NEWSLETTER

HUNTINGTONS QUEENSLAND

October 2011

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FROM THE PRESIDENT

Dear Friends

In September this year the International HD Conference was held in Melbourne. In 1997 I was fortunate to attend the first International HD Conference held in the Southern Hemisphere in Sydney and it was great to see the same commitment to research into a cure and/or treatment for HD with many of the conference speakers still as active in research as they were fourteen years ago. Although there is a greater understanding of HD there is no cure but like you all, I live in hope and at each conference the increase in knowledge and understanding continue to give me more hope.

In the Vancouver International Conference in 2009 there was a "late and breaking" research paper titled "*Suppression of Mutant and Normal Huntington with CNS or Peripheral Infusion of Antisense Oligonucleotides"* and in Melbourne a follow up paper was presented "*Antisense Oligonucleotide Therapy for the Treatment of Huntington's Disease".* Although these words may be scary the research is about reducing the level of the Huntington protein in the brain and shows how from basic research these projects will lead to clinical trials. If you are interested to learn more, check out the HD Buzz website http://hdbuzz.net/

I'd also like to take this opportunity to remind everyone that 2011-12 memberships fell due in July, so if you haven't already renewed your membership, please do so at your earliest convenience.

All the best!

Gerry Doyle, President

DIARY DATES

November 2011

1st November	Coffee Catch Up Group
5-11th November	Respite Holiday
16th November	Brisbane East Family Support Group
21st November	Northern NSW – meet with Mark Bevan from AHDA (NSW)
24th November	Ipswich Family Support Group
28th November	Gold Coast Family Support Group (to be confirmed)
To be advised	Mackay regional trip
To be advised	Bundaberg / Fraser Coast regional trip

December 2011

5th December	Sunshine Coast Family Support Group
7th December	Pine River Peninsula Family Support Group
9th December	Toowoomba Family Support Group
13th December	Annerley Day Respite Christmas party / Break up
14th December	Brisbane East Family Support Group
15th December	Brisbane Carers' Group
18-21st December	Young Families Respite Holiday (Hervey Bay)

This new (print) format Newsletter has been printed free of charge by the office of Graham Perrett, Federal Member for Moreton. Our kind thanks to Graham.

FROM THE OPERATIONS MANAGER

Hi to all our members and general readers. There are many things to report as well as there being a question I would like to ask your advice on. Since the last Newsletter we have had the Huntington's Disease World Congress 2011 in Melbourne, as well as our AGM, our 35th Anniversary celebrations and some other interesting developments that I would like to tell you about.

But first I would appreciate some feedback from the membership. It is regarding the issue of what terminology would be best suited to use, when referring to our people who have Huntington's Disease. These/you people are the main focus of our (Huntingtons Queensland's) reason for being, and for our activities. 'Clients' seems too formal and business like, although we pride ourselves on providing a professional service. 'Friends' or 'mates' could be presumptuous, even though it refers to our desire to reach out on a personal level. 'Patients', although it does have some validity, doesn't catch the relationship that we see existing between the Association and the people. 'Families' is close but it also includes the rest of the family members, who we are also very interested in supporting. 'Huntingtons people' while it may be correct, is a bit too impersonal. So there you have my ideas on the matter. Please help me out and set your thoughts into finding the right words to use. The person coming up with the best suggestion, or any suggestions at all, can claim a cup of caramel coffee (substitutions allowed) with me, my thanks, and a good chat here at Florence Dannell House.

