Huntington Study Group (HSG) Conference 2024 – Day 3

Read updates from clinical trials and scientific research on Huntington's disease from Day 3 of the 2024 Huntington Study Group conference.


By Dr Leora Fox and Dr Sarah Hernandez **November 13, 2024**

Edited by Dr Sarah Hernandez

We're back for the 3rd and final day of the Huntington Study Group (HSG) Conference. You can also read updates from day1 and day 2. They saved the best for last - family day! Follow along for our last day of HSG!

Demystifying research

Family Day is opening with a talk from Dr. Martha Nance, a neurologist from the University of Minnesota. This "Demystifying Research" session will walk through the basics of research studies, participation, and how science leads to treatments. She reminds us of the benefits and challenges of working on HD research. For example, it's caused by a single gene and has a wonderful, engaged participant community, but it's rare, complex, and affects the brain.

HSG 2024 was held in downtown Cincinnati, bringing Huntington's disease research and clinical trial updates to the Buckeye State.

Now Martha is revisiting the basics of genetics, how our genes are composed of a letter code that we represent with the letters A, C, T, and G. HD is caused by a change to a single gene called huntingtin, abbreviated HTT.

Within the huntingtin gene, everyone has repeats of the letters CAG - most people have between 10 and 26. Those with 40 or more will go on to develop HD. 36-39 repeats may or may not lead to HD symptoms in someone's lifetime. CAGs of 27-35 can sometimes lead to longer repeats in the next generation - so the parent might not have HD, but their children could inherit more repeats and develop symptoms. It's important to note that none of these ranges are absolutes; other genes and environmental factors can affect HD and its onset.

Martha reminds us that genes (DNA) can be made into genetic copies (RNA) which are used to make the cell's building blocks (proteins). She also lists the different types of research approaches that can be productive for learning more about a disease and developing treatments.

Observational studies and surveys help researchers understand how genetics, biology, and symptoms connect, or how symptoms affect people's lives. Examples are MyHDStory, JOIN-HD, CHANGE-HD, and ENROLL-HD.

Other studies focus on the biology of HD to study the "downstream effects" - what happens to brain cells because of a genetic change, like inflammation, damage, and dysfunction, and how to help clean up any cellular "trash", like unused protein fragments or toxic proteins.

Martha talks about some of the approaches to treating HD, like targeting the underlying CAG repeats, addressing dysfunction in cells, lowering huntingtin, and focusing on symptoms to improve quality of life.

She discusses some of the nuances of huntingtin lowering and the many approaches being explored. Designing drugs to "stick" to the RNA message, focusing on one or both copies of huntingtin, how to deliver these potential treatments - there are many ways to address these challenges with novel science.

She also lists the different drugs already available for helping with HD symptoms, and mentions new ideas that have gone from basic research to drug development, like trying to slow down the gradual expansion of CAG repeats that can happen in brain cells over time (somatic instability).

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Martha is now talking about how we measure the progression of HD and determine eligibility for trials. One example is a CAP score, a formula that takes into account CAG repeat size and age to determine an "expected" age of onset. This of course varies by individual.

She also touches on historical and current ways to separate HD into "stages." For research purposes, today's scientific and clinical community uses the HD-ISS.

Bridging research to treatment

The next session is a panel discussion and Q&A on clinical research participation, involving patients, researchers, doctors, and other community members who are here to speak about their experiences and answer questions about the path from research to treatment.

Topics that came up included perseverance despite setbacks, learning from clinical trials that didn't end as expected, frustration with eligibility criteria, and contributing to research through participation in observational studies.

All of the panelists encouraged the audience to get involved with research and with their local communities in any way that they can, whether that's a study of a medication, an observational trial, or simply connecting with others in the community to spread awareness and receive support.

HD biology and basics

The afternoon session begins with Dr. Victor Sung, a neurologist (and community advocate) at the University of Alabama who focuses on HD. He's speaking about HSG's work in the HD space from research basics to the clinic.

Vendors were present in an exhibit hall, where companies could showcase how they hope their medicines will work to treat Huntington's disease. Here, Spark Therapeutics shows deep brain structures affected in HD.

He's got a great analogy for thinking about DNA repair and lengthening of CAG repeats - the two strands of DNA act like a stuck zipper that gets off track, mismatching with the opposite side. The attempt to fix the lopsided zipper adds even more CAGs by accident.

We've heard a lot about the biomarker NfL, which is released from damaged brain cells and goes up over the course of HD. Victor likens the release of NfL to a tornado, where things get flung around - the more damage, the bigger the tornado.

