



NEWSLETTER

HUNTINGTONS QUEENSLAND

February 2012

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FROM THE PRESIDENT

Dear Friends

I am looking forward in 2012 to another successful year for Huntingtons Queensland. Over the last couple of years we have put in place the Rotary Scholarship to support our families with assistance for education expenses. Please contact the office or our staff to get the details of this programme.

Most of you would be aware of the grant of \$300,000 we received last year from the Department of Communities that is to be used to provide aids and equipment for HD families. The programme, called HQAssist, is now well established and if you would like to find out more please contact our Welfare Staff.

Fundraising is a key activity for all charity organisations such as ours. We are always looking for new ways to fundraise so if you have any ideas please feel free to contact us with your suggestions.

Gerry Doyle, President

DIARY DATES

FEBRUARY 2012

Wed 8/2/12

Thu 9/2/12

Wed 15/2/12

Fri 17/2/12

Mon 20/2/12

Mon 20/2/12

Wed 22/2/12

Fri 24/2/12

Tue 28/2 - Fri 2/3/12

Wed 29/2 - Fri 2/3/12

MARCH 2012

Tue 28/2 - Fri 2/3/12

Wed 29/2 - Fri 2/3/12

Fri 9/3/12

Mon 12/3/12

Wed 14/3/12

Wed 21/3/12

Fri 23/3/12

Wed 28/3/12

APRIL 2012

Tue 3/4/12

Wed 4/4/12

Friday 13/4/12

Mon 16/4/12

Wed 18/4/12

Fri 20/4/12

Fri 20/4/12

Mon 23/4/12

Mon 30/4–Wed 2/5/12

TBA

Coffee Catch Up Group

Brisbane Carers Support Group

Brisbane East Family Support Group

Toowoomba Family Support Group

Ipswich Family Support Group

Gold Coast Family Support Group

Coffee Catch Up Group

Pine Rivers Peninsula Family Support Group

Townsville Regional Visit

Mackay, Rockhampton & Gladstone Regional Visit

Townsville Regional Visit

Mackay, Rockhampton & Gladstone Regional Visit

Sunshine Coast Family Support Group

Brisbane Carers Support Group

Coffee Catch Up Group

Brisbane East Family Support Group

Burnett Family Support Group

Coffee Catch Up Group

Ipswich Family Support Group

School Holiday Activity

Toowoomba School Holiday Activity

Gold Coast Family Support Group

Brisbane East Family Support Group

Toowoomba Family Support Group

Pine Rivers Peninsula Family Support Group

Brisbane Carers Support Group

Bundaberg Fraser Coast Regional Trip

Coffee Catch Up Group

FROM THE OPERATIONS MANAGER

Greetings and best wishes to all for 2012! Let us all work together towards making the best that we can of this, sometimes hard to understand, and sometimes very enjoyable, adventure we call life. At the beginning of this year we can continue to focus on living every day in the present, but wonder at what might come in the future as well. Without getting ahead of myself, I am in awe at the stage of 'the hunt' that we Huntingtons hunters are in. Research continues to gather momentum and clinical trials get closer. In the mean time we concentrate on the here and now, and do our best to stand together and do as much as possible for each other. That is the way of the warrior.

I have one more reflection on time, this one in a more light hearted manner. If you refer to my poetry selection for this newsletter, you may find the answer that will allow us all to throw away the botox etc. Without giving the game away, the answer is in the mirrors.

It is approaching twelve months for my involvement with Huntingtons. None of this was in my world a year ago. What a surprise I had coming. What a great surprise. What great people, what a great organisation, what a worthy and formidable cause to become involved in. Last year was mainly learning about Huntington's Disease and Huntingtons Queensland. This year I will be becoming more active in the Welfare Service. You can expect me to be popping up more at support groups and having the chance to meet more of you. I also will be placing more emphasis on HD Awareness. There is great opportunity to increase awareness of Huntington's Disease, not only within the general public, but with GPs, other medical professionals, other organisations such as nursing homes, equipment suppliers, and last but not least, those potential providers of funds – the politicians. After much to-ing and fro-ing to find suitable dates for HD Awareness Week, we have settled on June and it will be HD Awareness Month. This will allow meetings for all of the support groups to fall within the awareness period. It will also allow time to plan some interesting and enjoyable activities. Included in this will be the launch of a Huntingtons Queensland's youth venture that Christine has been working very hard at developing.

The subject of awareness activities leads me to the next major focus that I will be working on this year – fund raising. A project I have been developing and one that I hope will be very enjoyable and also successful as a fundraiser this year, is music/film nights. Between the time of writing, and your reading this, we will have staged the preview of our first music night. The format of this night is the screening of two Helmut Lotti DVDs on a specially made three by two metre screen, indoors with stereo sound. Helmut Lotti is a Flemish Belgian tenor singer and songwriter. He has sold over 13 million albums worldwide and received over 90 platinum and 70 gold albums. Well known overseas, he is mainly known in Australia through the Ovation TV Channel. Lotti does volunteer work as an ambassador for UNICEF. While I cannot know your taste in music, there is every chance you will enjoy your introduction to Helmut Lotti.