Huntington's Disease World Congress 2011 was held in Melbourne, September 11th to 14th. We were represented by staff (Christine, Lesley and Theressa and myself), Gerry representing the committee, and the HD community including Cliff and Jenny Farmer, and a number of family members. It was a great experience and an informative and encouraging one as well. It allowed me to broaden my experience by speaking to, and hearing from a wide cross section of people. From an organisational point of view it allowed me to meet with the other Australian HD organisations as well as those from overseas. The avalanche of technical and highly specific information about HD was staggering for me personally. It was a challenge to my stamina and to my thinking powers. But at the same time this was very encouraging. I most certainly **cannot** report that nothing much is happening. It is impossible to rate the many very top quality presentations, but one memorable and impressive one for me personally was titled 'Huntington's Disease – Yes We Can' by Professor Sarah Tabrizi from London. Another highlight was the part increasingly being played by the HD Buzz website http://hdbuzz.net as a source of information across a wide range of subjects, written especially for the layman to understand. Most encouraging from the conference were the details of various advanced research programs and the details of a number of clinical trials that will be commencing within the next two years. Expert opinion seems to be that we are no longer at the beginning, we are not yet at the end or even at the beginning of the end, but we can safely say that we are at the end of the beginning. No one needs to point out how large the challenge is, or how slow the progress has been, but it is worth remembering that *there is solid progress* on a number of fronts.

On Thursday evening 22nd October we held the Annual General Meeting at the Sunnybank Community & Sports Club. The meeting was attended by approximately twenty people. Our annual report including the financial report from our recent audit was accepted. At the meeting, Robert Westley was elected as our new vice president; Heather Whye was elected as our new Treasurer and Marty Harmsworth was elected as a new committee member. Congratulations and thank you to Robert, Heather and Marty. While on the subject of personnel changes, we are pleased to announce that Theressa Byrne has now been appointed as a full time member of the Welfare Team.

After the AGM another ten or so members joined us to celebrate 35 years of Huntingtons Queensland as an organisation, with dinner and some light entertainment. The dinner and venue were a credit to the Sunnybank Club, especially Fred Law and his team in the Terrace Restaurant. Cliff Farmer made an interesting and encouraging address about the history of Huntingtons Queensland, and the view forward into the future. Will Stanfield, the 2010 Australian 'Man from Snowy River' recital champion, enthralled us with his introduction and setting of the scene, and then his rendition of this timeless classic. I could practically smell the smells and hear the sounds of the horses and their chains. Then Will backed up again as the Knight Sir Stodge, and was joined by Anne Stanfield as the elegant Queen, Cliff Farmer as a very impressive King, and myself as the narrator, for a humorous presentation of selections from the CJ Dennis work 'The Glugs of Gosh'.

Back to business matters. I am pleased to report that our new HQ-Assist program, to supply equipment to those affected by HD is now in operation. We are in the process of ramping up this service and we welcome enquiries, where items of equipment can be of assistance. I am also pleased to report that Christine's efforts to expand the services we provide by way of support groups are going very well. Christine has recently added two new support groups, one in the Ipswich area with seventeen attendees and seven apologies for the first meeting. Both these groups are focused on younger people and we are expecting them to expand even further in the near future. Well done to the entire Welfare Team.

Finally I can report that since our last Newsletter we have received the second installment of a grant of $10,000 per year for three years from the Sunnybank Community & Sports Club. This grant provides support for our youth program. It has already enabled family respite holidays and school holiday outings. Most recently we were able to send the child of one of our families to a youth leadership camp. Thank you and well done Sunnybank Community & Sports Club.

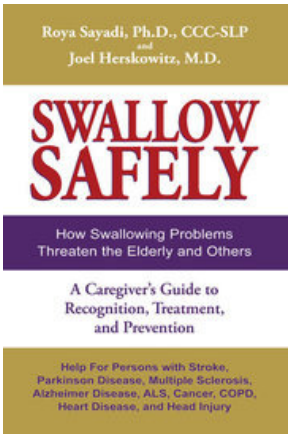
I wish you all strength and good spirits in continuing the hunt. You are not alone.

Michael McLean, Operations Manager

FROM THE WELFARE DESK…

Library Lending Service As part of our commitment to provide professional services to families affected by HD, Huntingtons Queensland continues to source relevant resources, books, journals, fact sheets, videos, research papers and more to help our families and those providing care for them to better understand HD. There are books about the testing process written by those who have gone through it themselves, books on HD, books about caring for someone with HD, family stories, clinical journals, and books not specifically about HD but which will also be insightful and we feel are relevant to our families and carers. For a list of all the books we have available to loan, please feel free to call our office and we would be more than happy to send you a list.

