"The 80th of Stem Cell Biology and Regenerative Medicine Forum"

Date：Apr 17th (Fri) 2015
Time : 18:00 ～ 19:30
Place：8th fl of New Hospital Building

（Internal Speaker）

18:00-18:30 Sanae Hamanaka (Division of Stem Cell Therapy, Center for Stem Cell Biology and Regenerative Medicine, IMUST)
Simultaneously generation of blood vessels and hematopoietic cells by way of blastocyst complementation with *Flk-1* KO mouse

（External Speaker）

18:30-19:30 Kazumasa Ogasawara (Division of Pathology and Disease regulation, Department of Pathology, Shiga University of Medical Science)
Establishment of a macaque system applicable to transplantation experiments in regenerative medicine

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Hosted by Center for Stem Cell Biology and Regenerative Medicine

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* Please register attendance at the reception desk.
* Next forum (the81th) will be held on May. 22nd (Fri) 18:00～ at Tommy Hall.
* Please contact tatsu-m@ims.u-tokyo.ac.jp, for Forum speaker recommendations

Simultaneously generation of blood vessels and hematopoietic cells by way of blastocyst complementation with *Flk-1* KO mouse

Sanae Hamanaka (Division of Stem Cell Therapy, Center for Stem Cell Biology and Regenerative Medicine, IMUST)

Shortage of donors and graft rejection are now the key constraint to organ transplants. To resolve these issue, we have developed the blastocyst complementation in which the pluripotent stem cells (PSCs) are injected into the blastocyst from organ deficient animal to generate deficient organ from injected PSCs. Recently, we have succeeded to generate pancreas in apancreatic mouse (*Pdx-1* KO mouse) by blastocyst complementation (Kobayashi, et al., Cell 2010). Injected iPSCs were contributed all pancreatic cell lineages, however, non-pancreatic lineage tissues such as blood vessels or nerves were chimera which is composed of PSCs and host cells. In case of organ transplantation accompanied by vascular anastomosis, it is known that MHC mismatch of the vascular endothelial cells become a target for graft rejection. To generate a rejection free transplantable organ, it is necessary to generate not only target organ but also vascular endothelial cells from PSCs.

To generate vascular endothelial cells, we performed blastocyst complementation with *vascular endothelial growth factor receptor-2* (*VEGFR-2/ Flk-1*) homozygous mutant (*Flk-1* KO) as host organ deficient animal which is embryonic lethality at 8.5~9.5 dpc due to early defect of endothelial and hematopoietic cells.

iPSC injected *Flk-1* KO chimera mice were survived to adulthood for over one year and vascular endothelial cells were generated from injected iPSCs. Moreover, we found that hematopoietic cells in *Flk-1* KO chimera mouse were also generated from donor iPSCs. It is suggested that the blastocyst complementation is effective with organ deficient animal which shows early embryonic lethal phenotype. Furthermore, vascular endothelial cells and hematopoietic cells are able to generate simultaneously by blastocyst complementation with *Flk-1* KO mouse as a host organ deficient animal.

Establishment of a macaque system applicable to transplantation experiments in regenerative medicine

Kazumasa Ogasawara (Division of Pathology and Disease regulation, Department of Pathology, Shiga University of Medical Science)

We have a colony of macaque fascicularis (crab-eating macaque, cynomolgus monkey) consisting of 700 individuals in which transplantation-related genes, major histocompatibility complex (MHC), have been determined. In more than five thousand macaques we analyzed so far including colonies outside of our facility, we found several MHC haplotypes and MHC homozygous macaques born in the Philippines. An MHC haplotype named HT4 consisted of an HT1 haplotype in the MHC class II region and an HT8 haplotype in the MHC class I region. Thus, we focused on macaques carrying these haplotypes to expand our macaque colony by means of intracytoplasmic sperm injection (ICSI).

We have established iPS cells from HT1-, HT4-, and HT8-homozygous macaques. Using the iPS cells from an HT1 homozygous macaque, we have performed a few trials in which differentiated cells from HT1-homozygous iPS cells were transplanted into HT1-heterozygous individuals. The HT1-homozygous cells differentiated from the iPS cells were transplantable more effectively to HT1-heterozygous individuals than to MHC-mismatched individuals. The results show that our macaque system is compatible with preclinical transplantation experiments before clinical applications in regenerative medicine.