We have permission from Helmut Lotti's management team to stage this, with no cost in royalties or infringement of copyright. Following on from this preview I will be holding two more similar nights at no charge, to audiences that will be selected from a wide range of places including nearby businesses and neighbours, our bank, lawyers, various people at the hospitals etc. The purposes of these two nights will be partly for Huntingtons Awareness, but mainly to encourage bookings for future ticketed performances. The attendees will be encouraged to organise a social club or other night from within their own workplace and/or friends. If you are interested in attending one of these free nights or later ticketed performances, please drop me a line. I trust that the product will impress our audiences and we will be building a mailing list of people interested in attending future performances. My aim is to spread our fundraising activities to beyond our membership and to provide people with a sense of them having received value for their contribution above and beyond it being a donation. The format of the event is portable and it can be easily transported to suitable venues at other and some regional locations. Members please don't be shy about asking me for Membership discount tickets. There is a



range of Helmut Lotti music available to us and we can stage more events based on Helmut Lotti if he proves popular. I anticipate also revisiting some of the popular musicals such as South Pacific, Oliver, Jesus Christ Superstar (not the old American movie but a later and far more superior British production). I am very open to requests and suggestions.

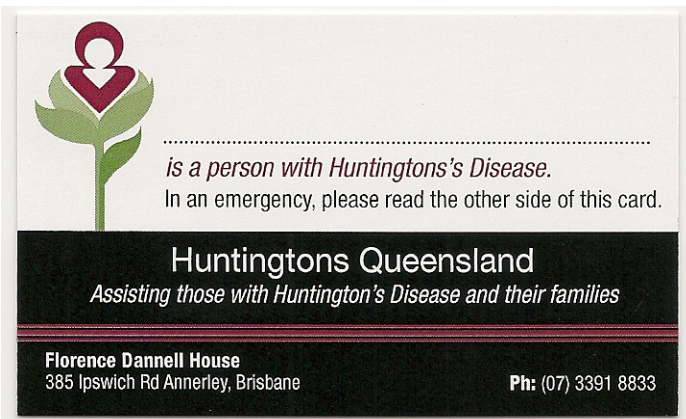
I hope to see you at one of these nights. Also don't forget a cuppa and chat with me is always on offer here at Annerley. Also if you are travelling some distance for appointments or other reasons to visit the city, please feel free to drop in and rest and freshen up here at your centre, either before or after you excursion to the city.

Michael McLean, Operations Manager

FROM THE WELFARE DESK...

In the last edition of our newsletter we highlighted some government and non-government schemes that some of our families might be entitled to which included the Patient Travel Subsidy Scheme, Disability Parking Permit, Queensland Companion Card, Carers Business Discount Card Queensland and the Taxi Subsidy Scheme. We had a great response from families wanting to find out more and have helped many people by completing applications and paperwork for them. We are glad that we were able to help and if there are any other families who would like us to help them to apply for these schemes and concessions and haven't contacted us yet (or maybe didn't get around to it because let's face it – Christmas is a pretty hectic time of year) then please feel free to give us a call. Some local councils may also have individual incentives and benefits for their residents, and so we would also urge you to let us know if you come across something, someone, or some service that has been of great help to you so that we can pass on the good word. This month I thought we'd let you know about a one of our initiatives that we have here at Huntingtons Qld that you may like to know a little more about.

Huntington's Disease ID Card



There are times, unfortunately, when people affected by HD may have found that others in the community might have had trouble understanding what they are trying to say, or misinterpret their involuntary movements or unsteady walk for something other than HD symptoms. Huntingtons Qld has an ID Card that we can issue for a person affected by HD. The idea behind this card is that you can show your card to someone if they are questioning your behaviour. The ID Card is printed with your name and states "(your name) is a person with Huntington's Disease. In an emergency, please read the other side of this card". On the back of the card it reads "I

have Huntington's Disease. It may affect my speech, movement, gait and behaviour. Please be patient and listen to me carefully". There is a space for us to write the name details for an emergency contact person, and the Card is given an official number that is recorded in a database – this means that issue of the card is controlled and only given to people with HD. This card is the size of a normal business card. We will also laminate it to protect it. The card is FREE! All you need to do is let us know you would like a card. Should you lose your card, just give us a call and we will reissue you with another card, it will have the same number, and it's STILL FREE. So how do you get one? Just give us a call and let us know. Too easy!

