Title of Project : Mechanisms of Generation, Maintenance, and Activation of Humoral Memory

Tomohiro Kurosaki
(Osaka University, WPI Immunology Frontier Research Center, Specially Appointed Professor)

Research Area : Immunology

Keyword : Immune memory

【Purpose and Background of the Research】

Organisms are protected from recurrent infections from pathogens in part, because the immune system has adapted itself, as a result of first exposure, to produce a specific anamnestic response that is more rapid and robust than the initial response.

In particular, humoral memory responses are characterized by faster kinetics of antibody production that is usually of higher affinity and greater quantity than a primary response. It is generally thought that B cells were selected into the long-lived pool of lymphocytes (called memory B cells) during the primary immune response, become re-activated and differentiate into immunoglobulin (Ig)-secreting plasma cells upon secondary exposure to antigen.

Despite such functional importance of memory B cells, molecular mechanisms underlying the rapid responsiveness and longevity of memory B cells are not clear. As a first step towards answering these issues, the following two specific questions should be clarified; (1) how are memory B cell generated? (2) where do these memory B cells reside?
In this project, by introducing a new imaging technology, we aim at answering these questions.

【Research Methods】

As a model exogenous antigen, we will use NP-hapten system, in which affinity maturation processes have been well established.

In terms of differentiation issue about how memory B cells are generated, we will establish the fate mapping system. It was previously believed that memory B cells come from germinal center (GC) B cells, whereas recent evidence suggests that generation of memory B cells does not necessarily require the GC processes, therefore raising the question about the previous belief. To clarify this issue, we will make a transgenic mouse line that permits mapping of the fate of Bcl6-expressing GC B cells and their progeny by indelibly marking them with enhance yellow fluorescent protein (EYFP) (called the fate mapping mice).

In terms of the localization issue, we will first try to identify the gene which is specifically expressed in memory B cells. Then, by using above fate mapping approach, we will make a transgenic mouse line that permits visualizing of memory B cells and their progeny by EYFP.

【Expected Research Achievements and Scientific Significance】

Vaccination is a typical therapeutic way to utilize the immune memory system; however not sufficient basic scientific knowledge has accumulated so far. One of the reasons is because we do not know the mechanisms of differentiation and activation processes of memory B cells.

Thus, new evidence generated by this project will contribute to development of a new type of vaccination way, thereby contributing to medical needs, too.

【Publications Relevant to the Project】

- Hikida, M., Casola, S., Takahashi, N., Kaji, T., Takemori, T., Rajewsky, K. and Kurosaki, T. PLCγ2 is essential for formation and maintenance of memory B cells. J. Exp. Med. 206, 681-689 (2009).
- Kurosaki, T., Shinohara, H. and Baba, Y. B cell signaling and fate decision. Ann. Rev. Immunol. (in press)

【Term of Project】 FY2009-2013

【Budget Allocation】 159,400 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.ifrec.osaka-u.ac.jp/jpn/laboratory/lymphocytedifferentiation/index.php
kurosaki@rcai.riken.jp