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Researchers Find Safer Way to Produce Stem Cell Alternative

Skin Cells Transformed Without Worrisome Use of Viruses

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Scientists have developed what appears to be a safer way to create a promising alternative to embryonic stem cells, boosting hopes that such cells could sidestep the moral and political quagmire that has hindered the development of a new generation of cures.

The researchers produced the cells by using strands of genetic material, instead of potentially dangerous genetically engineered viruses, to coax skin cells into a state that appears biologically identical to embryonic stem cells.

"It's a leap forward in the safe application of these cells," said Andras Nagy of Mount Sinai Hospital in Toronto, who helped lead the international team of researchers that described the work in two papers being published online today by the journal Nature. "We expect this to have a massive impact on this field."

In addition to the scientific implications, the work comes at a politically sensitive moment. Scientists are anxiously waiting for President Obama to follow through on his promise to lift restrictions on federal funding for research on human embryonic stem cells. Critics of such a move immediately pointed to the work as the latest evidence that the alternative cells make such research unnecessary.

"Stem cell research that requires destroying embryos is going the way of the Model T," Richard M. Doerflinger of the U.S. Conference of Catholic Bishops said. "No administration that values science and medical progress over politics will want to divert funds now toward that increasingly obsolete and needlessly divisive approach."

Scientists, however, while praising the work as a potentially important advance, said it remains crucial to work on both types of cells because it is far from clear which will turn out to be more useful.

"The point is, we don't know yet what the end potential of either of these approaches will be," said Mark A. Kay of Stanford University. "No one has cured any disease in people with any of these approaches yet. We don't know enough yet to know which approach will be better."

Because embryonic stem cells are believed capable of becoming any kind of tissue in the body, scientists believe they could eventually lead to treatments or even cures for a host of ailments, including heart disease, diabetes, and Alzheimer's and Parkinson's diseases. In 2001, President George W. Bush restricted federal funding for human embryonic stem cell research to prevent taxpayer money from

encouraging the destruction of human embryos, which is necessary to obtain the cells.

The alternative cells, known as induced pluripotent stem cells, or iPS cells, appear to have many of the same characteristics as embryonic stem cells but are produced by activating genes in adult cells to "reprogram" them into a more primitive state, bypassing the moral, political and ethical issues surrounding embryonic cells. Until now, however, their use has been limited because the genetic manipulation required the use of viruses, raising concerns the cells could cause cancer if placed in a patient. That has triggered a race to develop alternative approaches.

"These viral insertions are quite dangerous," Nagy said.

In the new work, Nagy and his colleagues in Toronto and at the University of Edinburgh in Scotland instead used a sequence of DNA known as a transposon, which can insert itself into the genetic machinery of a cell. In this case, the researchers used a transposon called "piggyBac" to carry four genes that can transform mouse and human embryonic skin cells into iPS cells. After the conversion took place, the researchers removed the added DNA from the transformed cells using a specific enzyme.

"PiggyBac carries the four genes into the cells and reprograms the cells into stem cells. After they have reprogrammed the cells, they are no longer required, and in fact they are dangerous," Nagy said. "After they do their job they can be removed seamlessly, with no trace left behind. The ability for seamless removal opens up a huge possibility."

A series of tests showed that the transformed cells had many of the properties of embryonic stem cells, Nagy said.

The researchers did their initial work on skin cells from embryos but say the approach should work just as efficiently in adult cells, and they plan to start those experiments.

"We do not expect that adult cells would behave significantly differently than the ones we are using currently," Nagy said.

In addition to producing safer cell lines that would be less likely to cause cancer in patients, the advance will enable many more scientists to begin working on such cells because they require no expertise or special laboratories necessary for working with viruses, he said.

"This opens up the possibility of working in this field for laboratories that don't have viral labs attached to them. A much larger number of laboratories will be able to push this field forward," Nagy said.

Other researchers praised the work.

"It's very significant," said George Q. Daley, a stem cell researcher at Children's Hospital in Boston. "I think it's a major step forward in realizing the value of these cells for medical research."

"It's very exciting work," agreed Robert Lanza, a stem cell researcher at Advanced Cell Technology in Worcester, Mass. "With the new work, we're only a hair's breadth away from the biggest prize in regenerative medicine -- a way to create patient-specific cells that are safe enough to use clinically."

Kay agreed that the work is promising but cautioned that much more research will be needed to prove that cells produced this way are safe. Many scientists are working on other approaches that may turn out to be safer and more efficient, he said.

"This is a step forward. The research is heading in the right direction. But there still may be room for improvement," he said.

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