Book Review Most people with Huntington's Disease at some time or another experience swallowing problems. This book, *Swallow Safely by Roya Sayadi and Joel Herskowitz*, helps the reader gain a better understanding of the stages of swallowing and how to recognise symptoms, which will benefit our HD carers. Whilst not specifically about HD (although there are a couple of references to HD throughout the book) the information is relevant and will be a great reference to those providing care to someone with HD who has a swallowing problem. There are also some strategies in the book about how to overcome, or minimise the swallowing with diagrams to help illustrate what is being explained.



Christine Fox, Senior Welfare Officer

HUNTINGTONS AWARENESS WEEK IS SET FOR THE 14th - 18th NOVEMBER 2011

A feature of this important week will be Wednesday evening, the 14th. We will be hosting an entertainment event at Florence Dannell House at Annerley featuring a screening of the music of Helmut Lotti. If you are not already aware of Helmut Lotti from the Ovation Channel then you are in for a big surprise. There will no charge for this event. We will be issuing a media release and information brochures and there will be promotional give-aways.

We have an HD poster featuring our President, Gerry, saying 'Who cares?…I do!" As a part of Huntingtons Awareness Week activities, I am calling for as many responses as possible - post cards, letters, emails, drawings etc to say, "I care about Huntingtons (*with your brief message or comment*)!" Let's add these to Gerry's poster to show to all the growing awareness and support for Huntington's Disease. *Please feel free to call us on **3891 8833** for more details.*

Report from the World Congress on HD

Melbourne Convention & Exhibition Centre
Australia
11-14 September 2011

By Mike Mclean, Operations Manager

The HD World Congress was held 11th to 14th September in Melbourne. Sunday 11th was, strictly speaking, a separate event, the International Huntington's Disease Association Family Day, also known as Marjorie Guthrie Day. Marjorie Guthrie was the wife of the early American folk singer Woodie Guthrie, who had Huntington's Disease. The theme for this day was Hope, Dignity & Awareness. Attendance was free, and the focus was on families and lay persons. After the welcomes and introductions, the topics included Youths Living with HD, Starting a Family, Relationships, Multidisciplinary Care, Coping Strategies, and Carers Living with HD. The keynote speakers were Nancy Wexler, whose long term scientific studies led to the discovery of the HD gene, and Charles Sabine, Emmy award winning TV journalist and pioneering spokesman for freedom of scientific research, and sufferers of dementia – in particular Huntington's Disease which has ravaged his family. Sunday evening, we were treated to the WCHD welcome reception and function.

Monday, Tuesday and Wednesday were the days of the actual World Congress. I have the program and some documentation that you are welcome to read at any time. It would be a very large undertaking to present a full review of the congress. There were many top level presentations that included questions and discussions. There was a very large and interesting poster presentation of work and findings on Huntingtons from all around the world; and there was the opportunity to network. For me, that meant meeting with the other Australian HD organisations and members from other countries in particular, Canada, Ireland, Israel, Sri Lanka and New Zealand. It was a pleasure to meet the owners of names, some of whom I have often seen and heard mentioned in regard to Huntingtons, names such as Michael Gattas geneticist, Trent Woodruff researcher (both from Brisbane) Andrew Churchyard (Melbourne) one of the congress organisers, and from overseas, Sarah Tabrizi, Nancy Wexler, Ed Wild, and Jeff Carroll. To give these outstanding people their full titles, and lists of contributions to our worthy cause, would itself fill the space that I have available for this report. I am attempting to present a sense of the overall flavour of the congress and to name a few names that impressed me, and with whom you may be familiar.

