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Hematopoietic reprogramming can lead to differentiated blood products for cell-replacement therapy

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Building upon previous work, researchers at the Icahn School of Medicine at Mount Sinai identified cells in the embryos of mice that are precursors to blood stem cells or hematopoietic stem/progenitor cells (HSPCs). In previous studies, they reprogrammed mouse skin cells in the lab to become HSPCs. Now, they have identified a precursor cell in the placenta and embryo of mice that can be matured in the lab to make HSPCs. Their study, titled, "Hematopoietic Reprograming In Vitro Informs in Vivo Identification of Hemogenic Precursors to Definitive Hematopoietic Stem Cells," establishes that the reprogramming process can work back and forth in blood cell development. Their results, published online today in the journal *Developmental Cell*, could eventually lead to a process of developing patient-specific HSPCs and more differentiated blood products for cell-replacement therapy.

The need for transplantable stem cells is great for patients suffering from blood diseases such as leukemia, lymphomas, multiple myeloma and immune deficiency. Researchers are looking at ways to produce large numbers of HSPCs in the laboratory and developing methods for growing patient-specific HSPCs. The reprogramming process developed by researchers at Icahn School of Medicine at Mount Sinai appears to mimic normal blood cell creation or developmental hematopoiesis -- going from precursor cells to cells that eventually become HSPCs. This technology could potentially provide a different source of stem cells and alleviate this problem.

The team analyzed mouse placentas and embryos for the presence of cells with the same phenotype as the precursor cells, and confirmed that they could be matured to HSPCs in the lab.

"To cure disease in the long-term, we need to be able to transplant something that can keep producing new blood cells and won't be rejected by the patient's body," said the senior author of the study, Kateri Moore, DVM, Associate Professor of Developmental and Regenerative Biology at the Icahn School of Medicine at Mount Sinai. "We are excited by the results of our study. The precursor cells can be matured in the lab to transplantable HSPCs. Our reprogramming process can inform developmental hematopoiesis and vice versa."

Other members of the research team included Ihor R. Lemischka, PhD, Professor of Developmental and Regenerative Biology, Pharmacology and Systems Therapeutics and member of The Black Family Stem Cell Institute and first author Carlos-Filipe Pereira, PhD, former Postdoctoral Fellow of Developmental and Regenerative Biology at the Icahn School of Medicine at Mount Sinai, currently an Assistant Professor at the University of Coimbra, Portugal, Cell Institute.

"Direct reprogramming studies can improve applications for regenerative medicine," said Dr. Lemischka. "Many investigators have attempted to do what we have been able to do growing HSPCs in vitro, but we been able to build upon this process that could move the field forward. The next step is to test these findings in humans."

"Our team has made great attempts to unlock this puzzle, working together for over 20 years in the fields of hematopoiesis and stem cell biology," said Dr. Moore, senior author of the study. "Our ultimate goal is to grow blood forming cells in the lab and improve efficiencies to generate patient-specific blood cells. This study brings us a step closer to reaching this goal."

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