



## News from the Hereditary Disease Foundation

### Reprogramming Brain Cells

Almost every month we learn new truths about Huntington's disease (HD) because of creative developments in science and technology.

Through a magical cocktail, Andrew Yoo, PhD and a team of scientists at Washington University School of Medicine in St. Louis have transformed skin cells from patients with HD directly into brain cells, specifically into medium spiny neurons of the brain. All these neurons die in HD. Who are the killers? DNA damage? Mitochondria that go awry?

"This is a powerful tool to investigate the reasons why particular brain cells with the disease-associated mutation become sick over time and eventually die," says Andrew Yoo. "In theory, we could model progression of the disease by reprogramming skin cells from patients at a range of ages, including before symptoms begin. And, if there are drugs or compounds that may help these patients, we can test them first in this system."



The Hereditary Disease Foundation (HDF) funded Andrew's research project entitled, "Modeling Huntington's Disease with Patient Neurons Generated by Direct Neuronal Reprogramming" in June 2017. He is Assistant Professor of Developmental Biology at Washington University.

Andrew is a critical scientist in the HDF's newly formed collaboration of "Gene Changers." Similar to the collaboration of Gene Hunters, who searched for a decade to find the Huntington's disease gene, the Gene Changers are breaking barriers. They have captured genes that make HD start earlier, and they discovered a gene that delays onset of HD by 23 years.

The path-breaking and creative strategy developed by Andrew and his team is helping us understand what drives the progression of HD. The reprogrammed brain cells can talk to us if we know how to ask the right questions and learn how to

understand their answers. They are the ultimate test tube for trying new ideas and developing novel treatments and cures.

<https://medicine.wustl.edu/news/altering-huntingtons-disease-patients-skin-cells-brain-cells-sheds-light-disorder/>

## **Exciting Results from Ionis Pharmaceuticals**

Ionis Pharmaceuticals recently announced successful results from a completed phase 1/2 study of the drug RG6042 in people with early stage Huntington's disease. The trial linked the two highest doses of the drug to a 40-60% drop in levels of the abnormal protein that causes HD. The pharmaceutical company Roche is working closely with Ionis on this research.



Sarah J. Tabrizi, FRCP, PhD, FMedSci, professor of clinical neurology, director of the University College London's Huntington's Disease Centre and the global lead investigator says, "For nearly twenty years, I have seen many families devastated from losses to this progressive neurodegenerative disease. With IONIS-HTT<sub>Rx</sub> (RG6042), the HD community has new hope for a therapy that can reduce the cause of HD, and therefore, may slow the progression and potentially prevent the disease in future generations, which is truly groundbreaking. I look forward to a longer-term, larger study that can establish the

benefit of reducing the toxic mutant huntingtin protein in people with HD."

The Hereditary Disease Foundation supports the brainstorming and research that has led to these promising results. C. Frank Bennett, PhD, Senior Vice President, Research at Ionis Pharmaceuticals and one of the company's founding members, is a longstanding member of our Scientific Advisory Board. Dr. Tabrizi was awarded our Leslie Gehry Brenner Prize for Innovation in Science in 2017 for channeling her passion for Huntington's disease research to discover effective new treatments that prevent or reverse the disorder. She is the global Principal Investigator for the world's first "gene silencing" clinical trial in HD, sponsored by Ionis Pharmaceuticals.

Nancy Wexler, President of the Hereditary Disease Foundation, celebrates this discovery, "Since discovering the HD gene in 1993, this marks a landmark momentous occasion for families with HD across the globe. To have the gene in our hands and turn it off is a spectacular accomplishment!"

<http://ir.ionispharma.com/news-releases/news-release-details/ionis-htt-rx-rg6042-top-line-data-demonstrate-significant>

## **HD on Television**

The critically acclaimed British drama "Call the Midwife" which airs on the BBC and on PBS, is airing a segment about a family impacted by HD in London during the 1960s. The segment has already aired in England and is scheduled to be on PBS

stations in the United States later in March or in April. Check your local listings if you would like to tune in.

## **What We Do**

The Hereditary Disease Foundation facilitates collaborative and innovative scientific research to further the understanding of Huntington's disease, a genetic disorder that typically strikes in early- to mid-adulthood, destroying brain cells, and bringing about increasingly severe disturbances in mood, cognitive ability, and movement. As a disease caused by a mistake in a single gene, Huntington's disease is an ideal model for the study of other brain disorders. Research organized by the Foundation led to the discovery of the genetic marker for Huntington's disease in 1983. The Foundation also organized and funded a decade-long international collaboration of over 100 scientists who, in 1993, discovered the genetic mutation that causes Huntington's. This work played an important role in the development of the Human Genome Project. For information visit <http://www.hdfoundation.org/>.