

Establishment of a diagnostics of autoimmune bone marrow failure by means of examination of antibody to hematopoietic stem Cells

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2003 Fiscal Year Final Research Report Summary

Establishment of a diagnostics of autoimmune bone marrow failure by means of examination of antibody to hematopoietic stem Cells

Research Project

Project/Area Number

14570969

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Hematology

Research Institution

Kanazawa University

Principal Investigator

CHUHJO Tatsuya Kanazawa University, University hospital, Assistant, 医学部附属病院, 助手 (00303298)

Co-Investigator(Kenkyū-buntansha)

NAKAO Shinji Kanazawa University, Graduate School of Medicine, Professor, 医学系研究科, 教授 (70217660)

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2002 - 2003

Keywords

autoantibody / aplastic anemia / PNH / DR15 / DRS-1 / helper T-cell / SEREX / MDS

Research Abstract

To identify candidate antigens in aplastic anemia (AA), we screened proteins derived from a leukemia cell line with serum of an AA patient and identified diazepam-binding inhibitor-related protein I (DRS-1). Enzyme-linked immunosorbent assay (ELISA) revealed high titers of anti-DRS-1 antibodies (DRS-1 Abs) in 27 (38.0%) of 71 AA patients displaying increased paroxysmal nocturnal hemoglobinuria (PNH)-type cells (PNH+), 2 (6.3%) of 32 PNH- AA patients, 5 (38.5%) of 13 PNH+ myelodysplastic syndrome (MDS) patients, and none of 42 PNH- MDS patients. DRS-1 gene was abundantly expressed in myeloid leukemia cell lines and in CD34+ cells derived from healthy individuals. Stimulation of T cells from an AA patient displaying high DRS-1 Abs with a putative CD4+ T-cell epitope (amino acid residues [aa's] 191-204) presented by HLA-DRI5, which overlapped with a hot spot (aa's 173-198) of DRS-1 Ab epitopes, gave rise to T cells cytotoxic for L cells (murine fibroblasts) that were

transfected with DRB 1[^]*1501 and DRS-1. Enzyme-linked immunospot assay demonstrated increased frequency of T-cell precursors specific to the DRS-1 peptide in other HLA-DR15+ AA patients displaying high DRS-1 Ab titers. These findings indicate that DRS-1 may serve as an autoantigen eliciting immune attack against hematopoietic stem cells in a subset of AA patients characterized by increased PNH-type cells.

Research Products (6 results)

All 2004 2003 2002

All Journal Article

[Journal Article] Diazepam-binding inhibitor protein 1 : a candidate autoantigen in acquired aplastic anemia patients harboring a minor population of paroxysmal nocturnal hemoglobinuria-type cells 2004 ▾

[Journal Article] Diazepam-binding inhibitor protein 1 : a candidate autoantigen in acquired aplastic anemia patients harboring a minor population of paroxysmal nocturnal hemoglobinuria-type cells 2004 ▾

[Journal Article] Polyclonal hematopoiesis maintained in patients with bone marrow failure harboring a minor population of paroxysmal nocturnal hemoglobinuria-type cells 2003 ▾

[Journal Article] Polyclonal hematopoiesis maintained in patients with bone marrow failure harboring a minor population of paroxysmal nocturnal hemoglobinuria-type cells 2003 ▾

[Journal Article] Clinical significance of a minor population of paroxysmal nocturnal hemoglobinuria-type cells in bone marrow failure syndrome 2002 ▾

[Journal Article] Clinical significance of a minor population of paroxysmal nocturnal he moglobinuria- type cells in bone marrow failure syndrome 2002 ▾

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