Huntington's disease therapeutics conference 2022 - Day 3

Check out research updates from Day 3 of the 2022 HD Therapeutics Conference #HDTC2022

By Dr Sarah Hernandez, Dr Leora Fox, Dr Rachel Harding, and Joel Stanton

March 08, 2022 **Edited by Professor Ed Wild**

Good morning! Today is the 3rd and final day of the #CHDI HDTherapeutics Conference in Palm Springs. Follow our feed today to get live updates!

Biomarkers and clinical tools

The fourth session of research talks will cover biomarkers and clinical tools for diagnosing, tracking, and treating HD. It is being introduced by Dr. Edith Monteagudo of CHDI and Dr. Niels Skotte, of University of Copenhagen.

The PET ligand is useful for lighting up the cortex and striatum

Biomarkers Task Force!

The first talk is by Dr. Cristina Sampaio & Dr. Robert E Pacifici, both from CHDI. They'll be discussing CHDI's Biomarker Task Force, focused on developing a strategy for moving biomarkers for HD forward.

Biomarkers are critical for drug development. They allow researchers to track how patients are progressing as their disease advances. They'll also be critical as the field moves forward

with treatments, because they'll allow researchers to determine if patients are getting better. CHDI and other organizations are committed to making biomarker data (and many other types of data) available in a way that can benefit the entire HD research and family community, not just an individual company. CHDI is focused on advancing biomarkers related to imaging (such as MRI scans), blood, and spinal fluid.

One molecule that didn't turn out to be a greatbiomarker in blood is expanded huntingtin. Even though it's directly involved in causing HD, it turns out it doesn't track well with disease progression. It seems like imaging is a strong bet in the biomarker field. Identifying biomarkers that can be assessed using imaging would give researchers a non-invasive way to continually track HD patients over time. Another key component of defining biomarkers is to find those that change with very early HD progression. This will allow researchers to start monitoring disease at the very earliest stages, before symptoms appear - a time when some think treatment needs to begin.

The lengthening of CAG repeats in some cells over time, known as somatic repeat expansion, is not only gaining interest because of the effects it has on age of disease onset, but it may also be useful as a biomarker. There are also ways to take advantage of "wearables" - digital devices, like watches, that people with HD can wear to gather lots of data in real time. These devices could track movement, sleep habits, and other metrics. CHDI has a 2-year goal for defining some of these important biomarkers and is eager to collaborate with the entire HD research community for this important project.

Biomarker discovery - the future is bright!

The next speaker is Dr. Jim Rosinski from CHDI. He'll be sharing his work using large datasets that will help profile people with HD for biomarker discovery. He feels "the future is bright!"

We are in a new age of data where scientists are able to measure thousands of changes in genetic messages and protein over time in many individuals. Using powerful analysis techniques, sorting through this data can be very valuable for drug development. Doing this requires a strong "pipeline," from being able to collect blood and spinal fluid samples from many people with HD, to developing the skills and software to understand the data. This is where observational studies like Enroll-HD and HDClarity come into play.

Samples donated by HD families who participate in these studies are essential for the many different types of analyses that can be made, by looking at how genes turn on and off, and examining changes in levels of different forms of RNA and protein. Looking at changes in protein levels across a brain area, organism, or group of people with a disease is known as proteomics. Using spinal fluid samples donated through the HDClarity study, researchers can link clinical data from Enroll HD with protein changes. Dr. Rosinski shared some exciting

preliminary data tracking many proteins in a large group of HDClarity participants. Looking at each individual protein alongside clinical data will help define biomarkers for disease progression and identify routes for drug design.

One biomarker that's been defined in HD is neurofilament light - NfL. It turns out, it's a really great biomarker! Dr. Rosinski found that just looking at this one protein can predict HD status! Wow! They also identified a few other proteins that are predictive of where a person might be in their HD symptoms. Ultimately, combining these findings could power more individualized care and treatment in HD.

The future is bright! Instead of scientists talking about IF we'll have a treatment for HD, they're focused on WHEN we get a treatment, we need biomarkers that will help us track how patients are doing. We've come a long way!

Next up is Dr. Aline Delva from KU Leuven. Dr. Delva will be describing her work using a type of imaging called PET. We recently wrote about it here: https://en.hdbuzz.net/319

PET ligands allow scientists and clinicians to visualize things inside the body or brain. This particular ligand is designed to stick to huntingtin and make it light up in a brain scanner, so levels can be tracked over time, and eventually during treatment. Dr. Delva is sharing new data from a human study where the PET ligand sticks to synapses, connection points between brain cells, to track their health over time, especially in areas of the brain that are most vulnerable to HD.