Young Families Respite Holiday



Each year Huntingtons Qld receives funding to host respite holidays for families affected by HD with young children. Many of these children find themselves caring for a parent at a young age (some people reading this may recall themselves in this role when they were young) and so we endeavour to provide an enjoyable family experience – happy childhood memories if you will – for these families. It also gives the kids the chance to meet others from HD Families, and often they are so surprised and maybe a little relieved to learn that they are “not the only one out there” going through this. So, from December 18th to 21st, Theresa and Christine took five families back to beautiful Hervey Bay for four days of sunshine, swimming, fishing and lots of fun. It’s not too hard to please the kids –as long as there is a pool they are quite happy and parents don’t see hide nor hair of their kids for hours at a time. One highlight of the holiday was by far the Wave Rider at the Wet Side Water Fun Park. It’s a free water adventure park with the feature being a wave making machine – in essence, the kids get to surf the waves in a relatively safe way and boy did they love that! (Let’s not forget the Dad’s who got in and had a go too!) The weather was perfect whilst we were there – and fishing off the Urangan Pier (for those of you who have been to Hervey Bay – that’s the really long one at the end of the Esplanade) at dusk enjoying pizza and playing in the sand as the tide went out to leave the flats for exploring – well that was a pretty popular night too. Oh, and let’s not forget the brekky bbq wraps in the park. Some of the kids went exploring again on the flats whilst the tide was out, the little ones played in the park and one of our Dads cooked up a great feast. I think it’s fair to say that everyone ate enough food to last a week. Another great holiday with some great families and kids.

Back to School Financial Assistance

Thanks to our Rotary Scholarship, Huntingtons Qld has some funding available to help families with the cost of sending kids along to school. How much funding we have to give to families varies from time to time, but if you have school aged children it’s worth giving us a call and we can tell you how to go about being a part of this. To be eligible, the children need to come from an HD family, and you’ll need to prove that you’ve had to spend money - which means we’ll need to see some invoices or receipts. But don’t worry if you’ve not kept any, we have ways around this and wouldn’t want you to miss out. You can also keep your receipts for preparing your tax returns as well. Families will receive a cheque once all requests have been received, sometime in the not too distant future. If you’d like to know more, be it for yourself or someone in your family, just give us a call and we can help. For those who have been in touch already, it won’t be too long now.

Huntingtons
Youth
Program
etc

The young families respite holiday and financial assistance with back to school costs are just a couple of ways we help young families with children. We have regular school holiday activities in several regions, we visit with families and refer them to support services specifically tailored to meet the needs of the family, not just the person with HD. We also work with schools (with parent’s okay), all with the goal to build relationships with the families and children, and to link them in with other kids in the same situation as themselves. In the coming issues we will let you know more about the ways that we can help young families with children, which will be a lead up to an official launch of this program – **HYPe** – which stands for **H**untingtons **Y**outh **P**rogram **e**tc. This will include a competition for the kids to decide on a logo design. Watch this space for more information, or give us a call if you’d like to more now.



On the front page of this Newsletter we have published the Welfare Schedule up till the end of April, with support group dates and regional trips penciled in. If you'd like to come along to any of these groups, or know someone that you think might like an invite, please let us know. We try to include as many families as we can, but we know there are people out there that we don't know about and welcome them along with open arms. Please don't forget, if you have any questions or concerns, or you're simply looking for someone to talk to, we are only a phone call away.

Christine Fox, along with Theresa Byrne and Lesley Park

Huntingtons Queensland Welfare Team

PS We have received a number of phone calls from people trying to contact Iris Simpson from Queensland Health. Iris is currently on indefinite leave but expects to be back in her office in March.

Here's a poem selected by our Ops Manager, Mike McLean.

The Mirror

By Edmund Burke, Irish Philosopher (1729 - 1797)

I look in the mirror
And what do I see?
A strange looking person
That cannot be me.

For I am much younger
And not nearly so fat
As that face in the mirror
I am looking at.

Oh, where are the mirrors
That I used to know
Like the ones which were
Made thirty years ago?

Now all things have changed
And I'm sure you'll agree
Mirrors are not as good
As they used to be.

So never be concerned,
If wrinkles appear
For one thing I've learned
Which is very clear.

Should your complexion
Be less than perfection,
It is really the mirror
That needs correction!!





HD research news.
In plain language.
Written by scientists.
For the global HD community.

Double success for huntingtin RNAi gene silencing

Clinical  **2 bits of good news for RNAi gene silencing in HD: it's safe over six months, and a way to treat bigger brain areas**

By Dr Ed Wild on January 24, 2012 Edited by Dr Jeff Carroll

Most HD researchers are pretty excited by the idea of 'silencing' the Huntington's disease gene, to reduce production of the harmful huntingtin protein. Two challenges - safety and delivery - are now closer to being solved thanks to collaborative work by academic and industry researchers.

