

Researchers create heart and blood cells from reprogrammed skin cells

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Stem cell researchers at UCLA were able to grow functioning cardiac cells using mouse skin cells that had been reprogrammed into cells with the same unlimited properties as embryonic stem cells. The finding is the first to show that induced pluripotent stem cells or iPS cells, which don't involve the use of embryos or eggs, can be differentiated into the three types of cardiovascular cells needed to repair the heart and blood vessels.

The discovery could one day lead to clinical trials of new treatments for people who suffer heart attacks, have atherosclerosis or are in heart failure, said Dr. Robb MacLellan, a researcher at the Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research and senior author of the study. Researchers also were able to differentiate the iPS cells into several types of blood cells, which may one day aid in treating blood diseases and in bone marrow transplantation.

“I believe iPS cells address many of the shortcomings of human embryonic stem cells and are the future of regenerative medicine,” said MacLellan, an associate professor of cardiology and physiology. “I’m hoping that these scientific findings are the first step towards one day developing new therapies that I can offer my patients. There are still many limitations with using iPS cells in clinical studies that we must overcome, but there are scientists in labs across the country working to address these issues right now.”

The study, which brought together stem cell and cardiology researchers at UCLA, appears online May 1, 2008 in the journal *Stem Cells*.

Last June, UCLA stem cell researchers were among several scientific teams that were the first to reprogram mouse skin cells into cells resembling embryonic stem cells, which have the ability to become every cell type found in the body. MacLellan and his team used UCLA's iPS cells in their study.

Although iPS cells are believed to be very similar to embryonic stem cells, further study needs to be done to confirm their differentiation potential. MacLellan's study proved that iPS cells can be induced into becoming cardiovascular cells, an important step in the confirmation process.

“Theoretically, iPS cells are able to differentiate into 220 different cells types,” said Dr. Miodrag Stojkovic, co-editor of Stem Cells. “For the first time, scientists from UCLA were able to induce the differentiation of mouse iPS cells into functional heart cells.”

In MacLellan's study, the iPS cells were cultured on a protein matrix known to direct embryonic stem cells into differentiating into cardiovascular progenitor cells, immature heart cells that can give rise to mature cardiac cells that perform different functions. The progenitor cells were then isolated from the other iPS cells that did not differentiate using a protein marker called KDR, a growth factor receptor expressed on the surface of the progenitor cells.

Once isolated, the cardiovascular progenitor cells were coaxed into becoming cardiomyocytes, or mature heart muscle cells that control heartbeat, endothelial cells, which form rudimentary blood vessels, and vascular smooth muscle cells, the specialized cells that line blood vessel walls. Once mature, the cardiomyocytes beat in the Petri dish.

Studies are under way now at UCLA to determine if human iPS cells behave the same way as the mouse cells behave. If they do, the time may

come when a person could use their own skin cells to create individualized iPS cell lines to provide cells for cardiac repair and regeneration, MacLellan said.

It is vital to be able to grow and isolate progenitor, or partially differentiated, cells that can create the three types of cardiac cells for potential clinical use. When embryonic stem cells are injected directly into the heart in animal models, they create tumors because the cells differentiate not only into cardiac cells but into other cells found in the human body as well. Likewise, using embryonic stem cells garnered from other sources than the patient could result in rejection of the injected cells.

The use of iPS cells may solve those problems. If the iPS cells come from the patient, rejection should not be an issue. Additionally, the use of cells that are already partially transformed into specific cardiac cell types may prevent tumor growth. The use of iPS cells also sidesteps the controversy some associate with deriving pluripotent stem cells from embryos or eggs, MacLellan said.

“Our hope is that, based on this work in mice, we can show that similar cardiovascular progenitor cells can be found in human iPS cells and, using a similar strategy, that we can isolate the progenitor cells and differentiate them into the cells types found in the human heart,” MacLellan said.

The article can be accessed at www.stemcells.com/papbyrecent.dtl .

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