



**Huntington's Disease
Society of America**

2018 Research Report



Table of Contents

- 2 Huntington's Disease Society of America Awards Five HD Human Biology Project Fellowships for 2018**
- 4 2018 Donald A. King Summer Research Fellowships**
- 6 HD Trialfinder: A Comprehensive Listing of HD Clinical Trials**
- 6 2018 Berman-Topper Family HD Career Development Fellowship**
- 7 2018 Hot Topics in HD Research**
- 9 HDSA Research Communications**
- 10 Clinical Trials Update**
- 13 2018 HD Research Conferences**
- 17 Huntington's Disease Society of America Announces Forty-Three 2018 HDSA Centers of Excellence**
- 20 A Special Thanks to the HDSA Scientific Advisory Board**

Hope shines brighter than ever that future generations may one day be free of HD



It has shaped up to be a year unlike any other for the HD community. In 2018, HDSA commemorated 50 years of service to the HD community and this year also marked the 25th anniversary of the identification of the huntingtin gene. This summer, a record number of people (1,046) attended the 33rd Annual HDSA Convention in Los Angeles, CA and the year culminated with the announcement from Roche/Genentech that the first ever Phase 3 clinical trial to test a huntingtin-lowering drug will begin in 2019 and will include sites in the United States.

The study will be called the GENERATION-HD1 study. The study name and Roche/Genentech team are inspired by HD families with the hope that "this will be the last GENERATION to suffer" from the ravages of this

hideous disease. News of this study has grabbed the attention of the global HD community. While the light of hope now shines brighter for all of us, we must not lose sight that much work remains before a finish line comes into sight.

GENERATION-HD1 and other HD trials will be long and require an unprecedented amount of commitment from not only HD families, but also the clinic staff that will run these studies. We know that the demand to participate in GENERATION-HD1 will outpace available spots, and this will undoubtedly be devastating news to many families. However, we are fortunate that there are many other companies currently testing or making plans to test innovative HD treatments. I hope that you enjoy reading about their progress in this year's HDSA Research Report.

As I look back on 2018, I am overwhelmed by the progress that has been made by the HD research community. When the calendar turns to 2019, I know that the HD families around the world will be ready to answer the call for brave research volunteers to get these disease-modifying trials completed... quickly. The scientific breakthroughs of this past year give me hope that 2019 will bring generations of HD families a step closer to seeing the finish line.

Thank you for all you do!



George Yohrling, PhD
HDSA Senior Director, Mission & Scientific Affairs



Rossana Foti



Richard Hickman



Michael Placzek



Isabelle St-Amour



Edith Pfister

Huntington's Disease Society of America Awards Five HD Human Biology Project Fellowships for 2018

In October 2018, HDSA announced that five research grants had been awarded under the Society's largest research initiative, the HDSA Huntington's Disease Human Biology Project. Totalling \$750,000, these grants represent HDSA's patient-centric research focus which brings basic and clinical researchers together to facilitate Huntington's disease (HD) science in the human condition, instead of in animal models, with the direct participation of people affected by HD.

HDSA received applications from researchers all around the world. Ultimately, grants were awarded to five research fellows, from Canada, Denmark and the United States.

The winners and titles of the 2018 HDSA HD Human Biology Project Grants are:

- *Dr. Rossana Foti, Postdoctoral Research Fellow, University of Copenhagen, Denmark: Epigenetic dysregulation of oligodendrocyte differentiation and myelinogenesis in Huntington's disease, and its relationship to disease-associated neuropsychiatric pathology. Using induced stem cells donated by HD patients with different types of symptoms, Dr. Foti will examine how changes to the brain's support cells contribute to the psychiatric symptoms of HD.*
- *Dr. Richard Hickman, Fellow in Neuropathology, Columbia University Medical Center: Aberrations in autophagy in the human brain of Huntington's disease: a post-mortem study with correlation to murine models. Dr. Hickman will study the systems that can remove debris from brain cells, and train with a world expert in the preparation and use of human brain tissue donated by individuals with HD.*
- *Dr. Edith Pfister, Instructor, University of Massachusetts Medical School: Alternative polyadenylation of the human HTT mRNA and its effect on mutant HTT accumulation. This work will explore changes in the length and location of different huntingtin mRNA and determine which ones make the best targets for huntingtin-lowering therapeutics.*

- *Dr. Michael Placzek, Instructor, Massachusetts General Hospital: COX-2 PET radiotracers for imaging early HD pathology in the living brain. This project focuses on the development of selective PET imaging radiotracers that can help track HD in the living brain and test the effectiveness of disease-modifying HD therapeutics.*
- *Dr. Isabelle St-Amour, Postdoctoral Fellow, Université Laval: Importance of microRNA biogenesis deficits in Huntington's disease. Dr. St-Amour will study how mutant huntingtin may affect the formation of micro-RNAs, which are important for controlling how healthy genes are expressed.*

For a complete summary of these five research projects, please visit www.hdsa.org/research.

Highlights from the Human Biology Project



Rocio Gomez-Pastor, PhD, University of Minnesota, 2016 Human Biology Fellow

Dr. Rocio Gomez-Pastor was funded between January 2017 and January 2018 to study how molecular chaperones coordinate proper folding and activity of neurons to prevent the progression of disease, resulting in two major publications. During this time, HDSA funding and connections helped her establish international collaborations and transition from a postdoctoral position at Duke University to a faculty position at the University of Minnesota, where she is now training undergraduate and graduate students in HD research.