He also revisits the HD-ISS staging system and how it is helping to design trials to slow down the progression of HD. Having a way to better define the pre-symptomatic and very early stages of HD will be an asset when deciding when to treat.

He notes that the field has evolved from vitamins (and even blueberries!) as experimental treatments, to a wide variety of genetic and biology-based approaches in just a decade. The field welcomes researchers to "throw their hats in the ring" and attack the challenge of HD from all angles.

Victor also reminds us that 2024 is the first time we've had four positive press releases so close together about milestones in huntingtin-lowering drug development (from Wave, uniQure, PTC Therapeutics, and Skyhawk).

Launching hope from the lab to the clinic

Our next speaker is HDBuzz's own Dr. Sarah Hernandez! Her talk is about hope in research, from the clinic, to experiments, to ideas. She's first sharing her own family's HD story and how far we've come from before the discovery of the HD gene to today.

Sarah's family background and discovering the story of Nancy Wexler's Gene Hunters led her to pursue a PhD and to study HD. She now heads up "all things science-y" at the Hereditary Disease Foundation, an HD research-focused nonprofit started by Nancy Wexler.

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She revisits the rapid-fire good news from the summer of 2024, which HDBuzz covered following press releases from Wave, uniQure, PTC Therapeutics, and Skyhawk. Sarah encourages a bird's-eye view of this positive news, which together is starting to show that HTT-lowering could become a successful treatment approach. She reminds us that there are even more HTT lowering strategies in the works, from companies like Latus Bio, Incisive Genetics, Atalanta Therapeutics, and Alnylum Pharmaceuticals.

She also mentions approaches to stopping the expansion of CAG repeats, from companies like Rgenta and LoQus23, or stem cell replacement therapies, in development by Neuexcell, Sana Biotechnology, and universities like UC Irvine and UC San Diego. Sarah also finds hope in basic research, like new tools to zoom in on single brain cells, and efforts to improve delivery of drugs to the brain through the nose, or using ultrasound!

Sarah shouts out the many HD organizations dedicated to care, support, research, and education in the US, like HDF, HDSA, HDBuzz, HDYO, HSG, HD-Reach, Help4HD, and more. She also reminds us that there is ongoing research into improving quality of life for people

with HD, through studies on sleep, lifestyle choices, and equity in research and care. A hopeful talk indeed!

Igniting hope for HD

The next session is a panel discussion on hope, from HD community members on their personal stories about what inspires them to keep pushing for treatments and cures for HD.

Erin Patterson, author of Huntington's Disease Heroes, shared her personal history with the disease, being gene positive as a caregiver for her father. She finds hope in the grace with which her father faces HD. She says even if there isn't a treatment in time for her, she knows that she'll be ok because of the way her dad approaches life.

Charles Sabine, OBE, founder of the HiddenNoMore Foundation, relays the hope that he helped foster when he orchestrated a meeting between Pope Francis and HD families. He made a movie about this encounter, called Dancing at the Vatican. Charles recently shared his story in a TED talk.

Dr. Karen Anderson shared that she gets hope from the HD families that come to community events like HSG. This wasn't the case when she first got into the HD field! She's worked with HSG on MyHDStory, which is an online research platform to connect people affected by HD, to better understand the needs of those living with HD, and break down barriers for clinical trial participation.

That's all from us for HSG 2024! HDBuzz had a great time sending live updates to the community and we hope you enjoyed the coverage!

The authors have no conflicts of interest to declare. For more information about our disclosure policy see our FAQ...

GLOSSARY

clinical trial Very carefully planned experiments designed to answer specific questions about how a drug affects human beings

observational A study in which measurements are made in human volunteers but no experimental drug or treatment is given

inflammation Activation of the immune system, thought to be involved in the HD disease process

therapeutics treatments

CAG repeat The stretch of DNA at the beginning of the HD gene, which contains the sequence CAG repeated many times, and is abnormally long in people who will

develop HD

biomarker a test of any kind - including blood tests, thinking tests and brain scans - that can measure or predict the progression of a disease like HD. Biomarkers may make clinical trials of new drugs quicker and more reliable.

somatic relating to the body

HTT one abbreviation for the gene that causes Huntington's disease. The same gene is also called HD and IT-15

RNA the chemical, similar to DNA, that makes up the 'message' molecules that cells use as working copies of genes, when manufacturing proteins.

NfL biomarker of brain health