It appears that these PET ligands can detect changes even in premanifest HD patients! This is great news because it gives researchers a tool to determine if a treatment is making a patient better before there are even noticeable HD-related changes. Next, Dr. Delva described her work looking at PET ligands that examined the huntingtin protein itself. The goal of this study was to determine if huntingtin could be used to track disease progression using PET technology. After testing the PET ligands in mouse and primate models, they did a small study in humans, and were able to figure out the best one to use, and find a safe and effective dose.

The results from the study showed that the PET ligand is useful for lighting up the cortex and striatum - brain regions that are particularly vulnerable in HD. While this is expected, it's exciting because it shows that this tool could work well for studying HD! A major advantage of these PET ligands is that they are examined using noninvasive, painless imaging techniques - similar to an MRI. So they can be done relatively easily and frequently on HD patients to track disease progression. All great qualities for a biomarker!

Next steps will be to expand these studies by testing the PET ligands in a larger group of people with HD. Such tools are now widely used and accepted in the Alzheimer's disease field, which sets a good precedent for their development in HD.
We're taking a break, but will be back shortly after refueling with some coffee! Stay tuned!

Digital Monitoring of HD

Up next is an exciting update from Drs. Peter McColgan and Jonas Dorn from Roche are here to provide an update from the GENERATION-HD1 trial of Tominersen. Appropriately, Dr. McColgan begins with an acknowledgement of the disappointment of HD families and thanks them for their incredible contributions to these studies.

The specific update for this talk is a discussion of some results from the digital monitoring platform - digital tools used to track HD progression in participants in Roche's various studies with tominersen. The trial participants had a smartphone to track measurements of HD-relevant symptoms, such as movement and cognitive changes. These are do-it-at-home versions of the kinds of tasks that physicians use to track HD in clinics.

Data was collected from 784 patients, with more than 350,000 days of tests recorded. That's a lot of information to process! Each participant spent 30-60 minutes per day, on average, conducting tasks on their phones. Many of the tasks reveal clear changes between HD patients and controls, including a speeded tapping task. This requires participants to quickly and repetitively tap a button, which becomes more difficult as HD progresses.

Because at-home testing is new, the team compared results for tests done at home, then repeated in a formal clinical setting. This resulted in excellent consistency - so collecting data at home seems feasible. Surprisingly simple tasks - including the speeded tapping - show very clear worsening during the course of the trial. This suggests these measures could be useful for future trials, and potentially save participants and families having to do so much in a clinic.

Dr. Dorn explains that there are some complexities in the digital data. For example, people who were doing worse on some tasks were more likely to stop completing the tasks early. Perhaps because those are the people with more severe symptom progression? For some of the tasks, including a "draw a shape" task, trial participants were clearly learning how to do the task faster. This is called a "practice effect," and it makes it tricky to generate useful data over a long time for those tasks.

A lot of work remains to digest these huge sets of data from the participants in Roche's tominersen trials. Expect to hear more from Roche as they continue to dive into the data.

In the next talk, Dr. Sarah Tabrizi (UCL) and Dr. Jeff Long (University of Iowa) will talk about the development of a staging system to help better define where a person is in their HD journey. This will be important for planning trials in people who haven't yet shown symptoms.

Staging systems are very important for grouping people with similar disease characteristics so they can be properly treated based on their current symptoms. This has been very helpful in fields like cancer treatment. HD needs this kind of staging system because it is still mainly diagnosed based on chorea, which can occur much later than other thinking and

mood changes. By analyzing tens of thousands of data sets from people with HD, a large consortium of researchers has been able to create a system with stages 0 through 3. This demonstrates the power of participating in studies like Enroll-HD.

At the scale's most basic level, 0 means the person has the gene but nothing else has changed, 1 is when biomarker changes can be detected (like in blood or brain images), 2 is changes measured in clinical tests, and 3 is when HD begins to affect day to day function.

Creating a scale for use by the entire clinical and research community is important for ensuring that care and research are consistent and we can learn as much as possible from every trial. The research community is now building powerful new tools around this existing scale. One example is a program to help determine whether an individual is a good fit for a clinical trial by taking into account their CAG repeat number, their age, and the results of many tests and brain images.

Roche Discussed their digital monitoring platform for HD

Combining and analyzing many measurements - brain images, tests of movement and thinking, shifts in abilities at home and work, potential changes in blood and spinal fluid - is a very powerful way to track progression and determine response to a drug. As with many aspects of HD, there can be a lot of variability within the four stages, and researchers are tackling ways to further define them based on things like age, genetics, and findings from exams in the clinic.