Charles Mosier, University of California, San Diego, 2016 Human Biology Fellow

Charles Mosier, a scientific associate in the laboratory of Dr. Vivian Hook, has funding from HDSA from January 2017 through the end of 2018. His project aims to provide insight into the biological molecules that interact with huntingtin, by applying large-scale statistics to RNA and protein data. With particular attention to juvenile onset HD and potential differences, his work has generated maps of huntingtin interaction hubs that are of great interest to CHDI Foundation for drug discovery.



Amber Southwell, PhD, University of Central Florida, 2015 Human Biology Fellow

Dr. Amber Southwell was funded between 2015 and 2018 to develop novel methods to improve upon ultrasensitive detection of huntingtin protein in cerebrospinal fluid. During the award period, she created and tested a series of huntingtin fusion proteins and selected the most effective ones to create antibodies and test in human brain tissue and cerebrospinal fluid. The types of assays Dr. Southwell is working on are highly sought after as biomarkers of disease progression for HD diagnostics and clinical trials. During the award period, Dr. Southwell was able to transition from postdoctoral researcher to lead her own team at the University of Central Florida and train the next generation of HD scientists. Two undergraduate students received HDSA's Donald King Summer Research Fellowships to carry out work in her laboratory during 2018.

2018 Donald A. King Summer Research Fellowships

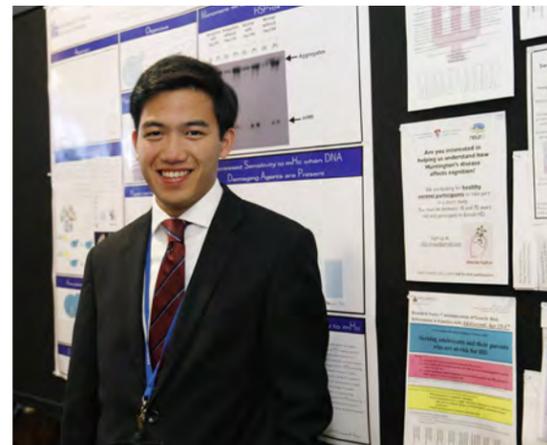
The Donald A. King Summer Research Fellowship provides summer salary funding to talented undergraduate students working in Huntington's disease research labs. The program was named in honor of HD advocate and 1999–2003 HDSA Board Chairman Donald King, who passed away in 2004. These summer fellowships were designed to facilitate meaningful discoveries about HD by helping bright student scientists to train and perform research alongside world HD experts. In 2018, HDSA awarded funding to four Donald King Fellows, who worked in their chosen laboratories during the summer of 2018.

- Jacob Friedman (University of Central Florida) worked with Amber Southwell, PhD using stem cells from male HD gene carriers to determine if a father's age affects CAG expansion.
- Ethan Smith (University of Central Florida) also worked under the guidance of Amber Southwell, PhD on a project that aims to clarify how the huntingtin protein makes its way to the cerebral spinal fluid (CSF) of HD mice.
- Wes Solem (Western Washington University) worked in the laboratory of Dr. Jeff Carroll to characterize a new HD mouse model that lacks huntingtin in its fat tissue.
- Scott Song (Amherst College) spent the summer working at Stanford University in the laboratory of Yanmin Yang, MD, PhD to investigate the function of calcium channels in HD cell cultures.

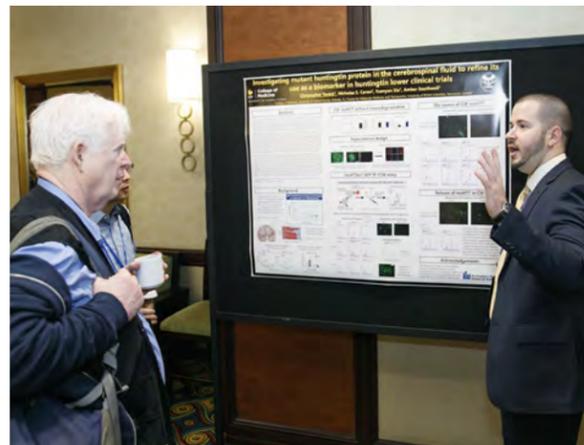
These fellows will be invited to present their findings at HDSA's 2019 Convention in Boston. The 2017 Donald A. King Summer Research Fellows are pictured presenting their posters at HDSA's 2018 Convention in Los Angeles.



Kiryung Kim, Columbia University



Paul Elizalde, Catholic University



Chris Yanick, University of Central Florida

Researchers Talk About HDSA Funding Programs

Without the support from the Huntington's Disease Society of America, this project would not have gotten off the ground. I am so grateful for the backing of this organization that provides so much for patients and family members affected by HD.

—Jacob Friedman, 2018 Donald King Fellow

Research Focus: Understanding why men are more likely to pass down a longer CAG repeat

Receiving grant support from the HDSA, where I know it was reviewed by researchers who think and care a lot about Huntington's disease, provides me with added confidence that the proposed project is of real interest to the Huntington's disease community. . . . I love that it puts me in contact with patients and their families. These encounters are immensely helpful; they are opportunities to obtain feedback from patients about the research.

