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How Stem Cells Could Fight Lou Gehrig's Disease

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Patients with Lou Gehrig's disease face a dismal prognosis. The only approved drug, Sanofi-Aventis's Rilutek, slows the fatal muscle-wasting disease by just a few months. Numerous experimental drugs have flopped in trials.

Can stem cells break the logjam?

That's the hope behind a path-breaking new collaboration between California Stem Cell, a biotech company in Irvine, Calif.; the charitable ALS Association; and a small Belgian drug discovery company. The concept is to use motor neuron cells the biotech firm has generated from embryonic stem cells to hunt for new drugs to treat amyotrophic lateral sclerosis, more commonly called ALS, or Lou Gehrig's disease.

The ALS Association, a patient advocacy group based in Calabasas Hills, Calif., will fund the research as part of its initiative to speed up the discovery of new drugs and therapies for ALS. Funding could amount to several million dollars if the research proceeds as planned, says Dr. Lucie Brujin, science director for the ALS Association.

"We're very excited about what this can do for us," says Brujin. "Before, we were using motor neurons from mice or rats."

Even then, adds Brujin, it was difficult to get a large enough quantity of the cells to use for research purposes. California Stem Cell's ability to deliver large quantities of human motor neuron cells is "a valuable new tool to use in the drug discovery process," says Brujin.

Embryonic stem cells offer the hope of providing an unlimited supply of living human cells for use in drug discovery and cell transplant therapy. The hard part is coaxing stem cells to turn into the various types of cells that are needed for research--muscle, bone, neuron, liver cell pancreas and so on.

"The hope of stem cells is just a hope and nothing more" without an efficient method of turning them into different types of adult cells, says Hans Keirstead, a stem cell researcher at University of California, Irvine, and a member of California Stem Cell's scientific advisory board.

He says the premise behind California Stem Cell is to create an efficient process for generating large, pure batches of various types of brain cells and other cells from embryonic stem cells. So far, his company has created motor neurons, heart muscle cells, neuronal progenitors and heart pacemaker cells.

Under the deal, California Stem Cell will ship batches of its motor neuron cells to BioFocus DPI, a U.K. company that provides research services to pharmaceutical and biotech companies. (BioFocus is a unit of Belgian drug discovery company Galapagos.) BioFocus will develop a test to screen the motor neurons against some 11,000 different gene-silencing fragments that will shut off a gene in the motor neuron cells.

"The aim is to rescue the cells from cell death, since ALS is a disease of cell death," says Katherine Hilyard, vice president for biological sciences at BioFocus DPI.

This process, which should take about a year, should allow BioFocus DPI to come up with a handful of drug targets. The next steps would be to determine if they translate into good drugs and, if so, develop a drug aimed at one or more targets.

Hilyard says BioFocus DPI previously worked with another company attempting to produce human motor neurons, but that company couldn't successfully turn the embryonic stem cells into motor neuron cells. "It would be impossible to do this research" without these motor neuron cells, she says. "We're all very pleased with this development."

Separately, the New York-based charity Project ALS is independently working on a similar project with researchers at Columbia University and the Harvard Stem Cell Institute. The Columbia and Harvard researchers it sponsors have already made billions of motor neurons from embryonic stem cells and hope to begin using them in drug screens this year, says Project ALS Research Director Valerie Estess.

With Kevin Eggan, a cellular biologist at Harvard, Project ALS is also making progress in taking skin biopsies from ALS patients and reprogramming those to become motor neurons. This will create cells in the lab dish that are genetically identical to those in the spines of ALS patients.

Until now, Estess notes, researchers have had to test their experimental ALS drugs on mice that have been genetically engineered to get the disease. Too often, the drugs work great in the mice and then "failed miserably in people," she says. "What stem cells will provide us in the very short term is much better disease models. They will allow us to screen drugs more effectively ... and will represent human disease more accurately."

Patients with ALS typically live for a mere three to five years after the disease is diagnosed. The disease attacks and kills motor neurons, the nerve cells responsible for movement. As motor neurons die, muscles grow weaker, and ALS patients have trouble speaking, chewing, swallowing and breathing. In its devastating last stages, people can become "locked in"--alive and conscious but unable to move an eyelash or communicate with the outside world in any way. ALS affects an estimated 30,000 people in the U.S.

There are several drugs now being tested to treat ALS, but all of them were first approved for some other disease. With any sort of luck, this new initiative could eventually lead to the first drug developed specifically to treat ALS.

In addition to its work in ALS, California Stem Cell is working with another charity, Families of Spinal Muscular Atrophy, to use motor neuron progenitor cells made from embryonic stem cells to treat this disease. SMA is a genetic disease that strikes children and causes muscles to waste away because they cannot make a crucial protein needed for motor neurons to survive. A trial for this therapy could begin next year.

