Innovations
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Generation of Engraftable Hematopoietic Stem Cells from Induced Pluripotent Stem Cells

Problem
HSCs from iPS cells are not able to stably engraft into bone marrow.

Technology Overview
Generation of iPS-derived, autologous HSCs engraftable in bone marrow.

IP Status
- Available for Licensing

Value Proposition
- Simple addition to cultures
- Safer than viral modification
- Small molecule is already approved by FDA (different indication) – proven safety
- Autologous transplantation

Market Attractions
- Cancer and other blood diseases

Development status
- Successfully tested *in vitro* and *in vivo* in mice

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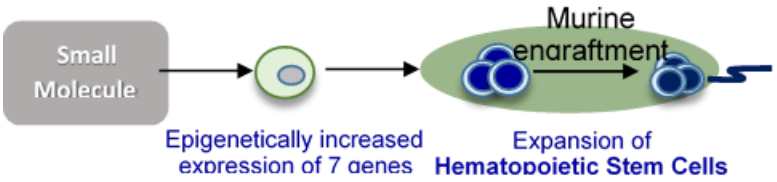
Problem: Bone marrow transplant is currently used to treat leukemia, lymphoma and genetic bone marrow failure disorders, but it can be highly risky especially when a closely matched donor is not available. Only one third of patients even have a viable donor for bone marrow transplantation. Generation of autologous hematopoietic stem cells (HSCs) engraftable in the bone marrow would improve safety and provide a source of cells for all HSC transplants without the need for donor matches. The challenge has been that iPS-derived HSCs do not engraft in the bone marrow when injected into immune deficient mice. Recently a study by Sugimura et al. (Nature, 2017) identified seven transcription factors (ERG, HOXA5, HOXA9, HOXA10, LCOR, RUNX1 and SPI1) that, when over-expressed in an iPS cell result in an engraftable HSC. However, over-expression of these seven genes by lentiviral transduction is not an ideal solution for several reasons including its cost, feasibility at commercial scale, and potential risk of harm from multiple over-expressed transcription factors.

Technical Solution and Key Value Propositions: A University of Colorado research group led by Dr. Michael Verneris has developed a novel process to create autologous HSCs that are engraftable in patient bone marrow. Human iPS cells are treated with a small molecule (SM1). SM1 changes the gene expression in iPS-derived HSCs, giving them a genetic signature associated with bone marrow engraftment in mice and the associated ability to engraft in mice.



In addition, treatment with SM1 resulted in more than two-fold expansion of HSCs over the course of 12 days of culture (figure 1), and led to increased iPSC-derived human HSC engraftment in immune-deficient mice (figure 2).

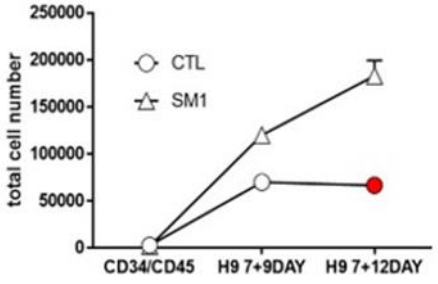


Figure 1. Treatment with the Small Molecule (SM1) showed more than two-fold expansion of HSCs over the course of 12 days of culture compared to control (CTL).

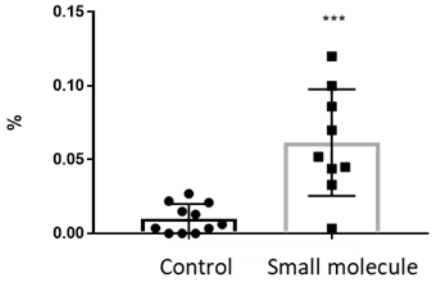


Figure 2. The percent human HSC engraftment is significantly higher in mice transplanted with iPS-derived stem cells treated with SM1 compared to control.