—Madeleine Sharp, MD, 2015 Human Biology Fellow and 2018 Convention Speaker

Research Focus: Cognitive symptoms of HD and response to rewards

The [HDSA] grant has been indispensable to my immediate work in HD research. In the long term, this type of independent funding greatly improves my chances of securing a position to pursue a full research program in the HD field.

—Tamara Maiuri, 2017 Berman-Topper Fellow and 2018 Convention Speaker

Research Focus: The role of DNA repair genes that could delay symptomatic onset

Grant support from the HDSA has provided me with the unique and rewarding opportunity as a non-PhD researcher to join the HD research community. . . . [it] is an exciting and rewarding contribution to a much broader effort of family members, scientists, caregivers, volunteers, and countless others working together to understand and treat the disease.

—Charles Mosier, 2017 Human Biology Fellow

Research Focus: Identifying huntingtin interactors in juvenile HD to speed drug discovery



HD Trialfinder: A Comprehensive Listing of HD Clinical Trials



Clinical trial recruitment is one of the biggest barriers to gaining knowledge about HD and testing drugs to treat it, so participating in a trial is a very meaningful way to contribute to HD research. To facilitate this process for both families and researchers, HDSA created HD Trialfinder, a clinical trials matching service. It's a way for individuals with Huntington's disease, caregivers, healthy volunteers, and physicians to connect with current research studies. HD Trialfinder includes an easy-to-use website and free call center staffed by trained HD clinical trial navigators.

Through involvement in the worldwide HD research community, HDSA keeps track of national, international, and local clinical trials so that the HD Trialfinder listing stays up-to-date with studies that need participants. Anyone can visit the website to read about ongoing studies, and by creating a profile for yourself, a loved one, or a patient, you can find out which nearby studies you are eligible for, and locate contact information to get involved directly.

There are many ways to get involved in HD research, whether that's a drug trial, a local imaging study, a yearly observational visit, a phone call from home, or even driving a friend or family member to their study appointment. Go to www.hdtrialfinder.org or call 1-866-890-6612 to get involved today.

2018 Berman-Topper Family HD Career Development Fellowship

Since 2016, HDSA has awarded four Berman-Topper Family HD Career Development Fellowships to young postdoctoral scientists who are committed to making HD research part of their career plan. This fellowship, made possible through the generosity of the Berman and Topper families and the CHDI Foundation, provides up to \$80,000 of funding yearly for three years.

This May, the 2018 HDSA Berman-Topper Family HD Career Development Fellowship was awarded to Dr. Rachel Harding at the University of Toronto. Her proposal, "Structural and biophysical investigations of DNA and DNA repair protein interactions with huntingtin," will examine close relationships between huntingtin and a set of proteins known to repair DNA. These DNA repair proteins have emerged recently as a promising area of focus in Huntington's disease research; they may play a role in age of symptomatic onset as well as increase survival and longevity of neurons.



Rachel Harding, Post-doctoral Fellow, SGC

Dr. Harding will conduct the research at the University of Toronto under the guidance of Dr. Cheryl Arrowsmith and with additional mentorship from Dr. Ray Truant at McMaster University. She will make use of highly collaborative research relationships to identify and select important DNA repair proteins, and apply her expertise in structural biology to help visualize how these molecules interact with huntingtin.

HDSA's scientific advisory board (SAB) was impressed with Dr. Harding's unique proposal. She has excellent communication skills, a productive publication record, and has been profiled for her open attitude towards data-sharing.

Through the HDSA Berman-Topper Career Development Fellowship she is recognized as having great potential to pursue an independent career in the field. She brings structural biology expertise and new energy to the study of HD, and is well-positioned to learn a great deal from her co-mentors, who are experts in high resolution microscopy and Huntington's disease. Dr. Harding's detailed study of how huntingtin bonds with DNA repair genes could break new ground in the field, and represents an exciting step in the direction of HD therapeutics.

2018 Hot Topics in HD Research

Excitement about HD research reached new heights this year, with lots of buzz around the forward movement of gene therapy trials, new fields of focus emerging from studies of the human genome, and renewed interest from the pharmaceutical industry. Some areas of interest include:

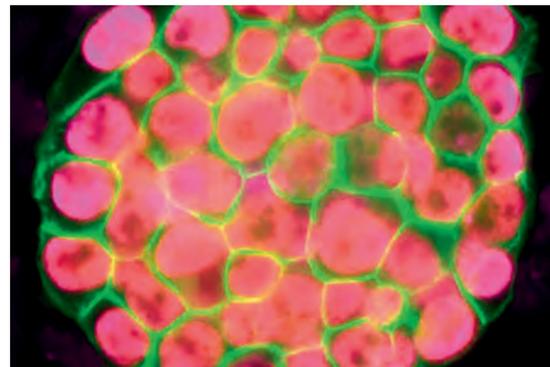
Huntingtin-lowering: The very first medical approach to target the genetic source of Huntington's disease, huntingtin-lowering therapy interferes with DNA or RNA to decrease the production of mutant huntingtin protein in the brain. Three clinical trials are currently underway. Roche Pharmaceuticals, known as Genentech in the United States, is carrying out a pivotal Phase III trial to test RG6042, formerly known as IONIS-HTTRx. There are expected to be 80-90 sites worldwide. Additionally, Wave Life Sciences has two huntingtin-lowering Phase 1b/2a trials underway, called PRECISION-HD 1 and PRECISION-HD 2. Videos of community presentations from Roche and Wave were recorded via webinar and at HDSA's 2018 Convention in Los Angeles, and are available on HDSA's website.

