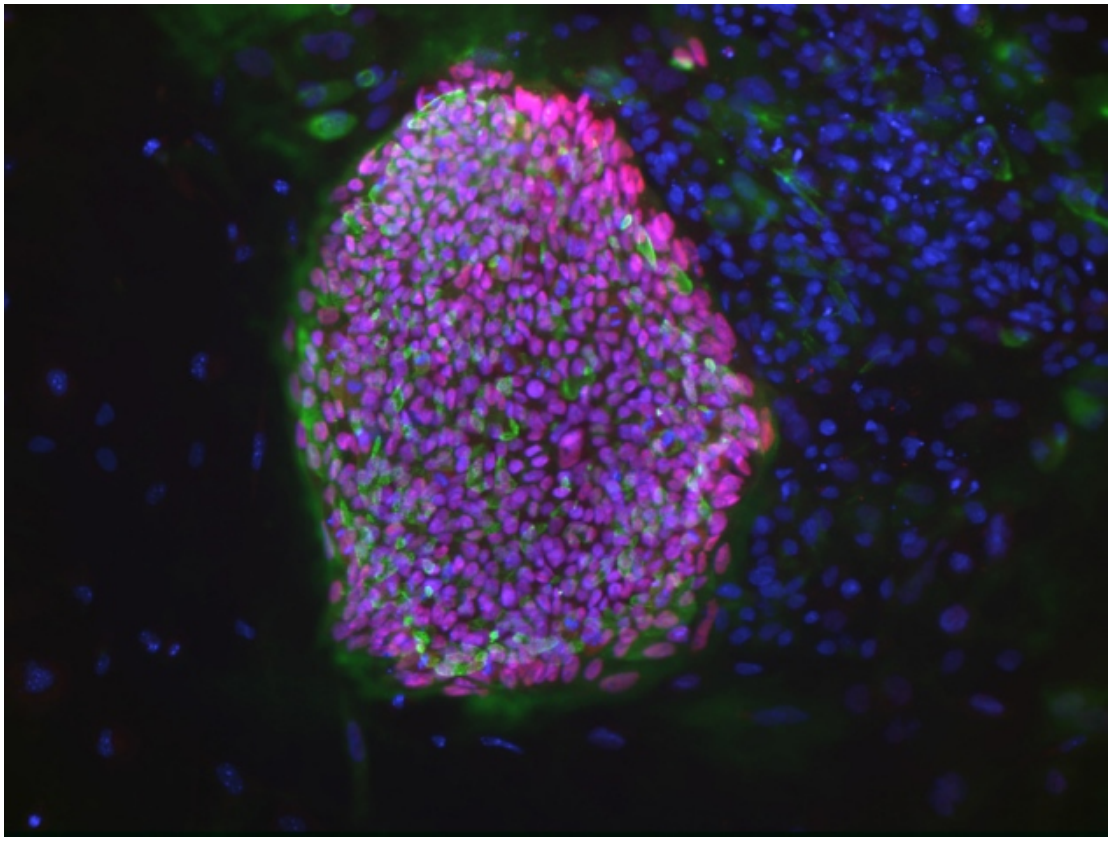
28 April 2014



Bjarki Johannesson, NYSCF

This colony of embryonic stem cells, created from a type 1 diabetes patient, is one of the first to be cloned from an adult human.

Two research groups have independently produced human embryonic stem-cell lines from embryos cloned from adult cells. Their success could reinvigorate efforts to use such cells to make patient-specific replacement tissues for degenerative diseases, for example to replace pancreatic cells in patients with type 1 diabetes. But further studies will be needed before such cells can be tested as therapies.

The first stem-cell lines from cloned human embryos were reported in May last year by a team led by reproductive biology specialist Shoukhrat Mitalipov of the Oregon Health & Science University in Beaverton (see 'Human stem cells created by cloning'). Those cells carried genomes taken from fetal cells or from cells of an eight-month-old baby[1], and it was unclear whether this would be possible using cells from older individuals. (Errors were found in Mitalipov's paper, but were not deemed to affect the validity of its results.)

Now two teams have independently announced success. On 17 April, researchers led by Young Gie Chung and Dong Ryul Lee at the CHA University in Seoul reported in *Cell Stem Cell* that they had cloned embryonic stem-cell (ES cell) lines made using i from two healthy men, aged 35 and 75[2]. And in a paper published on *Nature*'s website today, a team led by regenerative

from an adult cell, Dolly the sheep, in 1996.

The studies show that the technique works for adult cells and in multiple labs, marking a major step. “It's important for several reasons,” says Robin Lovell-Badge, a stem-cell biologist at the MRC National Institute for Medical Research in London.

At present, studies to test potential cell therapies derived from ES cells are more likely to gain regulatory approval than those testing therapies derived from induced pluripotent stem (iPS) cells, which are made by adding genes to adult cells to reprogram them to an embryonic-like state. Compared with iPS cells, ES cells are less variable, says Lovell-Badge. Therapies for spinal-cord injury and eye disease using non-cloned ES cells have already been tested in human trials. But while many ES cell lines have been made using embryos left over from fertility treatments, stem cells made from cloned adult cells are genetically matched to patients and so are at less risk of being rejected when transplanted.

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Lovell-Badge says cloned embryos could also be useful in other ways, in particular to improve techniques for reprogramming adult cells and to study cell types unique to early-stage embryos, such as those that go on to form the placenta.

Few, however, expect a huge influx of researchers making stem cells from cloned human embryos. The technique is expensive, technically difficult and ethically fraught. It creates an embryo only for the purpose of harvesting its cells. Obtaining human eggs also requires regulatory clearance to perform an invasive procedure on healthy young women, who are paid for their time and discomfort.

About ten years ago, making human ES cells from cloned embryos was among the hottest areas of research, recalls Egli. Most stem-cell biologists shifted focus as convenient technologies for making iPS cells became established, but Egli did not. “I didn't think it was right to only try one approach when it was so important to find cures for these diseases,” he says.

He thinks that iPS cell lines work well for drug screening and basic research questions, but it is still unclear whether iPS cells or ES cells will work best as therapies. “If you had a choice, you would pick the one from nuclear transfer rather than iPS,” he says. This is because iPS cells often do not become completely reprogrammed or may become warped during the reprogramming process, which could make them less stable.

Even if cloned ES cells do prove better suited for therapy, creating a different ES cell line for each patient would probably not be necessary, says Robert Lanza, chief scientific officer at Advanced Cell Technology in Marlborough, Massachussetts, and a co-author on the *Cell Stem Cell* paper. Instead, he imagines, scientists would create banks of cell lines that could serve patients needing replacement tissues.

Rogue scientists

— and which is illegal in many countries. But Mitalipov thinks that rogue scientists attempting to do this are unlikely to succeed for technical reasons.

“We never got any offspring in the monkey, and we tried hard,” he says. Over several years, his team transplanted hundreds of cloned monkey embryos from laboratory dishes into healthy monkeys; only one embryo implanted successfully, and it stopped developing after two months[4].

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