【Grant-in-Aid for Specially Promoted Research】

Biological Sciences

Title of Project： Comprehensive analysis of innate immunity

Shizuo Akira
(Osaka University, Immunology Frontier Research Center, Professor)

Research Project Number：15H05704　Researcher Number：50192919
Research Area：Immunology
Keyword：Innate immunity, mRNA stability, M2 macrophage, Inflammation

【Purpose and Background of the Research】

Studies bridging innate immunity and various diseases are rapidly progressing. We revealed the physiological roles of TLR family molecules and downstream signaling pathways, which are critical for pathogen recognition, by generating knockout mice. These molecules are involved not only in pathogen recognition, but also in arteriosclerosis, cancer, metabolic syndrome and other diseases. TLR activates a signaling pathway that results in the production of cytokines, chemokines and various molecules associated with the immune response. Although most components of the innate immune signaling pathway, such as TLR, have been elucidated, the physiological roles of various TLR signaling-inducible genes remain unclear. Among them, we recently identified two inducible genes: Regnase-1 and Jmjd3. Studies of the former gene has led to the novel research field "**Control of mRNA stability in the immune response**", and that of the latter molecule Jmjd3 to another new research field "**Characterization of M2 macrophage subsets responsible for distinct pathophysiology**".

【Research Methods】

Our research methods are as follows: mRNA stability project 1) Analysis of the Regnase-1 expression mechanism and its role in different tissues. 2) Identification and functional analysis of new molecules involved in mRNA control by Regnase-1. M2 macrophage project 1) Identification of disorder-specific M2 macrophages and investigation of its physiological roles. 2) Comprehensive analysis of gene expression levels in disorder-specific M2 macrophages Identification and functional analysis of new molecules involved in the differentiation and activation of M2 macrophages.

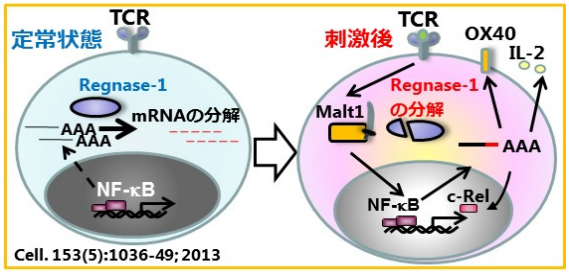

Figure1　Regulation mechanism of Regnase-1 in CD4+ cell

【Expected Research Achievements and Scientific Significance】

We have succeeded in developing a novel concept for the mechanisms underlying the actions of the innate immune system, including the control of **mRNA stability** and its link to inflammation as well as the presence of distinct **M2 macrophage** subsets in diseases. The results of these studies are expected to help unravel the immune regulation mechanisms underlying various diseases.

【Publications Relevant to the Project】

・Uehata T, et al.Cell.153:1036-49 (2013) (Figure1)
・Satoh T, et al.Nature.495:524-28 (2013) (Figure2)

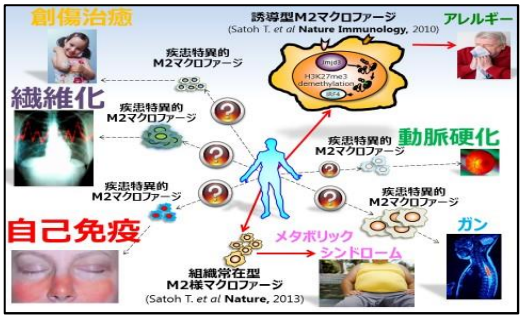

Figure2 disorder-specific M2 macrophages

【Term of Project】

FY2015-2019

【Budget Allocation】

433,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://hostdefense.ifrec.osaka-u.ac.jp/ja/index.html
sakira@biken.osaka-u.ac.jp