This is an even more refined way to help recruit the right people for trials than current methods, which use clinical scores (you may have heard of CAP or PIN). This conference is a great venue for presenting novel tools like this because so many players in HD research are present.

It's lunch time for us here in sunny CA. We'll be back after the break to share exciting updates from various HD clinical trials. Tune back in soon!

Clinical and Human data

We're back for the last session of the conference! We'll be sharing exciting talks focused on recent clinical trials.

Up first are Dr. Jamie Hamilton and Dr. Mark Guttman from University of Toronto who will be introducing this clinical session. Dr. Guttman is acknowledging the resilience of the HD community over the past few years and the continued hope to be found in clinical trials.

Tominersen in the spotlight

The first talk this afternoon is from Dr Peter McColgan and Dr Lauren Boak from Roche. They will be giving us an update on tominersen, the huntingtin-lowering drug under investigation in the Phase III GENERATION HD1 study. Lauren is kicking things off - she has shared the slides of the Roche presentation through this link if you want to follow along or look at these later: https://bit.ly/3sH1faG

Roche has several approaches for lowering huntingtin. They're not just using tominersen to lower total huntingtin, but they also have programs to specifically reduce levels of the expanded huntingtin copy and other tools they're exploring. It's encouraging to hear that Roche is committed to HD. But today Lauren will just be focusing on what they learned in GENERATION-HD1 with their tominersen program. The final analysis of the data from this trial is ongoing.

There are in fact 3 different trials Roche is conducting where data analysis is not yet complete - the Natural history study, GEN-PEAK study and GENERATION HD1 but today the focus will be on the halted phase 3 GENERATION HD1 study. Lauren is now recapping the data from animal models which informed the trial. These were used to determine the dose of tominersen in the GENERATION HD1 study - 120 mg every 8 or 16 weeks which Roche predicted would lower huntingtin by 25-45%.

Now Peter will tell us about the analysis they've done so far of the data from GENERATION-HD1. Levels of expanded huntingtin were reduced in both the 8 and 16 week groups as predicted. This suggests tominersen was engaging the target. However, when they looked at certain scores that measured overall how participants were doing, people who were treated with tominersen did worse than people who were treated with placebo, particularly when treated every 8 weeks.

Peter shares that more adverse events (side effects) were seen for folks who got the drug more frequently, fitting with the trend we see with the overall scores for patients in the different drug groups. Our previous session taught us a lot about biomarkers for HD. One biomarker we learned about was NfL. Unexpectedly, Roche found that NfL levels went up after tominersen dosing. They're still not sure why this is.

Tominersen lowered huntingtin levels but the trial did not reach its endpoints and did not improve symptoms in patients. Scientists are now working hard to understand why.

Roche have been looking at the data collected from patients in the trial after they stopped taking tominersen. 84% of patients stayed in the trial even after dosing was halted which is very helpful for Roche scientists to try and figure out what happened. The number of

patients that stayed in the trial following the dosing halt is a true testament to HD patients. From this it's evident that the HD community is passionate about participating in research and contributing to finding a treatment.

Changes in brain structure were reported for patients in the trial with bigger changes seen for patients who took the drug more frequently. Peter suggested there may be some recovery of the brain structure after dosing was stopped, but analysis of this data is ongoing. Roche scientists used a common clinical measurement called UHDRS which looks at lots of different signs and symptoms of HD. Looking at this score after dosing was halted, no significant difference was seen between people who did or did not receive the drug in the trial.

A similar pattern is seen in another clinical measurement called total functional capacity, which measures daily function in activities at home and work. There was no statistically significant difference between patients after dosing was stopped. Roche wanted to divide people in the trial into groups to see whether severity of symptoms might have played a role in how they responded to the drug. This was done after the trial was designed, known as a post-hoc analysis - so all results must be taken with a pinch of salt.

As we previously wrote, Roche thinks that younger participants who had less advanced symptoms of HD might have done somewhat better in the trial than older more advanced ones. https://en.hdbuzz.net/316

BUT! This is not a statistically significant finding and is the subject of heated debate by scientists in the field. Roche have sliced and diced the data in lots of different ways to work out if the drug was beneficial for a subgroup of patients. Another factor is how much drug the patients were exposed to which they work out by measuring the drug in spinal fluid.