The main advantages of attending the Congress for me personally was the degree of hope and encouragement that is provided and supported, by both the amount of, and the calibre of, the work being done right around the world. There is a great deal of work being done. There is a wide range of areas of research in which progress is being made, with a real depth to both the researchers and the research being done. Elsewhere I have paraphrased Professor Sarah Tabrizi's quote of Winston Churchill's famous summary (from a completely different field of endeavour): "This is not the end. It is not even the beginning of the end. But it is perhaps, the end of the beginning." Alongside the research is the very impressive array and depth of work in the field of caring and support for those with, and the families of people who are affected by Huntingtons. We all look forward to the final solution, but in the mean time I am pleased to be able to say that there is a lot being done in care and support. We realise that no matter what we provide in these areas, we all wish that we could do more. But we should all be encouraged by that half of the glass which is full. In Queensland we can be proud of the world class facility we have access to, ie the monthly HD Clinic at the Royal Brisbane and Women's Hospital. A significant feature of the Clinic is the 'one stop shop' nature, by means of the access to multidisciplinary specialists on the one occasion. Many HD organisations from around the world applaud Queensland for its HD Clinic.

There is also an outstanding model of care for Huntingtons in the Netherlands. The type of service that we provide at the Brisbane monthly Clinic is a standardised service in the Netherlands. They reinforce our approach and exceed our service delivery describing the benefits thus:

> *'Integrated multidisciplinary care increases the standards of care and the quality of life of HD patients and informal caregivers. The capacity of informal caregivers increases, the functioning of the patient improves and gaps in health care will be closed and / or prevented. Nursing home admission can be postponed and costs are reduced as the efficiency of care increases.'*

They also have a live-in facility for 50 people that is truly impressive. Of course everything comes down to funding, but they have set the benchmark for which we should all strive. Comparisons are not for the sense of egos or winning, but to help adjust our aims and dreams, and to encourage others to go for it.

Space limitations ensure that I have to omit more than I can include when reviewing the presentations at the Congress. But it would be impossible not to spend some time on the presentation entitled 'Huntington's Disease – Yes We Can', by Professor Sarah Tabrizi, professor of Clinical Neurology from London. Sarah is one of those people who exudes energy and enthusiasm, has a massive workload, but is not too busy to stop and talk and to offer encouragement and help. She has the gift of being able to fully load a presentation with so much technical information, but even though a lot goes over one's head, one retains an awful lot, as well as the overall message that she is making. And this message is one of hope.

Professor Tabrizi described 'A virtual explosion of HD research in the past two decades:

- Literally thousands of papers published
- Cell culture models and high throughput screening systems
- Many different animal models developed - fly, worm, fish, rat, sheep, monkey…
- Many important insights into disease mechanisms in HD.

Professor Tabrizi reports that real potential treatments are in the pipeline and that there are clinical trials on humans scheduled to commence within the next two years. She reports that there are many more targets in development. Other presenters also explained how developments in 'biomarkers' and other clinical tools, allow meaningful tests and measurements for trialled treatments.

Professor Tabrizi listed six promising research programs:

1. Reducing production of the mutant protein (gene silencing)
2. Helping cells get rid of the mutant protein (clearance by autophagy)
3. Reducing inflammatory toxins
4. Supporting neurons
5. Restoring healthy gene regulation
6. Improving energy production

Mention was made also of the progress in and the benefits of delaying the onset of HD.

I also found Peter Harper's address 'Looking Back on Huntington's Disease. How can the Past Help us to Understand the Present and Contribute to the Future' very interesting, informative and inspiring.

A recurrent theme that is evident from my discussions with Christine, Theressa and Lesley, our welfare staff, who also willingly and enthusiastically braved the torrent of information and viewpoints that comprised the conference, is that as time goes by, and the dust settles, particular presentations and parts of presentations remain with us and grow in importance with regard to the influence that they have on our thinking and understanding of matters Huntington. Connections and the broadening of knowledge and experience derived from relevant networking, features with all four of us. We all have our highlights from the conference some of which include:

- Sarah Tabrizi – details above.
- Tony Hannan's positive work on environmental enrichment, brain plasticity and reserve – a positive view interesting for carers and people living with HD.

