自己免疫性再生不良性貧血における自己抗原の解析：CD4陽性T細胞エピトープの同定

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Analysis of autoantigens in immune-mediated aplastic anemia-identification of an epitope of a CD4^+ T-cell clone

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Research Abstract

To determine an epitope of a CD4^+ T-cell clone, ZN1, that appears to have an essential role in the development of aplastic anemia, we attempted to establish a system to screen a peptide capable of stimulating this T-cell clone using CLIP-replacement Ii-chain gene expression vectors. ZN1 was immortalized using infection with Herpesvirus saimiri. Stimulation with cultured bone marrow mononuclear cells (BMMCs) in the presence of IL-3 and GM-CSF induced DNA synthesis by ZN1. When monoclonal antibodies (mAbs) against HLA-DR, HLA-DR2 or HLA-DQ were added to the culture, both anti-DR and anti-DR2 mAbs inhibited DNA synthesis by ZN1 in

response to cultured BMMCs, suggesting restriction ** antigen recognition by HLA-DR2. Then, we transfected COS7 cells with a DR2 b gene plasmid and a DR a chain plasmid. Flow cytometry confirmed expression of DR2 by the COS7 transfectant. We are now testing interferon-γ excretion by ZN1 stimulated by the HLA-DR2-COS7 that was transfected with CLIP-replacement Ii chain gene vectors.
In relation to this project, we screened cDNA library derived from the patient's bone marrow mononuclear cells using serological identification of antigens by recombinant expression cloning to identify autoantigens in AA. IgG antibodies recognizing α globin (residue 1-101, α globin^<1-101>) was detected in the patient's serum. Immunoblotting using recombinant α globin^<1-101> detected the specific antibodies in 21 of 25 (84.0%) AA patients. When the patient's lymphocytes were stimulated with α globin^<1-11>, a low percentage of CD8* T cells reactive to this peptide were generated. The cultured T cells showed cytotoxicity against HLA-A*0201^+JY cells that were pulsed with this peptide. Addition of T cells stimulated by α globin^<1-11> to autologous CD34^+ cells reduced the number of colonies derived from BFU-E and CFU-GM to nearly a half of the control, α globin may serve as a target of immune system attack in AA patients possessing HLA-A-*0201.

Research Products (13 results)

All Other

All Publications

[Publications] Wang H, Chuhjo T, Yamazaki H, Shiobara S, Teramura M, Mizoguchi H, Nakao S: "Relative increase of granulocytes with a paroxysmal nocturnal haemoglobinuria phenotype in aplastic anaemia patients : the high prevalence at diagnosis"Eur J Haemaol. 66. 200-205 (2001)

[Publications] Ishiyama K, Karasawa M, Miyawaki S, Ueda Y, Noda M, Wakita A, Sawanobori M, Nagai H, Nakao S: "Aplastic anaemia with 13q-: a benign subset of bone marrow failure responsive to immunosuppressive therapy"Br J Haematol. 117. 747-750 (2002)

[Publications] Feng X, Chuhjo T, Nakao S, et al.: "An a globin peptide presented by HLA-A^*0201 on hematopoietic progenitor cells is a target of immune system attack in aplastic anemia"Blood. 98(Suppl). 700a (2001)

[Publications] Wang H, Chuhjo T, Yasue S, Omine M, Nakao S: "Clinical significance of a minor population of paroxysmal nocturnal hemoglobinuria-type cells in bone marrow failure syndrome"Blood. 100. 3897-3902 (2002)

[Publications] Miura Y, Thoburn CJ, Bright EC, Chen W, Nakao S, Hess AD: "Cytokine and chemokine profiles in autologous graft-versus-host disease(GVHD) : interleukin 1O and interferon gamma may be critical mediators for the development of autologous GVHD"Blood. 100. 2650-2658 (2002)

[Publications] Ishiyama K, Chuhjo T, Wang H, Yachie A, Omine M, Nakao S: "Polyclonal hematopoiesis maintained in patients with bone marrow failure harboring a minor population of paroxysmal nocturnal hemaglobinuria-type cells"Blood. (in press). (2003)

[Publications] 中尾眞二: "看護のための最新医学講座-血液・造血器疾患"日野原重明, 井村裕夫, 岩井郁子, 北村聖監, 北村聖 編(中山書店). 106-116 (2001)

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[Publications] Miura Y., Thoburn C.J., Bright E.C., Chen W., Nakao S., Hess A.D.: "Cytokine and chemokine profiles in autologous graft-versus-host; disease (GVHD): interleukin 10 and interferon gamma may be critical mediators for the development of autologous GVHD."Blood. 100. 2650-2658 (2002)

[Publications] Ishiyama K., Chuhjo T., Wang H., Yachie A., Omine M., Nakao S.: "Polyclonal hematopoiesis maintained in patients with bone marrow failure harboring a minor population of paroxysmal nocturnal hemaglobinuria-type cells."Blood. (in press)

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