Several companies and academic researchers are working on therapies that also target huntingtin mRNA using RNA interference (RNAi) and short hairpin RNA (ssRNA) approaches. Delivery of these therapies to the brain is accomplished by delivery of viral vectors — adeno-associated virus (AAV). These therapies are in preclinical development and are being tested in mice and in larger mammals.

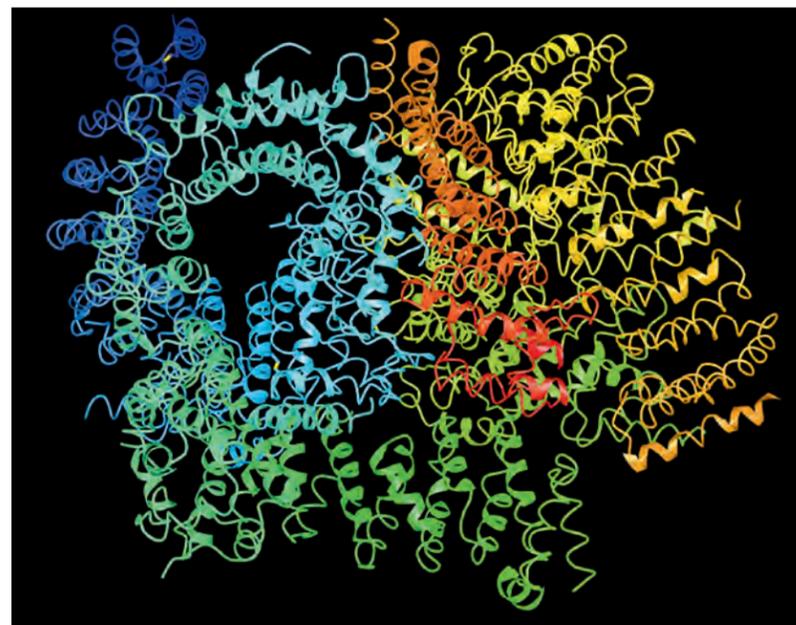
2018 Hot Topics in HD Research (continued)

Stem cells: 2018 marked the formation of an international network to study stem cells in Huntington's disease. Research in this field has advanced considerably over the past decade, with the goal of developing methods to replace or support brain cells that are damaged in HD. In May of 2018 HD scientists kick-started a global initiative, co-championed by Dr. Anne Rosser and HDSA board member Dr. Leslie Thompson. HDSA's Dr. George Yohrling was invited to attend the first conference in California, where experts discussed their recent findings and had the opportunity to form new collaborations to tackle their common goal of developing stem cell-based HD therapies. HDSA also featured an April webinar by stem cell researcher Dr. Jack Reidling who is collaborating with Dr. Thompson to test stem cell replacement techniques in the brains of mice.

Huntingtin structure: To figure out how mutant huntingtin can do so much damage to the brain, scientists have long wanted to take a snapshot of the protein's actual shape. This has been difficult to do because of huntingtin's large size and floppy structure. In 2018, a group of German scientists finally cracked it by using an extremely powerful microscope and capturing huntingtin with one of its many dance partners, a protein called HAP40. Apparently huntingtin looks like a pair of headphones! This structural information is a milestone for researchers and could help to inform us about the best angle of attack for a future drug.



Microscopic view of induced pluripotent stem cells captured at the UCLA Broad Stem Cell Research Center

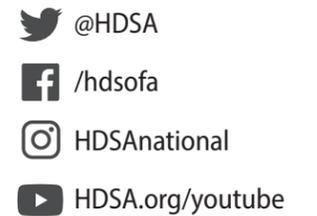


The structure of huntingtin protein

HDSA Research Communications

HDSA is committed to delivering timely and accurate updates about recent Huntington's disease clinical trials and laboratory research that builds upon our knowledge of HD.

Research Webinars: Monthly presentations from HD experts around the globe, featuring direct Q+A sessions for attendees to ask researchers and medical professionals about their findings. All webinars are recorded and shared on HDSA's YouTube channel. Among this year's topics were stem cell replacement therapy, exercise and physical therapy, and huntingtin lowering.



This Week In HD Research Blog: New in 2018, Dr. Leora Fox, HDSA's Manager of Research and Mission Programs, provides a weekly roundup of breaking HD medical news, HDSA research activities, scientific funding announcements, and historical moments in HD research at www.hdsa.org/blog.

FAQ Documents: When news stories or clinical trial announcements generate confusion within the community, HDSA responds with answers to frequently-asked questions.



HDBuzz: HDSA is a proud founding supporter of www.hdbuzz.net, a website dedicated to clear and effective communication about current research studies. The editors of HDBuzz are the dynamic duo of Ed Wild and Jeff Carroll, who also make fabulous yearly presentations at HDSA's Convention. This year's topics included novel HD animal models, participation in observational trials, a collaborative industry partnership to speed HD drug development, and even an HDSA Q&A about huntingtin-lowering.

Social Media: HDSA Communications and Research staff work together to make sure that the scientific news stories we share are accurate and relevant to families.

Convention Research Forum: The 2018 HDSA Convention featured the story of the development of the first huntingtin-lowering therapy, told collaboratively by ten speakers, from the team that discovered the HD gene to the head of the HD division at Roche Pharmaceuticals, who will conduct the upcoming clinical trial. This story highlighted the important role of brave HD families in the drug development process.



