Hereditary Disease Foundation 2018 Year in Review

2018 Leslie Gehry Brenner Prize for Innovation in Science Awarded to Dr. C. Frank Bennett Whose Work Made the First Clinical Trials in Huntington's Disease Possible

Frank Bennett of Ionis Pharmaceuticals has developed antisense therapies for Huntington's disease. IONIS-HTT$_{Rx}$ is designed to treat patients with HD and is the first and only drug to demonstrate reduction of neurotoxic abnormal huntingtin protein, the underlying cause of HD, in patients.

We are honored to recognize Frank for his innovative work in bringing us a totally novel class of drugs. His idea to use the body's own molecular capacity to create new medicine is revolutionary.

Roche has licensed the drug from Ionis and is poised to begin phase 3 clinical trials to lower the amount of the abnormal huntingtin protein, the underlying cause of HD. These trials will take place in the U.S. and abroad, and we are eagerly anticipating the outcome.

Our 2018 International Conference

The world's foremost HD and rare disease researchers came to Boston for the Hereditary Disease Foundation's 11th biennial "Milton Wexler Celebration of Life" conference. Over 250 scientists from across the globe came together to share their latest unpublished research findings. They explored the most cutting-edge approaches to brain research and discussed new ways to design and create therapies. Diverse research questions and methods converged on the common goal of developing novel therapies for HD and other disorders.

Our 2018 Workshop

In October, the Hereditary Disease Foundation organized and led a Milton Wexler Interdisciplinary Workshop of 30 researchers focused on modifier genes. These genes play a significant role in why some people develop Huntington's disease at a young age, and others develop the disease when they are much older. The first two Genetic Modifier Workshops of 2016 and 2017 focused on the introduction and updates of two potential genetic modifiers. This year, the 2018

Workshop encompassed conversations and updates with a broader focus on potential hot topics and avenues for developing therapies and different perspectives.

Workshops always provide the chance for both young and experienced scientists to come together to brainstorm, share ideas and data, and collaborate, setting aside competitive barriers to work together to advance research and find solutions. Collaboration is key – HDF Workshops, like the biennial conference, provide an essential forum for open discussions that turn into partnerships.

Our 2018 50th Year Symposium and Dinner

Over 200 guests attended the 2018 Symposium and Dinner at the Harvard Club of New York City. Dr. Shirley Tilghman, President Emerita and Professor of Molecular Biology and Public Affairs at Princeton University presented the keynote address. She spoke about how genes are organized in the genome and are regulated during early development. Dr. Tilghman is a world-renowned leader in the field of molecular biology whose brilliant scientific career as a mammalian development geneticist has advanced our understanding of Huntington's disease and other disorders. A member of the National Research Council's committee that set the blueprint for the United States effort in the Human Genome Project, she also was one of the founding members of the National Advisory Council of the Human Genome Project for the National Institutes of Health. During postdoctoral studies at the National Institutes of Health, she made a number of groundbreaking discoveries while participating in cloning the first mammalian gene, and then continued to make scientific breakthroughs as an independent investigator at the Institute for Cancer Research in Philadelphia.

Dr. C. Frank Bennett, senior vice president for research and franchise leader for neurological programs at Ionis Pharmaceuticals, gave a mesmerizing talk about his work developing antisense therapeutics for neuromuscular and neurological diseases. In 2005, Frank started a program to develop antisense therapies for Huntington's disease. IONIS-HTT_{Rx} is designed to treat patients with HD and is the first and only drug to demonstrate reduction of the neurotoxic abnormal huntingtin protein, the underlying cause of HD, in patients. Ionis is partnering with Roche for phase 3 of the trial, which is set to begin in the U.S. and abroad soon. This is a groundbreaking advance for the field of HD!

At the dinner that followed, Gala Chair Karen Newman announced that the event had raised $800,000 to support the Foundation's critical work. Kate and Justin Miner of the band Miner treated us all to a moving and spirited musical performance. Kate's mother and two sisters have the expanded version of the

HD gene. Kate is actively engaged with the medical community and policymakers to help find a cure for HD and raise awareness.

Our Scientific Leadership Expansion in 2018

Our Scientific Advisory Board (SAB), composed of distinguished scientists from around the world, sets the scientific priorities of the Foundation, reviews grant and fellowship applications, and selects the most promising research projects to fund. In 2018 the Board elected five extraordinary scientists to the SAB. We welcome these individuals to the HDF family:

- **Myriam Heiman, Ph.D.**, The Broad Institute of MIT and Harvard
- **A. Jenny Morton, Ph.D.**, University of Cambridge
- **Harry T. Orr, Ph.D.**, University of Minnesota
- **Christopher E. Pearson, Ph.D.**, The Hospital for Sick Children, University of Toronto
- **Sarah J. Tabrizi, FRCP Ph.D., FMedSci**, UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square.

See our current Scientific Advisory Board members.

Our New 2018-2019 Postdoctoral Fellowship and Research Grant Awardees

In July the Foundation's current research recipients were joined by these additional award recipients:

Anne Ast
Mentor: Erich E. Wanker, Ph.D.
Institution: Max-Delbrück-Center for Molecular Medicine, Germany
Project Title: *Manipulating seeding activity and proteotoxicity of amyloidogenic HTT aggregates by targeted amino acid exchanges*

Alejandro Mas-Monteys, Ph.D.
Institution: University of Pennsylvania, The Children's Hospital of Philadelphia
Project Title: *Novel approaches for knock down control*

Ellen Penney, M.D., Ph.D.
Institution: Massachusetts General Hospital
Project Title: *R-loops in HD: Somatic Expansion and DNA Repair*

Anna Pluciennik, Ph.D.
Institution: Thomas Jefferson University
Project title: *Crosstalk between DNA repair pathways in Huntington's disease*

Piere Rodriguez, Ph.D.
Mentor: Judith Frydman, Ph.D.
Institution: Stanford University
Project Title: *Dissection of the functional and structural communication within the Huntingtin protein and its interaction with the human TRiC chaperonin*

Matthew Scaglione, Ph.D.
Institution: Medical College of Wisconsin
Project Title: *Analysis of a novel class of molecular chaperones that suppress polyglutamine aggregation*

Learn about our Research Grants.

Together We Can Do This!

The Hereditary Disease Foundation has a long tradition of funding extremely novel and catalytic work of promising young investigators who do not have access to funding from major institutions. We fund pilot studies which help seed grants so investigators can apply elsewhere.

Many of our distinguished Scientific Advisory Board, as well as other scientists prominent in the field today, began their careers with a grant from our Foundation. We have nurtured many careers early on – the HDF is often credited with guiding "generations of researchers" to dedicate their life's work to studying Huntington's disease and related brain disorders such as Alzheimer's, Parkinson's and ALS.

YOU ARE THE FOUNDATION'S TRUE PARTNERS IN RESEARCH.

Over 90% of the Foundation's contributions are modest gifts. These gifts have a tremendous cumulative impact on the research we are able to fund.

Your contribution counts – whatever the amount!

Together we can do this!

Innovating Research…Discovering Cures

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