Researchers achieve another stem cell milestone: Revert human skin cells to embryonic stem cell-like state

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Harvard Stem Cell Institute researchers have successfully turned back the clock on human skin cells, causing them to revert to an embryonic stem cell-like state from which they can become any cell in the body.

The work, published online Sunday by the journal *Nature*, is an independent report similar to the stem cell breakthrough announced in November simultaneously by scientists in Japan and at the University of Wisconsin. That work, too, induced skin cells to revert to cells very similar to embryonic stem cells, called “induced pluripotent stem cells” (iPS)

“Pluripotency,” or the ability to develop into any other cell in the body, is a much desired trait of embryonic stem cells, which are extracted from several-day-old embryos and then cultured in the lab.

The need to destroy the embryo when extracting the stem cells is at the heart of a societal schism over the research, with some saying it is wrong to destroy nascent life to conduct scientific research and others saying that there is no harm in destroying embryos that would never be allowed to develop beyond the blastocyst stage, particularly to search for cures to disease.

George Daley, an HSCI Principal Faculty member and a Harvard Medical School associate professor of biological chemistry and

molecular pharmacology, noted that “despite success in generating iPS cells, we are not abandoning our efforts to derive new human stem cell lines by nuclear transfer.

“We are not yet certain which type of cell will prove most useful for medical applications,” Daley said, whose lab is at Children's Hospital Boston. “Besides, nuclear transfer is an experimental method that asks very important questions that will never be answered by reprogramming skin cells with defined genes.”
The collaborative work was led by Daley and conducted by researchers at the Harvard Stem Cell Institute, Children’s Hospital Boston, the Dana-Farber Cancer Institute, Harvard Medical School, and Brigham and Women’s Hospital.

Daley said the work built off research in other labs conducted a year earlier in which four genes were packed into a virus and inserted into animal skin cells, causing them to revert to a pluripotent form. Daley and his team used the human analogs of those same four factors to cause human skin cells to become pluripotent. In their work, they found that two of the factors, called Oct4 and Sox2, plus one of the two remaining factors, either Klf4 or Myc, were required for the process to work. It worked best, however, when all four factors were present.

While the advance has been hailed as a way to continue with promising stem cell work while avoiding the sticky ethical dilemmas posed by the need to destroy embryos, Daley said the same caveats apply to his work that applied to the research from Japan and Wisconsin: among the factors used to get the skin cells to transform into the pluripotent state are ones known to cause cancer.

“In the mouse, this same combination of genes cause tumors; we’d assume that’d be the case in human cells,” Daley said.

Though that hurdle may need to be overcome before the technique can be used in treatments administered directly to patients, the iPS cells can immediately be used to create cell lines from patients known to have specific diseases, with the aim of re-creating these diseases to study in the lab.

Daley said his team is interested in using the induced pluripotent cells to create cell lines from patients with various blood diseases, including sickle-cell anemia and Fanconi anemia, a hereditary disease where the bone marrow doesn't produce enough new cells to replenish the blood.

While the cells can provide a new way to create disease-specific tissue, Daley said it won't supplant the current method, which involves transplanting the nuclei of cells from a patient with a disease into eggs to generate a disease-specific cell line.

"This is an exciting new development and alternative approach to getting stem cells, being very effectively pursued by George Daley and Konrad Hochedlinger at the HSCI," said Doug Melton, Co-Director of the Harvard Stem Cell Institute and Co-Chairman of the Department of Stem Cell and Regenerative Biology. "It is good news because it provides yet another way for us to explore using stem cells to find new treatments for disease," Melton said.

Source: Harvard University

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