Important new step toward producing stem cells for human treatment

September 25 2008

Konrad Hochedlinger

(PhysOrg.com) -- A team of Harvard Stem Cell Institute (HSCI) scientists has taken an important step toward producing induced pluripotent stem (iPS) cells that are safe to transplant into patients to treat diseases.

Excitement over the ability of researchers to create this form of stem cell by inserting four genes into adults cells has thus far been tempered by the fact that the genes have been inserted using retroviruses, which have the potential to turn on cancer genes and trigger tumor growth.

But today Konrad Hochedlinger and HSCI colleagues at Massachusetts General Hospital and Joslin Diabetes Center report having created mouse iPS cells using harmless adenoviruses that ultimately disappear

from the new cells and therefore do not integrate into their DNA like the retroviruses.

“The adenoviruses infect the cells” carrying the genes needed for cellular reprogramming, “but are cleared by the cells after a few cell divisions,” said Hochedlinger, an assistant professor in Harvard’s new inter-school Department of Stem Cell and Regenerative Biology (SCRB). “This wouldn’t be harmful in any way because the DNA of the new cells remains unaffected,” he said.

The report by the Hochedlinger group appears in today’s on-line edition of the journal *Science*.

Harvard Stem Cell Institute co-director Doug Melton, who is also co-chair of SCRB, said “this paper by the Hochedlinger’s group is another in a series by one of the leading labs, whose work is aimed at making stem cells from patient samples. In this advance, the use of viruses that integrate into the host genome have been eliminated, making the process easier and the end product, the induced pluripotent stem cell, that much more safe.”

It has previously been believed that the viruses carrying the four essential transcription factors had to be integrated into the genome of the target cell in order for adult cells to be reprogrammed into pluripotent stem cells, “but we’ve shown that you don’t need integration of the virus into the genome to produce iPS cells,” Hochedlinger said.

Hochedlinger and colleagues Mathias Stadtfeld – the study’s lead author, Masaki Nagaya, Jochen Utikal, and Gordon Weir – head of HSCI’s Diabetes Program, have used the new technique to create iPS cells from mouse skin cell, and mouse fetal and adult liver cells.

“We get stem cell lines,” said Hochedlinger. “They are all pluripotent” –

meaning that they can become any type of cell –"and they have no traces of the adenovirus." Even more important, he said, thus far none of the mice carrying the new cells lines have shown any signs of developing tumors – and tumors were being frequently reported in mice carrying the cell lines created using retroviruses.

"The next step is to reproduce this work using human cells, and there's no reason why it can't work," Hochedlinger said, adding that "this basically provides us with a system with which to test the question of whether iPS cells are the equivalent of human embryonic stem cells. That's a question that, in my opinion, hasn't been answered yet."

As Hochedlinger and his colleagues have been working to find viral substitutes for the use of retroviruses in the production of iPS cells, some HSCI researchers are reported to be looking for chemicals that might be used in place of viruses, and some of those experiments are said to be quite promising.

The work reported today was supported by grants from the Harvard Stem Cell Institute, and by a National Institutes of Health New Innovator Award Hochedlinger received last year.

Provided by Harvard University