MARCH 2022 - VOL. 24

NEWSLETTER

HUNTINGTON'S DISEASE TASMANIA

Providing a voice for people with Huntington's disease and their families

Beanies

As we say goodbye to long summer days, we turn our thoughts cool Autumn and cold Winter windy, frosty weather. Its time to invest in a new beanie to keep us warm. Our wonderful family member Barbara has boosted our supplies of beautiful hand knitted in various colours.

You can purchase one from our online shop via our website. www.huntingtontasmania.org.au

In this issue

From the President's Desk

Hi Everyone,

Welcome to the first Newsletter for 2022. It is great to start a New Year feeling refreshed, energized and focussed on our mission to support, advocate and serve those impacted by Huntington's in Tasmania.

We hope you had an enjoyable break and have remained well during this time of uncertainty for us all. Living with a pandemic can be stressful for everyone. There are often many people who are relying on us, and it becomes easy to forget about taking care of ourselves. Try to schedule some time each day for yourself. As little as ten minutes a day will make the world of difference.

I am very excited by the year ahead. There will be challenges, but I am confident that with the strength of our new Board, we can turn them into great opportunities.

We have started the year by advertising for our Executive Officer position with applications closing on March 12th. A lot of lobbying and hard work have gone into this position becoming a reality so we are all feeling very excited. Our advertisement for a new volunteer Treasurer has also been very well received. We hope to have some announcements to make in the next newsletter.

Some events to look forward to

- Youth Group meets on the first Sunday of each month. For more information please see page 6
- End of Life Choices (Volunteer Assisted Dying Act) with the Hon Michael Gaffney MLC.
  Devonport April 30th Paranaple Centre Devonport. (Aberdeen Room) 11:00am - 2:00pm
  Hobart Date and Venue to be confirmed.
- Light it up 4 HD and other events for International Huntington's Disease Awareness Month

North-West support Group

Plans are underway for a North-West HD support Group to commence in Devonport and Wynyard in the coming months.

I hope you all enjoy the last few weeks of the warm weather, stay safe.

Kind Regards

Pam Cummings

Condolences

It is with a heavy heart that I advise of the death of Lucy Williams in the early hours of Sunday 20th March following a short illness. Lucy and her husband Les have been involved in Huntington's Tas since it began. During that time Les held many positions, having retired a few years ago he remains a life Member of the Association.

We send our love and Sympathy to Les and his family at this very sad time.

Evaluating health literacy in individuals with a neurological condition and caregivers

Are you living with a neurological condition?
Do you support someone living with a neurological condition?
Are you interested in undertaking a survey on health and e-health literacy (the ability to find, understand, and use online and offline health information)?

This study is observational and will provide us with information needed to develop novel health and e-health literacy interventions for people living with neurological conditions and caregivers.

What do I need to do?

Complete an online survey containing questions on health literacy and e-health literacy. If you wish, you can also decide to participate in workshops on ehealth interventions.

If you are interested in participating, please scan the QR code below or copy the link into your web browser:

https://redcap.link/miikb66x

For further information please contact:
Dr Travis Cruickshank or A/Prof Mandy Stanley
Chief Investigators | Email: spin@ecu.edu.au

