

Translational hematology research for aging and cell therapy using non-human primate hematopoietic stem cells

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Non-human primate (Rhesus macaque) is a potentially more instructive species in which to model human hematopoiesis and aging, based on the close phylogenetic relationship between macaques and humans, and similar telomere lengths, lifespans, and hematopoietic system. To study clinically-relevant aspects of aging and cell therapy, we proposed to engineer rhesus macaque hematopoietic stem and progenitor cells (HSPCs) using lentiviral genetic barcode or CRISPR/Cas9 followed by autologous transplantation. My talk will focus on my recent studies; 1. The impact of aging on hematopoiesis; To investigate the hematopoietic aging, we compared the clonal output of thousands of genetically barcoded HSPCs in aged vs young macaques after autologous transplantation. 2. Engineering HSPCs to enable immunotherapy for acute myeloid leukemia (AML); To avoid an non-tumor toxicity in myeloid cells, we proposed a novel approach to the treatment of AML, CD33 KO HSPC derived hematopoietic system resistant to anti-CD33 CAR-T cells while enabling specific targeting of AML. Our data provide insight into the translational hematology research for aging and cell therapy, which is relevant for designing transplantation and immunotherapy strategies.