Keynote Address Speakers (LtoR): George Yohrling (HDSA), Erik Lundgren (Roche), Blair Leavitt (UBC), Ed Wild (UCL), Any Fedele (California), Doug Macdonald (CHDI Foundation), Robert Pacifici (CHDI Foundation), Holly Kordasiewicz (Ionis), Anne Smith (Ionis), James Gusella (MGH/Harvard) told the story of the development of the first drug to specifically target the disease causing protein, huntingtin.

Clinical Trials Update

Changes to Enroll-HD Coming to Meet Demands of HD Clinical Trial Pipeline



In May, HD investigators from around the world convened in Quebec, Canada for the Inaugural Enroll-HD Congress. There, updates were provided on the progress made to date with this global initiative. As of November 1, 2018, there are over 16,000 active participants enrolled at 156 active sites in 18 countries around the world. Once an additional 50 or so clinical sites complete the start-up process, Enroll-HD will have over 20,000 participants in more than 200 sites.

Enroll-HD is an observational study that is just one component of the entire Enroll-HD research platform that serves to enable all future HD clinical studies. Enroll-HD is sponsored and managed by CHDI Foundation, a not-for-profit biomedical research organization dedicated to rapidly developing therapies that slow the progression of Huntington's disease.

While these numbers may sound impressive, only 18% of the active participants in Enroll-HD are categorized as pre-manifest. The goal is to increase this percentage to 40% over next five years. A major reason for this is to better understand HD in gene positive individuals BEFORE they ever show symptoms, but we also need to ensure that a pipeline of potential clinical trial participants are at the ready when numerous companies seek to commence huntingtin-lowering trials in this important population.

It was also announced that a new, less burdensome protocol will be started in 2019 for patients in the more advanced stages of HD. This study will be called Enroll-HD Lite. Initially, it will be tested in 10–15 sites with about 500 patients around the globe before it is expanded more widely.

Roche/Genentech Initiates Pivotal Phase 3 Clinical Trial of Huntingtin-lowering Drug RG6042



After a decade of preclinical development and a successful safety trial by Ionis Pharmaceuticals, in 2018 a promising huntingtin-lowering drug was bought by Roche Pharmaceuticals and is now being tested in a Phase 3 clinical trial. The drug, formerly IONIS-HTTRx, is now known as RG6042. It is an antisense oligonucleotide (ASO), a short string of DNA-like molecules that can stick to huntingtin RNA and stop huntingtin protein from being made. The goal of this large trial is to understand whether the drug can slow or improve symptoms for people with HD.

The 660 participants needed to complete this pivotal trial must have early manifest HD. This means they have begun to show movement symptoms and may have difficulty driving and working, but are still able to maintain many of their independent activities at home, such as cooking and self-care. Specifically, participants must be ages 25–65, with a clinical diagnosis of HD, an independence score of 70 or more, and a CAP score of more than 400.

Participants will be split into three groups, and every person involved will have a lumbar puncture (spinal injection) monthly for 25 months. One group will receive a placebo, one group will receive RG6042 every other month, and one group will receive RG6042 every month. Each person will also have blood work, MRIs, tests of thinking and movement, and wearable technologies to monitor their activity at home.

Roche/Genentech spent many months planning this trial and selecting sites, which are beginning to open one by one as their hospital or university regulations come through. HDSA continues to provide timely updates to trial information, opportunities to interface with Roche/Genentech representatives, and answers to frequently asked questions from the community. Stay informed at www.hdtrialfinder.org and at www.hdsa.org.

The Next “Wave” of Huntingtin-lowering: PRECISION-HD



Wave Life Sciences is a genetic medicines company based in Cambridge, Massachusetts. Wave is testing huntingtin-lowering therapies in two ongoing clinical studies, called PRECISION-HD 1 and PRECISION-HD 2. The trials are currently taking place in Canada and Poland and involve lumbar punctures (spinal injections) to deliver antisense oligonucleotide (ASO) therapies to the brain in patients with HD. These therapies, WVE-120101 and WVE-120102, act by binding to mutant huntingtin mRNA and preventing the formation of the toxic mutant huntingtin protein.

The Wave Life Sciences ASOs are “stereopure,” ensuring that the drug’s shape is always the same, which could lead to greater efficiency of action in the body. They also specifically attack mutant huntingtin RNA while leaving the healthy form relatively intact. This is achieved by targeting single-letter genetic differences called SNPs (pronounced “snips”) between a person’s two copies of huntingtin. However, not everyone with HD has these genetic differences; between the two ASOs, it is estimated that around 70% of people with HD would be eligible.

SNP testing and administration of the ASOs in two Phase 1b/2a clinical studies began in Poland and Canada in 2017–2018 and is projected to begin at several US sites in 2018–2019. Each drug will be administered to approximately 60 individuals each, provided that no red flags arise for safety. Among the very first group of patients, half received a single low dose of the drug, and half received a placebo. If no immediate safety issues are identified, later participants in the study will be randomized 3:1 to receive multiple doses of the drug. Top-line safety results from these studies are expected in 2019, and HDSA will continue to provide updates about this novel therapy entering the huntingtin-lowering space.