MSWA

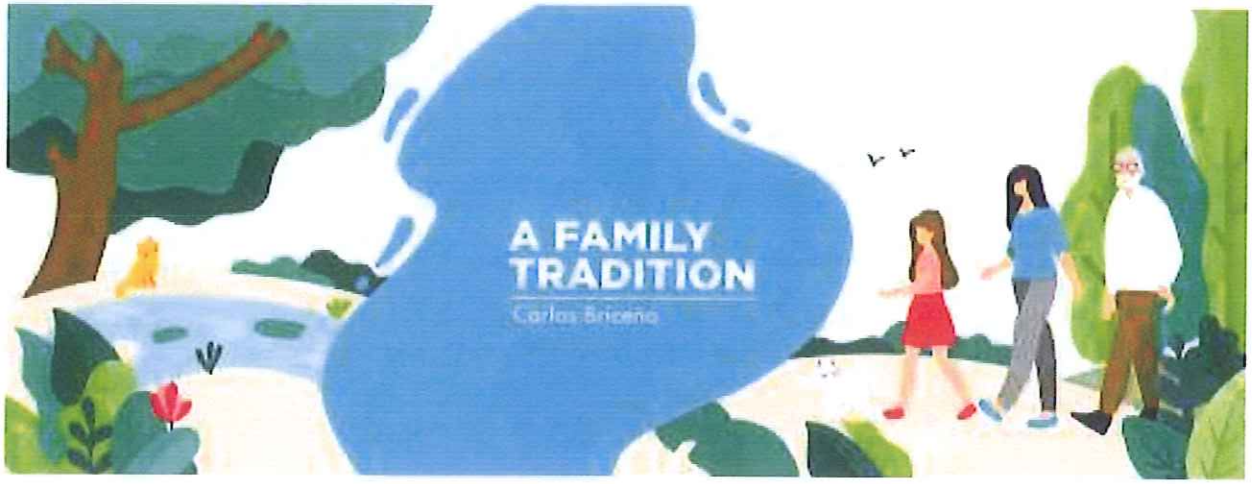
WE KNOW NEURO

AUSTRALIA ECU EDITH COWAN UNIVERSITY

Encouraging Difficult Conversations About Huntington's Disease

huntingtonsdiseasenews.com/2022/02/21/encouraging-difficult-conversations-about-huntingtons-disease/

February 21, 2022



Earlier this month, my wife and daughter, Jill and Alexus, respectively, participated in a panel discussion about Huntington's disease (HD). The topic was difficult conversations.

Jill and Alexus are both gene-positive for HD, but they each had different reasons for accepting the invitation to participate. Alexus said, "I love talking about myself." Jill, who is more private, said that as uncomfortable as talking about herself would be, she had agreed because she hoped that what she shared would make people feel less alone during their Huntington's journey.

Some questions that were posed included: While raising your kids, how did you talk to your children about HD? Do you have any advice for families who are just learning about HD? Does your family talk about testing? What advice do you have for families who have different views or values regarding testing? Can you tell us about your dating experiences? How open are you about sharing about HD on social media?

Recommended Reading
January 12, 2022 Columns by B.J. Viau

Changing Our Mindset About Genetic Testing for Huntington's Disease

I share these questions because they are important topics for discussion among families affected by HD.

One point that Jill and Alexus made was the importance of being open to talking about the disease. A poignant moment during the discussion was hearing a man who had tested positive share how refreshing it was to hear people talking about HD so openly,

because in his family, which included several gene-positive members, that was not the case.

I heard the pain in his voice. It's difficult enough to have HD, but to feel as alone as he seemed to be must be crushing.

That was not the only time I felt sad during the discussion.

Who wants to hear that Jill didn't like planning for the future when she was younger, before her diagnosis, because she always assumed she would die young from HD. Or that Alexus considered it normal when she was a child that her grandfather, who was gene-positive, got his nutrition through a feeding tube.

To some, talking about HD and acknowledging it as a deadly reality that will usually cause intense suffering is the equivalent of dipping their hands into a pot of boiling water. But not acknowledging or talking about it will not make the disease, or the great emotional and financial toll usually associated with it, disappear.

A major reason I am able to write about HD in this space is because Jill gave me permission to do so. She really does prefer her privacy. But she has told me that, as long as she has breath, she will continue to be open about sharing her experiences and emotions in the hope that she made just one person feel less afraid and alone.

I hope her mindset and courage inspire others to have the difficult conversations they have been trying to avoid.

YaYAPSS

Youth and Young Adult Peer Support Service
Provided by the Huntington's Disease Association of Tasmania

Our first YaYAPSS (Youth and Young Adult Peer Support Service) face to face group session was held on Sunday 6th March. It was a wonderful opportunity for young people aged 12 to 30 years to meet, gain support, listen to and talk to others about their experiences with HD.
Kayla and Mike, who run the program, provide wonderful support in a non-threatening environment. Everyone is welcome to join them on the 1st Sunday of each month.

If you would like more information please contact Kayla or Mike on 0412 142 520

Hobart Support Group

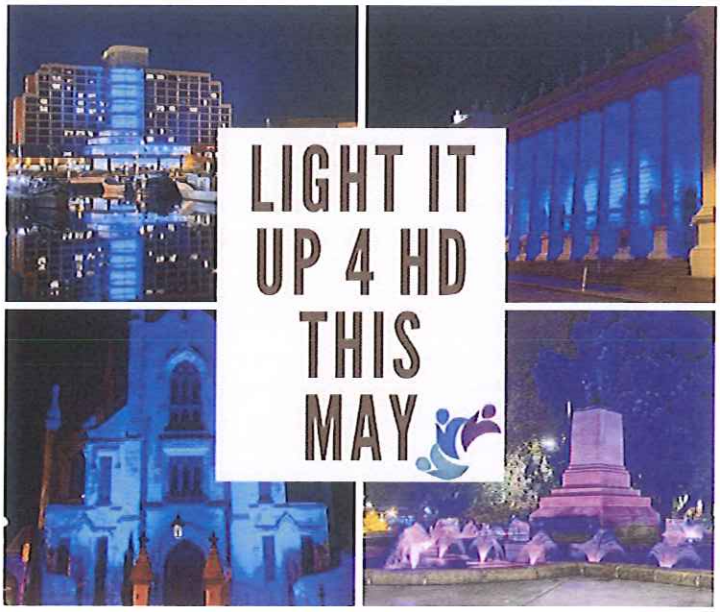
If you live in or near Hobart, you are welcome to join the Hobart Support Group.