- Jim Gusella's presentation on genetic modifiers – discussion of genetic factors other than the CAG repeat length in the progression of the disease which could provide clues for treatment options.
- Colin Master's interesting and encouraging discussion of how research and drug treatments for Huntingtons can benefit from the work carried out in the better funded area of Alzheimer's research.
- Michael Hayden's discussion of the presentation of older individuals with Huntingtons and what that means in terms of overall numbers of people presenting with the disease.
- Michael Guttman's discussion of Huntingtons diagnosis as a spectrum rather than an event.
- David Crauford made the point about behavioural aspects of Huntingtons being relatively under researched and misunderstood, and his plea for neurologists to focus less on depression and to focus on apathy and irritability.
- Martha Nance delivered the reminder that there is never 'nothing we can do', and the encouragement that this provides when sometimes we feel overwhelmed by the magnitude of some of the issues facing people with HD and their families.
- Personal stories by three young people affected Huntingtons, Matt, Jessica and Clint. Reflections of their personal journeys as children growing up with a parent having Huntingtons.
- Raymond Roos from the Netherlands who ran a 'Patient Education Program' to see if they could:
  1. Reduce the incidence of depression and negative moods,
  2. Increase the quality of life,
  3. Delay symptom onset,
  4. Increase Awareness.

  The outcomes of the Program were very positive and the details are soon to be published.
- The Scottish Association has a brilliant resource called the 'Roadmap to HD'.

If you would like further details on any of these topics, we have a range of literature from the conference. This includes the WCHD 2011 program, a list of abstracts for the presentations, a printout of the Sarah Tabrizi presentation slides, a copy of the 'Scottish' roadmap, details of the Netherlands care and residential programs, and of Raymond Roos' 'Patient Education Program'. We welcome your interest in matters HD generally and in particular on information from the World Congress.

GALENEA & CHDI FOUNDATION ANNOUNCE COLLABORATION TO IDENTIFY KEY SYNAPTIC DYSFUNCTION IN HUNTINGTON'S DISEASE

Program aims to pave the way for novel drug discovery.

Press release Sept 6th 2011 8:00 am

http://www.marketwatch.com/story/galenea-and-chdi-foundation-announce-collaboration-to-identify-key-synaptic-dysfunction-in-huntingtons-disease-2011-09-06

CAMBRIDGE, Mass. and NEW YORK, Sept. 6, 2011 /PRNewswire via COMTEX/ - Galenea Corp. and CHDI Foundation, Inc. have announced a collaboration to identify synaptic dysfunction linked to Huntington's Disease (HD) utilizing Galenea's proprietary synaptic transmission drug discovery platform. Mounting evidence indicates that mutant huntingtin protein, the molecular defect in HD, disrupts normal synaptic function, contributing to the behavioral, cognitive, and motor symptoms of this devastating neurodegenerative disorder.

Galenea's innovative platform will provide new insights into the disease mechanism and, ultimately, offer a different approach to the discovery of therapies for HD. "The application of Galenea's high throughput platform to investigate synaptic transmission dysfunction in HD will be very informative to developing drugs that target, in a very precise way, the molecular underpinnings of cognitive and behavioral defects in HD," said Ramee Lee, PhD, Director, Early Discovery Initiative at CHDI. "We are excited to work with Galenea to determine whether EEG signatures in rodent HD models are reflective of the synaptic dysfunction seen in HD patients. Such information could significantly facilitate HD preclinical drug discovery efforts," added George Yohrling, PhD, Director, Target Assessment at CHDI.

Dysfunctions in synaptic transmission, the fundamental process by which neurons communicate, play a critical role in many central nervous system diseases, including HD. Galenea's platform examines synaptic transmission on multiple levels. Galenea's MANTRA (TM) (Multiwell Automated Neuro Transmission Assay) system, a revolutionary high throughput screening assay, monitors synaptic events at the cellular level using primary neuronal cultures. At the network level, Galenea has developed a state-of-the-art system for establishing in vivo electroencephalography (EEG) measures of behaviors in rodent disease models by monitoring brain and behavioural activities in parallel. The collaboration will employ this two-pronged approach to identify and characterize the synaptic defects that occur in HD at both the neuronal and network levels.