The Scoop on Four HD Drug Trials in 2018



The LEGATO-HD trial being carried out by Teva Pharmaceuticals was a Phase 2 study designed to test whether laquinimod could improve movement symptoms in people with HD. In August of 2018, we learned that unfortunately this Phase 2 study failed to meet its primary endpoint, so the development of laquinimod for HD will not continue.



The PRIDE-HD study, also run by Teva, was a Phase 2 study to test the efficacy of pridopidine for improving movement symptoms in HD. We learned in 2018 that PRIDE-HD did not meet its primary endpoint of improving movement symptoms, but trial participants showed mild improvements in measures of independence in daily life. However, this trial is currently on hold and is not likely to continue in the near future.



The STAIR trial is a Phase 2 study being carried out by Azevan Pharmaceuticals to test SRX246, a drug designed to treat aggression and anxiety in HD. In September 2018, the STAIR trial finished recruiting more than 100 participants, and the community is awaiting the results of the analysis.



The SIGNAL trial is an ongoing Phase 2 study by Vaccinex that is currently recruiting at 20 sites in the US. The trial is testing the safety and tolerability of an antibody called VX15, given as a monthly IV infusion. VX15 has the potential to target inflammation in the HD brain, which is being measured through MRI.

2018 HD Research Conferences

Genentech/Roche Announces US & Canadian Locations of Observational Natural History Study



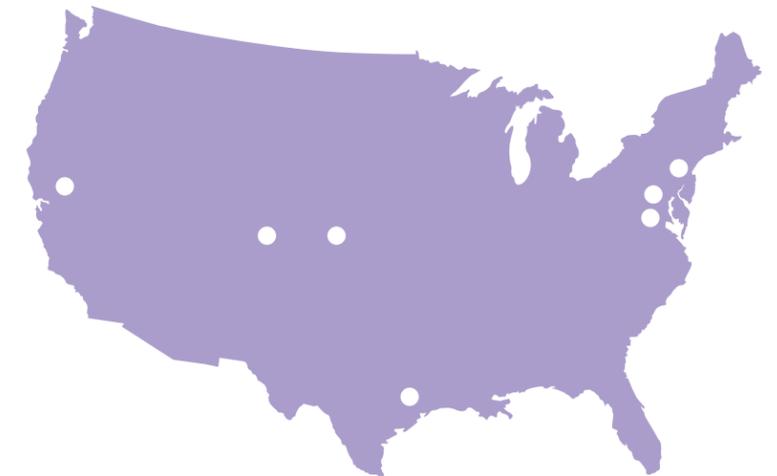
Genentech
A Member of the Roche Group

At the Huntington Study Group Meeting in Houston, Genentech/Roche announced the US and Canadian locations for their Natural History Study. This study does not involve drug treatments. It will monitor people with early manifest HD by testing their symptoms and measuring their mutant huntingtin levels over time. It will last for 16 months and includes an initial screening, 4 clinic visits with lumbar punctures and other assessments (at baseline and at months 3, 9, and 15), and 2 phone check-ups (at months 6 and 12). Around 100 people age 25–65 will be recruited. The 7 US study locations will be:

- Columbia Health Sciences/NYS Psychiatric Institute (NY)
- Georgetown University (DC)
- Hereditary Neurological Disease Center (Kansas)
- Johns Hopkins University (MD)
- Rocky Mountain Movement Disorders Clinic (Colorado)
- University of California, Davis Medical Center
- University of Texas Health Science Center- Houston

Please note that each of these sites must obtain their own internal approvals before they formally start recruiting for this study. Not all of these sites are recruiting yet; specific information about this study will be available shortly at www.hdtrialfinder.org and at the government's clinical trials website: <https://clinicaltrials.gov/ct2/show/NCT03664804>

As a reminder, HDSA does not control participation in this trial; recruitment is likely to take place through existing doctor/patient relationships. Genentech/Roche has also provided a Clinical Trial Information Support Line at 1-888-662-6728.



2018 CHDI Therapeutics Conference Update: Who said 13 is an Unlucky Number?

Results of the Ionis Huntingtin Lowering Trial Presented at the 13th Annual CHDI Therapeutics Conference in Palm Springs

While many saw the December 11, 2017 press release from Ionis Pharmaceuticals announcing their Phase 1b/2a trial of their antisense oligonucleotide (ASO) targeting huntingtin was successful, researchers had to wait until March 1, 2018 at 13th annual CHDI HD Therapeutics Conference in Palm Springs to see the top-line results from this groundbreaking study. Dr. Anne Smith (Ionis) and Dr. Sarah Tabrizi (University College London) gave a tag-team presentation on the overview of the HTT-Rx study and results. The primary objective of their study was to test the Ionis ASO for safety in HD patients. They found that at the highest dose tested (120mg), the ASO was safe and well-tolerated. As an added bonus, they reported that the drug successfully lowers mutant huntingtin protein in the cerebral spinal fluid, or CSF, in a dose dependent manner. We expect the full dataset to be published in a peer-reviewed journal soon.

Huntingtin lowering approaches are getting a lot of attention lately, but researchers are not putting all their eggs in one basket when it comes to treating HD. Stem cells hold great promise to help us better model HD in a laboratory setting and may themselves serve as therapeutic agents for HD.

A panel of five researchers provided updates on how a variety of different stem cell based approaches for HD. HDSA's own Scientific Advisory Board member, Dr. Leslie Thompson presented her recent work that transplantation of human neural stem cells into an HD mouse model could rescue functional deficits in the animals.