Peter is now sharing data which suggests people in the trial exposed to less of the drug might have fared slightly better, but, again, there are not enough people to power these statistical analyses. A lot of folks working on making medicines for HD will learn from this trial to help inform the design of future clinical trials, including which types of drugs, dosing, and delivery might work best. The data seem to indicate that younger less advanced HD patients might be better candidates for huntingtin lowering, and that lower drug doses may be more beneficial. This doesn't mean it couldn't help a wider population, but it's useful for designing the next trial.

In a new phase II study, Roche plans to enroll younger people with HD, with less advanced symptoms, and to use 2 new doses. These were not disclosed in the talk, but they would be lower than the doses used in the GENERATION-HD1 study. Peter is now talking us through how this younger cohort fits into the new HD-ISS staging which was described in the talk by Prof. Tabrizi earlier in the day. This new system will be important to help define exactly which people might benefit from huntingtin-lowering drugs like tominersen.

The Q&A is lively and technical! No details have been shared yet about the potential Phase II trial, but it will once again rely on the strength and enthusiasm of future participants and their families.

Gene therapy for early stage HD

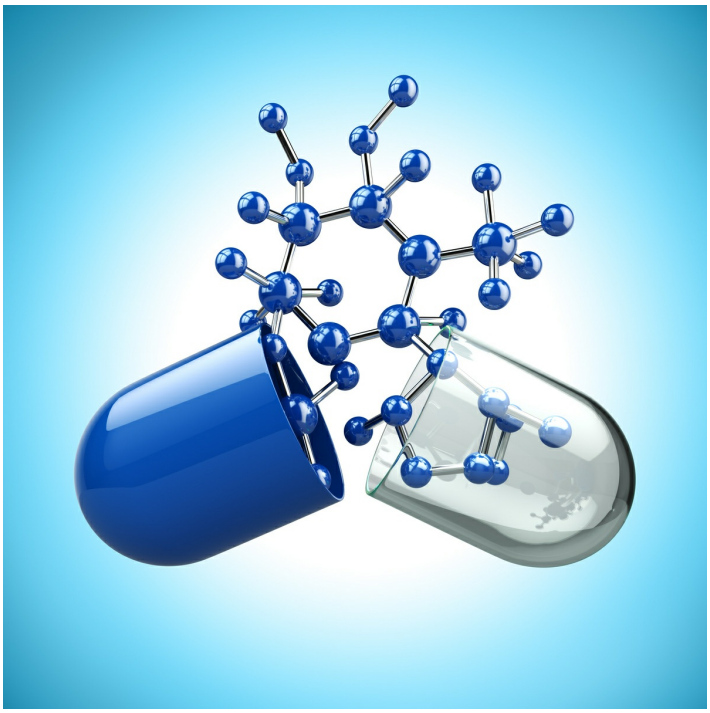
Next up is neurosurgeon Dr David Cooper from uniQure who will give us an update on the gene therapy trials, HD-GeneTRX-1 and HD-GeneTRX-2, for their one shot drug called AMT-130 which they are testing to treat early-stage HD. Dr. Cooper describes the structure of the drug - a harmless virus particle filled with instructions to make a set of RNA that leads to the lowering in of the Huntigntin gene into regions it is injected into. In this case, deep brain structures.

UniQure did a lot of studies of their drug in a range of different HD models including cells in a dish as well as monkeys and pigs. These studies informed their studies now underway in people with HD. The deep parts of the brain impacted most in HD - the “striatum” - are tricky to reach, and hard to infuse with uniQure’s viral particles. Decades of work have led to procedures for infusing brain structures to maximize how much is treated with drug.

AMT-130 lowers total huntingtin - the normal and the expanded forms of the protein. uniQure’s goal isn’t 100% reduction of huntingtin, but to significantly lower levels, for life, after a single injection. There are two studies - one in Europe and one in the US, with 15 and 26 patients respectively. There will be patients with low dose, higher doses, or placebo.

The primary objective of both studies is to establish whether the treatment is safe and tolerated. Additional objectives include trying to understand if - as predicted by the mouse work done - the therapy is persistent for years after a single injection As with many trials, there are limitations in who can participate in the study. For example, participants must be able to handle anesthesia. Given the ongoing pandemic, this means that people must be 8-12 weeks past any COVID infection so omicron has made things more tricky.

The current goals are to include people with at relatively early stages of HD, and people whose deep brain regions are preserved enough to safely inject them with the drug. This is the first gene therapy for HD, and the first time anyone has done as many brain injections as uniQure is planning to do - 6! This gives them the best chance to cover the whole striatum with a single surgical procedure. Each surgery is reviewed by a team of neurosurgeons, who must all agree that the planned surgeries are likely to be safe.



