造血幹細胞の発生・自己複製に関わる分子クローニ ングとその機能解析

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Research Project

Research Abstract

Molecular cloning of self-renewal factors for hematopoietic stem cells and analysis of those gene

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For regeneration therapy using hematopoietic stem cells(HSCs), it is necessary to expand HSCs in vitro effectively. We tried to analyze the self-renewal and maintenance of immature phenotype so called, "HSC's stemness" for in vitro expansion of HSCs. In this experiment, we focused on receptor tyrosine kinase, TIE2, which is expressed on the tried and an above the light cells (TSCs).

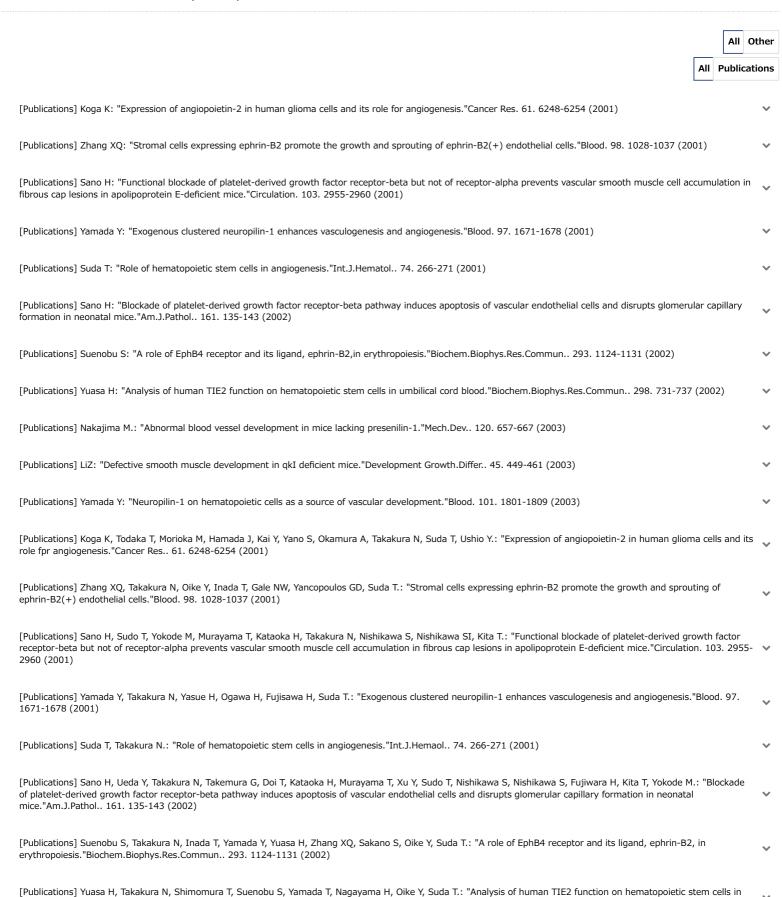
We found that proliferation of HSCs are observed near ECs forming capillary in hematopoietic organ, such as fetal liver, bone marrow and so on and such HSCs produce angiopoietin-1(Ang1), a ligand for TIE2. Then, we analyzed the function of TIE2 for sternness by using constitutively active form of TIE2. Result showed that TIE2 activation promote several kinds of biological phenomena such as anti-apoptosis, delay of cell cycle, and enhancement of cell adhesion to matrix. Moreover, upon an

activation of TIE2 on ECs and hematopoietic cells(HCs), those cells selectively adhered with each other tightly. This suggests that Ang1 from HSCs stimulates TIE2 on both HSCs and ECs in the foci and becomes trigger for cell adhesion and stemness of HSCs.

Based on these experiments, we tried to isolate TIE2 activation associating gene using micro-array methods and obtained several candidate genes. E11, a novel gene of putative transcriptional factor, expresses on several stem cells in variety of organ and targeted disruption of this gene led to early embryonic lethality before HSCs develop. We will try to establish knock out mice those have HSCs specifically disrupted of E11 gene and analyze this gene in hematopoiesis precisely. Moreover, we isolated a candidate gene, galectin-3, that may associate with cell adhesion between HSCs and ECs. We have started to generate a transgenic mice expressing galectin-3 on HSCs and ECs under the transcriptional control of TIE2 promoter and will analyze the stemness of HSCs using this mice.

Research Products (22 results)

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