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Stem Cell Technology: First Neurons Created From ALS Patient's Skin Cells

ScienceDaily (Aug. 1, 2008) — Harvard and Columbia scientists have for the first time used a new technique to transform an ALS (amyotrophic lateral sclerosis, or Lou Gehrig's disease) patient's skin cells into motor neurons, a process that may be used in the future to create tailor-made cells to treat the debilitating disease.

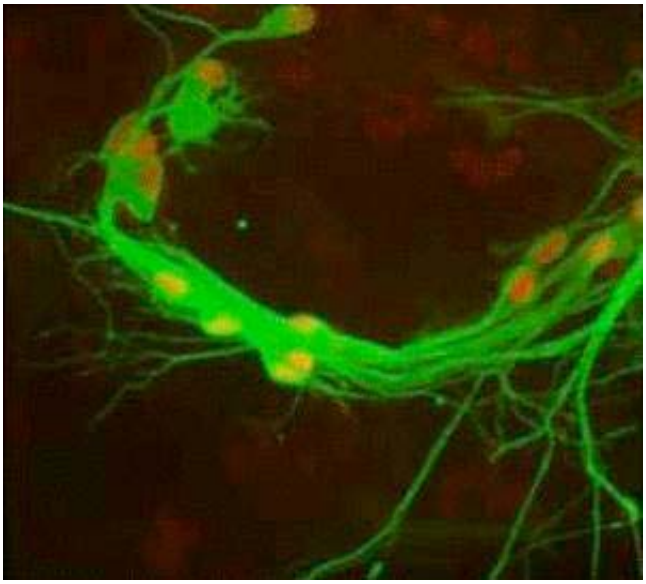

Image of motor neuron. (Credit: Courtesy Dimos, Rodolfa et al)

The research – led by Kevin Eggan, Ph.D. of the Harvard Stem Cell Institute – will be published July 31 in the online version of the journal Science.

This is the first time that skin cells from a chronically-ill patient have been reprogrammed into a stem cell-like state, and then coaxed into the specific cell types that would be needed to understand and treat the disease.

Though cell replacement therapies are probably still years away, the new cells will solve a problem that has hindered ALS research for years: the inability to study a patient's motor neurons in the laboratory.

ALS is caused by the degeneration and death of motor neurons, the nerve cells which convey nerve impulses from the spinal cord to each of the body's muscles. The death of motor neurons leads to paralysis of these muscles, including those involved in swallowing and breathing, and ultimately leads to death of the patient. The disease affects about 30,000 people in the United States.

"Up until now, it's been impossible to get access to the neurons affected by ALS and, although everyone was excited by the potential of the new technology, it was uncertain that we would be able to obtain them from patients' skin cells," says co-author Chris Henderson, Ph.D., professor of pathology, neurology and neuroscience, co-director of the Center for Motor Neuron Biology and Disease at Columbia, and senior scientific advisor of the Project A.L.S./ Jenifer Estess Laboratory for Stem Cell Research. "Our paper now shows that we can generate hundreds of millions of motor neurons that are genetically identical to a patient's own neurons. This will be an immense help as we try to uncover the mechanisms behind this disease and screen for drugs that can prolong life."

The motor neurons were created using a new technique that reprograms human adult skin cells into cells that

resemble embryonic stem (ES) cells. The technique used to make these cells – called induced pluripotent stem (iPS) cells – was a major advance in the field that was first reported last November by researchers in Japan and Wisconsin. Those studies used skin cells from healthy adults, but it remained unknown whether iPS cells could be created with cells from chronically-ill patients and then transformed into neurons. The Columbia-Harvard team, in this paper, showed this was possible using an ALS patient's skin cells.

Columbia clinician-researchers Wendy Chung, M.D., Ph.D., Herbert Irving Assistant Professor of Pediatrics in Medicine, and Hiroshi Mitsumoto, M.D., D.Sc., the Wesley J. Howe Professor of Neurology at Columbia, obtained skin cells from an 82-year-old ALS patient. In the Project A.L.S. laboratory, Columbia researchers Dr. Henderson and Hynek Wichterle, Ph.D., assistant professor of pathology, and colleagues cultured the cells and contributed expertise needed for identifying iPS cell-derived motor neurons. Finally, Harvard researchers, led by Kevin Eggan of the Harvard Stem Cell Institute, successfully used the new technique to reprogram the skin cells into iPS cells and differentiate them into motor neurons.

Scientists had originally hoped to create neurons and other adult cells using "therapeutic cloning," in which DNA from a patient is inserted into a donated egg to create embryonic stem cells. That technique, however, has still not been successful in humans, and is also hindered by a shortage of donated eggs.

If the iPS technique holds its promise in producing neurons and other cells for research, it will probably replace the "therapeutic cloning" approach, Dr. Henderson says, but there are still lots of questions about the iPS-derived neurons.

"We don't know yet how similar they are to the motor neurons in ALS patients," he says. "While the cells exhibit many properties that are typical of motor neurons, we don't yet know whether they will be prone to degeneration that will allow us to mimic the disease in the culture dish and therefore to screen potential drugs."

Researchers at Columbia and Harvard are already collaborating to investigate the cells with the ultimate goal of determining how they differ from a healthy person's motor neurons.

"Project A.L.S. has always maintained that collaboration between scientists is the answer to understanding and treating this disease," Valerie Estess, founder and research director, Project A.L.S. "We are thrilled to have catalyzed the Harvard-Columbia collaboration that led to this discovery."

"Therapeutic use of the cells is probably a long way off," Dr. Henderson says. "Right now there are safety issues with iPS cells, including a risk of cancer. We also don't know how to reintroduce cells into a sick adult in a way that will be beneficial. All these hurdles need to be overcome first before we can think about using the cells to treat disease, but we can start immediately to evaluate them as a tool for drug discovery."

The Columbia and Harvard researchers were supported by the Harvard Stem Cell Institute, Project A.L.S., the SMA Foundation, MDA Wings Over Wall Street, the Claire and Leonard Tow Charitable Foundation, the Spina, Drago and Bowen Families, Ride for Life and the New York Stem Cell Foundation.

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