

Stem cells help explain varied genetics behind rare neurologic disease

March 30 2017

Researchers at Case Western Reserve University School of Medicine have successfully grown stem cells from children with a devastating neurological disease to help explain how different genetic backgrounds can cause common symptoms. The work sheds light on how certain brain disorders develop, and provides a framework for developing and testing new therapeutics. Medications that appear promising when exposed to the new cells could be precisely tailored to individual patients based on their genetic background.

In the new study, published in *The American Journal of Human Genetics*, researchers used stem cells in their laboratory to simultaneously model different genetic scenarios that underlie neurologic disease. They identified individual and shared defects in the cells that could inform treatment efforts.

The researchers developed programmable stem cells, called induced [pluripotent stem cells](#), from 12 children with various forms of Pelizaeus-Merzbacher Disease, or PMD. The rare but often fatal genetic disease can be caused by one of hundreds of mutations in a gene critical to the proper production of nerve cell insulation, or myelin. Some children with PMD have missing, partial, duplicate, or even triplicate copies of this gene, while others have only a small mutation. With so many potential causes, researchers have been in desperate need of a way to accurately and efficiently model genetic diseases like PMD in [human cells](#).

By recapitulating multiple stages of the disease in their laboratory, the researchers established a broad platform for testing new therapeutics at the molecular and cellular level. They were also able to link defects in brain cell function to patient genetics.

"Stem cell technology allowed us to grow cells that make myelin in the laboratory directly from individual PMD [patients](#). By studying a wide spectrum of patients, we found that there are distinct patient subgroups.

This suggests that individual PMD patients may require different clinical treatment approaches," said Paul Tesar, PhD, study lead, Dr. Donald and Ruth Weber Goodman Professor of Innovative Therapeutics, and Associate Professor of Genetics and Genome Sciences at Case Western Reserve University School of Medicine.

The researchers watched in real-time as the patients' stem cells matured in the laboratory. "We leveraged the ability to access patient-specific brain cells to understand why these cells are dysfunctional. We found that a subset of patients exhibited an overt dysfunction in certain cellular stress pathways," said Zachary Nevin, first author of the study and MD/PhD student at Case Western Reserve University School of Medicine. "We used the cells to create a screening platform that can test medications for the ability to restore cell function and myelin. Encouragingly, we identified molecules that could reverse some of the deficits." The promising finding provides proof-of-concept that medications that mend a patient's cells in the laboratory could be advanced to clinical testing in the future.

The stem cell platform could also help other researchers study and classify genetic diseases with varied causes, particularly other neurologic disorders. Said Tesar, "Neurological conditions present a unique challenge, since the disease-causing [cells](#) are locked away in patients' brains and inaccessible to study. With these new patient-derived [stem](#)

cells, we can now model disease symptoms in the laboratory and begin to understand ways to reverse them."

Provided by Case Western Reserve University

Citation: Stem cells help explain varied genetics behind rare neurologic disease (2017, March 30)
retrieved 26 April 2024 from

<https://medicalxpress.com/news/2017-03-stem-cells-varied-genetics-rare.html>

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.