We're big fans of *gene silencing*. Like many Huntington's disease researchers, we think it's the approach most likely to produce an effective treatment for HD.

Gene silencing involves using a specially designed drug to intercept a message molecule, called *RNA*, that's produced from the HD gene and tells cells to make the harmful *huntingtin protein*. The effect of the drug is that cells make less of the protein.

Put even simpler, *gene silencing* is like a stop sign for mutant huntingtin.

Rapid progress

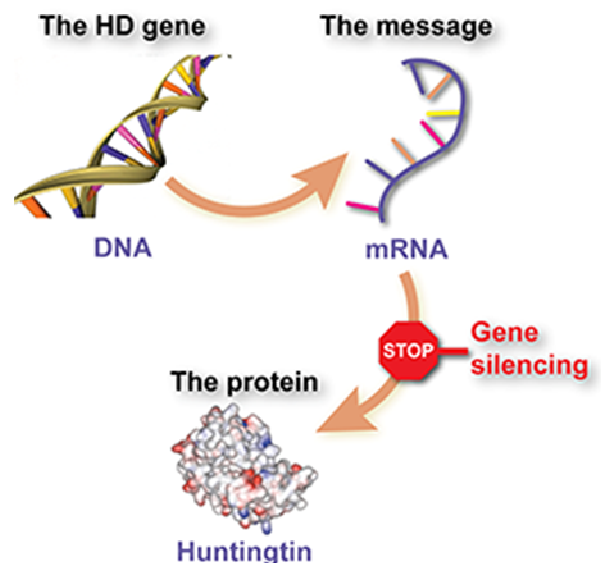
So far, *gene silencing* for HD, in various forms, has cleared every hurdle it's encountered. It's now been tested in several mouse and rat models of HD, and not only slowed down progression but actually produced improvement in both symptoms and brain damage. It seems that the brain can actually recover — to some extent — if only levels of the harmful protein can be lowered a bit.

The remaining hurdles

Several research teams are heading for human trials of *gene silencing* in HD. But there are a few remaining challenges to address before that can happen.

The first is **safety**. Unexpected side effects are always possible, and could be dramatic, since we're talking about drugs that are injected or infused directly into the nervous system, and interact directly with our cells' genetic machinery.

Another is **delivery**. *Gene silencing* drugs can't be given as pills or injections into the blood, because they wouldn't be let into the brain. So they have to be introduced directly into the nervous system. Depending on the structure of the drug, this means an operation to introduce needles or tubes into either the spine or the skull. Sounds drastic, but if the treatment is effective, it'll be worth it.



Gene silencing reduces huntingtin production by preventing its RNA message being read by cells



The delivery problem doesn't stop there though, because once the drug is in the head, it has to get **inside** our brain cells to work its genetic wizardry.

The *gene silencing* menu

Gene silencing researchers have to make several choices before they begin a treatment trial. Here's a checklist to help you understand future news stories.

First, we have to decide on the **structure** of the drug. The two basic choices are **RNAi** drugs, which are chemically similar to the body's *RNA* message molecules; and **ASO** drugs, which are slightly different but may be better absorbed by cells.

The second choice is what **target** to choose: both copies of the HD gene, or just the mutant one. Targeting both — called **non-specific silencing** — is easier, but switching off the 'normal' gene might be dangerous. Targeting just the mutant gene — called **allele-specific silencing** — may be safer but is much harder to do.

The third choice is **destination** — where will the drug go? *RNAi* drugs don't naturally spread far, so the drug has to be delivered right into the substance of the brain. Drugs that spread further, like *ASOs*, could be infused into the fluid around the brain or, if we're lucky, at the base of the spine.

Fourth, we need to decide on **delivery**. Will the drug be given on its own, packaged in a virus or pumped at pressure, to increase its spread through the brain?

The fifth choice is **treatment regime**. Should we give a one-off treatment or infuse the drug over weeks or months? Right now we don't know how long the effects will last, so this has to be worked out by comparing different regimes.

“The RNAi drug spread further than you'd get with simple injections. A lot further, in fact.”

Whenever you read about *gene silencing* research, it's helpful to figure out up front, which option has been selected for each of these choices.

Three come along all at once

At the recent HD World Congress in Melbourne, HDBuzz reported on exciting presentations from several *gene silencing* research groups. Then in November, we brought you news of the first safety trial of huntingtin *gene silencing* using *RNAi* in

a *primate* brain.

Now, two further scientific papers have been published — each the fruit of collaboration between academic researchers and biotechnology companies. Both papers involved Minneapolis-based company Medtronic and the team of Dr Zheming Zhang at the University of Kentucky.

Six-month safety

The November report of *RNAi* safety in primates was quite a short study — six weeks. The new study by Medtronic and Zhang's team, reported in the journal *Brain*, was also done in rhesus monkeys, but lasted a full six months.

