

Imperfections mar hopes for reprogrammed stem cells

(Reuters) - When scientists announced 5 years ago they could reprogram ordinary skin cells into behaving like embryonic stem cells, religious conservatives and others who opposed the use of stem cells cheered the advance.

But while they have proven to be a powerful new way to study human disease, the reprogrammed cells -- known as induced pluripotent stem cells, or iPS cells -- are no substitute for embryonic stem cells.

"This has strong policy implications," Dr. George Daley of the Harvard Stem Cell Institute and Harvard Medical School said in a telephone interview.

"It has not ever been a scientifically driven argument that iPS cells are a worthy and complete substitute for embryonic stem cells," Daley said. "Those arguments were always made based on political and religious opposition to embryonic stem cells."

Stem cells are the body's master cells, the source material for all other cells. Proponents of embryonic stem cells say they could transform medicine, providing treatments for blindness, juvenile diabetes or severe injuries.

Scientists typically harvest embryonic stem cells from leftover embryos at fertility clinics. But the issue has been a point of controversy for some religious conservatives, who believe the destruction of any human embryo is wrong.

When they were first discovered in 2006, induced pluripotent stem cells looked like a perfect solution to this ethical debate.

Instead of destroying an embryo, iPS cells are made in a lab from ordinary skin or blood cells. Using various methods, scientists introduce three or four genes that return these cells to an embryonic-like state in which they, too, are able to turn into any type of cell.

And because iPS cells can be made with tissue from people with known genetic diseases, scientists can use them to study how diseases develop or to test the effectiveness of drugs.

Already, researchers have made iPS cells from patients with Gaucher's disease, Down Syndrome, Parkinson's and diabetes.

In February, a team from Stanford University in California used iPS cells to make beating heart cells that replicate a rare heart defect found in children with Timothy syndrome, a disorder also characterized by autism symptoms.

SERIOUS PROBLEMS

But recently, scientists have started to raise concerns about iPS cells.

Last year, a group led by Dr. Robert Lanza, chief scientific officer of Advanced Cell Technology, compared batches of iPS cells to embryonic stem cells and noticed the iPS cells died more quickly and were much less capable of growing and expanding.

"It was the first study showing there were problems. No one wanted to believe it," Lanza said in a telephone interview.

In July, Daley's team reported more problems in the journal Nature, showing that iPS cells retain a bit of memory of their prior life as adult tissue, which could limit their use.

And earlier this month, an international team led by researchers at the University of California San Diego found genetic mutations in 22 iPS cell lines taken from seven different labs.

"There are serious problems with this iPS cell technology that still need to be solved," Lanza said.

He said abnormalities in iPS cells could raise flags among regulators that these cells could cause problems in people.

Advanced Cell won U.S. Food and Drug Administration approval last year for a clinical trial to treat a progressive form of blindness called Stargardt's macular dystrophy, and in January it won FDA approval to start using embryonic stem cells to treat macular degeneration.

Those followed Geron Corp's success last year in winning the FDA's nod for the first-ever approved study of human embryonic stem cells to treat people whose spinal cords have been crushed.

"The gold standard cells at the present time are embryonic stem cells," Lanza said.

But the political path for embryonic stem cells is still murky. The Obama administration overturned the strictest of the limitations imposed by former President George W. Bush on using federal funds for the research, but last summer that policy was challenged in court.

A U.S. appeals court has ruled that funding could continue while the government appeals, but grants from the National Institutes of Health have been frozen and unfrozen and the court battles are continuing.

UNIQUE ROLE

Stem cell scientists are not giving up on iPS cells, but instead of a replacement for embryonic stem cells, they see them filling a unique research role.

Dr. Jack Kessler of Northwestern University Feinberg School of Medicine in Chicago led a team that coaxed iPS cells into becoming a type of memory cell in the brain that dies off early in people with Alzheimer's disease.

"The beauty of iPS cells for this kind of study is that it gives us the ability to create human neurons with different genetic backgrounds, and specifically with genetic backgrounds with the disease of interest," Kessler said.

That cannot be done with embryonic stem cells, whose potential for future disease is unknown.

"There is no such thing as developing human embryonic stem cells with Alzheimer's disease," Kessler said.

Kessler and others see the newly discovered problems with iPS cells as a setback in efforts to use them in people to treat diseases.

"Do I personally think we will ultimately be able to use iPS cells for treatments? I do."