

Gladstone scientist converts human skin cells into functional brain cells

July 28 2011

A scientist at the Gladstone Institutes has discovered a novel way to convert human skin cells into brain cells, advancing medicine and human health by offering new hope for regenerative medicine and personalized drug discovery and development.

In a paper being published online today in the scientific journal *Cell Stem Cell*, Sheng Ding, PhD, reveals efficient and robust methods for transforming adult <u>skin cells</u> into neurons that are capable of transmitting <u>brain signals</u>, marking one of the first documented experiments for transforming an adult human's skin cells into functioning <u>brain cells</u>.

"This work could have important ramifications for patients and families who suffer at the hands of neurodegenerative diseases such Alzheimer's, Parkinson's and Huntington's disease," said Lennart Mucke, MD, who directs <u>neurological research</u> at Gladstone. "Dr. Ding's latest research offers new hope for the process of developing medications for these diseases, as well as for the possibility of cell-replacement therapy to reduce the trauma of millions of people affected by these devastating and irreversible conditions."

The work was done in collaboration with Stuart Lipton, M.D., Ph.D., who directs the Del E. Webb Neuroscience, Aging and <u>Stem Cell</u> <u>Research</u> Center at Sanford-Burnham Medical Research Institute. Dr. Ding, one of the world's leading chemical biologists in stem-cell science, earlier this year joined Gladstone and the faculty at the University of



California San Francisco (UCSF), as a professor of <u>pharmaceutical</u> <u>chemistry</u>. Gladstone, which is affiliated with UCSF, is a leading and independent biomedical-research organization that is using stem-cell research to advance its work in its three major areas of focus: cardiovascular disease, neurodegenerative disease and <u>viral infections</u>.

Dr. Ding's work builds on the cell-reprogramming work of another Gladstone scientist, Senior Investigator Shinya Yamanaka, MD, PhD. Dr. Yamanaka's 2006 discovery of a way to turn adult skin cells into cells that act like embryonic <u>stem cells</u> has radically advanced the fields of cell biology and stem-cell research.

Embryonic stem cells—"pluripotent" cells that can develop into any type of cell in the human body—hold tremendous promise for regenerative medicine, in which damaged organs and tissues can be replaced or repaired. Many in the science community consider the use of stem cells to be key to the future treatment and eradication of a number of diseases, including heart disease and diabetes. But the use of embryonic stem cells is controversial—which is one reason why Dr. Yamanaka's discovery of an alternate way to obtain human stem cells, without the use of embryos, is so important.

Dr. Ding's work extends Dr. Yamanaka's by offering still another method for avoiding the use of embryonic stem cells and creating an entirely new platform for fundamental studies of human disease. Rather than using models made in yeast, flies or mice for disease research, all cell-reprogramming technology allows human brain, heart and other cells to be created from the skin cells of patients with a specific disease. The new cells created from the skin cells contain a complete set of the genes that resulted in that disease—representing the potential of a far-superior human model for studying illnesses, drugs and other treatments. In the future, such reprogrammed skin cells could be used to test both drug safety and efficacy for an individual patient with, for example,



Alzheimer's disease.

"This technology should allow us to very rapidly model <u>neurodegenerative diseases</u> in a dish by making nerve cells from individual patients in just a matter of days—rather than the months required previously," said Dr. Lipton.

In the experiments being reported today, Dr. Ding used two genes and a microRNA to convert a skin sample from a 55-year-old woman directly into brain cells. (MicroRNAs are tiny strands of genetic material that regulate almost every process in every cell of the body.) The cells created by Dr. Ding's experiments exchanged the electrical impulses necessary for brain cells to communicate things such as thoughts and emotions. Using microRNA to reprogram cells is a safer and more efficient way than using the more common gene-modification approach. In ensuing experiments, Dr. Ding hopes to rely only on microRNAs and pharmaceutical compounds to convert skin cells to brain cells, which should lead to more efficient generation of cells for testing and regenerative purposes.

"This will help us avoid any genome modifications," said Dr. Ding. "These cells are not ready yet for transplantation. But this work removes some of the major technical hurdles to using reprogrammed cells to create transplant-ready <u>cells</u> for a host of diseases."

Dr. Ding is a senior investigator at the Gladstone Institute of Cardiovascular Disease and a UCSF professor of pharmaceutical chemistry. Dr. Ding, who performed the work described in this paper at The Scripps Research Institute, has pioneered the development and application of innovative chemical approaches to stem-cell biology and regeneration.



Provided by Gladstone Institutes

Citation: Gladstone scientist converts human skin cells into functional brain cells (2011, July 28) retrieved 5 May 2024 from

https://medicalxpress.com/news/2011-07-gladstone-scientist-human-skin-cells.html

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