CELEBRATING TRANSFORMATIVE RESEARCH

HEREDITARY DISEASE FOUNDATION 2023 SYMPOSIUM & GALA

THE HEREDITARY DISEASE FOUNDATION FUNDS THE MOST PROMISING, INNOVATIVE, AND PARADIGM-CHANGING RESEARCH TO CURE HUNTINGTON'S DISEASE.

GOOD EVENING!

We are excited to be with you tonight, our community of Huntington's disease family members and friends, researchers, clinicians, advocacy partners, pharmaceutical industry experts, Partners in Research, generous donors and loyal supporters.

It is an honor to lead the Hereditary Disease Foundation. Meeting people in the HD community who share our personal experiences with this disease fuels our passion for funding the most promising and innovative research. We draw inspiration from people like HDF Board member Tacie Fox who—as you will hear tonight—openly shares her family's challenges, strength and hope in the face of Huntington's disease.

Tonight's gala celebrates the transformative research funded by the Hereditary Disease Foundation and the dedication of our scientists. We're also proud to highlight the initiatives launched in recent years, such as our Research Spotlight Webinar Series, Young Investigator Forums, and the newly established Transformative Research Awards.

The Hereditary Disease Foundation is committed to supporting renowned and emerging scientists in HD research, fostering collaborations for rapid advancements. Over the past three days, we hosted two scientific workshops, bringing together over 50 researchers, many of whom are with us tonight, to discuss exciting advances and new technologies shaping HD research.

We invite you to learn more about the Hereditary Disease Foundation, its innovative research, and engage with experts and HDF board members present tonight. Ask questions, visit our website, and consider supporting our work because the research we fund together can be transformative.

With gratitude,

Meghan Donaldson
Chief Executive Officer

Karen Newman
Chair, Board of Directors

HEREDITARY DISEASE FOUNDATION AT A GLANCE

WE FUND GROUNDBREAKING HUNTINGTON'S DISEASE RESEARCH

HDF Transformative Research Awards stimulate revolutionary advances by providing scientific teams with 2-year grants of up to $1 million for projects with the potential to change the course of Huntington's disease.

HDF Postdoctoral Fellowships fund the work of promising junior scientists and cultivate interest in HD research by encouraging scientists early in their careers.

HDF Grants provide seed funding to experienced HD researchers, enabling them to collect preliminary data that can lead to securing major long-term funding from other sources.

WE BRING THE HUNTINGTON'S DISEASE COMMUNITY TOGETHER

HDF Small Workshops enable researchers from varying disciplines and at different career points to brainstorm and explore new directions towards treatments for HD.

HDF Research Webinars spotlight brilliant scientists discussing their work in non-technical language for the general public - we hope you will join us!

HDF Conferences bring together international experts in HD and other neurological disorders to determine new ways to identify therapies.
Next August, the Hereditary Disease Foundation is proud to be hosting HD2024, our biennial Milton Wexler Symposium, which will bring together some 300 of the world's foremost experts in HD and other neurological diseases. For three days, scientists will share their latest discoveries and explore cutting-edge research approaches, sparking discussions of new ways to design and create therapies.

JEFFERY W. KELLY, PHD

Lita Annenberg Hazen Professor of Chemistry
The Scripps Research Institute
National Academy of Sciences
American Academy of Arts and Sciences
2022 Breakthrough Prize in Life Sciences
2023 Wolf Prize in Chemistry

Dr. Jeffery Kelly's groundbreaking research on protein misfolding and aggregation has led to therapeutic strategies for a range of devastating neurogenerative and cardiovascular diseases. He is a member of the Scientific Advisory Board of the Hereditary Disease Foundation.

Dr. Kelly discovered the first regulatory agency-approved drug that slows the progression of the neurodegenerative disease familial amyloid polyneuropathy and the cardiac disease senile systemic amyloidosis (tafamidis; Pfizer), both caused by the aggregation of the protein transthyretin.

Currently, his lab is focused on the discovery of first-in-class drugs that would slow the progression of multiple neurodegenerative diseases by modulating organismal protein homeostasis (e.g. autophagy) and/or neuroinflammation. Dr. Kelly has published over 390 scientific papers, he has placed 45 trainees in tenured or tenure-track academic positions, and 60 trainees in biotechnology and pharmaceutical positions.