PTC-518 And Branaplam are oral HTT lowering agents

Image credit: Maxx Studio

No two brains are exactly the same, so each patient's brain scans have to be carefully analyzed before surgery. A harmless contrast agent is injected along with the AMT-130 which helps the surgeons see exactly where the injected material spreads to. This allows the surgeons to confirm successful delivery of the drug across the entire targeted region. In the first 4 patients treated, all left the hospital the next day without any serious complications. Similarly, no bad changes were observed in brain imagery during this first year after the patients were treated with AMT-130.

Despite the challenges posed by the pandemic, the US cohort is nearly completely treated, and the first few patients in Europe have been treated. UniQure are now fine-tuning the surgical procedures which are needed to inject the AMT-130 into the brain, to make sure that the drug is going to the right regions every single surgery and that the surgery is not taking too long to do. What they've learned about the surgical procedure will help inform a planned third trial group (cohort) in the US in the near future.

We're taking a quick break before we head into the final talks of the conference, covering updates from some of the other clinical trials underway right now.

Innovations that led to SELECT-HD

First up after the break is Dr. Michael A Panzara from Wave Life Sciences. Dr Panzara will be telling us about the phase 1b/2a clinical trial called SELECT-HD, which is testing an expanded huntingtin-specific lowering therapy. Wave makes anti-sense oligonucleotides or ASOs which target the huntingtin "message" molecule in the cell, to lower levels of huntingtin protein. This is similar to the approach Roche took with Tominersen except their drug only targets expanded huntingtin.

PRECISION-HD1 and PRECISION-HD2 were trials testing two ASOs against expanded huntingtin. Although the drugs were safe, they did NOT lower huntingtin as expected. Both trials used drugs which were specific to expanded huntingtin as they target genetic signatures called SNPs (“snips”) - parts of genetic code that differ between gene copies - only found on the expanded huntingtin gene.

Wave have since developed another ASO drug called WVE-003 that targets a different SNP and has updated chemistry. This drug can be tested in some of the HD animal models as they also have the SNP targeted by WVE-003 and the results so far are promising. Wave is hopeful that this new approach will allow for more effective lowering of harmful huntingtin at lower doses of ASO, while leaving the healthy form of huntingtin intact. It is being tested now in a new trial called SELECT-HD.

When Wave tested their new and (hopefully) improved drug in HD mouse models, the drug lowered levels of expanded huntingtin by at least 50% and this effect was sustained for about 3 months. The scientists at Wave also checked if unexpanded huntingtin was affected by this new drug. HD mouse models treated with the drug did not have any significant change in their unexpanded huntingtin levels - good news! Wave also tested their drug in monkeys to see how it dispersed in the brain. They wanted to ensure that all of the important regions would get a sufficient dose of the drug - these data were also very encouraging.

In order for people with HD to be enrolled in the SELECT-HDclinical trial, they must have the SNP which the drug targets, so Wave have developed a diagnostic test to check thiss. Wave are designing the trial to be “adaptive” - this means that based on the data, they might change the dose or frequency of dosing of the drug while the trial is ongoing. But these changes won’t affect results since they’re being planned for in the beginning.

Deep brain stimulation in HD

Next up is Dr. Jan Vesper, from Heinrich Heine University in Düsseldorf to discuss HD-DBS. This is a proposed pilot trial for deep brain stimulation in people with HD. Deep brain stimulation is a procedure that uses electrical signals to stimulate the brain. A pilot trial was conducted nearly 10 years ago now which showed that some HD movement symptoms were reduced when people with HD were treated with deep brain stimulation.

A much larger trial called HD-DBS was then run across multiple sites around the world, which looked to measure lots of different clinical signs and symptoms of HD in participants who received the treatment or the placebo. To ensure participant safety, the inclusion and exclusion criteria were extensive, so it took a pretty long time to recruit people for the trial, but eventually 48 participants were recruited from Germany, Austria, and France, and about half received the placebo treatment. All data were collected in January of this year and analysis is ongoing. Today we will hear some of the preliminary findings.

For both groups in the trial, those treated with the deep brain stimulation and those who received placebo, some people improved but others got worse. So it doesn't seem that this treatment is especially promising for folks with HD. Some patients did improve in the trial but its not clear why this might have been and there were no significant differences between those who received the treatment or placebo. Despite the disappointing outcome, researchers developed and refined surgical techniques in this trial that could be applied to future studies in HD and other diseases.

