

Growing human brain cells in the lab

October 10 2017





Credit: Gladstone Institutes



Li Gan, PhD, wants to find treatments to help patients with Alzheimer's disease. Like most researchers, she's hit a few major roadblocks.

When researchers like Gan find potential new drugs, they must be tested on human <u>cells</u> to confirm they can benefit patients. Historically, these tests have been conducted in <u>cancer cells</u>, which often don't match the biology of human <u>brain</u> cells.

"The problem is that brain cells from actual people can't survive in a dish, so we need to engineer <u>human cells</u> in the lab," explained Gan, senior investigator at the Gladstone Institutes. "But, that's not as simple as it may sound."

Many scientists use induced <u>pluripotent stem cells</u> (iPSCs) to address this issue. IPSCs are made by reprogramming <u>skin cells</u> to become stem cells, which can then be transformed into any type of cell in the body. Gan uses iPSCs to produce brain cells, such as neurons or <u>glial cells</u>, because they are relevant to neurodegenerative disease.

Human brain cells derived from iPSCs offer great potential for drug screening. Yet, the process for producing them can be complicated, expensive, and highly variable. Many of the current methods produce cells that are heterogeneous, or different from one another, and this can lead to inconsistent results in drug screening. In addition, producing a large number of cells is very costly, so it's difficult to scale up for big experiments.

To overcome these constraints, Michael Ward, MD, PhD, had an idea.

A New Technique Is Born

"I came across a new method to produce iPSCs that was developed at Stanford," said Ward, a former postdoctoral scholar in Gan's lab who is



now an investigator at the National Institutes of Health. "I thought that if we could find a way to simplify and better control that approach, we might be able to improve the way we engineer human brain cells in the lab."

Ward and his colleague Chao Wang, PhD, discovered a way to manipulate the genetic makeup of cells to produce thousands of neurons from a single iPSC. This meant that every engineered brain cell was now identical.

"I was truly motivated by our initial results," said Gan, who is also a professor of neurology at UC San Francisco. "I had observed too much variability using the traditional method, which made reproducing experiments quite problematic. So, the ability to produce homogeneous human brain cells was very exciting."

The team further improved the technique to create a simplified, <u>two-step</u> <u>process</u>. This allows scientists to precisely control how many brain cells they produce and makes it easier to replicate their results from one experiment to the next.

Their technique also greatly accelerates the process. While it would normally take several months to produce brain cells, Gan and her team can now engineer large quantities of them within 1 or 2 weeks, and have functionally active neurons within 1 month.

The researchers realized this new approach had tremendous potential to screen drugs and to study disease mechanisms. To prove it, they tested it on their own research.

They applied their technique to produce human neurons by using iPSCs. Then, they developed a drug discovery platform and screened 1,280 compounds. Their goal is to identify the compounds that could lower



levels of the protein tau in the brain, which is considered one of the most promising approaches in Alzheimer's research and could potentially lead to new drugs to treat the disease.

"We showed that we can engineer large quantities of human brain cells that are all the same, while also significantly reducing the costs," said Wang, Gladstone postdoctoral scholar. "This means our technology can easily be scaled up and can essentially be used to screen millions of compounds."

A Powerful Tool for the Entire Scientific Community

"We have developed a cost-effective technology to produce large quantities of human brain cells in two simple steps," summarized Gan. "By surmounting major challenges in human neuron-based drug discovery, we believe this technique will be adopted widely in both basic science and industry."

Word of this useful new technology has already spread, and people from different scientific sectors have come knocking on Gan's door to learn about it. Her team has shared the new method with scores of academic colleagues, some of whom had no experience with cell culture. So far, they all successfully repeated the two-step process to produce their own cells and facilitate scientific discoveries.

Details of this new technique were also published on October 10, 2017, in the scientific journal *Stem Cell Reports*.

With some of the roadblocks out of the way, Gan hopes more discoveries will soon help the millions who suffer from Alzheimer's disease.

More information: Chao Wang et al. Scalable Production of iPSC-



Derived Human Neurons to Identify Tau-Lowering Compounds by High-Content Screening, *Stem Cell Reports* (2017). <u>DOI:</u> <u>10.1016/j.stemcr.2017.08.019</u>

Provided by Gladstone Institutes

Citation: Growing human brain cells in the lab (2017, October 10) retrieved 2 May 2024 from <u>https://medicalxpress.com/news/2017-10-human-brain-cells-lab.html</u>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.