This group is open to anyone with a connection to Huntington's Disease. Those with HD, family, carers and other support services. Come and have a chat, hang out, ask questions and connect with our HD community.

This group welcomes all ages, however minors should be accompanied by an adult for the initial meeting.

For further information please call Alex on 0458 450 705 or Mike on 0406 997 811

MAY IS THE INTERNATIONAL AWARENESS MONTH FOR HUNTINGTON'S DISEASE



As May is fast approaching we are calling out to all businesses and land marks to light up purple and blue to help raise awareness for Huntington's Disease.

Participating businesses and landmarks will receive State, National and International recognition as well as Social Media coverage from Huntington's Disease Tasmania.

For further information on how to register please call (03) 6431 3403 or email huntingtontas@outlook.com.au

CALLING ALL MOTORCYCLE RIDERS!

This May riders from around the nation are putting on their tutus to raise awareness for Huntington's Disease.

We would love for Tasmanians to get involved and help raise awareness and funds for Huntington's Disease

We welcome motorcycle groups and individual riders to participate.

Purple tutus represent those with Juvenile Huntington's Disease
Blue tutus represent adults with Huntington's Disease

To register your interest please call us on (03) 6431 3403 or email huntingtontas@outlook.com.au

Hold your own fundraiser this May to help support Tasmanians living with this incurable disease.

Register by calling (03) 6431 3403 or email huntingtontas@outlook.com.au

Oral drug may change the story for huntingtin lowering

Researchers with PTC Therapeutics recently published exciting new findings - a promising new huntingtin lowering drug that can be taken as a pill. Will this change how we move forward with huntingtin lowering?

By Dr Sarah Hernandez and Dr Jeff Carroll February 01, 2022 Edited by Dr Rachel Harding

Huntingtin lowering has gained lots of attention in HD research, and for good reason. It was the first potential treatment designed to directly target the cause of HD – the huntingtin protein. But there are limitations to current huntingtin lowering approaches: they require delivery to the spinal fluid or brain surgery for delivery, can show limited distribution within the brain, and don't cross the blood-brain barrier (which is why they require a lumbar puncture or brain surgery). They also don't reduce huntingtin outside of the brain in "peripheral" tissue.

Scientists from PTC Therapeutics recently published their work in the prestigious journal Nature Communications describing a series of drug molecules that lower huntingtin which can be taken orally, and show distribution throughout the brain and body. These are results that would have sounded like science fiction even 5 years ago. But in a post-2020 world, wonders never cease! So let's dive into what their data show and what it means for huntingtin lowering.

Needle in a haystack

PTC started by screening a huge library of molecules – around 300,000 different ones! They tested each of these molecules on cells derived from HD patients. This is a promising first pass for identifying molecules of interest because it screens molecules for effects they'll have in cells from humans. Often times, drugs don't work the way scientists thought they would if studies are only done in animal models before being tested in people. First looking in human cells suggests the drug molecules will have the intended effect in the only organism we're most interested in – people.

Finding HTT-C2 was like finding a needle in a haystack. HTT-C2 is not only able to lower huntingtin, but it can also be taken as a pill and crosses the blood-brain barrier – traits that make this drug seem almost too good to be true.

Changing the message

From those 300,000 molecules, PTC's scientists narrowed in on two promising molecules that were able to lower huntingtin in human cells. Both molecules are "splice modulators", meaning that they can lowers huntingtin levels by changing the way the message that produces the huntingtin protein is read. The scientists at PTC went on to analyse these molecules in different experiments, and also looked at a very similar molecule they called HTT-C2.

You can think of each gene like a story book. When the sequence for the gene, or story, is over, the final part reads "The End" to signal to the cell that the sequence for that gene is complete. These splicing modulators work by moving the last page up, so the story reads "The End" before the end of the sequence. Because the story no longer makes sense, the cell destroys that message and doesn't make the associated protein. Just like you would toss a book that made no sense with a premature ending and read, "Once upon a time, The End".

