



News from the Hereditary Disease Foundation

Racing Towards A Cure

As the Hereditary Disease Foundation (HDF) celebrates our 50th anniversary, we are pleased to launch this newsletter highlighting the outstanding HDF funded research being done by scientists around the world. Innovative research is crucial to curing Huntington's disease (HD) and other brain disorders. A key research area scientists currently are exploring is the mechanisms of three newly discovered genes. Two of these genes produce a younger onset of Huntington's disease symptoms. The third gene makes a protein that is protective – delaying onset of Huntington's disease by as many as 23 years. We want to turn this third gene into a medicine that pushes HD out of our lifespan. When we energize our efforts by funding novel, innovative research projects, the cure will come more quickly!

Setting Scientific Priorities

The Hereditary Disease Foundation's Scientific Advisory Board is composed of an international group of 27 distinguished scientists. They review grant and fellowship applications and select the most innovative and promising research projects to fund. We kick off this issue by introducing the Chair of our Scientific Advisory Board, Anne B. Young, MD, PhD.

Anne is Chair Emerita, Department of Neurology, Massachusetts General Hospital; Distinguished Julieanne Dorn Professor of Neurology, Harvard Medical School; Member, Royal College of Physicians, England; Member, American Academy of Arts and Sciences; and Member, National Academy of Medicine.



Anne has been actively involved in HD research for four decades. She participated in the Hereditary Disease Foundation's Venezuela Collaborative Project from 1981 until 2002, as a neurologist on the research team doing field work. In Venezuela, Anne focused on making accurate diagnoses of persons affected by HD. She also helped collect blood, skin and other samples generously donated by the Venezuelan family members.

Anne and her husband, the late John B. ("Jack") Penney, Jr., MD, created new models of how the basal ganglia control movements. They based their theories on data from animal and postmortem human brain samples. They

discovered, through clever experiments, how the basal ganglia are organized to affect movement in Huntington's, Parkinson's disease, dystonia and other disorders. The basal ganglia control movement, reward, emotions and memory. Anne and Jack's model suggested the design of therapies that could help many diseases. One prediction from their model was that Deep Brain Stimulation of the subthalamic nucleus or medial pallidum should help Parkinson's disease.

Anne was recruited in 1991 to Harvard Medical School and Massachusetts General Hospital as the hospital's first female head of a department. She founded and designed the Mass General Institute for Neurodegenerative Disease (MIND) in 2001 to accelerate the discovery of new and effective therapies for these disorders.

Anne Young and David Housman, PhD, also on our Science Advisory Board, founded Effective Therapeutics LLC.

In addition to serving as Chair of the Scientific Advisory Board, Anne plays a key role as Vice Chair of our Board of Directors. She received the Hereditary Disease Foundation's Leslie Gehry Brenner Prize for Innovation in Science in 2016.

Meet the Scientists

Each year the Hereditary Disease Foundation awards grants to scientists who are devoting their careers to changing the lives of families affected by Huntington's disease. Two awardees are Leslie Thompson, PhD, at the University of California, Irvine; and Steven Finkbeiner, MD, PhD, at the J. David Gladstone Institute, University of California, San Francisco. They are collaborating on our new "Genetic Modifiers Projects." Genetic modifiers are genes that impact the age when someone begins to show symptoms of the disease.

Leslie and Steve's research project is titled, "Assessment of Whole Genome Sequencing -Derived Genetic Modifiers in Differentiated HD-Derived iPSCs."

Renowned researchers in the Huntington's disease field and long-time collaborators, Leslie and Steve were founding members of a consortium established by the National Institutes of Health. The consortium received funding from HD organizations, including the Hereditary Disease Foundation, to develop human neuron models of Huntington's disease by reprogramming patient cells to be stem cells and then directing those stem cells to become neurons.



Leslie Thompson, PhD, and Steven Finkbeiner, MD, PhD

The two investigators developed a collaborative project for the Hereditary Disease Foundation to evaluate genes that may modify Huntington's disease. Potential modifying genes will be analyzed in human neurons made from stem cells from HD patients. The impact of each potential modifying gene and their effects will be studied.

Leslie will use sophisticated techniques to look globally at how those genes affect the expression of other genes in cells. She will specifically look at whether modulation of potential HD modifier genes affects the gene expression changes that she previously found associated with HD neurons. HD neurons express a specific pattern of getting sick and being healthy. Leslie and Steve are first testing how the specific changes make HD start early or late.

Steve will use special robotic microscopes he invented to test whether modulation of potential HD modifier genes affects degeneration of human HD neurons. These special microscopes let them follow individual cells, much like patients in a clinical trial, to sensitively measure effects of potential HD modifier genes on specific pathways and neurodegeneration. The results from the two approaches will be integrated into a deeper molecular and cellular understanding of how other genes, besides the HD gene, affect HD. If new genes are discovered they will be included in their studies. This will provide a better understanding of how HD occurs and the identification of therapeutic targets that could lead to new treatments.

The Huntington's Disease Community

The Hereditary Disease Foundation focuses on funding research toward treatments and cures for Huntington's disease. For more information visit: www.hdfoundation.org

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