LESLIE GEHRY PRIZE FOR INNOVATION IN SCIENCE

2023 RECIPIENT

VANESSA C. WHEELER, PHD

Center for Genomic Medicine
Massachusetts General Hospital
Harvard Medical School

Dr. Vanessa Wheeler's research on somatic instability laid the groundwork for what has become the most prolific topic in Huntington's disease research this decade, as understanding somatic instability is thought by many leading scientists to be the route to the cure.

Huntington's disease is caused by a genetic expansion in a gene called huntingtin. When the expansion reaches a certain threshold, the person carrying that expansion will go on to develop HD if they live long enough. Over time, the expansion within the huntingtin gene increases in certain areas of the body – notably, the brain. This biological phenomenon of an increase in genetic expansion is called "somatic instability." Scientific data now suggests that somatic instability is the cause of brain cell death in HD.

Well before the term "somatic instability" was on the lips of every HD researcher, Dr. Wheeler was connecting dots related to this biological phenomenon and making connections for how it participates in HD pathology. Dr. Wheeler has been focused on somatic instability as the root cause of HD since the mid-2000s.

ABOUT THE PRIZE

Each year, the Hereditary Disease Foundation presents the prestigious Leslie Gehry Prize for Innovation in Science. This award of $100,000 was created by HDF Founding Director and world-renowned architect Frank Gehry and his family to honor the memory of his late daughter Leslie, a gifted artist, painter, photographer, and filmmaker.

Previous Recipients

2022: Dr. Steven Finkbeiner, Gladstone Institutes and the University of California, San Francisco
2021: Prof. Elena Cataneo, University of Milan, Italy
2020: Dr. Ai Yamamoto, Columbia University
2019: Dr. Scott Zeitlin, University of Virginia
2018: Dr. C. Frank Bennett, Ionis Pharmaceuticals
2017: Dr. Sarah J. Tabrizi, University College London, England
2016: Dr. Anne B. Young, Massachusetts General Hospital, Harvard Medical School
2015: Dr. Beverly Davidson, Children's Hospital of Philadelphia, University of Pennsylvania
2014: Dr. X. William Yang, University of California, Los Angeles
2013: Dr. Leslie Thompson, University of California, Irvine
2012: Dr. Gillian Bates, University College London, England
2010: Dr. David Housman, Massachusetts Institute of Technology

NANCY S. WEXLER YOUNG INVESTIGATOR PRIZE

2023 RECIPIENT

CHIARA SCARAMUZZINO, PHD

Grenoble Institut des Neurosciences, France

Dr. Chiara Scaramuzzino carried out her postdoctoral training with Dr. Frederic Saudou, investigating communication between brain cells using microscopic chips that mimic circuitry in the brain. She recently accepted an independent position and is focused on defining molecular mechanisms underlying the breakdown of brain cell communication in neurodegenerative diseases, such as Huntington's.

Communication amongst brain cells is critical for a healthy brain. In HD, communication signals break down between two key brain structures that are the most affected by this disease, the cortex and striatum. Normally, these brain regions can send each other molecular messages, called neurotropic factors, that aid in the survival of brain cells. In HD, neurotropic molecular messages from the cortex don't reach the striatum, causing brain cells in the striatum to die. Dr. Scaramuzzino's work uncovered that the striatum-to-cortex communication loop is also impaired in HD. She aims to restore transmission of these fundamental neurotrophic molecular messages to restore communication between these two brain regions in HD.

ABOUT THE PRIZE

Each year the Hereditary Disease Foundation presents the Nancy S. Wexler Young Investigator Prize to a researcher whose work reflects the highest caliber of excellence, diligence, and creative thinking. The prize recipient is selected by the Hereditary Disease Foundation Scientific Advisory Board.

Previous Recipients

2022: Dr. Natalia Barbosa, Stanford University
2021: Dr. Sarah Hernandez
University of California, Irvine
2020: Dr. Osama Al-Dalahmah, Columbia
University Irving Medical Center

TRANSFORMATIVE RESEARCH AWARDS

The Transformative Research Awards were made possible through a partnership between the Hereditary Disease Foundation and a generous group of anonymous donors. Established in 2023, this award is designed to move the most innovative work in Huntington's disease from concept to practice by funding collaborative research teams who are focused on creating new ways to move toward a disease-modifying treatment and provide transformational new insights to the HD research field.