"We are pleased to be collaborating with CHDI who bring deep expertise and resources to the collaboration. Our vision is to translate initial discoveries that emerge from this critical first step into novel drug candidates that positively impact the lives of Huntington's disease patients," said Mark Benjamin, DSc, Galenea's President and CEO. David Gerber, PhD, VP of CNS Research added, "The opportunity to apply Galenea's platform to the discovery of synaptic-based therapeutics for HD is ideal. I am confident that this collaboration will yield new insights into the underlying pathology of this disease and ultimately new therapeutic candidates."

SOURCE: Galenea Corp

'THE HD VIEW' – Help 4 HD RADIO BLOG PREMIERED ON OCTOBER 4th 2011

Greetings!

Introducing "The HD View" - another fabulous program brought to you by HD Support Groups and Help 4 HD on Blog Talk Radio. It is my sincerest desire to reach the JHD and HD community in a very special way. As we break through communication barriers with "The HD View", let's have some fun too. We have an incredible panel of prominent JHD/HD community members to discuss your questions and concerns.

About The HD View

Tune in on the first Monday of the month (unless otherwise posted) at 3:30 pm PT/6:30 pm ET/11:30 pm UK time to "The HD View". This is a new program brought to you by HD Support Groups and Help 4 HD on Blog Talk Radio.

We will be discussing current topics and concerns from the JHD and HD community with a little music mixed in. Our incredible panel of prominent individuals within the JHD and HD community will be available to discuss your questions. With their experience and knowledge, we can face the challenges of Huntington's disease together.

Link is www.blogtalkradio.com/help4hd

Love and peace to all, Melissa Biliardi

help4hd@yahoo.com

BIOMARKER FOR HUNTINGTON'S DISEASE IDENTIFIED

http://www.sciencenews.org/view/generic/id/334911/title/Biomarker_for_Huntington%E2%80%99s_disease_identified

Measures of gene activity indicate illness progression, treatment effectiveness

By Nick Bascom Web edition: Tuesday, October 4th, 2011

Scientists on the trail of treatments for Huntington's Disease may have found a way to track their success. A new study reports that patients with Huntington's Disease have higher levels of expression of a gene called H2AFY in their blood compared with healthy people. What's more, patients treated with a drug that slows the effects of the disease had reduced levels of H2AFY activity compared with people given a placebo.

The results suggest that H2AFY could serve as a tool for monitoring the progression of the disease and an indicator of whether prospective treatments are working, researchers report online October 3 in the Proceedings of the National Academy of Sciences.

“Biomarker identification for Huntington’s disease is critically important for clinical trials,” says Leslie Thompson, director of the Interdepartmental Neuroscience Program at the University of California, Irvine, who was not involved in the study.

Huntington’s disease is a hereditary movement disorder marked by involuntary bodily twitches and jerks. The damage the disorder does to nerve cells also causes severe depression and impairs a patient’s ability to reason clearly. “It’s a devastating disease,” and one for which there is no cure, says neurologist Clemens Scherzer of Brigham and Women’s Hospital in Boston, who led the new study.

Although some promising treatments are now being tested in clinical trials, one roadblock in their development has been sorting out whether candidate drugs actually halt progression of the disease. To address this problem, Scherzer and colleagues sought a biomarker - a biological indicator they could easily measure - that would provide them with a snapshot of the state of a patient’s disease.

Casting a wide net, the research team analyzed expression data from every gene in the blood cells of more than 100 people. Eight people had Huntington’s disease, and more than 80 had other neurological conditions. Compared with the other participants, the Huntington’s patients had elevated levels of H2AFY expression - levels that were as much as two times higher compared with those of healthy people.

