Hats off to brain donors on Brain Donation Awareness Day

May 7 is Brain Donation Awareness Day. Today we highlight the selfless donation that many HD families have made, sending our gratitude, sharing research updates made with those precious brains, and detailing resources for brain donation.

By Dr Sarah Hernandez | May 07, 2024 | Edited by Dr Rachel Harding

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If you're a frequent reader of HDBuzz, you may have noticed that our articles increasingly thank Huntington's disease (HD) families for their generous and selfless brain donations. That's because more and more research is making use of human brains, leading to a better understanding of HD in people. All of that is only possible because of the fantastic HD community that supports HD researchers. So today, May 7th, on Brain Donation Awareness Day, we tip our hats to each and every HD family member who has very generously donated a brain to HD research. Serendipitously, this falls during HD awareness month!

Why is brain donation so important?

Humans are the only species that naturally get HD. We have lots of animals that model HD, but those have all been created in a lab. While they're important for answering some types of questions about the disease, they can't ever truly replicate every disease feature we see in people. To understand exactly what HD is doing, we need samples from people.

On Brain Donation Awareness Day, we send our deepest THANK YOU to all who have selflessly donated brains to advance HD research.

While researchers have some models from people, like skin cells that can be turned into brain cells in a dish, these still can't tell us everything that's going on inside the complex human brain. To get the clearest picture of how HD affects the human brain as a whole, human brain donations are needed.

Using scientific experiments to analyze human brains from people with HD allows researchers to dissect the interaction between distinct types of brain cells, understand how amounts of molecules change as HD progresses, and much more. As technology advances, researchers are using molecular mapping to determine what's going on at a cell-by-cell level.

What are we learning about HD from donated brains?

Overall, researchers are learning *lots* from studying human brains generously donated by HD families! They are answering questions about why certain brain cells are more vulnerable in HD, what other types of cells in the brain are doing, and how somatic expansion plays a role in when and why nerve cells in the brain get sick. Below are some examples of how these precious materials are used to advance HD research, many from recent talks we heard at the CHDI therapeutics conference earlier this year.

Cell death and brain health

Tony Reiner from the University of Tennessee Health Science Center is using tools to visualize different forms of the huntingtin protein throughout the brain. The huntingtin protein comes in lots of different flavors - expanded, fragmented, clumped, and others. Tony and his group are mapping these different forms of huntingtin in the human brain to try and understand the cause and effect for how different huntingtin flavors may contribute to specific brain cells getting sick.

Osama Al-Dalahmah from Columbia University Irving Medical Center uses human HD brains to study a star-shaped cell called an astrocyte. Astrocytes help maintain health and function of nerve cells in the brain. Osama's team found that the more sick brain cells there are, the more the astrocytes are trying to make things better again. Understanding how HD affects astrocytes may help us understand how to improve health of the whole brain.

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Better understanding somatic expansion

Christopher Walsh from Boston Children's Hospital and Harvard Medical School is using human HD brains to look at somatic expansion - the increase in the CAG number in some cell types over the course of someone's lifetime. Because there seems to be a link between somatic expansion and disease progression, lots of scientists are trying to better

understand it. Chris is identifying single letter changes in the DNA code that are linked to somatic instability. These specific changes define a genetic “signature” that can be used to track cells, which can help scientists understand how the brain changes over someone’s lifetime.

Matthew Baffuto from the lab of Nat Heintz at Rockefeller University is using human HD brains looking at epigenetics - inherited labels on the genetic code that make it easier or harder for a gene to be made into a message or protein. Matthew is mapping these labels on genes that control somatic expansion and mapping those in cells in the brain that have high or low amounts of expansion. His work will shine light on how epigenetics can be used to understand how HD affects drivers of disease, like somatic expansion.

Tracking CAG expansions on a cell-by-cell level

Nat Heintz from Rockefeller University has been using human HD brains to try and understand how somatic expansion is connected to cell death. Using fancy technology, Nat and his team are able to look at the number of CAGs in each cell in the brain. Because we know which cells are vulnerable in HD, this gives researchers an idea of the contribution that expansions play in cell death. Surprisingly, they found that it isn’t just the cells that die that have large CAG expansions, perhaps suggesting there’s more to the story for why brain cells are dying in HD.

The partnership between the HD community and researchers, particularly through brain donation, will help us find a treatment and get across the finish line.

Bob Handsaker from the lab of Steve McCarroll at Harvard Medical School and the Broad Institute is mapping CAG lengths on a cell-by-cell basis. They’ve measured CAG numbers up to 1000 CAGs long in some cells! They’re mapping when in disease rapid CAG expansion happens. They find that when cells get 150 or more CAGs, genes that should be off are turned on and others that should be on are turned off. Bob thinks this leads to toxicity and eventually death of the brain cells that undergo this rapid CAG expansion.

Where can I go for more information?

We realize the thought of donating a brain - the organ that encompasses the essence of you or your loved ones - is a tricky topic. It's also important to acknowledge that brain donation is not something that everyone might participate in due to religious, cultural, personal, or other reasons.

If you think brain donation might be right for you or is something you are interested in learning more about, it does need to be thought about in advance. The key for brain donations is to set them up before people pass. The sooner the brain is received after death, the more preserved cells and tissues will be and the more scientists can learn.

If this is something you're interested in learning more about, you can find information from:

> **"So much of the science that happens in the lab wouldn't be possible without the HD community. "**

- The Brain Donor Project
- Huntington's Disease Society of America
- Huntington Society of Canada
- HD organizations in your home country
- Local academic institutions

Our deepest gratitude to those who have donated

The past few years have brought a massive increase in the number of studies using human brains. The advent of fancy new techniques that allow researchers to examine brains at a cell-by-cell level has increased the amount of information gathered from these brains and has helped ask and answer complicated questions.

So much of the science that happens in the lab wouldn't be possible without the HD community. That is particularly true for studies using human brains. The findings that come from those studies get us closer to understanding HD in people, and closer to a treatment. Science, particularly HD science, relies on a partnership between the researchers and the HD family community.

Today, on Brain Donation Awareness Day, we send our deepest gratitude to the amazing HD community for standing hand-in-hand with HD researchers so that we can cross the finish line together, treatment in hand.

Sarah Hernandez is an employee of the Hereditary Disease Foundation, which has provided or is providing funding to several researchers mentioned in this article. For more information about our disclosure policy see our FAQ...

GLOSSARY

huntingtin protein The protein produced by the HD gene.
therapeutics treatments
somatic relating to the body