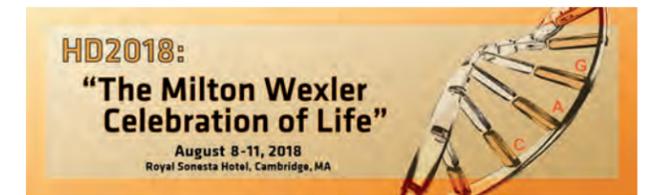
Work stemming from the landmark 2015 Genome-Wide Association Study (GWAS) is also becoming a very attractive area of focus for HD drug hunters. The GWAS study and subsequent follow up studies are identifying that the expression of certain genes other than huntingtin can have a direct impact on the age of onset of HD symptoms. Interestingly, many of these genes appear to be involved in how our bodies repair damage to our DNA. Researchers such as Dr. Ricardo Pinto, 2016 HDSA Berman-Topper HD Career Development Fellow, are working to validate these genes with the hope that the work could launch new drug discovery efforts.

(Left): Robert Pacifici, Chief Scientific Officer of CHDI Foundation presents a check to Louise Vetter, President and CEO of HDSA. Team CHDI took part in a grueling 100 mile Tour de Palm Springs bike race this February. Together, they raised \$38,411 to support HDSA's mission.



(Above): Dr. Sarah Tabrizi presents the results of the Ionis HTT-Rx trial to a standing room only audience at the 13th Annual CHDI HD Therapeutics Conference held February 25-March 1, 2018 in Palm Springs, CA.

HD2018: The Milton Wexler Celebration of Life



The Milton Wexler Celebration of Life is a biennial scientific conference organized by the Hereditary Disease Foundation to assemble the world's foremost Huntington's disease and rare disease researchers. The HD2018 meeting, held in Boston, Massachusetts in August 2018, hosted nearly 250 participants from all over the world who came together to share their latest research findings. Topics ranged from protein structure to modern computational analyses, from established animal models to recent clinical successes. Diverse research questions and methods converged on the common goal of developing novel therapies for HD and other rare disorders.

The opening session featured an interview with a woman affected by HD and her husband, highlighting day-to-day challenges and bringing to light many unanswered clinical questions to motivate ongoing research. A clinical session focused on the development of Ionis-HTTRx (RG6042), the huntingtin-lowering therapy in development by Roche Pharmaceuticals (known as Genentech in the United States) that has shown great promise in early clinical trials. Three keynote talks highlighted some hot topics in recent Huntington's disease research: dysfunction and removal of toxic proteins, DNA repair, and the application of cutting-edge scientific tools. Additional sessions addressed other neurodegenerative diseases like spinocerebellar ataxia, explored non-invasive ways to deliver therapies to the brain, and highlighted new animal models.

"Datablitz" sessions showcased work from the next generation of young researchers, and featured several HDSA-supported Human Biology Project and Berman-Topper Fellows. Speaker invitations are selective, so it was encouraging to note that HDSA's researchers are being recognized by the wider HD science community and requested to participate in this collaborative conference.

HD-COPE Providing Patient and Caregiver Input to the HD Drug Development Process



The Huntington's Disease Coalition for Patient Engagement (HD-COPE) was formed in late 2017 to add quality to all aspects of clinical trials through patient representative input. Patient-oriented input is critical to ensure that future HD therapies meet the needs of the patient community, speed up recruitment and decrease drop-out from clinical trials.

HD-COPE is a global coalition of the leading HD patient advocacy organizations who have united to give families affected by Huntington's disease a direct voice in HD clinical research. By expanding patient involvement beyond participation in trials as a subject, HD-COPE seeks to ensure that clinical research means research carried out 'with' or 'by' members of the community, rather than it being 'to' or 'about' them.

HD-COPE Providing Patient and Caregiver Input to the HD Drug Development Process (continued)

In 2018, members of the HD-COPE traveled to London for training with some of the world's leading HD scientists. In addition, input from the group has been in high demand. Roche/Genentech, Wave Life Sciences, uniQure and CHDI Foundation all met with them during the course of the year to help shape their clinical plans.

The HD-COPE members are the:

- European Huntington's Association
- Huntington's Disease Society of America and
- Huntington's Society of Canada.



(Left): HD-COPE team in London preparing to meet with Dr. Sarah Tabrizi and her HD team at the University College London in February.



(Left): HD-COPE team with uniQure leadership at their headquarters in Lexington, Massachusetts.

Huntington's Disease Society of America Announces Forty-Three 2018 HDSA Centers of Excellence



This February, HDSA announced that forty-three outstanding Huntington's disease care facilities were awarded the designation of HDSA Center of Excellence for 2018.

The 2018 HDSA Centers of Excellence program expanded to 43 Centers from 41 last year. Since 2015 the program has grown from just 20 – a 115 percent increase in four years. The HDSA Centers of Excellence are multi-disciplinary care teams with expertise in Huntington's disease that share an exemplary commitment to bringing comprehensive care.

With the continued growth of the program, HDSA is bringing more 'boots on the ground' to support HD affected families across the United States with care locations in 30 States plus the District of Columbia. In addition, four Centers have partner sites to expand care in Oregon, California, Tennessee, Mississippi, and Alabama. This year, HDSA awarded a total of \$1,264,250 to the Centers of Excellence program, an increase of \$104,500 from last year.

