"The Stem Cell Biology and Regenerative Medicine Symposium"

Date：Oct 19th (Mon) 2015
Time : 13:00 ～ 15:00
Place：8th fl of New Hospital Building

（Speaker1）

13:00-14:00 Fernando Camargo (Associate Professor Stem Cell Program, Children's Hospital Boston Department of Stem Cell and Regenerative Biology, Harvard University)
In vivo Stem Cell Clonal Dynamics

（Speaker2）

14:00-15:00 Margaret A. Goodell (Professor, Baylor College of Medicine)
DNMT3A in Normal and Malignant Hematopoiesis

Hosted by Center for Stem Cell Biology and Regenerative Medicine

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* Please register attendance at the reception desk.
* Next forum (the86th) will be held on Oct. 22th (Thurs) 18:00～ at Tommy Hall
* Please contact tatsu-m@ims.u-tokyo.ac.jp, for Forum speaker recommendations

In vivo Stem Cell Clonal Dynamics

Fernando Camargo (Associate Professor Stem Cell Program, Children's Hospital Boston Department of Stem Cell and Regenerative Biology, Harvard University)

Tremendous progress has been achieved in the characterization of the hematopoietic system over the past two decades. Historically, the main experimental approach used to elucidate and define these cellular relationships in the bone marrow (BM) has been the transplantationassay. For this reason, most of our knowledge about the in vivo properties of hematopoietic stem cells (HSCs) and progenitor cells has been derived from studies in the transplant context. Because of the lack of tractable systems, the mechanistic nature of non-transplant hematopoiesis has remained largelyunexplored. Over the past several years, my laboratory has developed novel genetic tools for the clonal tracing and imaging of hematopoietic populations in the unperturbed niche that aim to bring insight into the biology of stem and progenitor cells in situ. Our work using a transposon-mediated cellular tagging approach indicated that progenitors, and not the classical long-term HSCs, are the cells mainly responsible for the day-to-day production of blood cells in the adult. Our data also suggested that lineage restricted progenitors are the main contributors to hematopoiesis at steady state. These data represent the first systematic analysis of clonal fate in an unperturbed hematopoietic niche and revealed a novel cellular mechanism for homeostatic blood regeneration. We have now utilized this clonal tracing model to bring insight into the dynamics of stem and progenitor biology during embryonic hematopoiesis and in the severely aged hematopoietic system. These data will be discussed at the meeting.

DNMT3A in Normal and Malignant Hematopoiesis

Margaret A. Goodell (Professor, Baylor College of Medicine)

Recent exome sequencing in hematologic malignancies identified frequent mutations in genes encoding epigenetic regulators, particularly those that control DNA methylation such as *DNMT3A*. We found that loss of *Dnmt3a* in mouse hematopoietic stem cells (HSCs) leads to increased self-renewal and inhibited differentiation. To study the role of these mutations in malignancies, we have introduced into mouse HSCs additional mutant genes that co-occur in patients. We have found that FLT3-ITD can synergize with mutations in *Dnmt3a* to lead to lymphoid or myeloid malignancies, influenced in part by the degree of DNMT3A activity that remains. We have also crossed *Dnmt3a* mutant and *Tet2* mutant mice in order to examine the type of malignancies that develop and the associated mechanisms. These and other recent studies on DNMT3A function will be presented.