Profiling of endothelial cell derived stem cell factors associating with the regulation of hematopoietic stem calls

2007 Fiscal Year Final Research Report Summary

Profiling of endothelial cell derived stem cell factors associating with the regulation of hematopoietic stem calls

Research Project

Project/Area Number

16390275

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Hematology

Research Institution

Osaka University (2006-2007)
Kanazawa University (2004-2005)

Principal Investigator

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Project Period (FY)

2004 – 2007

Keywords

hematopoietic stem cell / self-renewal / self-renewal / galectin-3 / PSF1

Research Abstract

Quiescence is thought to be one of important feature of hematopoietic stem cells (HSCs) for the prevention of exhaustion in bone marrow (BM) adult hematopoiesis. Recently, it has suggested that HSCs change their cell cycle status from cycling population to quiescent one between 3 and 4 weeks after birth. However, the precise molecular mechanism of induction in quiescence of HSCs is not fully understood. Although Tie2, a receptor tyrosine kinase expressed on HSCs has been suggested to regulate quiescence of HSCs, its role is not clearly known. Therefore, we isolated molecules affected by Tie2 activation and analyzed the function of those molecules. We isolated a novel evolutionarily conserved DNA replication factor, PSFI (Partner of SLD5-1) in HSCs. In one-year-old PSF1(+/-) mice, the pool size of stem cells and

progenitors is decreased. While young PSF1(+/-) mutant mice develop normally, are fertile, and have no obvious differences in hematopoiesis in the steady state compared with wild-type mice, intravenous injection of 5-fluorouracil (5-FU) is lethal in PSF1(+/-) mice due to a delay in induction of HSC proliferation during ablated BM reconstitution. Our data indicated that PSF1 is required for acute proliferation of HSCs in the BM of mice. Moreover, we found that galactose binding lectin-3 (galectin-3; Gal-3) upregulated by Tie2 activation plays a role in quiescence of HSCs. HSCs from mice harboring conditionally overexpressed Gal-3 under the control of the Tie2 promoter progressed slowly through the cell cycle because of induction of p21. By contrast, cell cycle of Tie2+HSC population from Gal-3-deficient mice was accelerated resulted in exhaustion of HSCs possessing long-term repopulating ability in adult BM. These indicated that Gal-3 is negative regulator of HSC cycling and has a crucial role in inhibition of exhaustion for adult hematopoiesis.

Research Products (39 results)

All | 2008 | 2007 | 2006 | 2005 | Other

All | Journal Article | Presentation | Book

[Journal Article] Spatial and temporal role of the apelin/APJ system in the caliber size regulation of blood vessels durinh angiogenesis 2008

[Journal Article] Involvement of MDR1 Function In Proliferation of Tumor Cells 2008

[Journal Article] Spatial and temporal role of the apelin/APJ system in the caliber size regulation of blood vessels during angiogenesis 2008

[Journal Article] EphB4 overexpression on B16 melanoma cells affects arterial-venous patterning in tumor angiogenesis 2007

[Journal Article] Cardiac stem cells in brown adipose tissue express CD133 and induce bone marrow non-hematonoietic cells to differentiate into cardiomyocytes 2007

[Journal Article] A novel approach for myocardial regeneration with educated cord blood cells cocultured with cells from brown adipose tissue 2007

[Journal Article] Expression of angiogenic and neurotrophic factors in the progenitor cell niche of adult monkey subventricular zone 2007

[Journal Article] Inhibition of Axonal Outgrowth in the Tumor Environment: Involvement of Class 3 Semaphorins 2007

[Journal Article] EphB4 overexpression on B16 melanoma cells affects arterial-venous patterning in tumor angiogenesis 2007

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[Journal Article] Inhibition of Axonal Outgrowth in the Tumor Environment : Involvement of Class 3 Semaphorins 2007

[Journal Article] Physiological pathway of differentiation of hematopoietic stem cell population into mural cells 2006

[Journal Article] Negative Regulation of VEGF-Induced Vascular Leakage by Blockade of Angiotensin II Type 1 Receptor 2006

[Journal Article] Role of hematopoietic lineage cells as accessory components in blood vessel formation 2006

[Journal Article] Cardiac progenitor cells in brown adipose tissue repaired damaged myocardium 2006

[Journal Article] Identification and characterization of mouse PSF1-binding protein, SLD5 2006

[Journal Article] Platelet derived growth factor receptor alpha is essential for establishing a microe nvironment that supports definitive ervthrouoiesis 2006

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[Journal Article] Identification and characterization of mouse PSFI-binding protein, SLD5 **2006**

[Journal Article] Platelet derived growth factor receptor alpha is essential for establishing a microenvironment that supports definitive erythropoiesis **2006**

[Journal Article] Hematopoietic cells regulate the angiogenic switch during tumorigenesis **2005**

[Journal Article] PSF1 is essential for Early Embryogenesis in mice **2005**

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[Journal Article] PSF1 is essential for Early Embryogenesis in mice **2005**

[Presentation] Molecular analysis of stemness and blood vessel formation regulated by Tie2 **2007**

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[Presentation] Involvement of hematopoietic stem cell population in angiogenesis **2007**

[Presentation] Galectin-3 induces quiescence of hematopoietic stem cells in the bone marrow niche **2007**

[Presentation] Galectin-3 induces quiescence of hematopoietic stem cells in the bone marrow niche **2007**

[Presentation] Analysis of molecules regulated by Tie2 on stemness and blood vessel formation **2006**

[Presentation] Analysis of molecules regulated by Tie2 on stemness and blood vessel formation **2006**

[Presentation] Analysis of molecules regulated by Tie2 on stemness and blood vessel formation **2005**

[Presentation] Analysis of molecules regulated by Tie2 on stemness and blood vessel formation **2005**

[Book] Involvement of MDRI Function In Proliferation of Tumor Cells

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