Institute of DNA Medicine
Department of Molecular Immunology

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General Summary

Our research interests have focused on the analysis of the basic immune system protecting against disease and of immune disorders, such as hypersensitivity diseases and autoimmune diseases.

Research Activities

Enhanced IgE levels in interleukin 31 transgenic mice

Interleukin (IL)-31 is a newly discovered T-cell-derived cytokine whose overexpression in transgenic mice produces a phenotype closely resembling Alzheimer disease. In Nc/Nga mice high expression levels of IL-31 are associated with increased levels of serum IgE. Enhanced expression levels of IL-31 correlate with IL-4 and IL-13 but not with serum IgE levels in atopic dermatitis or allergic contact dermatitis.

To investigate the function of IL-31 and to confirm the possible association of IL-31 with serum IgE levels, transgenic mice that overexpress IL-31 were established under the control of cytomegalovirus enhancer/chicken beta-actin promoter.

Comparison of transgenic mice with littermate nontransgenic mice at 7 weeks of age showed a tendency for serum IgE levels to be increased in transgenic mice. Serum IgE levels in IL-31 transgenic mice with severe dermatitis were significantly higher than those in nontransgenic or other transgenic mice with mild or moderate dermatitis. Total IgE levels in 13-week-old transgenic mice were significantly higher than those in 7-week-old transgenic mice, but no age-related changes in serum IgE levels were observed in nontransgenic mice. However, no significant difference in the production of IL-4 or interferon-γ were found between nontransgenic and transgenic mice. Although our data do not reveal the mechanism of IgE expression in IL-31 transgenic mice, they do suggest that IgE levels in the mice correlate with the severity of the dermatitis induced by IL-31.

Abnormal telomerase activity and telomere length in T and B cells from patients with systemic lupus erythematosus

To evaluate the clinical significance of telomerase activity and telomere length in T and B lymphocytes from patients with systemic lupus erythematosus (SLE), CD3+ (T cell) and CD19+ (B cell) lymphocytes were isolated from the peripheral blood of patients with SLE and healthy control subjects by means of magnetic-bead-coupled antibodies. The telomerase activity of lymphocytes was measured with the telomeric-repeat amplification protocol. Telomere length was measured with flow cytometry fluorescence *in*

situ hybridization.

The telomerase activity of T cells was significantly higher in patients with either active or inactive SLE than in control subjects but was lower than the telomerase activity of B cells in patients with active SLE and was not correlated with the SLE disease activity index. The telomerase activity of B cells was significantly higher than in controls only in patients with active SLE and was strongly correlated with the SLE disease activity index. Four laboratory results, the anti-double-strand DNA antibody titer, the IgG level, the C3 level, and the CH50 level, were correlated with B-cell telomerase activity. Telomere length in T cells was significantly shorter than in control subjects. In contrast, the telomere length in B cells did not differ significantly from that in control subjects.

These results suggest that: 1) T cells are continuously activated in patients with SLE, 2) this activation alone does not cause the disease to develop, and 3) the disease manifests when B cell activation also occurs. Although it is not clear whether B-cell activation is mediated by T cells, the inhibition of B-cell activation may at least lead to the suppression of disease activity.

Publications

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