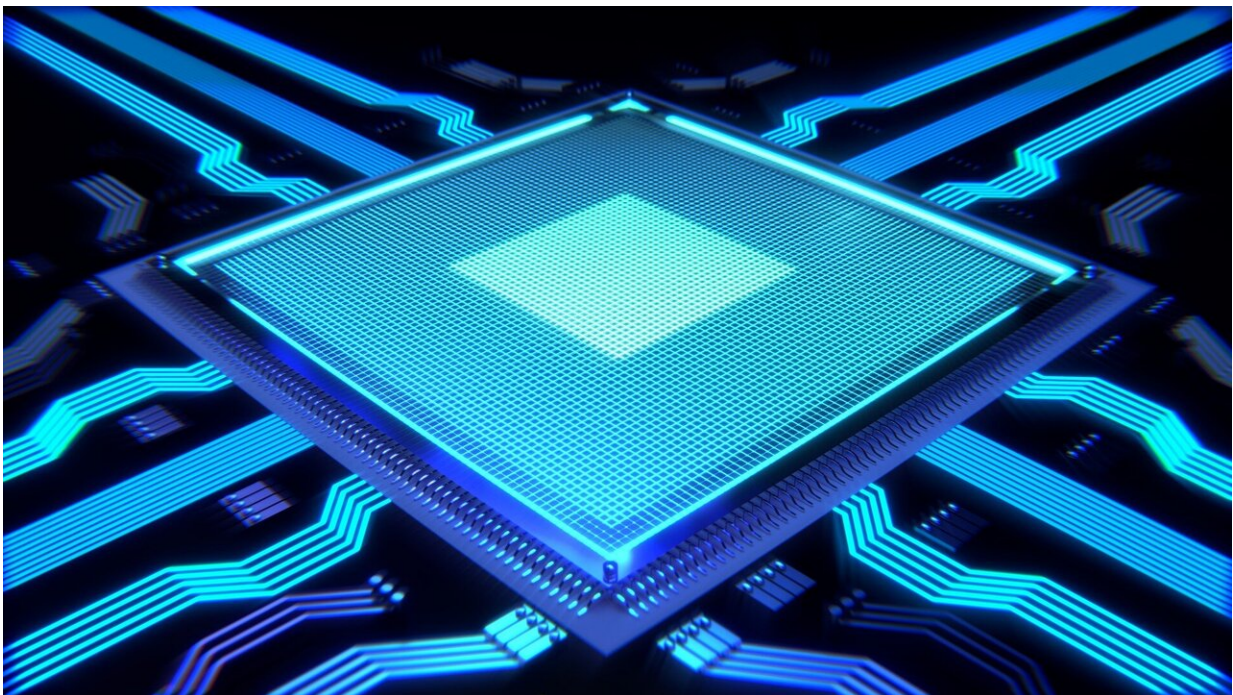


# Researchers create 3D model for rare neuromuscular disorders, setting stage for clinical trial

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A scientific team supported by the National Institutes of Health has created a tiny, bioengineered 3D model that mimics the biology of chronic inflammatory demyelinating polyneuropathy and multifocal motor neuropathy, a pair of rare, devastating neuromuscular diseases.

The researchers used the organ-on-a-chip, or "tissue chip," model to show how a drug could potentially treat the diseases. They provided key preclinical data for a drug company to submit to the U.S. Food and Drug Administration to get authorization for testing in a clinical trial.

This work provides one of the first examples of scientists using primarily [tissue](#) chip data for an FDA Investigational New Drug application to test the efficacy of a candidate drug in people with [rare diseases](#). The [drug company](#) Sanofi started recruiting participants into a Phase 2 clinical trial in April 2021. The drug was tested for safety previously and approved by the FDA for a different indication.

The tissue chip research was led by Hesperos, Inc., an Orlando-based company partially funded by a Small Business Innovation Research grant from NIH's National Center for Advancing Translational Sciences (NCATS). This study could open the door to studying and developing new therapies for other rare diseases by establishing a new avenue for repurposing existing drugs for rare diseases. Most of the known 7,000 rare diseases do not have effective treatments. Researchers often lack animal models for studying rare disease biology and testing potential drugs.

"This marks an important milestone in the evolution of the use of tissue chips," said Lucie Low, Ph.D., scientific program manager for the NCATS Tissue Chip for Drug Screening initiative. "We know that pharmaceutical companies are using tissue chips internally. Submitting data to [regulatory agencies](#) generated from tissue chip platforms is a powerful indicator of their growing promise."

James Hickman, Ph.D., chief scientist at Hesperos, and his colleagues described the development of the model and their research results in *Advanced Therapeutics*. In these diseases, the [immune system](#) makes proteins called antibodies that damage [nerve cells](#) and slow down

messages moving from the brain to the muscles. This can make it hard for people to move their arms, hands and legs. Current treatments can help, but often are inconsistent.

The researchers developed a tissue chip model consisting of two cell types: motoneurons and Schwann cells. Motoneurons transmit messages from the brain to muscles. Schwann cells help the signals move more quickly. The model could mimic functional characteristics of the diseases, allowing the scientists to see how a drug was working by determining whether the brain's messages to muscles were slowing down or not.

The researchers showed that exposing the cells to blood serum from people with these rare diseases caused a shower of immune system antibodies against the cells. This made the motoneuron signals move more slowly. After treatment with TNT005, a drug that blocks the immune system reaction, the cells and the message speed returned to normal.

"We're confident that our system can reproduce what happens to a patient, including the disease symptoms and disease progression," said Hickman. "It's important to create functionally relevant patient models that will mimic what is seen in clinical trials."

Approximately 90% of promising therapies fail in clinical trials because animal models used in preclinical testing are not good at predicting how people will respond. To improve that [success rate](#) and help get more treatments to people who have few options, scientists are exploring the uses of tissue chips. Designed to support living [human tissues](#) and cells, tissue chips mimic the structure and function of human organs and systems, such as the lungs, heart and liver. Researchers are studying their uses in many areas, including for testing the safety and effectiveness of candidate drugs and modeling diseases.

The potential clinical uses of tissue chip data are growing. Recently, an NIH-supported research team at Harvard University's Wyss Institute reported using a tissue chip model to generate data on the effectiveness of a repurposed drug for treating lung damage from COVID-19 infection. In the NCATS-funded Clinical Trials on a Chip program, several projects examine how tissue chip data can help researchers design more useful clinical trials. This might include using such data to predict which patients in a trial are most likely to respond to a therapy.

"Creating a platform that can predict human responses to a [drug](#) in a rare disease could lead to exciting new opportunities in research," said Low. "If tissue [chip](#) data can be generated that inform the decisions made before early human trials, this could reduce the risks to vulnerable populations."

**More information:** John W. Rumsey et al, Classical Complement Pathway Inhibition in a "Human-On-A-Chip" Model of Autoimmune Demyelinating Neuropathies, *Advanced Therapeutics* (2022). [DOI: 10.1002/adtp.202200030](#)

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