"The 86th of Stem Cell Biology and Regenerative Medicine Forum"

Date：Oct 22nd (Thu) 2015
Time : 18:00 ～ 19:30
Place：8th fl of New Hospital Building

（Internal Speaker）

18:00-18:30 Susumu Goyama (Associate Professor Division of Cellular Therapy
The Institute of Medical ScienceThe University of Tokyo)
UBASH3B-CBL axis regulates myeloid proliferation in human preleukemia induced by AML1-ETO

（External Speaker）

18:30-19:30 Yoshio Katayama (Junior Associate Professor, Hematology, Department of Medicine, Kobe University Hospital, PRESTO, Japan Science and Technology Agency)
Eyes on non-hematopoietic tissues to understand hematology: lympho-hematopoietic microenvironment regulated by inter-organ communication

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Hosted by Center for Stem Cell Biology and Regenerative Medicine

---Information---
* Please register attendance at the reception desk.
* Next forum (the87th) is not yet fixed.
* Please contact tatsu-m@ims.u-tokyo.ac.jp, for Forum speaker

UBASH3B-CBL axis regulates myeloid proliferation in human preleukemia induced by AML1-ETO

Susumu Goyama (Associate Professor Division of Cellular Therapy The Institute of Medical ScienceThe University of Tokyo)

The t(8;21) rearrangement, which creates the AML1-ETO fusion protein, represents the most common chromosomal translocation in acute myeloid leukemia (AML). Clinical data suggest that CBL mutations are a frequent event in t(8;21) AML, but the role of CBL in AML1-ETO-induced leukemia has not been investigated. In this study, we demonstrate that CBL mutations collaborate with AML1-ETO to expand human CD34+ cells both in vitro and in a xenograft model. CBL depletion by shRNA also promotes the growth of AML1-ETO cells, demonstrating the inhibitory function of endogenous CBL in t(8;21) AML. Mechanistically, loss of CBL function confers hyper-responsiveness to thrombopoietin and enhances STAT5/AKT/ERK/Src signaling in AML1-ETO cells. Interestingly, we found the protein tyrosine phosphatase UBASH3B, which is known to inhibit CBL function, is upregulated by AML1-ETO through transcriptional and miR-9-mediated regulation. UBASH3B depletion induces an aberrant pattern of CBL phosphorylation and impairs proliferation in AML1-ETO cells. The growth-inhibition caused by UBASH3B depletion can be rescued by ectopic expression of CBL mutants, suggesting that UBASH3B supports the growth of AML1-ETO cells partly through modulation of CBL function. Our study reveals a role of CBL in restricting myeloid proliferation of human AML1-ETO-induced leukemia, and identifies UBASH3B as a potential target for pharmaceutical intervention.

Eyes on non-hematopoietic tissues to understand hematology: lympho-hematopoietic microenvironment regulated by inter-organ communication

Yoshio Katayama (Junior Associate Professor, Hematology, Department of Medicine, Kobe University Hospital, PRESTO, Japan Science and Technology Agency)

Hematopoietic stem/progenitor cells (HSCs/HPCs) possess the ability to maintain the entire population of blood cells throughout life and to replenish the hematopoietic system after transplantation into marrow-ablated recipients. Bone marrow is the primary organ for hematopoiesis, in which HSCs/HPCs reside in microenvironment adapted to supporting their ability, called a “niche”. The skeletal and the hematopoietic systems are two different research lines now being united through the definition of a new function of bone-forming osteoblasts, as a regulatory microenvironment for hematopoiesis. In addition to the accumulation of knowledge about niche cells themselves, novel findings about cells regulating environmental function (niche modulators) have also recently emerged, such as sympathetic nervous system and mature hematopoietic/skeletal cells. Furthermore, recent studies have revealed that the skeletal system regulates primary lymphoid organs, and glucose/fat energy metabolism in association with brain and liver. Inter-organ communication governs lympho-hematopoiesis, and the deviation of this network may result in HSCs/HPCs mobilization, hematologic disorders, and aging.