Let's look at what the researchers studied, using the checklist above:

1. Structure: this was a trial of an *RNAi* drug.
2. Target: both copies of the gene were targeted — non-specific knockdown.
3. Destination: the substance of the brain — the striatum, to be exact, which is affected early in HD patients.
4. Delivery: the drug was packaged into an empty virus, called AAV2.
5. Treatment regime: a one-off injection into five sites on each side of the brain

It's also worth noting that 'normal' monkeys were used, with no expanded copies of the HD gene. So, this trial could only measure protein changes and safety — it can't predict improvement in patients.



After treatment, the monkeys were observed for six months, looking at their general health and movement control. The surgery was well tolerated, and no new problems were seen in the treated animals.

As hoped, levels of *huntingtin protein* fell significantly in the treated regions. At each injection site, protein levels were reduced over an area about six millimeters across — in volume, that's about three M&M's worth per brain. It may not sound like much, but in a human brain that could make a big difference, and remember these measurements were made 6 months after the one-off treatment.

Thankfully, the drug caused no harmful brain changes like *inflammation*, infection or *neuron* damage.

So, the drug did its job of reducing protein levels, and treatment didn't appear to produce any harmful effects. The authors reckon that six monkey months equates to about 18 human months. Sounds good — but as the authors point out, it could take even longer in humans for good or bad effects to emerge.



Measuring brain volumes is more fun when you do it with M&Ms. For the record, a single milk chocolate M&M has a volume of about 600 cubic millimeters.

An innovative delivery method

The other new paper came from a three-way collaboration between the University of Kentucky team, Medtronic, and *RNAi* drug company Alnylam Pharmaceuticals. It was published in the journal *Experimental Neurology*.

This was also a study of non-specific knockdown *RNAi*, delivered into the striatum of monkeys.

What distinguishes this work is the innovative delivery method. A technique called **convection enhanced delivery (CED)** was used. This involves placing tubes through the skull and into the substance of the brain. The top end of the tube is connected to a small pump that constantly squirts the drug down the tube under pressure. This pressure is the key — it causes the drug molecule to spread much further than it otherwise would.

CED is already used to get chemotherapy drugs to spread further within brain tumors. But would it work to deliver an *RNAi* drug?

First, the drug was pumped into the brain for seven days. Only one side of the brain was treated, so that the other could be used for comparison. A range of doses and infusion rates was used, to find the best combination. Then, a 28-day infusion was tried. Cleverly, the team made harmless radioactive modifications to the drug, that enabled them to measure exactly how far it had spread.

The drug did its job of reducing huntingtin levels, and the tubes and infusions didn't particularly harm the brain.

But was the additional hassle of fitting tubes and pumps worth it — did the drug spread further? In short, yes.

Measurements showed that the *RNAi* drug reached much further than you'd expect with simple injections. If both sides of the brain had been treated, huntingtin levels would have been reduced in about eleven M&Ms'-worth of brain.

In a nutshell...

Before these two papers came out, we already knew that huntingtin could be lowered in the monkey brain using *RNAi*. Now we can add two major check-marks to our wish-list: first, silencing works and is safe over longer periods, and second, there are ways of getting the drug to spread further.

What could go wrong?

Cautious optimism is a wise approach here. There are certainly some things that could go wrong on the way to human trials, or during them.



These *primate* trials have shown that lowering huntingtin levels is safe in healthy monkeys. But that doesn't mean it's definitely safe in human patients. Human brains are much bigger and more complex than monkey brains. So the treatment could be less effective, or more dangerous, simply because of the species difference.

It's also possible that the healthy protein somehow protects the brain from its harmful brother in humans. If that's the case, silencing both copies could unexpectedly do more harm than good.

The brains of people with HD symptoms are probably more fragile and difficult to operate on, too. The bits of the brain that need treating are smaller than normal, because of shrinkage caused by HD. So the operations may be harder and more risky.

Finally, detecting success might be difficult in humans, because the disease progresses slowly, and we can't examine patient brains under the microscope.

But never forget — all of these problems are being worked on together by some of the best scientific minds in the world, all focused on making effective treatments a reality for patients.

2012 — the year of *gene silencing* for HD?

Could 2012 be the year of *gene silencing* for HD patients? Will we see one or more human trials in the coming months? On the strength of progress so far, we actually believe that's a reasonable thing to hope for, and several groups are working hard to make it a reality. The first trials will be small, and will be carried out slowly and with great caution, because safety is the prime concern. But if all goes well, larger trials will follow.

The authors have no conflicts of interest to declare.

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HUNTINGTONS ASSOCIATION QLD

FUNDRAISING SOCIAL GOLF DAY

Take out your diary, book up Sunday 11th March and invite your friends or just come along and join a team at our next golf day.

