www.chicagotribune.com/news/nationworld/chi-stemcell_21nov21,1,7049489.story

chicagotribune.com

Major leap for stem cells

Researchers reprogram human skin cells to behave like embryonic stem cells

By Jeremy Manier

Tribune staff reporter

November 21, 2007

In an advance that could transform stem-cell research and accelerate progress toward treating patients with personalized replacement tissue, American and Japanese researchers report they have reprogrammed ordinary human skin cells to behave like embryonic stem cells.

By inserting four key genes into the cells, the scientists say they created a form of stem cell that can grow into virtually any kind of tissue -- a feat that previously required destroying embryos to extract cells. The discovery may clear a path for researchers to produce stem cells more easily and without the ethical issues of embryo destruction.

Testing the cells in human patients will require overcoming many obstacles, including potential risks from the viruses the groups used to place the genes in the cells. Experts also said the method will not completely replace use of embryonic stem cells, which they will need at least as a "gold standard" for assessing the new cells, called induced pluripotent stem (iPS) cells.

Even so, abortion opponents were quick to embrace the technique, described in research released Tuesday by the journals Cell and Science, and hailed the results as evidence that embryo-destroying research is no longer necessary.

Many researchers normally cautious about the significance of such alternative methods said the iPS cells already have started to change the field of stem-cell research. Dozens of labs have raced to try the technique since August 2006, when the Japanese team, led by Shinya Yamanaka of Kyoto University, demonstrated the approach using mice.

Reprogramming adult cells has been the Holy Grail of the field all along, said George Daley, a researcher at the Harvard Stem Cell Institute. Like many experts, he said he was shocked the two teams seem to have reached that goal so quickly.

"It's just a spectacular, spectacular advance," Daley said. "It will change everyone's thinking about the field."

Yamanaka's success with human cells was announced by Cell at the same time a separate study on the method by University of Wisconsin-Madison researcher James Thomson appeared online in Science.

Many experts found the technique especially intriguing because, in theory, it could allow researchers to take a patient's cells and reprogram them to make stem cells that match his immune system. Previously scientists had proposed doing that by making embryonic clones of the patient and extracting stem cells, but that alternative was technically difficult and laden with ethical objections.

The potential of iPS cells was instantly clear to Dr. Jack Kessler, a stem cell researcher and chair of neurology at Northwestern University. Kessler said his team decided to start exploring the new techniques last year within a week of Yamanaka's report on mice.

"This is groundbreaking, brilliant work," he said. "I don't care who you speak to in the field; you won't find anybody who doesn't find this exciting."

A spokeswoman for President Bush, who has restricted federal funding for work on embryonic stem cells, said Bush was "very pleased" that the studies showed how to harness the capabilities of stem cells without destroying embryos.

"By avoiding techniques that destroy life, while vigorously supporting alternative approaches, President Bush is encouraging scientific advancement within ethical boundaries," spokeswoman Dana Perino said.

Thomson, who co-discovered human embryonic stem cells in 1998, said political barriers have hindered all such work and stressed that the new research would not have been possible without insights gained from embryonic cells.

"My feeling is that the political controversy set the field back about four to five years," Thomson said. He credited Bush with providing some funds for the field starting in 2001 but said Bush's funding limits "represented very bad public policy as far as I'm concerned. The field has been much slower taking off than it would have been otherwise."

Both Yamanaka and Thomson said work on iPS cells should proceed alongside research on embryonic stem cells. But Thomson added Tuesday that if the technique proves successful enough, embryonic stem cells "will gradually be used by fewer and fewer labs."

Several experts said the most fundamental step forward came in Yamanaka's study using mouse cells. By studying which genes are most active in the embryonic stem cells of mice, his team was able to identify four genes that seemed crucial to stem cells' ability to produce many different tissue types. Inserting the genes in ordinary mouse cells gave them the properties of embryonic stem cells.

"That was really a fascinating piece of work, and the end of a lot of workmanlike trial and error," said Evan Snyder, director of the stem cell research center at the Burnham Institute in California.

Once the mouse result was published, teams around the world launched efforts to see if it would work with human cells. No one knew if those four genes would do the same job in both species, and Thomson's group in Wisconsin wound up succeeding with a slightly different mix of genes.

In essence, the groups were trying to take the ordinary cells back in time, to a point in early embryonic development when the fates of an embryo's cells are not fixed. The roots of such work can be traced to the birth in 1996 of Dolly the sheep, the first animal cloned from an adult cell.

Dolly showed that researchers could reset an adult cell's clock by placing its nucleus in an egg cell. Thomson said the challenge was to find a faster and more practical approach that could reset that clock by manipulating just a few genes.

Both teams used viruses to introduce the suite of genes into the cells. One hurdle now will be to find ways of adding the genes without viruses, or removing the viruses once they've done their work.

In addition, one of the genes the Japanese team used is also an oncogene, meaning it has been linked with certain types of cancer. Thomson's group avoided using that gene, and other researchers say they are already pursuing safer ways of making the cells.

Initial testing suggests that, like embryonic stem cells, the iPS cells can form any type of tissue. Thomson said his group likely will take a closer look at how well the cells can be coaxed into forming cardiac cells, which could be transplanted into patients with heart problems, and dopamine-producing brain cells, which might offer new treatments for Parkinson's disease.

Rev. Tadeusz Pacholczyk, director of education at the National Catholic Bioethics Center in Philadelphia, said the findings could shift the stem cell debate. "This approach provides medical advantages as well as clear moral advantages," Pacholczyk said. "That's an amazing development."

Snyder and other scientists who have backed embryonic stem cell research fear the new finding may hamper efforts to lift Bush's funding limits.

"Every time we get a headline like this, some policymakers say, 'OK, now we can stop funding embryonic research, and you guys can get jobs at McDonald's,'" Snyder said.

"But this means there's a whole new area of research that Congress needs to fund, and you've got to compare all the cells head to head."

---

jmanier@tribune.com