system, and also stimulate CD4Th1 cells and cytotoxic T cells in the acquired immunity. On the other hand, NKT cells control the immunity system to maintain transplantation tolerance, or to prevent the development of various autoimmune diseases. However, it is not clear at present how the NKT cells acquire their dual functional activities during their development.

In the present proposals, we are going to determine the precursor cells of NKT cells, analyze the mechanisms of development and differentiation of NKT cells, and investigate the mechanisms of acquisition of dual functional activities, such as protection and regulation mediated by NKT cells during their development.

【Expected results】

The physiological function of NKT cell is essential for host defense, such as protection against infectious disease and control of cancer development, and also important for immune regulation, such as allergic responses, protection of autoimmune disease development, and maintenance of transplantation tolerance. By using NKT cloned mice we generated by direct transfer of mature NKT cell nucleus into enucleated unfertilized egg, it is expected to elucidate their mechanisms of NKT cell development and function, leading to further development of strategy for clinical applications.

【References by the principal researcher】

- The NKT cell system: bridging innate and acquired immunity. *Nat. Immunol.* Taniguchi, M., Seino, K., and Nakayama, T. 4:1164-1165, 2003.
- Generation of Cloned Mice by Direct Nuclear Transfer from Natural Killer T Cells. *Current Biology*. Inoue, K., Wakao, H., Ogonuki, N., Miki, H., Seino, K., Nambu-Wakao, R., Noda, S., Miyoshi, H., Koseki, H., Taniguchi, M., and Ogura, A. 15:1114-1118, 2005.

【Term of project】 FY2006 - 2010

【Budget allocation】 23,600,000 yen

【Homepage address】

<http://www.rcai.riken.go.jp/indexE.html>