To further study the gene as a candidate biomarker, Scherzer began collaborating with Steven Hersch and colleagues at Massachusetts General Hospital, who were conducting a clinical trial of a compound called sodium phenylbutyrate as a potential therapeutic drug for Huntington’s.

The collaborators measured H2AFY activity in blood cells of trial participants before and after they began taking sodium phenylbutyrate. As patients continued to take the compound, the researchers found decreasing H2AFY activity - a sign that the drug-like compound might be slowing the nerve-cell damage inflicted by the disease.

Scherzer says he hopes that H2AFY and other biomarkers like it will help speed the development of new treatments for the disease. “The key is to make clinical trials for Huntington’s disease more efficient,” he says.

TECHNOLOGY HELPING TO BREAK THE CURSE OF HD

http://www.heraldsun.com.au/news/more-news/scarlett-born-to-a-life-free-of-dads-curse/story-fn7x8me2-1226134260521

By Daniel Hoy from Herald Sun September 12, 2011 12:00A

Sean Egan with wife Annabelle and daughter Scarlett. Picture: Bruce Magilton *Source:* Herald Sun

The same technology that enabled Sean Egan to find out if he carried the defective Huntington's Disease gene also enabled him to bring a child into the world who would live free of the deadly curse.

When Mr. Egan was 16, his father died as a result of Huntington's Disease. The Frankston school teacher, now 43, knew he had a 50-50 chance of carrying the gene that would shorten his life. So in 2002, he decided to discover if he actually did, or did not, carry the gene. The results were positive.

"(Before I found out) I spent a lot of time worrying if I had the gene," he said. "I'd go to bed thinking about it. I felt (that) if I was going to worry, I wanted to have something to worry about."

Last year, he faced another tough question. Should he start a family? "My wife was keen for a family but we both felt we couldn't bring a child into the world who had (Huntington's) or even had a chance of having it," he said. "I couldn't do that."

Mr. Egan and his wife, Annabelle, used IVF and pre-genetic testing to ensure their baby did not carry the disease. Mrs. Egan's eggs were fertilised using IVF and three days later doctors tested the cells for the gene. The eggs without the gene were implanted. Seventeen months ago, baby Scarlett was born without a life sentence.

Mr. Egan hopes the trial into Huntington's drug PBT2 will bring about a cure. But he's not counting on it. "I can't afford to get my hopes up when it's a long way down the track from being successful with mice and rats to getting on the market," he said.

For now, Mr. Egan focuses on staying fit and healthy. "There is some scientific evidence that if you stay active physically you can delay onset and delay progression," he said.

PRANA BIOTECH'S NEW TRIAL OF PBT2 IN HD: THE LOWDOWN

This article is reprinted courtesy of the HD Buzz website.

Prana Biotech's PBT2 trial in Huntington's Disease: what we know so far & what copper has to do with the mutant protein

By Dr Ed Wild (http:/en.hdbuzz.net/people/Ed Wild) on October 03, 2011 Edited by Dr Jeff Carroll (http:/en.hdbuzz.net/people/Jeff Carroll)

Prana Biotech has announced a Phase 2 clinical trial in Huntington's Disease patients in Australia and the USA. Here's what we know so far about the trial, the company, the drug and the friendship between copper and the mutant huntingtin protein.

PBT2 clinical trial announced

A new international clinical trial of a drug that might slow the progression of Huntington's Disease is bound to cause excitement. With the trial's launch coinciding with the opening of the Huntington's Disease World Congress, and the company behind the trial is based in the town hosting the Congress, headlines are sure to follow.

So you may already have heard that Prana Biotech's drug PBT2 will be tested in an international clinical trial, beginning late 2011 in Australia and the USA. We're here to give you as much detail as we can about the trial and the drug, as well as examining the evidence that PBT2 might work in Huntington's disease.

No, not that kind of copper!

The trial

Drug trials involving humans are divided into three phases.

Phase 1 is when healthy volunteers are given a drug for the first time. In **Phase 2**, the drug is given to patients with symptoms for the first time, but the main aim is to check it's safe and doesn't make things worse. **Phase 3** trials are much larger, involving many hundreds of volunteers, and aim to provide the evidence required to get a drug approved.