To be held at the Howeston Golf Course at 100 Creek Road Birkdale.

Last year was a wonderful success with lots of fun and prizes. We raised \$2500 so we're hoping for another great day.

For details, please see the flyer included in this Newsletter.

We'd love to see you there!



FDA Approved Recruitment of 100 HD patients for Prana's PBT2 [Reach2HJD] Clinical Trials in US and Australia 1-3-2012

Prana Biotechnology given the green light to begin Huntington's Disease clinical trial in the U.S.

<http://www.proactiveinvestors.com.au/companies/news/23774/prana> - biotechnology given the green light to begin Huntingtons Disease clinical trial in the US.

Wednesday, January 04, 2012 by Angela Kean - Prana Biotechnology (ASX:PBT) has received approval from the United States Food and Drug Administration to begin recruiting patients for the company's first clinical trial using PBT2 in physical movement symptoms, progressively impacts the mind and emotions as well. The disease causes incapacitation and death about 15-25 years after onset. The disease affects 30,000 people in the U.S. and about 70,000 worldwide.

According to Prana, there are currently no drugs in development that have established clinical evidence for treating cognitive decline. Prana is developing PBT2 for the treatment of both Alzheimer's and **Huntington's Disease**. Previous research by the company has shown that PBT2 can improve synaptic activity in neurons needed for memory. The randomised, double-blind, placebo-controlled trial will enroll 100 patients with early to mid-stage Huntington's Disease at clinical sites in the U.S. and Australia. The aim of this trial is to demonstrate safety, motor benefits and the same cognitive benefits for Huntington's patients that it has already demonstrated in Alzheimer's patients treated with PBT2.

FDA Approval to Commence Huntington's Disease Clinical Trial Using Prana's PBT2

<http://www.4-traders.com/news/FDA-Approval-to-Commence-Huntington-s-Disease-Clinical-Trial-Using-Prana-s-PBT2--13954181/>

01/03/2012 | 06:59 pm

PBT2

Huntington Study Group appointed to coordinate the trial and start recruitment

Melbourne - 4 January, 2012: Prana Biotechnology (NASDAQ:PRAN; ASX:PBT) today announced that it has received approval from the United States Food and Drug Administration (FDA) to start recruiting patients for the company's first clinical trial using PBT2 in patients with Huntington's Disease (HD).

Prana's Investigational New Drug Application (IND) is now open. "The opening of this IND for a Phase 2 study follows an extensive review of PBT2 data by the FDA and reflects a favourable analysis from the FDA to support the study of PBT2 in Huntington's Disease patients", commented Geoffrey Kempler, Prana's Executive Chairman.

Huntington's Disease is a complex and severely debilitating genetic, neurodegenerative disease, for which there is no cure. The disease often affects young adults and, whilst associated with severe physical movement symptoms, progressively impacts the mind and emotions as well. The disease causes incapacitation and death about 15-25 years after onset.

The Company has appointed the Huntington Study Group (HSG) to coordinate the trial. HSG will commence recruitment of patients for the trial, named "Reach2HD, at clinical sites across USA and in Australia. The randomised, double-blind, placebo-controlled trial will enroll 100 patients with early to mid-stage Huntington's Disease. The Principal Investigator on the study is Dr. Raymond Dorsey of Johns Hopkins University Medical Center. The protocol synopsis appears below in Appendix 1.

Ira Shoulson, Professor of Neurology, Pharmacology and Human Science at Georgetown University (Washington DC) and the Chair of the Executive Committee of the Huntington Study Group said "PBT2 attracted our attention as an experimental drug with the potential to bring real benefit to Huntington's Disease patients who suffer from a range of motor, behavioural and cognitive symptoms. The favourable signals from the PBT2 trial in Alzheimer's Disease are particularly promising".

The disease affects 30,000 people in the US and about 70,000 worldwide. There are no drugs in development that have established clinical evidence for treating cognitive decline. Prana aims, in this trial, to demonstrate safety, motor benefits



and the same cognitive benefits for Huntington's patients that it has already demonstrated in Alzheimer's patients treated with PBT2.

Appendix 1 - Protocol synopsis

Title: A randomised, double-blind, placebo-controlled study to assess the safety and tolerability, and efficacy of PBT2 in patients with early to mid-stage Huntington's disease (HD)

Number: PBT2-204

Study Name: Reach2HD

Objectives:

Primary Objective: To evaluate the safety and tolerability of two dose levels of PBT2 when administered orally once daily over 26 weeks in patients with HD.

Secondary objectives: Determine the effect of PBT2 after 26 weeks in patients with HD on:

1. Cognition
2. Motor function
3. Behaviour
4. Functional abilities
5. Global function
6. Plasma and urine biomarkers
7. Brain volumes and function (imaging), and
8. To evaluate the Pharmacokinetics of PBT2 in patients with HD.

