【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Agricultural Sciences)

Title of Project : Redefinition of intractable inflammatory diseases based on mast cell activation syndrome

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Research Project Number : 16H06383 Researcher Number : 80145820
Research Area : Agriculture
Keyword : Disease prevention and control

【Purpose and Background of the Research】

Mast cells are distributed over the connective tissue widely, and it is well known that a great variety of inflammatory mediators are released from the cells after by binding of pathogen ingredient or IgE antibody to their specific receptors eventually resulting in contribution to the innate immunity or induction of the nonspecific inflammations such as allergic responses.

It is also well known that mast cells located in the microenvironment are associated with the development of intractable inflammatory diseases, but its molecular mechanisms have not been understood by the simple reaction system as stated above. In addition, chemical mediators have material specificity for release kinetics over having many kinds including a species. Released chemical mediators might derive the pathological conditions through peripheral blood in a distant part, and in late years a new concept called "mast cell activation syndrome" was proposed. In this study, I investigate mast cell activation mechanisms involved in the affected sites and identify the functional molecules that induce pathological conditions in a variety of animals suffering from the yet unknown intractable inflammatory diseases. Thus, I do redefinition from a new viewpoint and aim at the development of novel diagnostic methods to identify and evaluate an etiology and pathological conditions of patients and the therapeutic drugs.

【Research Methods】

1) Examine species specificity, tissue specificity, and differentiation specificity of mast cells derived from various animals based on the surface molecules, the quantitative and qualitative data, and the reactive difference with various stimulants. 2) Using various intractable inflammatory disease models, assay chemical mediators derived from mast cells by blood and tissues and evaluate the effectiveness as diagnosis parameters. 3) Clarify the action of the specific chemical mediators from the viewpoint of itch and pain by knock-in or knock-out methods. Furthermore, I identify the target molecules and establish effective control methods of the mast cell activation syndrome.

【Expected Research Achievements and Scientific Significance】

This research project is based on much knowledge provided so far. I focus on an etiology and a process of the aggravation systematically, and the viewpoint that added not only the biochemical point of view but also physicochemical point of view in a species, a local site, the difference at the differentiation stage of mast cells. It clarifies the significant involvement of the mast cell activation syndrome in the development of intractable inflammatory diseases, and it may greatly change the treatment policy by identification of novel effective diagnosis parameters. Social significance is extremely big as well as scientific significance by a companion diagnosis.

【Publications Relevant to the Project】

・Hamilton, M.J. *et al.* Mast cell activation syndrome: A newly recognized disorder with systemic clinical manifestions. J. Allergy Clin. Immunol. 128:147-152 (2011).
・Tanaka, A. *et al.* Mast cells function as an alternative modulator of adipogenesis through 15-deoxy-delta-12, 14-prostaglandin J2. Am. J. Physiol.-Cell Physiol. 301:C1360-C1367 (2011).

【Term of Project】

FY2016-2020

【Budget Allocation】

144,900 Thousand Yen

【Homepage Address and Other Contact Information】

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