Embryonic-like Cells Advance Toward Disease Treatment

By Constance Holden
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Two papers published this week appear to bring closer the day when embryonic-like stem cells can be used to treat human diseases. One study describes what scientists say is the safest method yet to produce these cells. The other reports success in using the cells to begin correcting a rare genetic disorder known as Fanconi anemia.

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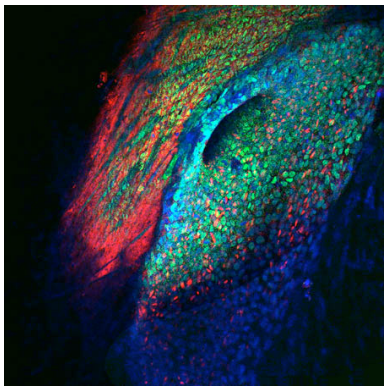

On track. Colonies of genetically corrected cells taken from Fanconi anemia patients show red and yellow, markers associated with pluripotency.

CREDIT: JUAN CARLOS IZPISÚA BELMONTE

Induced pluripotent stem (iPS) cells were first reported in 2006 by Shinya Yamanaka, a researcher at Kyoto University in Japan (*Science*, 7 July 2006, p. 27). Because embryos are not destroyed to create them, they have been hailed as a way out of the ethical dilemma posed by human embryonic stem cells. IPS cells are grown in culture from body cells, through the addition of genes that cause them to revert to pluripotency--the stage in which they can potentially develop into any type of body cell.

But there has been a snag: Introducing foreign genes into a cell can cause cancer. So researchers have spent the past 2 years experimenting with various other ways to activate the cell's own pluripotency genes. In April, scientists at The Scripps Research Institute in San Diego, California, reported success in using proteins to reprogram the genes in mice (*Science*NOW, 3 April).

Now, a team of U.S. and Korean scientists led by Kwang-Soo Kim at Harvard Medical School in Boston says it has achieved the same feat with human cells.

Using skin cells from newborns, the scientists overcame a major hurdle to reprogramming: the difficulty in getting the necessary proteins to cross the cell membrane. To do the job, they used a short segment of amino acids known to enable the HIV virus to invade cells. Although the efficiency was about one-tenth that of other methods, with about 1 in 100,000 cells turning into iPS cells, the resulting iPS cells passed all the usual tests to demonstrate that they are indeed pluripotent, the group reports in the journal *Cell Stem Cell*. "After a few more flight tests--in order to assure everything is working properly--it should be ready for commercial use," claims co-author Robert Lanza of Advanced Cell Technology Inc. in Worcester, Massachusetts, in a press release. It's a "huge step," agrees stem cell biologist Tim Townes of the University of Alabama, Birmingham, who was not affiliated with the study.

Things may also be looking up for using iPS cells to treat human diseases. Reporting online this week in the journal *Nature*, Juan Carlos Belmonte of the Salk Institute in San Diego and colleagues in Spain say they have successfully generated genetically tailored iPS-derived blood stem cells that could potentially treat patients with Fanconi anemia. A disease of bone marrow failure, the condition can cause skeletal deformities and increases cancer and anemia susceptibility. First, the researchers took skin cells from patients and introduced genes to correct the defective mutations. They then turned the cells into iPS cells, reprogramming them the way Yamanaka did: using a virus to ferry in four key reprogramming genes. Finally, the researchers cultured them into blood stem cells of the type that could potentially be injected into patients to reverse their disease. "This is, to our knowledge, the first demonstration that iPS cell technology can be used for the generation of patient-specific, disease-corrected cells," says Belmonte.

Townes calls the work a "fantastic" advance. Still, he cautions that it will take years to develop a therapy. A treatment "would combine two highly experimental therapies: cell transplants and gene therapy," notes Belmonte. And better reprogramming techniques must be developed, he says, because the safe methods so far reported "are just not efficient enough" for reprogramming cells from Fanconi anemia patients.

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