Number of Patients: 100 patients will be randomized into the study

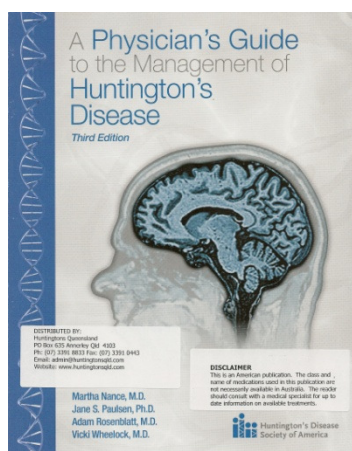
Key Patient Criteria – early to mid-stage Huntington's Disease

BOOK REVIEW

A Physician's Guide to the Management of Huntington's Disease

Third Edition

By Martha Nance MD, Jane S Paulsen PhD, Adam Rosenblatt MD, Vicki Wheelock MD



Whilst a cure for Huntington's Disease has yet to be found, research into the disease continues with improvements in understanding of its *genetic, biochemical and neuroanatomic basis*. A new publication which adds to the literature on Huntingtons and brings together all the understandings of the past ten years is the new edition of "The Physician's Guide to the Management of Huntington's Disease".

This Guide is organised along similar lines to the previous edition, with sections on the movement, cognitive and psychiatric disorders and provides several generally accepted pharmacological and non-pharmacological treatments for each issue. The new guide also addresses additional material of interest to the reader, notably multidisciplinary team care for HD, Juvenile HD, management of late stage HD and a review of current areas of interest in research.


Whilst the guide is intended primarily as a resource for doctors there are many areas of interest for the lay reader in furthering their understanding of HD. It also reiterates the belief that whilst a cure may still be sometime in the future, there is no substitute for creative and thoughtful treatment of HD symptoms. The Physician's Guide is available to borrow now from the Huntingtons Qld Library, and will be available at a later date as a downloadable PDF.





Another article from HD Buzz

TRACK-HD reveals changes in HD mutation carriers, empowering future trials

Clinical  Follow-up data from TRACK-HD study proves that we have the tests we need to successfully run drug trials for HD

By Prof Anne Rosser on December 05, 2011 Edited by Dr Jeff Carroll

The results of a two-year study of HD mutation carriers, called TRACK-HD, have just been released. These results prove that a number of changes, including thinking ability and brain changes, occur early in people carrying the HD mutation. Most importantly, these changes are suitable for use as endpoints in future clinical trials for drugs to prevent or delay the onset of HD.

What is TRACK-HD and why is it important?

The longitudinal results of the TRACK-HD study were published today in Lancet Neurology. TRACK-HD is a study that involved people positive for the HD gene, but without symptoms ('premanifest') and people who were in the very early stages of the condition ('early manifest').

TRACK-HD followed (or 'tracked') individuals over a period of two years to see if it was possible to pick up subtle changes that occurred even before the disease had become manifest. These changes are referred to as 'biomarkers' and will be important for both clinical diagnosis and for running clinical trials of new treatments.

Why do we need biomarkers?

'Biomarkers' are biological measures that can be used to follow change in disease status. A wide range of measures can be considered, ranging from the levels of specific chemicals in blood or urine, to changes that can be measured on a brain scan, to scores in a memory and thinking test.

The important point about biomarkers is that they can be measured repeatedly, and can be given a value that allows us to compare between individuals, and also to follow the changes in an individual over time.

Without biomarkers, we have to measure change using clinical scales. This is the approach that has been used in most studies involving HD patients to date. Clinical scales rely on questionnaires, or a clinician's observation of a patient's symptoms.



TRACK-HD is a study designed to observe changes over time in people carrying the HD mutation.



Although clinical scales can be used for this purpose, they aren't very reliable because they depend on the judgment of a clinician. For example, a doctor may have to rate the amount of movement problems a patient has. Anything that depends on human judgment tends to be rather variable.

In light of this variability, trials have had to include many more patients, which makes them more expensive and difficult to run. This problem is magnified if we want to run trials on premanifest people, as our clinical scales are very poor at measuring any change at all in this situation.

“The TRACK-HD results are important in that they will allow doctors and scientists to select better tests for clinical trials.”

Because of these problems with clinical scales, high quality clinical trials with premanifest subjects will be very heavily dependent on identifying suitable biomarkers.

All HD-affected people would like to run trials to prevent or delay the onset of HD, but this would be very difficult or impossible to do using clinical scales as an outcome measure.

As well as being important for the future of clinical trials, biomarkers may be useful for doctors trying to diagnose the onset of disease in an individual who has had a predictive test. At the moment, the only way to do this is to follow someone in the clinic over a period of years to try to assess whether their condition is changing.

How did TRACK-HD work?

