Molecular analysis of pathogenesis on Sjogren ' s syndrome and its application of new diagnosis and therapy

Yoshio Hayashi

(The University of Tokushima Graduate School, Institute of Health Biosciences, Department of Oral Molecular Pathology, Professor)

【Outline of survey】

The aim of this project is to elucidate the role of α-fodrin autoantigen which render in vivo immunoregulation of autoimmune responses in primary Sjogren's syndrome (SS). We investigate molecular analysis of pathogenesis on SS and its application of new diagnosis and therapy for human SS. Previously, we reported that a cleavage product of 120-kd α-fodrin may be an important autoantigen on the development of primary SS. Accumulated evidences suggest an important role of apoptosis in disease pathogenesis of SS, but little is known about the events triggering T cell invasion of the target organs in prelude to organ-specific autoimmune diseases. Cleavage of certain autoantigens during apoptosis may reveal immunocryptic epitopes that could potentially induce autoimmune responses. We speculate that an increase in enzymatic activity of apoptotic proteases is involved in the progression of α-fodrin proteolysis during apoptosis.

【Expected results】

The apoptosis associated breakdown product, 120-kd α-fodrin, may have an important role in the development of human Sjogren ' s syndrome (SS). Production of autoantibodies and proliferative T cell responses against cleavage product of α-fodrin might be an important clue that could shed light on the novel mechanisms by which tissue-specific apoptosis contributes to the disease development. The development of SS appears to be dependent on autoantigen cleavage through caspase cascade, and caspase-inhibitors might provide a new therapeutic option directed at reducing tissue damage. Moreover, it is feasible for the future possibility that a peptide analogue of autoantigen could be used as an immunotherapeutic agent.

【References by the principal researcher】

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【Term of project】 FY 2005 — 2009 | **【Budget allocation】** 86,100,000 yen

【Homepage address】 http://www.dent.tokushima-u.ac.jp/english/