ASHBi SEMINAR

2025
5.12 MON
16:30-18:00

Venue **Conference Room** ◀◀◀ Onsite Only
B1F, Faculty of Medicine Bldg. B

Registration

Lecturer **Pierre Savatie** Ph.D.
Professor, Stem Cell and Brain Research Institute, INSERM, Lyon, France

Irene Aksoy Ph.D.
Researcher, Stem Cell and Brain Research Institute, INSERM, Lyon, France

"The challenges of pluripotent stem cell-based germline chimeras"

Lecturer: **Pierre Savatier, Ph.D.**

Pluripotent stem cells have long been used to produce knockout mice via germline chimera technology. However, aside from the rat, this approach has not been successfully applied to other mammals. I will describe our long-term efforts to generate rabbit embryonic stem cell (ESC) and induced pluripotent stem cell (iPSC) lines. Building on our investigation of the pluripotency continuum in rabbit embryos, I will demonstrate that rabbit iPSCs can be reprogrammed using KLF2, ERAS and PRMT6, which enables them to efficiently colonize host embryos. These chimeric embryos develop into fetuses and newborn rabbits, with iPSCs contributing up to 100 % to certain organs. Notably, female rabbits generated via this method are healthy and transmit the iPSC genome to their offspring, confirming germline chimerism. This advancement lays the groundwork for developing rabbit models of human disease and, when extended to non-human primates, could enable the generation of monkey models that capture complex genetic traits beyond the scope of conventional CRISPR-based embryo editing.

"Molecular and cellular mechanisms underlying embryo colonization by pluripotent stem cells in primates"

Lecturer: **Irene Aksoy, PhD**

Generating interspecies chimeras with primate pluripotent stem cells (PSCs) remains a major challenge. Unlike mouse embryonic stem cells (ESCs), which efficiently colonize host embryos, human and non-human primate (NHP) naïve PSCs exhibit poor integration, regardless of the host species. After dissociation, these cells slow DNA replication, stall in G1, and differentiate prematurely, suggesting an intrinsic inability to remain mitotically active during colonization. The pre-implantation embryo may also impose selective pressures that eliminate foreign cells via cell competition. To investigate this, we assessed naïve PSCs from humans, chimpanzees, rhesus monkeys, and marmosets in both in vitro competition assays and in vivo embryo injections. Chimpanzee PSCs consistently outcompeted human, rhesus, and marmoset PSCs in vitro and exhibited superior colonization efficiency in rabbit, pig, bovine, and cynomolgus monkey embryos. Single-cell transcriptomics revealed adaptive transcriptional changes in chimpanzee PSCs during colonization. Mechanistically, ERK and AKT signaling pathways enhance primate PSC survival in chimeric environments. ERK inhibits BIM to prevent apoptosis, while AKT reduces BAX activity. Leveraging these insights, we developed a small-molecule cocktail that improves human iPSC colonization. These findings establish a link between cell competition and chimera formation, providing a framework for optimizing primate PSC-embryo integration and producing intra- and inter-species chimeras.

Organizer : Institute for the Advanced Study of Human Biology (WPI-ASHBi), Kyoto University
Host: Dr. Tomonori Nakamura
Contact: ashbi-event@mail2.adm.kyoto-u.ac.jp