TRACK-HD was funded by the CHDI foundation and started in January 2008. It enrolled 117 premanifest individuals, 116 people with early HD and 116 people without HD, for comparison. Because the assessments were complex and time-consuming there was a limit to how many patients could be assessed in an individual clinic, and so the study took place between several sites in Canada, France, the Netherlands and the UK.

Participants had a 'baseline' visit at the start of the study, another at the end of year one, and one at the end of year two. The baseline visit for each patient occurred between January and August, 2008. PREDICT-HD is another study, coordinated from the University of Iowa, which uses complementary (and partially overlapping) assessment tools.

What were the measures used in TRACK-HD?

A variety of assessments were used that aimed to measure changes across a wide range of symptoms in HD, including involuntary movements, slowing and irregularity of movements, eye movements, memory and thinking tests, and assessment of behaviour. The participants were also assessed using clinical scales already in routine use, as this allows a comparison to be made between the new findings and the measures we already use.

The assessments were designed to be as objective to remove as much human judgment as possible. For example, rather than relying on a physician's observations, the movement assessments used a sensor that could be held between the forefinger and thumb. The same type of device can be pushed with the tongue to test how constant the pressure is; while this sounds odd, it turns out to be an indirect measure of movement problems.

Rather than being written down and transcribed by hand, readings were made directly and stored electronically. Another example of the advanced technology in TRACK-HD is the use of sophisticated eye tracking equipment to measure the very rapid tiny movements made by the eyes.

In addition to the clinic tests, scans of the brain were performed to measure how the volume of certain brain structures changed, and blood was taken and stored.



Now we need to work on measurements sensitive enough to detect change and test drugs before symptoms begin



What were the findings in TRACK-HD after two years?

The study revealed a lot of changes in the early symptomatic HD group over time. The most sensitive was loss of brain volume, but there were also changes in the memory and thinking and movement tasks. There were also measurable changes in eye movements, but they require more development before they could be used in clinical trials. Few of the behavioral tests showed reliable changes, although a test of reduced motivation looks more promising and provides a basis for further work.

Not surprisingly, it was much harder to see changes in the premanifest group. Because there is a relationship between the number of CAG repeats in someone’s mutant HD gene and the expected age of onset of HD symptoms, researchers can crudely predict whether someone is ‘close to’ or ‘far from’ expected onset of symptoms. When the premanifest subjects were divided this way, researchers could see more changes in the brain scans of the group predicted to be closer to onset.

Where does this leave us and where next?

Some data from TRACK-HD has been previously published, in particular, the ‘cross-sectional’ data, which was a comparison of the differences between the premanifest and early HD groups at their first visit to the clinic. The cross sectional data has been useful, but the data presented in this current publication is much more valuable, because it follows individuals over time.

This follow-up study specifically describes the clinical and brain scan changes in the group over the study period, but some of this data will continue to be analyzed and so we should expect further publications in the future. Of particular interest, the researchers are continuing to analyze the blood samples for chemical changes.

The TRACK-HD results are important in that they will allow doctors and scientists to select better tests for clinical trials. They will also facilitate much better estimates of the numbers of patients needed for these trials. Clinical trials are very expensive to run and also hold a certain amount of risk for participants, so, although it is important to make sure trials have sufficient patients to get an answer, it is also important not to include patients unnecessarily.

In addition, very large trials would tie up a lot of patients and would result in fewer trials being conducted overall. This is going to become an even more important issue as more drugs come along to be tested. TRACK-HD helps us understand exactly how many subjects we need for each trial.

There are some things that we don’t know yet about the TRACK-HD data. In particular, we don’t know whether it is possible to modify the observed changes with treatment. If we do find a drug that makes HD symptoms better, will it also modify the behavioral and brain scan changes revealed by TRACK-HD? This is the gold-standard for defining a ‘*biomarker*’, which will enable subsequent trials to be run even more efficiently.

It is also not known whether changes in a specific *biomarker* are related to a change in how a person functions. We’re less interested in biomarkers that change in response to a drug if that drug doesn’t also make the patient any better. All of these are questions for the future, so we should expect more publications from the TRACK-HD team.

Trending topics this month from HD Buzz:

animal-model	biomarkers
disease-modifying	mouse-model
stem-cells	HDAC-inhibition
communication	

For more information on these topics go to: www.hdbuzz.net



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Huntingtons Queensland
is a not-for-profit service organisation.
Established in 1976.

Our Mission is:

To provide professional support and advocacy for all persons affected by Huntington's Disease in Queensland.

Our Services Include:

- Providing individual and family support
- Facilitating the HD Day Respite Program
- Facilitating support group meetings
- Recreational activities for families with young children
- Organising respite holidays
- Providing information to families and health professionals
- Distributing a regular Newsletter
- Co-ordinating the annual HD Awareness activities
- Fundraising activities

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