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Scientists Reach Stem Cell Milestone

By Alice Park

After nearly a decade of setbacks and false starts, stem-cell science finally seems to be hitting its stride. Just a year after Japanese scientists first reported that they had [generated stem cells by reprogramming adult skin cells](#) — without using embryos — American researchers have managed to use that groundbreaking technique to achieve another scientific milestone. They created the first nerve cells from reprogrammed stem cells — an important demonstration of the potential power of stem-cell-based treatments to cure disease.

Led by Kevin Eggan at the Harvard Stem Cell Institute and Christopher Henderson at Columbia University, the 13-person team reported online today in *Science Express* that they had generated motor neurons from the skin cells of two elderly patients with a rare form of ALS, or Lou Gehrig's disease, a progressive neurodegenerative condition. The new study marks an important first step on the road toward real stem-cell-based therapies, and also answers several plaguing questions about the pioneering stem-cell technique known as induced pluripotent stem cell, or iPS, generation.

iPS was first described by Japanese biologist Shinya Yamanaka, who, in 2007, showed that the introduction of four genes into an adult human skin cell could reprogram it back to an embryonic state (Yamanaka had reported the same achievement in mice the previous year). Like embryonic stem cells, these reprogrammed adult cells could be coaxed into becoming any other type of cell — from skin to nerve to muscle. But researchers questioned whether the new stem cells would behave as predictably or as safely as embryonic stem cells, or whether iPS would consistently yield usable cells. "Our work shows that the original method developed by Yamanaka works great," says Eggan.

Researchers also questioned whether iPS would work with delicate cells from older people or with cells taken from patients with disease (Yamanaka used skin cells from healthy middle-aged people in his study). Eggan and Henderson tackled both issues at once, by working with cells from two siblings, ages 82 and 89, who both had ALS. It turned out that generating iPS cells from older patients proved no more difficult than growing

them from younger ones, says Eggan. "This study puts those issues definitively to rest," he says. "It opens the door to being able to make patient-specific stem-cell lines [to treat] diseases that affect people very late in life, like Parkinson's or Alzheimer's disease."

In the lab, Eggan's group has successfully turned stem cells into motor neurons, the cells that connect the spinal cord to the body's muscles and which degenerate in ALS. But researchers have not been able to prove that these cells will be clinically useful — that is, whether the new nerve cells will work as well as healthy ones in the spinal cord of a patient. Testing the viability of cells made from iPS stem cells is still a long way off, mostly because iPS requires the use of viruses to deliver the time-reversing genes into adult cells — that works in the lab, but it is not yet safe for patients. To use iPS cells in patients, researchers would have to find a way to reprogram adult cells using chemicals, rather than genes.

There are other, more immediate payoffs of the new study. For one thing, it gives researchers a better understanding of how ALS progresses. Because the new nerve cells have the same genetic makeup as the patients' own diseased cells, Henderson says, they may very well develop signs of the disease in culture, allowing researchers to watch ALS unfold before their eyes. "Our lack of understanding of the disease process is preventing us from developing more efficient cures," says Henderson. "Because the disease is happening in the spinal cord, we don't have access to living samples of neurons undergoing the disease process. But now we have in the culture dish the very cells affected by the disease."

One theory about the cause of ALS is that motor nerves die after exposure to a toxic compound released by other nerve cells in the spinal cord. The Harvard and Columbia groups are hoping to test that idea in the lab: if the cells in culture release the same agent, then finding drug compounds that block the damaging effects of the toxin could preserve neurons and hold off the paralyzing effects of the disease.

The answers to those questions, says Eggan, may come in a matter of "months, not years." It's still unclear whether the new iPS nerve cells can live up to the gold standard of cells created from human embryonic stem cells, but Eggan, Henderson and their colleagues are confident that their current achievement brings stem-cell science one step closer to the original and ultimate goal: cures for diseases such as ALS, Alzheimer's and diabetes.

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