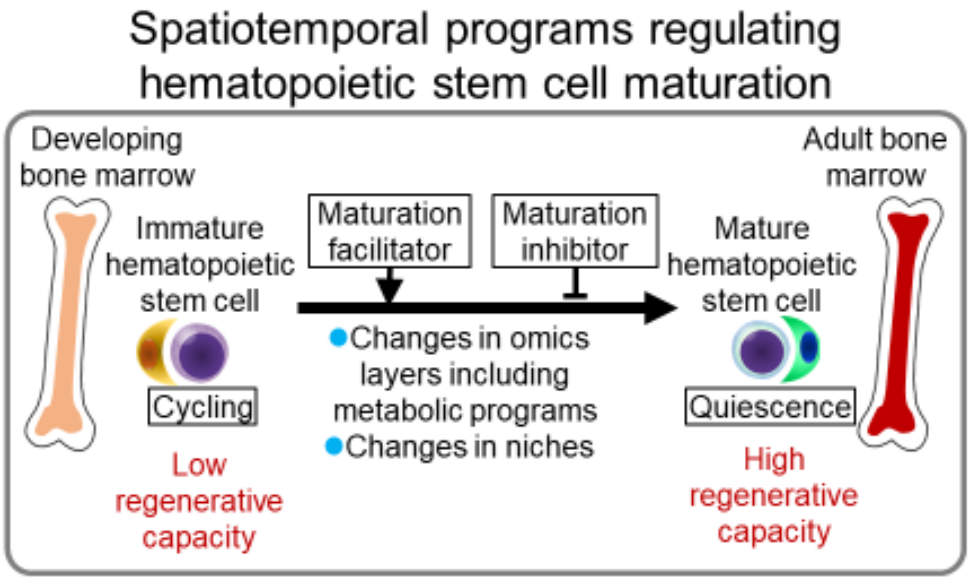
Spatiotemporal programs regulating hematopoietic stem cell maturation

TAKUBO Keiyo

Project Director, Department of Stem Cell Biology,
National Center for Global Health and Medicine Research Institute

In blood cells, maturation is associated with acquisition of cell cycle quiescence in hematopoietic stem cells (HSCs) with high regeneration capacity of entire blood system. Maturation of HSCs and their niches likely contributes to high engraftment capacity after HSC transplant. However, expanded HSCs or induced HSCs from pluripotent cells show immature phenotypes including loss of quiescence with low stem cell capacity. In this project, we will define mechanisms that underlie hematopoietic maturation and resulting technologies that improve transplantation. We will evaluate transcriptional/epigenetic/metabolic programs associated with maturation-related changes in HSC metabolism using single cell analysis.

We will also model HSC maturation using a novel HSC culture mimicking the physiological niche by testing candidate factors that induce HSC maturation. Furthermore, we will evaluate the effect of microenvironment changes on HSC maturation. We will assess dynamics of HSCs and niche cells in maturating BM using intravital multiphoton imaging technique. Our studies should reveal mechanisms underlying HSC maturation at cellular and molecular levels, suggest how to enhance HSC maturation and improve expansion of HSCs and generation of transplantable HSCs from pluripotent cells in vitro.



■ URL http://www.ri.ncgm.go.jp/department/pro/04/abstract.html