Selective targeting of huntingtin

One drawback of splicing modulator drugs like those PTC identified, over other approaches that are specifically designed to only target the huntingtin sequence, are "off-target effects". Drugs like HTT-C2 can also change where "The End" is placed in other genes. But the good news is that HTT-C2 seems to primarily affect huntingtin over other genes at low doses. When experiments were done to examine all the genes in treated cells, widespread effects weren't observed even at dose levels far higher than would ever be used. This suggests that HTT-C2 is surprisingly able to discriminate between just the huntingtin gene, despite the potential to alter levels of other genes.

Effects are adjustable and reversible

But all the previous experiments were done on cells in a dish. What happens when you give HTT-C2 to an entire organism? Does it have the same effect? Can it lower huntingtin in the brain? To answer those questions, PTC's researchers turned to mouse models of HD.

"This new type of approach, that accomplishes huntingtin lowering with a pill, could be a game changer for patients who have been hesitant about more invasive types of approaches. "

Mice were fed HTT-C2 every day. Yes, you read that correctly – the mice were given this drug orally. This is a huge difference from previous huntingtin lowering therapeutics! For those who have followed the huntingtin lowering field, previous therapeutics have required either lumbar puncture or brain surgery, neither of which are ideal. This new type of approach, that accomplishes huntingtin lowering with a pill, could be a game changer for patients who have been hesitant about more invasive treatments.

Encouragingly, the more HTT-C2 the mice were given, the more huntingtin was lowered. This is great news because it suggests HTT-C2 dosage can be actively adjusted to change how much huntingtin is lowered. We don't yet know how much total huntingtin should be lowered in people to produce beneficial effects without being harmful, so this is a massive safety advantage – if huntingtin isn't lowered enough, more drug can be given, and if huntingtin is lowered too much, the dose can be reduced.

Another exciting finding is that the effects of HTT-C2 were quickly reversible. Just 10 days after treatment stopped, huntingtin levels returned to that which was observed prior to treatment. This is another major safety advantage – the "washout" of this drug is very fast, meaning the time it takes for the drug to leave a patient's system will be relatively quick. If a negative consequence is observed after HTT-C2 is given, the effects can be quickly reversed. However, 10 days is the washout timeline in mice and this will likely be different in people.

Reduces huntingtin in the brain and body

HTT-C2 treatment targets both the expanded and unexpanded copies of huntingtin, unlike current ASO-based approaches by Wave Life Sciences that will only target the expanded copy. Because the unexpanded huntingtin copy is still needed to carry out its normal jobs inside cells, it's important to track how much of both copies are being lowered.

Splice modulators change the genetic story – they move the ending up so it no longer makes sense to the cell. The same way we would throw away a book that said "The End" half way through, the cell degrades the genetic message that no longer makes sense.

When researchers looked at the brains of HD mice dosed with HTT-C2, they saw about 50% reduction of both expanded and unexpanded huntingtin throughout the whole brain. This included in regions most sensitive to HD, which suggests HTT-C2 is having an effect in the areas where it's needed most.

Huntingtin is expressed in all cell types of the body, not just the brain. So while we know about the effects of HD in the brain because changes there control the most apparent parts of the disease like mood changes and chorea, there are also effects in other tissues like the heart and muscles. Because of this, it may also be beneficial to lower huntingtin in all tissues, not just the brain.

When the authors assessed how much HTT-C2 lowered huntingtin in tissue outside of the brain, they found it was actually much higher than in the brain – it was lowered over 90%! While research suggests a 50% reduction would be tolerated, 90% is likely too much.

For safety reasons, the researchers at PTC further tweaked the drug by changing the chemical structure – resulting in another a drug they called HTT-D3. When given to mice, HTT-D3 showed huntingtin lowering in both the brain and body to equal levels of around 50%.

"Splice modulators, like HTT-D3 from this paper and PTC-518 from PTC's drug discovery program, seem to check all the boxes – they lowers huntingtin both inside and outside of the brain, they can be taken orally, they bypasses the blood-brain barrier, and they're selective for huntingtin. "

What's next for splice modulators in HD?

Splice modulators are an exciting new approach for huntingtin lowering. Encouragingly, a similar drug called risdiplam has already been granted FDA approval and is currently being used to treat another neurodegenerative disease, spinal muscular atrophy. This strengthens the possibility that something similar can be used to treat HD.

While HTT-D3 was used as a proof-of-concept drug in this paper, PTC Therapeutics is moving forward with a different drug discovered using their pipeline. This drug is called PTC-518. The Phase 1 safety trial for PTC-518 in non-HD individuals is ongoing, but interim results suggest the trial is going well. So far, the drug has been well tolerated with no adverse events. Huntingtin is being engaged by the drug and expression is being reduced in a dose-dependent manner, similar to what was observed in mouse models. Their Phase 2 trial in HD patients is planned to start by the end of 2022.

