マイナー組織適合抗原高親和性T細胞レセプター遺伝子導入による特異的CTLの誘導

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2007 Fiscal Year Final Research Report Summary

Induction of cytotoxic T lymphocytes specific for minor histocompatility antigen through transferringThell receptor gene

Research Project

Project/Area Number
18591049
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
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Project Period (FY)
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minor histocompatibility antigen / leukemia / stem cell transplantation
Research Abstract

In hematopoietic SCT from HLA-matched donors, allogeneic immune reactions such as GVHD and GVL effect are induced by disparities in minor histocompatibility antigens (mHas) between donor and recipient. CD62L has been reported to act as an mHa based on analysis of the outcome of allogeneic SCT. To identify peptides derived from CD62L that may be involved in GVL effect, we prepared all possible 18 different 9-mer peptides derived from CD62L that include codon 213 in one of the 9 positions, and tested for cytotoxic T-cell precursors specific to any of these peptides in patients after CD62L-disparate SCT. PBMC obtained from 5 patients with I-ILA-A*2402 who developed GVHD following transplantation were incubated with autologous monocyte-derived DCs or HLA-A*2402-transfected T2 cells which were pulsed with the 9-mer peptides, or incubated with the peptides only, and 1FN-gamma secretion from PBMC after 16 hours incubation was examined. Two to 4 different recipient-type peptides for each patient induced higher IFN-gamma secretion than the others. By stimulating PBMC with the peptide-pulsed T2-A24 cells, T-cell lines specific for 4 peptides were obtained. The cultured T cells efficiently lysed peptide-pulsed T2-A24 cells as well as HLA-A*2402-positive lymphoblastic cell line cells that were disparate with CD62L. Addition of mAbs against HLA-class I blocked this cytotoxicity. WIC stabilization assay demonstrated that the 4 peptides bound to the cell surface and HLA complex stabilized. These results suggest these peptides may serve as mHas capable of inducing GVL effect, and CTLs recognizing CD62L-derived polymorphic peptides may have therapeutic value in treating relapsed leukemia after SCT.

Research Products (40 results)

(40 results)					
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All	ournal Article (24 results) (of which Peer Reviewed: 12 results)	Presentation	(16 resu	ılts)
[Journal Article] CD16(+)CD56(-)NK cells in the peripheral b graft-versus-leukemia effect	d of cord blood transplant	recipients: A unique subset of NK cells poss	sibly associated	d with 2008	~
[Journal Article] Mechanism of decrease of oral bioavailability	cyclosporin A during imm	unotherapy upon coadministration of amph	otericin B	2008	~
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[Journal Article] Mechanism of decrease of oral bioavailability	cyclosporin A during imm	unotherapy upon coadministration of amph	otericin B	2008	~
[Journal Article] Living-donor lobar lung transplantation for b bronchiolitis obliterans recur in transplanted lungs?	ncho-bronchiolitis obliteran	s after allogeneic hematopoietic stem cell ti	ransplantation	: does 2007	~
[Journal Article] Macrophage colony-stimulating factor enhan	s rituximab-dependent cell	ular cytotoxicity by monocytes		2007	~
[Journal Article] Prospective phase II trial to evaluate the co transplantation with fludarabine and busulfan	lications and kinetics of chi	merism induction following allogeneic hema	atopoietic sten	n cell 2007	~
[Journal Article] Immature platelet fraction for prediction of	elet engraftment after allo	geneic stem cell transplantation		2007	~
[Journal Article] Roles of DRB1(*)1501 and DRB1(*)1502 in	e pathogenesis of aplastica	nemia.		2007	~
[Journal Article] Safety and efficacy of foscarnet for preempt	therapy against cytomega	lovirus reactivation after unrelated cord blo	od transplanta	ation. 2007	~
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[Journal Article] Safety and efficacy of foscarnet for preempt	therapy against cytomega	lovirus reactivation after unrelated cord blo	od transplanta	ation 2007	~

[Journal Article] Immunoglobulin preparations attenuate organ dysfunction and hemostatic abnormality by suppressing the production of cytokine lipopolysaccharide-induced disseminated intravascular coagulation in rats.	es in 2006	~
[Journal Article] Graft rejection and hyperacute graft-versus-host disease in stem cell transplantation from non-inherited maternal antigen comple HLA-mismatched siblings.	ementary 2006	~
[Journal Article] Reduced-intensity unrelated cord blood transplantation for treatment of metastatic renal cell carcinoma: first evidence of cord-bloversus-solid-tumor effect.	2006	~
[Journal Article] Successful treatment of minimal residual disease-positive Phiadelphia chromosome-positive acute lymphoblastic leukemia with in followed by reduced-intensity unrelated cord blood transplantation after allogeneic peripheral blood stem cell transplantation.	natinib 2006	~
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[Presentation] A novel strategy for the treatment of acute GVHD: removal of excessive inflammatory cytokines using the absorbent	2008	~
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[Presentation] 過剰炎症性サイトカイン吸着除去による急性GVHD治療開発	2008	~
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