

# New stem cell technique improves genetic alteration

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UC Irvine researchers have discovered a dramatically improved method for genetically manipulating human embryonic stem cells, making it easier for scientists to study and potentially treat thousands of disorders ranging from Huntington's disease to muscular dystrophy and diabetes.

The technique for the first time blends two existing cell-handling methods to improve cell survival rates and increase the efficiency of inserting DNA into cells. The new approach is up to 100 times more efficient than current methods at producing human embryonic stem cells with desired genetic alterations.

“The ability to generate large quantities of cells with altered genes opens the door to new research into many devastating disorders,” said Peter Donovan, professor of biological chemistry and developmental and cell biology at UCI, and co-director of the UCI Sue and Bill Gross Stem Cell Research Center. “Not only will it allow us to study diseases more in-depth, it also could be a key step in the successful development of future stem cell therapies.”

This study appears online this week in the journal *Stem Cells*.

Donovan and Leslie Lock, assistant adjunct professor of biological chemistry and developmental and cell biology at UCI, previously identified proteins called growth factors that help keep cells alive. Growth factors are like switches that tell cells how to behave, for example to stay alive, divide or remain a stem cell. Without a signal to

stay alive, the cells die.

The UCI scientists – Donovan, Lock and Kristi Hohenstein, a stem cell scientist in Donovan’s lab – used those growth factors in the current study to keep cells alive, then they used a technique called nucleofection to insert DNA into the cells. Nucleofection uses electrical pulses to punch tiny holes in the outer layer of a cell through which DNA can enter the cell.

With this technique, scientists can introduce into cells DNA that makes proteins that glow green under a special light. The green color allows them to track cell movement once the cells are transplanted into an animal model, making it easier for researchers to identify the cells during safety studies of potential stem cell therapies.

Scientists today primarily use chemicals to get DNA into cells, but that method inadvertently can kill the cells and is inefficient at transferring genetic information. For every one genetically altered cell generated using the chemical method, the new growth factor/nucleofection method produces between 10 and 100 successfully modified cells, UCI scientists estimate.

With the publication of this study, the new method now may be used by stem cell scientists worldwide to improve the efficiency of genetically modifying human embryonic stem cells.

“Before our technique, genetic modification of human embryonic stem cells largely was inefficient,” Hohenstein said. “This is a stepping stone for bigger things to come.”

Scientists can use the technique to develop populations of cells with abnormalities that lead to disease. They can then study those cells to learn more about the disorder and how it is caused. Scientists also

possibly could use the technique to correct the disorder in stem cells, then use the healthy cells in a treatment.

The method potentially could help treat monogenic diseases, which result from modifications in a single gene occurring in all cells of the body. Though relatively rare, these diseases affect millions of people worldwide. Scientists currently estimate that more 10,000 human diseases are monogenic, according to the World Health Organization. Examples include Huntington's disease, sickle cell anemia, cystic fibrosis and hemophilia.

Source: University of California - Irvine

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