Spatiotemporal regulation of antigen recognition and activation of T cells

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【Outline of survey】

T cells play central role in immune regulation, and start immune responses by interacting dendritic cells which had uptaken and processed antigen. Upon contact, T cells create "Immunological synapse" in the interface between T cells and DCs. However, we found that antigen recognition and activation by T cells are mediated by "TCR microclusters" which are formed prior to Immunological synapse. This finding leads us to revise the current idea on the mechanism of T cell activation. Thus, in this project, we will analyze (1) activation regulation by the quality and quantity of antigen, and the involvement of self-peptide recognition, (2) identify all signal molecules involved in the microcluster among the TCR signaling molecules, (3) the relationship between co-stimulatory signals mediating positive/negative regulation of T cell activation or lipid raft and microclusters. We will develop new system, which enables to analyze three-dimensional analysis of the cell-cell interaction. Furthermore, We will analyze by using in vitro and in vivo imaging technique how the signal regulation to lead the activation of NF-AT vs. NF-kobo results in different functional diversification in independent or cooperative manners.

【Expected results】

・The analysis will clarify new regulatory mechanism of T cell activation at the molecular level on the basis of the new concept of TCR microclusters. It will also enable us to analyze temporal and spatial regulation of sustained activation.

・The functional role of self-peptide recognition for T cell activation by the analysis of the activation of TCR microclusters will be analyzed which may clarify the fundamental question of self-nonself discrimination.

・The analysis will lead to the development of new inhibitors targeting on temporal and spatial regulation by analysis of the molecular recruitment, cluster formation, and dynamism/equilibrium.

【References by the principal investigator】

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【Term of project】 FY2007− 2011	【Budget allocation】 18,000,000 yen (2007 direct cost)

【Homepage address】 http://web.rcai.riken.jp/en/labo/signaling/