PRESS RELEASE
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UCLA SCIENTISTS HAVE ISOLATED THE FIRST STAGES OF TISSUE PRODUCTION FROM HUMAN EMBRYONIC STEM CELLS

Scientists at the UCLA Broad Stem Cell Research Center have described a population of cells that mark the very first stage of differentiation of human embryonic stem cells as they enter a developmental pathway that leads to production of blood, heart muscle, blood vessels and bone.

Researchers hope that these cells could one day be used for clinical treatments of a wide range of medical conditions as the discovery may help scientists create better and safer tissues for use in regenerative medicine. It also will allow scientists to better understand the differences between pluripotent stem cells, which can become every cell in the body, and cells that have lost their pluripotency and are on their way to becoming specific types of tissue cells.

The study appears today in the early online edition of the peer-reviewed journal Proceedings of the National Academy of Sciences.

"Scientists are very interested in understanding how cells that are pluripotent are directed to become specific tissues," said Dr. Gay Crooks, a professor of pathology and laboratory medicine and senior author of the study. "We want to know what it is that switches on and off to make a pluripotent cell no longer be pluripotent. In this study, we found a cell population that can help us understand these processes, as it is such a close relative to embryonic stem cells, but has lost the ability to be pluripotent."

During early development, human embryonic stem cells can follow three distinct developmental pathways to form the primary germ cell layers: the mesoderm, the ectoderm and the endoderm. These three germ cell layers then become all the tissues in the human body. In this study, Crooks and her team studied human embryonic stem cells that followed the mesoderm pathway, which gives rise to blood cells, blood vessels, cardiac cells, muscle, cartilage, bone and fat.

Dr. Denis Evseenko, lead investigator on the studies and an assistant researcher in the pathology and laboratory medicine department at UCLA, placed human embryonic stem cells into culture and, after three or four days, found a small subset of the cells that had lost a key cell surface marker characteristic of the pluripotent state and had gained a new marker that is a hallmark of mesodermal cells. Because the markers are displayed on the cell surface, Crooks said, specific antibodies can be used to isolate the human embryonic mesodermal progenitors (hEMP cells) from the other cells in culture.

"The hEMP cells are the earliest stage of cells that are transitioning from human embryonic stem cells into the cells of the mesoderm," she said. "While these hEMP cells appear to be committed to forming mesoderm, they have not yet determined what type of mesodermal tissue they will become. Because of this we hope they may serve as a source to produce large numbers of blood, bone or muscle cells, once we learn how to drive them further along the correct pathway."

Crooks's research program focuses on making blood stem cells from human embryonic stem cells. Studies have shown that the blood stem cells created from human embryonic stem cells in the lab lack some of the functions possessed by the blood stem cells found in bone marrow or umbilical cord blood. As a result, the blood from embryonic stem cells does not develop into an optimal immune system. Crooks hopes that hEMP cells could be used to create blood stem cells as powerful and potent as those found in bone marrow and cord blood, cells that would be safe to use in human to treat such diseases as leukemia and sickle cell anemia.

The hEMP cells were tested extensively to ensure they had lost the ability to form teratomas, encapsulated tumors with tissue or organ components. The ability to create teratomas is a hallmark of embryonic stem cells.

"Researchers agree that it is not a good idea to use pluripotent stem cells in people because of the risk that they might form teratomas," Crooks said. "The hEMP cells we isolated did not have the ability to make teratomas, so they should be a safer choice when thinking about developing therapies for use in humans."

Crooks and Evseenko are now studying how to best direct the hEMP cells into all the mesoderm cell lineages, including blood cells, and manipulate the cells so they become functional cells as they proliferate and differentiate.

The study was funded by the California Institute of Regenerative Medicine and the UCLA Broad Stem Cell Research Center.

The stem cell center was launched in 2005 with a UCLA commitment of $20 million over five years. A $20 million gift from the Eli and Edythe Broad Foundation in 2007 resulted in the renaming of the center. With more than 200 members, the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research is committed to a multi-disciplinary, integrated collaboration of scientific, academic and medical disciplines for the purpose of understanding adult and human embryonic stem cells. The center supports innovation, excellence and the highest ethical standards focused on stem cell research with the intent of facilitating basic scientific inquiry directed towards future clinical applications to treat disease. The center is a collaboration of the David Geffen School of Medicine, UCLA's Jonsson Cancer Center, the Henry Samueli School of Engineering and Applied Science and the UCLA College of Letters and Science. To learn more about the center, visit our web site at http://www.stemcell.ucla.edu. To learn more about the center, visit our web site at http://www.stemcell.ucla.edu.

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