The Transformative Research Awards are the largest grants ever awarded by the Hereditary Disease Foundation.

The Hereditary Disease Foundation is thrilled to announce the recipients of our inaugural Transformative Research Awards. Congratulations to the two all-star collaborative teams, one led by Dr. Beverly Davidson of the Children's Hospital of Philadelphia and University of Pennsylvania, and the other led by Dr. Ricardo Mouro Pinto of Massachusetts General Hospital and Harvard Medical School, who will each receive funding of $1 million over the next two years to advance their work toward developing treatments for Huntington's disease.

Dr. Davidson's and Dr. Mouro Pinto's teams each use cutting-edge methods but take different approaches to advance Huntington's disease research and, if successful, could lead to truly transformative therapies for Huntington's disease. Breakthroughs in research that will bring about disease-modifying treatments for HD will not come unless HD research receives funding. The Hereditary Disease Foundation is excited to be able to offer dedicated funds that will transform the therapeutic landscape of HD research and lead to clinical trials.

TRANSLATIONAL STUDIES ON PIAS1 AND MSH3 KNOCKDOWN FOR HUNTINGTON'S DISEASE

Beverly Davidson (principal investigator), Leslie Thompson and Jang-Ho Cha (co-investigators)

Beverly Davidson, PhD of Children's Hospital of Philadelphia and the University of Pennsylvania will collaborate with **Leslie Thompson, PhD** from the University of California, Irvine, and **Jang-Ho Cha, MD, PhD** from Latus Biosciences.

Their project will target two proteins using an adeno-associated virus (AAV) that can be injected into the brain at very small volumes and achieve wide distribution throughout the brain. MSH3 is involved in a biological phenomenon called "somatic instability," which is the molecular stutter in the CAG repeat that causes HD to expand over time in vulnerable tissues, particularly the brain. PIAS1 has been shown to significantly improve symptoms in mice that model HD.

Dr. Davidson has been working on Huntington's disease for decades, most recently specializing in developing and improving viral delivery strategies for HD therapeutics. She also has experience moving promising drug targets to primate models. Dr. Thompson is a renowned leader in stem cell research and has extensive experience working with various models of HD mice. Dr. Cha has worked in the pharmaceutical sector for decades and is well-versed in taking drugs from conception to clinic. Both Drs. Thompson and Cha were key members of the research team that traveled to Venezuela annually on a quest to find the gene that causes HD. This all-star team capitalizes on their own specific skill sets while collaborating to move novel approaches toward the clinic.

THERAPEUTIC TARGETING OF SOMATIC CAG EXPANSIONS WITH PRECISE CRISPR BASE EDITING

Ricardo Mouro Pinto (principal investigator), James Gusella, Benjamin Kleinstiver, David Liu (co-investigators), Benjamin Deverman, Joseph Nabhan, Cathleen Lutz, and Vanessa Wheeler (collaborators)

Ricardo Mouro Pinto, PhD of Massachusetts General Hospital and Harvard Medical School will work with a large team of experts including **James Gusella, PhD**, **Benjamin Kleinstiver, PhD** and **Vanessa Wheeler, PhD**, of the same institutions; **David Liu, PhD** and **Benjamin Deverman, PhD** from the Broad Institute of MIT and Harvard; **Joseph Nabhan, PhD** from Vesigen Therapeutics; and **Cathleen Lutz, PhD**, **MBA** from the Jackson Laboratory.

Their project will develop genome editing therapeutics that target the cause of the CAG repeat expansion in Huntington's disease. Their goal is to permanently halt somatic instability with a one-and-done (gene editing) approach to the brains of mice that model Huntington's disease.

Dr. Mouro Pinto, who has been dedicated to Huntington's disease research since his postdoctoral studies in 2015, has assembled a formidable team. Dr. Gusella, a pioneer in HD research since the 1970s, played a pivotal role in identifying the disease-causing gene. Dr. Kleinstiver is a genome editing expert. Dr. Liu invented base editing, a modified CRISPR technology central to this project. Dr. Deverman specializes in virus development. Dr. Nabhan excels in therapeutic packaging for brain delivery. Dr. Lutz is renowned for mouse model development. Dr. Wheeler, a mentor to Dr. Mouro Pinto, has devoted her career to understanding somatic instability's impact on Huntington's disease. Each team member brings essential expertise to the project.

