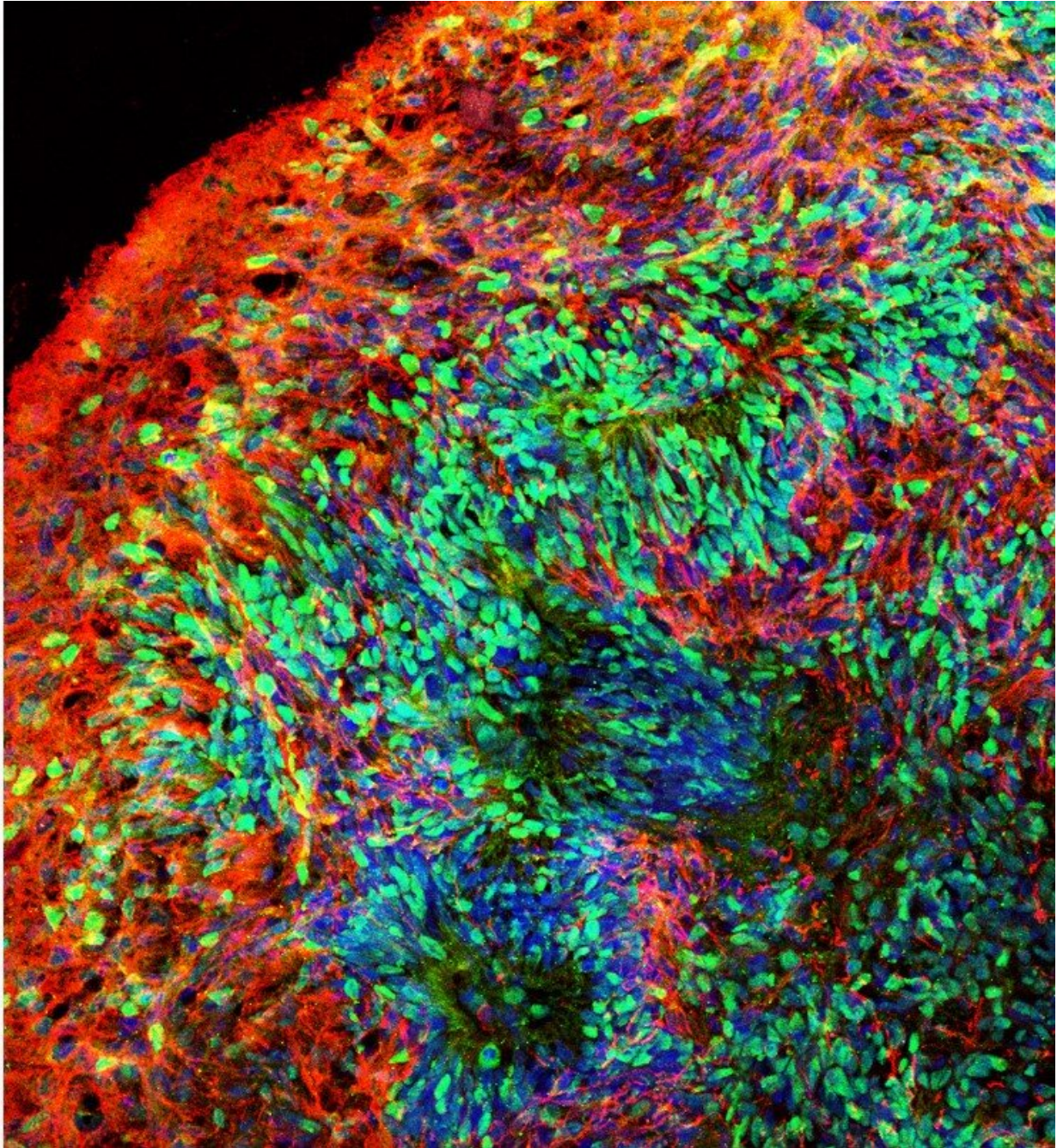


# Targeting key gene could help lead to Down syndrome treatment

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A living 3D "organoid" model of the brain generated from Down syndrome human stem cells. Credit: Ranjie Xu/Rutgers University-New Brunswick

Targeting a key gene before birth could someday help lead to a treatment

for Down syndrome by reversing abnormal embryonic brain development and improving cognitive function after birth, according to a Rutgers-led study.

Using [stem cells](#) that can turn into other cells in the brain, researchers developed two [experimental models](#)—a living 3-D "organoid" model of the brain and a mouse brain model with implanted [human cells](#)—to investigate [early brain development](#) linked to Down syndrome, according to the study in the journal *Cell Stem Cell*. The study focused on [human chromosome 21](#) gene OLIG2.

"Our results suggest the OLIG2 gene is potentially an excellent prenatal therapeutic target to reverse abnormal embryonic brain development, rebalance the two types of neurons in the brain—excitatory and inhibitory, and a healthy balance is critical—as well as improve postnatal cognitive function," said Peng Jiang, assistant professor in the Department of Cell Biology and Neuroscience at Rutgers University-New Brunswick.

Usually, a baby is born with 46 chromosomes, but babies with Down syndrome have an extra copy of chromosome 21. That changes how a baby's body and brain develops, which can lead to mental and physical challenges, according to the U.S. Centers for Disease Control and Prevention. Down syndrome is the most common chromosomal condition diagnosed in the United States, affecting about one in 700 babies, and about 6,000 infants are born each year with the condition.

The researchers obtained skin cells collected from Down syndrome patients and genetically reprogrammed those cells to human-induced [pluripotent stem cells](#) (hiPSCs). Resembling embryonic stem cells, the special cells can develop into many different types of cells, including brain cells, during early life and growth and are useful tools for drug development and disease modeling, according to the National Institutes

of Health.

Using brain cells derived from stem cells with an extra copy of chromosome 21, the scientists developed the 3-D brain organoid model, which resembles the early developing human brain. They also developed the mouse brain model, with stem cell-derived human brain cells implanted into the mouse brain within a day after the mice were born. They found that inhibitory neurons—which make your brain function smoothly—were overproduced in both models, and adult mice had impaired memory. They also found that the OLIG2 gene plays a critical role in those effects and that inhibiting it led to improvements.

The combination of the brain organoid and mouse brain model could be used to study other neurodevelopmental disorders such as autism spectrum disorder. It may also help scientists better understand the mechanisms in Alzheimer's disease. Down syndrome patients often develop early-onset Alzheimer's disease, Jiang noted.

**More information:** *Cell Stem Cell* (2019). [DOI: 10.1016/j.stem.2019.04.014](https://doi.org/10.1016/j.stem.2019.04.014)

Provided by Rutgers University

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