"The 87th of Stem Cell Biology and Regenerative Medicine Forum"

Date：Feb 8th (Mon) 2016
Time : 13:00 ～ 14:30
Place：Auditorium in 1st Building

（Internal Speaker）

13:00-13:30 Yuki Taya (Division of Stem Cell Therapy The Institute of Medical Science The University of Tokyo)
Valine starving permits hematopoietic stem cell transplantation without chemoirradiative myeloablation

（External Speaker）

13:30-14:30 Kazuhito Naka (Department of Stem Cell Biology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan)
A Nutrient Supply Essential for CML Stem Cells

Hosted by Center for Stem Cell Biology and Regenerative Medicine

---Information---

* Please register attendance at the reception desk.
* Next forum (the88th) will be held on Feb 22nd.
* Please contact tatsu-m@ims.u-tokyo.ac.jp, for Forum speaker recommendations

Valine starving permits hematopoietic stem cell transplantation without chemoirradiative myeloablation

Yuki Taya (Division of Stem Cell Therapy The Institute of Medical ScienceThe University of Tokyo)

Hematopoietic stem cells (HSCs) have the potential to provide the entire range of blood cells throughout the lifespan, maintaining the hibernation state in specialized bone marrow (BM) microenvironment called niches. Although various types of cells and proteinous factors have been proposed to control hematopoiesis, little is known about environmental factors crucial for the maintenance, survival and function of HSCs in vivo. Here we found that endogenous small molecules such as amino acids are differentially distributed to bone tissues in mice. Functional analysis of various amino acids revealed that self-renewal of HSCs is lost under in vitro culture conditions without some amino acids especially valine. Consistent with these in vitro data, the mice fed a diet deficient in valine exhibited a massive decrease in the frequency of BM HSCs. Furthermore, dietary deficiency of valine could vacate BM niches and promote engraftment of donor HSCs. These findings indicate a critical role for valine metabolism in the maintenance of HSCs and raise the possibility that in vivo reduction of valine may become third conditioning method for HSC transplantation.

A Nutrient Supply Essential for CML Stem Cells

Kazuhito Naka (Department of Stem Cell Biology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan)

A nutrient supply specific to the rare chronic myelogenous leukemia (CML) stem cell population could provide a target for novel therapeutics aimed at eradicating these cells. In this study, we surveyed global metabolic differences between murine normal hematopoietic stem cells (HSCs) and CML stem cells using sophisticated metabolomics techniques. Strikingly, we found that CML stem cells took up significantly higher levels of dipeptide species than normal HSCs. Once internalized, these dipeptide species activated nutrient signaling via a pathway involving p38MAPK and the stemness transcription factor Smad3, which promotes CML stem cell maintenance. Importantly, pharmacological inhibition of dipeptide uptake inhibited CML stem cell activity *in vivo*. Collectively, our results demonstrated that dipeptide species support CML stem cell maintenance by guaranteeing an essential nutrient supply *in vivo*, and thus point towards a potential novel therapeutic target for CML treatment.