THANK YOU

The Hereditary Disease Foundation extends a special thanks to our Partners in Research, generous donors, and corporate sponsors this year.

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Our research program is supported by a partnership between generous donors and HDF-funded scientists. We welcome new partners to join us in pursuing game-changing scientific research that will make a powerful difference in the lives of families around the world impacted by Huntington's disease and other neurodegenerative disorders.

The research we fund together can be transformative.

The future of Huntington's disease research is exciting, promising and hopeful. The cure for HD is on the horizon. Your support will make a difference.

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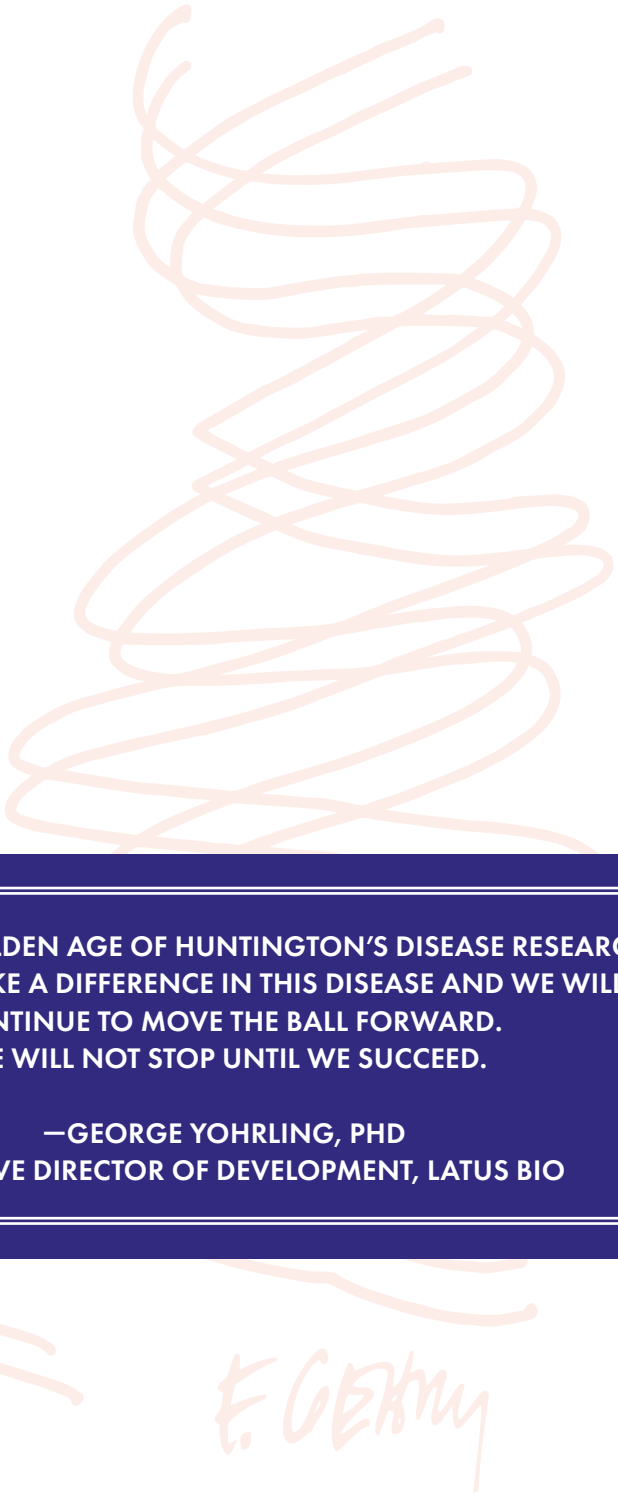

THIS IS THE GOLDEN AGE OF HUNTINGTON'S DISEASE RESEARCH. WE CAN MAKE A DIFFERENCE IN THIS DISEASE AND WE WILL CONTINUE TO MOVE THE BALL FORWARD. WE WILL NOT STOP UNTIL WE SUCCEED.

—GEORGE YOHRLING, PHD
EXECUTIVE DIRECTOR OF DEVELOPMENT, LATUS BIO

Hereditary Disease Foundation