

Elucidation of tolerance mechanism against peripheral target antigens in autoimmune diseases

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【Outline of survey】

It remains to be elucidated how tolerance breaks down in patients with autoimmune diseases. In this study we attempt to clarify autoimmune mechanism and develop disease-specific therapeutic strategies with less side effects using pemphigus, an autoimmune blistering skin disease, as a model disease. Previously, we have generated an active mouse disease model for pemphigus by a unique approach using adoptive transfer of lymphocytes from autoantigen knockout mice to autoantigen-expressing mice. We have also developed self-reactive B cell transgenic mice and found a possible new mechanism of peripheral tolerance. In this study, we have the following plans; 1) To clarify the molecular and cellular mechanisms for the new mechanism of peripheral tolerance, 2) To clarify the pathophysiological roles of long-lived plasma cells in autoimmune diseases, 3) To identify and characterize T cells which are directly involved in autoantibody production, 4) To develop active disease mouse model for other tissue-specific autoimmune diseases by our approach using adoptive transfer of autoantigen-knockout lymphocytes.

【Expected results】

The current dogma for the peripheral tolerance is based on the findings using mouse models expressing artificial antigens in various tissues. Our attempt is quite unique and will bring benefits to basic and clinical medicine by elucidating the mechanisms of peripheral tolerance against disease-involved autoantigen in physiological conditions

【References by the principal researcher】

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【Term of project】 FY 2005 - 2009

【Budget allocation】 85,500,000 yen

【Homepage address】 <http://web.sc.itc.keio.ac.jp/derma/index-jp.html>