Development of the new animal model for systemic sclerosis using the immunologic function of CD19 and CD22

2000 Fiscal Year Final Research Report Summary

Development of the new animal model for systemic sclerosis using the immunologic function of CD19 and CD22

Research Project

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10357008

Research Category

Grant-in-Aid for Scientific Research (A).

Allocation Type

Single-year Grants

Section

展開研究

Research Field

Dermatology

Research Institution

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systemic sclerosis / CD19 / CD22 / B lymphocytes / tight skin mouse 1 / autoimmunity / animal model

Research Abstract

CD19 regulates intrinsic B lymphocyte signaling thresholds. To determine a role of CD19 expression in autoantibody production, we have assessed autoimmunity in a transgenic mice (CD19TG) with subtle 15-29% CD19 increases. Various autoantibodies were produced in CD19TG mice, demonstrating that small changes in CD19 expression can induce autoantibody production. Similar changes in CD19 expression were found on B cells from patients with systemic sclerosis (SSc). CD19 density on blood B cells from SSc patients was significantly (～20%) higher compared with normal individuals, while CD20, CD22, and CD40 expression were normal. These results

suggest that modest changes in the expression or function of CD19 may shift the balance between tolerance and immunity to autoimmunity.
Tight skin (Tsk) mice overall reflect the skin sclerosis in human SSc, but do not precisely mimic the immunologic abnormalities in human SSc. Based upon the results described above, we chose the immunologic function of CD19 for the development of new mouse model of SSc. Tsk mice were mated with CD19TG mice that overexpress CD19 by 2.6-fold or CD19 knock-out (KO) mice to generate CD19TG Tsk or CD19KO Tsk mice. In CD19TG Tsk mice, IgG anti-topoisomerase I antibody levels were elevated compared with wild-type mice, which was not observed in Tsk mice. Furthermore, the production of various autoantibodies was induced in CD19TG mice. This suggests that CD19TG Tsk mice would be the SSc animal model that most precisely reflect immunologic abnormalities in human SSc. However, skin sclerosis in CD19TG Tsk mice did not increase compared with Tsk mice. In contrast, the development of skin sclerosis was significantly inhibited in CD19KO Tsk mice in which the various immunologic abnormalities were almost completely abolished. Thus, expression and function of CD19 may also play a critical role in the development of skin sclerosis in Tsk mice.

Research Products (4 results)

All Other

All Publications

[Publications] Sato S,Hasegawa M,Fujimoto M,Tedder TF,Takehara K: "Quantitative genetic variation in CD19 expression correlates with autoimmunity."J Immunol. 165. 6635-6643 (2000)

[Publications] Sato S: "CD19 is a central response regulator of B lymphocyte signaling thresholds governing autoimmunity."J Dermatol Sci. 22. 1-10 (1999)

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[Publications] Sato S, Hasegawa M, Fujimoto M, Tedder TF, Takehara K: "Quantitative genetic variation in CD19 expression correlates"with autoimmunity.J Immunol. 165. 6635-6643 (2000)

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