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Researchers succeed in programming blood forming stem cells

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By transferring four genes into mouse fibroblast cells, researchers at the Icahn School of Medicine at Mount Sinai have produced cells that resemble hematopoietic stem cells, which produce millions of new blood cells in the human body every day. These findings provide a platform for future development of patient-specific stem/progenitor cells, and more differentiated blood products, for cell-replacement therapy.

The study, titled, "Induction of a Hemogenic Program in Mouse Fibroblasts," was published online in *Cell Stem Cell* on June 13. Mount Sinai researchers screened a panel of 18 genetic factors for inducing blood-forming activity and identified a combination of four transcription factors, Gata2, Gfi1b, cFos, and Etv6 as sufficient to generate blood vessel precursor cells with the subsequent appearance of hematopoietic cells. The precursor cells express a human CD34 reporter, Sca1 and Prominin1 within a global endothelial transcription program.

"The cells that we grew in a petri dish are identical in gene expression to those found in the mouse embryo and could eventually generate colonies of mature blood cells," said the first author of the study, Carlos Filipe Pereira, PhD, Postdoctoral Fellow of Developmental and Regenerative Biology at the Icahn School of Medicine.

Other leaders of the research team that screened the genetic factors to find the right combination included Kateri Moore, DVM, Associate Professor of Developmental and Regenerative Biology at the Icahn School and Ihor R. Lemischka, PhD, Professor of Developmental and

Regenerative Biology, Pharmacology and Systems Therapeutics and Director of The Black Family Stem Cell Institute at The Mount Sinai Medical Center.

"The combination of gene factors that we used was not composed entirely of the most obvious or expected proteins," said Dr. Lemischka. "Many investigators have been trying to grow hematopoietic stem cells from embryonic stem cells, but this process has been problematic. Instead, we used mature mouse fibroblasts, picked the right combination of proteins, and it worked."

"This discovery is just the beginning of something new and exciting and can hopefully be used to identify a treatment for blood disorders," said Dennis S. Charney, MD, Anne and Joel Ehrenkranz Dean of the Icahn School of Medicine at Mount Sinai and Executive Vice President for Academic Affairs at The Mount Sinai Medical Center.

According to Dr. Pereira, there is a critical shortage of suitable donors for blood stem cell transplants. Donors are currently necessary to meet the needs of patients suffering from blood diseases such as leukemia, aplastic anemia, lymphomas, multiple myeloma and immune deficiency disorders. "Programming of hematopoietic stem cells represents an exciting alternative," said Pereira.

"Dr. Lemischka and I have been working together for over 20 years in the fields of hematopoiesis and stem cell biology," said Dr. Moore, senior author of the study. "It is truly exciting to be able to grow these blood forming cells in a culture dish and learn so much from them. We have already started applying this new approach to human cells and anticipate similar success."

Provided by The Mount Sinai Hospital