The HDSA Centers of Excellence provide an elite team approach to Huntington's disease care and research. Patients benefit from expert neurologists, psychiatrists, therapists, counselors and other professionals who have extensive experience working with families affected by HD and who work collaboratively to help families plan the best HD care program throughout the course of the disease. Applications to become an HDSA Center of Excellence are open to all clinics in the United States who share HDSA's commitment to high-quality, comprehensive care and access to clinical research. In short, the Centers of Excellence are the epitome of the help and hope that has guided HDSA's mission for fifty years.



**Huntington's Disease Society of America
Announces Forty-Three 2018 HDSA
Centers of Excellence**

Albany Medical College (NY)
Beth Israel Deaconess Medical Center (MA)
Cleveland Clinic (OH)
Colorado Neurological Institute
Columbia Health Sciences/NYS Psychiatric Institute (NY)
Dartmouth-Hitchcock Medical Center (NH)
Duke University (NC)
Emory University (GA)
Georgetown University (DC)
Hennepin County Medical Center (MN)
Indiana University
Johns Hopkins University (MD)
Massachusetts General Hospital
Northwestern University (IL)
Ochsner Health System (LA)
Ohio State University
Rush University Medical Center (IL)
Stanford University (CA)
University of Alabama, Birmingham
University of California, Davis Medical Center
University of California, Los Angeles
University of California, San Diego
University of California, San Francisco
University of Colorado
University of Florida
University of Iowa
University of Louisville (KY)



**Huntington's Disease Society of America
Announces Forty-Three 2018 HDSA
Centers of Excellence**

University of Nebraska Medical Center
University of Pennsylvania
University of Pittsburgh Medical Center (PA)
University of Rochester (NY)
University of South Carolina School of Medicine
University of South Florida
University of Tennessee – Memphis
University of Texas Health Science Center- Houston
University of Utah
University of Vermont, Frederick Binter Center
for Parkinson's Disease & Movement Disorders
University of Virginia
University of Washington (WA)
University of Wisconsin
Vanderbilt University Medical Center (TN)
Virginia Commonwealth University
Washington University School of Medicine (MO)
•
LEVEL 1 PARTNER HD CLINICS
Kaiser Permanente (CA)
Oregon Health Sciences University
Cole Neuroscience Center, University of Tennessee Medical Center
University of Tennessee, Erlanger Medical Center
University of Mississippi Medical Center
University of South Alabama

Yellow = New COE for 2018

A Special Thanks to the HDSA Scientific Advisory Board

We are grateful to the Scientific Advisory Board (SAB) members who so generously donate their time and talent as volunteers! The HDSA SAB is comprised of leading experts in their fields. The role of the SAB is to provide scientific review of research proposals to ensure that the research programs at HDSA are scientifically sound, pertinent and provide a high impact to the HD research community. Additionally, the SAB advises the HDSA Board of Trustees and management on a range of issues influencing the scientific direction of the Society. The current members of the HDSA SAB are:

- Michelle Gray, PhD, Assistant Professor, University of Alabama-Birmingham (Chairwoman)
- Neil Aronin, MD, Professor and Chairman of Endocrinology and Metabolism, University of Massachusetts Medical School
- Susan Browne, PhD, Director, Teva Pharmaceuticals
- Jang-Ho Cha, MD, PhD, Global Translational Medicine Head, Neuroscience, Novartis Institutes for BioMedical Research
- Kenneth Fischbeck, MD, NIH Distinguished Investigator, Chief, Neurogenetics Branch
- David Howland, PhD, Director, CHDI Foundation
- Blair Leavitt, MD, PhD, Professor, University of British Columbia
- Marcy MacDonald, PhD, Professor, Harvard Medical School, Massachusetts General Hospital
- Melissa Moser, Community Representative
- Harry Orr, PhD, Professor, University of Minnesota
- Leslie Thompson, PhD, Professor, University of California at Irvine



Shown (left to right):
Leora Fox, PhD,
Harry Orr, PhD,
Neil Aronin, MD,
Kurt Fischbeck, PhD,
Susan Browne, PhD,
Louise Vetter,
George Yohrling, PhD,
David Howland, PhD,
Leslie Thompson, PhD,
Blair Leavitt, MD, PhD,
Michelle Gray, PhD

 Huntington's Disease
Society of America

HDSA 34

BOSTON

■ 34TH ANNUAL ■
HDSA CONVENTION
JUNE 27-29, 2019

For More Info Visit www.HDSA.org/convention

Huntington's disease (HD) is a fatal genetic disorder that causes the progressive breakdown of nerve cells in the brain. It deteriorates a person's physical and mental abilities often starting in their prime working years. Currently, there is no cure for Huntington's disease.

Every child of a parent with HD has a 50/50 chance of inheriting the faulty gene that causes Huntington's disease. Today, there are approximately 30,000 symptomatic Americans and more than 200,000 individuals at-risk of inheriting the disease.

Our Mission: To improve the lives of people with Huntington's disease and their families.

Our Vision: A world free of Huntington's disease.

The Huntington's Disease Society of America (HDSA) is the premier nonprofit organization dedicated to improving the lives of everyone affected by HD. From community services and education to advocacy and research, HDSA is the world's leader in providing help for today and hope for tomorrow for people with HD and their families.



505 Eighth Avenue, Suite 902
New York, NY 10018
1-800-345-HDSA
www.hdsa.org