Now we are onto the development of oral huntingtin-lowering drugs! Two companies are working on these treatments for HD. Presenting first is Brian Beers, from PTC Therapeutics. He will be telling us about PTC518, a huntingtin lowering drug which can be taken by mouth.

PTC518 - Update!

In mouse models of HD, PTC518 has been shown to effectively lower the levels of total huntingtin and preclinical data looked very promising. PTC tested their drug in healthy volunteers and showed the drug was having the desired genetic effect of messing with the huntingtin recipe, known as RNA splicing. They were also able to determine a safe and tolerable dose of PTC-518. The scientists also looked at what happened when they stopped treating with the drug and showed that the effects could be rapidly reversed. This is great news if the data suggests dosing of the participants need to be stopped for any reason.

They are sharing the new study design, which will involve two groups of participants who will get either a low or a high dose for 12 weeks. 162 patients will be recruited in this trial which they aim to begin in the first quarter of 2022. PIVOT-HD will be the new phase II clinical trial, which aims to demonstrate that PTC518 works to reduce huntingtin levels in people with HD and they will track important biomarkers to see how the drug is working. PTC will look at the safety of the drug as well as changes to the levels of huntingtin protein, the biomarker NfL, different clinical measurements of HD signs, and symptoms.

The trial is about to get going in the US, UK, France, Germany and Australia. Hopefully we will be hearing updates from PTC soon!

Branaplam - an oral HTT lowering molecule

The final talk of the conference will be from Dr Beth Borowsky, from Novartis Pharmaceuticals. We will hear some updates about the VIBRANT-HD, a phase 2b trial investigating the huntingtin lowering drug, branaplam.

Dr Borowsky explains how taking a drug by mouth has a lot of benefits for patients compared to other therapies delivered by more taxing routes, such as spinal injections or brain surgery. A pill can also work on the whole body, rather than just the brain, and the effects can be reversed!

Branaplam was originally developed for a fatal childhood disorder called SMA, but in an amazing twist of science was found to also lower huntingtin, so Novartis redirected their efforts towards HD. Branaplam targets machinery which processes genetic messages, called splicing machinery. Changing how messages are spliced can affect how much protein is made from the message, so drugs that modify splicing can change the levels of proteins in the cell.

In a phase I study, the drug was tested for the first time in adults to figure out a safe amount and frequency of dosing. This was important because branaplam was developed to treat SMA in children. VIBRANT-HD is a phase IIb study which will test branaplam for the first time in adults with HD to work out what dose of the drug needs to be administered to lower huntingtin.

Branaplam is given as an oral liquid that patients drink once per week. Different patients will be given different doses so Novartis can work out what dose will work best for a second phase of the trial.

Lots of clinical measurements will be collected from participants in the trial, including levels of various biomarkers, like huntingtin and NfL. Recruitment for this trial is underway and hopefully we'll hear updates on how the trial is proceeding soon!

That's all folks! Thanks so much for following along. You can read our daily reports for the CHDI conference at https://hdbuzz.net

---

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

GLOSSARY

Total Functional Capacity A standardized rating scale for function in HD, used to assess capacity to work, handle finances, perform domestic chores and self-care tasks

statistically significant Unlikely to have arisen by chance, according to a statistical test

deep brain stimulation direct stimulation of the brain using electrical impulses through tiny wires.

huntingtin protein The protein produced by the HD gene.

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

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

anti-sense the half of the DNA double-helix that is mostly used as a backup, but

sometimes produces message molecules

phase III The phase in the development of a new treatment where clinical trials are conducted using many patients, to determine whether the treatment is effective

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.

splicing the cutting up of RNA messages, to remove non-coding regions and join together coding regions.

placebo A placebo is a dummy medicine containing no active ingredients. The placebo effect is a psychological effect that causes people to feel better even if they're taking a pill that doesn't work.

primate a group of mammal species including monkeys, apes and humans

somatic relating to the body

chorea Involuntary, irregular 'fidgety' movements that are common in HD

cohort a group of participants in a clinical research study

UHDRS A standardized neurological examination that aims to provide a uniform assessment of the clinical features of HD

ASOs A type of gene silencing treatment in which specially designed DNA molecules are used to switch off a gene

magnetic resonance A technique using powerful magnetic fields to produce detailed images of the brain in living humans and animals

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

single nucleotide polymorphisms a single-letter spelling difference in a gene. SNPs, pronounced 'snips', are common and most don't change the function of the gene.

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