A cure for Lou Gehrig's disease is sought in tiny cells, big data

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Before diving too deeply into this story on Lou Gehrig's disease research, you should know about a technique that manipulates an adult's blood or skin cell into behaving like an embryonic stem cell.

Once reverted into that primitive state, this new cell can be directed to become any other type of cell in the human body.

Funded by an $8 million federal grant awarded last month, UC Irvine researchers are leading a team of six institutions studying Lou Gehrig's disease using stem cells generated through this reprogramming method.

The cells are known as induced pluripotent stem, or iPS, cells. Researchers involved in the NeuroLINCS program said they might be key to learning why Lou Gehrig's disease strikes patients who did not inherit the neurological condition, and aid in discovering new drug treatments for it.

For the study, the iPS cells will be derived from the blood cells of 12 people with Lou Gehrig's disease and turned into motor neurons, the nerve cells that control voluntary muscle movements.

Before iPS cells, researchers' options for studying nerve cells were limited to those taken from mice, or actual embryonic stem cells.

"You're not destroying any embryos, not destroying any fetuses, and the biggest advantage is the genetic material does not change. The DNA or whatever the patient
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harbors, a certain mutation, a problem with the DNA code, that is maintained when you convert to iPS,” said Dhruv Sareen, a neurobiology researcher with Cedars-Sinai Board of Governors Regenerative Medicine Institute.

Researchers will upload their information – and there will be a vast amount of it – into a shared database where analysts will look for commonalities to help doctors better diagnose and treat the disease. Along with UCI and Cedars-Sinai, participants include researchers from Johns Hopkins University, UC San Francisco, Massachusetts Institute of Technology, and the Gladstone Institute of Neurological Disease,

Lou Gehrig’s disease, or amyotrophic lateral sclerosis, attacks motor neurons, causing them to degenerate. It leaves the mind intact as it wilts muscles and freezes joints. In the grip of its most severe stage, patients can no longer speak, eat or breathe on their own.

Sareen called it one of the more deadly neurological diseases, with most patients dying within four to five years after diagnosis.

The woman heading up NeuroLINCS, Leslie Thompson, is renowned for her work with Huntington’s disease, another degenerative motor neuron condition. But unlike the majority of Lou Gehrig’s cases, the cause of Huntington’s is known: It is a genetic defect.

A small number, 5 percent to 10 percent, of Lou Gehrig’s cases are inherited.

When studying motor neurons, Thompson and her team will look for “signatures,” characteristics that make them unique. They will expose the nerve cells to proteins, genes, chemicals and anything else with which they might come in contact in the brain, to see how those factors change them or their activity.

Cedars-Sinai’s regenerative medicine institute is generating the iPS cells for the project. It delivered versions derived from healthy skin cells last week for the control group, and is sending iPS cells from ALS patients this week.

“We want to be able to create in a dish the motor neurons that mirror an individual patient’s disease so we can see how quickly or slowly degeneration occurs,” the institute’s director, Clive Svendsen, said. “We also want to be able to interact with the disease model and see if we can slow it down in the dish. If so, theoretically, we should be able to slow it down in the patient as well.”
The grant from the National Institutes of Health will cover six years of research. Along the way, Thompson and her team will have to meet certain milestones. The first is building infrastructure for the database and determining how to upload the information.

“We keep track of things in our own lab, but we’re not used to sharing it with others,” Thompson said. “We’ve had ways we’ve been sharing, through publications, and there are some centralized databases and sources that are available – but not at this level. This is going to take a whole new type of technology to handle this type of data set, and computational analysis. It really is really innovative.”

Ryan Lim is a UCI graduate student working in Thompson’s lab. He said one nerve cell has about 500 gigabytes of data, “and that’s just the tip of the iceberg.”

One gigabyte in a cell phone’s data plan is the equivalent of sending or receiving 50,000 e-mails, streaming 33 hours of music, viewing 1,000 web pages and posting 2,800 photos on Facebook, according to the consumers group Citizens Utility Board.

Svendsen said data-analysis teams will collaborate to create computer programs to pull all the information together.

“Scientists often focus on very small things, such as a single signaling pathway in cells or a single gene or protein that is involved in some way with disease development, but identifying and correcting one component rarely leads to a cure,” he said. “This is especially true in the brain because its networks are very complex.”

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