Splice modulators, like HTT-D3 from this paper and PTC-518 from PTC's drug discovery program, seem to check all the boxes – they lower huntingtin both inside and outside of the brain, they can be taken orally, they bypasses the blood-brain barrier, and they're selective for huntingtin. In a year of tough news for HD research, it almost seems too good to be true. But right now the data looks very promising and the HD community is eager for some promising news.

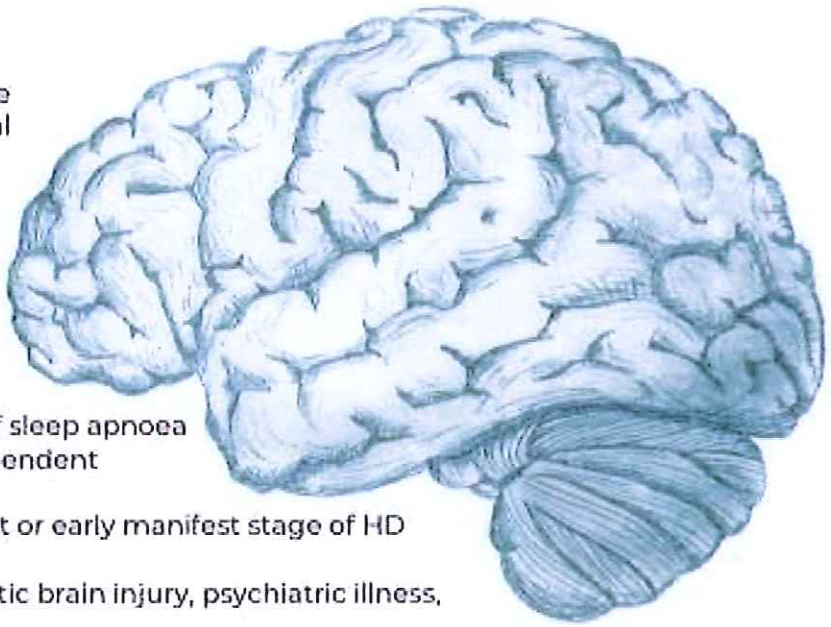
The authors have no conflicts of interest to declare. For more information about our disclosure policy see our FAQ... on our website https://en.hdbuzz.net

SLEEP AND GUT HEALTH IN HUNTINGTON'S DISEASE

We are looking for people with and without Huntington's disease (HD) to take part in a study investigating sleep quality and the gut.

Who are we?

This study is being led by Dr Yifat Glikmann-Johnston, Professor Julie Stout, and Emily Fitzgerald (Clinical Neuropsychology PhD candidate) from the Stout Lab at Monash University.



You may be eligible if:

- You're aged 18-65
- You're not a shift worker
- You do not have a diagnosis of sleep apnoea
- You're not drug or alcohol dependent
- You do not have HD
- You are within the premanifest or early manifest stage of HD
- You are gene negative for HD
- You have no history of traumatic brain injury, psychiatric illness, or learning disability
- You have no diagnosis of irritable bowel syndrome, coeliac disease, Crohn's disease or diabetes
- You have not travelled across three zones in the last month

What will I need to do?

- Provide a stool sample to assess gut function
- Wear an activity monitor, like a FitBit, and complete a sleep diary every day for 14 days
- Complete a set of online questionnaires
- Complete a set of cognitive tasks via mobile and telehealth
- This study will be conducted from your home, which means you don't need to travel anywhere to participate!

Reimbursement

You will be reimbursed up to $120 upon completion of the study

MONASH University

For more information contact: Meg Rankin (03) 9903 4695
Med-HDsleepgutstudy@monash.edu

MUHREC Project IDs:
27008 & 23253

Membership

Become a Member

Membership is an important way to support our organization.

Your membership will provide strength when advocating for better services for our HD community.

To join go to our website — www.huntingtontasmania.org.au

HD Happenings

We are looking for photos and stories to be included into our newsletter. It is a great opportunity for families to get involved and share with other HD families their photos and stories. Whether you're affected by HD yourself, a carer or family member we would love to hear from you.

HUNTINGTON'S DISEASE TASMANIA

Head Office
Office 4, Brownell Place
11 Wilson Street
Burnie, TAS 7320

www.huntingtonstasmania.org.au
Phone (03) 6431 3403
Email: huntingtontas@outlook.com.au

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