

Scientists turn skin cells into brain cells

June 7 2012

Scientists at the Gladstone Institutes have for the first time transformed skin cells-with a single genetic factor-into cells that develop on their own into an interconnected, functional network of brain cells. The research offers new hope in the fight against many neurological conditions because scientists expect that such a transformation-or reprogramming-of cells may lead to better models for testing drugs for devastating neurodegenerative conditions such as Alzheimer's disease.

This research comes at a time of renewed focus on Alzheimer's disease, which currently afflicts 5.4 million people in the United States alone-a figure expected to nearly triple by 2050. Yet there are no approved medications to prevent or reverse the progression of this debilitating disease.

In findings appearing online today in *Cell Stem Cell*, researchers in the laboratory of Gladstone Investigator Yadong Huang, MD, PhD, describe how they transferred a single gene called Sox2 into both mouse and human skin cells. Within days the skin cells transformed into early-stage [brain stem cells](#), also called induced [neural stem cells](#) (iNSCs). These iNSCs began to self-renew, soon maturing into neurons capable of transmitting [electrical signals](#). Within a month, the neurons had developed into neural networks.

"Many [drug candidates](#)-especially those developed for [neurodegenerative diseases](#)-fail in clinical trials because current models don't accurately predict the drug's effects on the [human brain](#)," said Dr. Huang, who is also an associate professor of neurology at the University of California,

San Francisco (UCSF), with which Gladstone is affiliated. "Human neurons-derived from reengineered skin cells-could help assess the efficacy and safety of these drugs, thereby reducing risks and resources associated with human trials."

Dr. Huang's findings build on the work of other Gladstone scientists, starting with Gladstone Investigator, Shinya Yamanaka, MD, PhD. In 2007, Dr. Yamanaka used four genetic factors to turn adult human skin cells into cells that act like embryonic stem cells-called induced pluripotent stem cells.

Also known as iPS cells, these cells can become virtually any cell type in the human body-just like embryonic stem cells. Then last year, Gladstone Senior Investigator Sheng Ding, PhD, announced that he had used a combination of small molecules and genetic factors to transform skin cells directly into neural stem cells. Today, Dr. Huang takes a new tack by using one genetic factor-Sox2-to directly reprogram one cell type into another without reverting to the pluripotent state.

Avoiding the pluripotent state as Drs. Ding and Huang have done is one approach to avoiding the potential danger that "rogue" iPS cells might develop into a tumor if used to replace or repair damaged organs or tissue.

"We wanted to see whether these newly generated neurons could result in tumor growth after transplanting them into mouse brains," said Karen Ring, UCSF Biomedical Sciences graduate student and the paper's lead author. "Instead we saw the reprogrammed cells integrate into the mouse's brain-and not a single tumor developed."

This research has also revealed the precise role of Sox2 as a master regulator that controls the identity of neural stem cells. In the future, Dr. Huang and his team hope to identify similar regulators that guide the

development of specific neural progenitors and subtypes of neurons in the brain.

"If we can pinpoint which genes control the development of each neuron type, we can generate them in the petri dish from a single sample of [human skin cells](#)," said Dr. Huang. "We could then test drugs that affect different neuron types-such as those involved in Parkinson's disease-helping us to put drug development for neurodegenerative diseases on the fast track."

Provided by Gladstone Institutes

Citation: Scientists turn skin cells into brain cells (2012, June 7) retrieved 14 July 2023 from <https://medicalxpress.com/news/2012-06-skin-cells-brain-lab.html>

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