Prana's PBT2 trial in Huntington's is a **Phase 2** trial — so, it'll be quite small overall, involving a hundred volunteers. In a press release, the company says it's aiming to involve about **15 sites** in Australia and the US — that means an average of six to seven volunteers per site. The trial will involve people with 'early' Huntington's disease. Broadly speaking, that means people who have HD symptoms like involuntary movements, that are fairly mild and don't prevent them walking, working or functioning at home.

Each early HD volunteer will be enrolled for **six months**, but because the company hasn't yet announced the full trial design, we can't tell you how many volunteers will be given the drug and how many a *placebo* pill, containing no drug, for comparison. Nor do we know what tests will be used to assess the effect of the drug, and whether the trial will involve things like *MRI* brain scanning.

"If metals can help proteins to do good, can they also contribute to the harm caused by abnormal proteins?"

Another unknown is which sites will be chosen for the trial in Australia and the USA, but Massachusetts General Hospital in Boston, USA and Johns Hopkins University in Baltimore have been confirmed as partners. Given Prana's local connection, we'll be surprised if Melbourne isn't also included as an Australian site.

The company has announced that the results are expected by **late 2013**.

Because it's a phase 2 trial, the main aims will be to make sure the drug is 'safe and well tolerated' — in other words, that it doesn't cause a worsening of symptoms or any unexpected side effects, and to settle on the best dose for larger phase 3 studies. But the company will also be hoping that the phase 2 trials will give a suggestion that PBT2 can change the disease in the right direction, to give the confidence to proceed to an expensive phase 3 trial.

The company

Prana Biotech is a relatively small pharmaceutical company, founded in Melbourne in 1997. In Hindu philosophy, 'prana' is a powerful, mysterious force that sustains life. Prana's research is rather more down-to-earth, though: it focuses on the interactions between proteins — the molecular machines that carry out most important functions in our cells — and metals.

The idea that our bodies rely on metals might sound odd but we're all familiar, at least from Popeye cartoons, with the idea that iron is essential for health. The same's true of many other metals — sometimes called 'trace elements'.

Proteins and metals: unexpected friends

Iron's a pretty good example of an important interaction between proteins and metals. Our blood carries oxygen from the air we breathe to our organs, inside our red blood cells. Those cells are red because they contain a red protein called hemoglobin. But the oxygen-carrying power of hemoglobin relies on a tiny amount of iron, locked deep inside the protein. Lack of iron causes anemia, which makes people pale and breathless because their blood can't carry enough oxygen.

PBT2 aims to prevent copper from sticking to the mutant huntingtin protein - a possible step on the road to Huntington's Disease. Researchers are increasingly aware that many proteins need a little help from metals to get their work done. But we also know that proteins can go bad, and cause harm. The mutant *huntingtin protein*, produced in the cells of people with an expanded HD gene, is a perfect example, but there are many others: Alzheimer's and Parkinson's are both diseases in which proteins cause harm and form clumps called '*aggregates*' in brain cells.

So if metals can help proteins to do good, can they also contribute to the harm caused by abnormal proteins? Increasingly, researchers think so, and that's the answer Prana is betting on.

Copper, PBT2 and Alzheimer's

Prana is particularly interested in the role played by **copper** in the harmful effects of abnormal proteins. PBT2 was developed as a treatment for Alzheimer's disease, where the protein that causes damage, '*amyloid*', becomes more sticky when copper atoms attach to it. PBT reduces the amount of copper that attaches to *amyloid*.

In a 2008 Phase 2 trial of PBT2, published in Lancet Neurology, treatment of Alzheimer's patients with PBT2 appeared to reduce the amount of *amyloid* protein in the spinal fluid that surrounds the brain, and the drug didn't cause serious side

effects. Prana is now planning further studies to look for effects of PBT2 on *amyloid* levels in the brain, and working towards a large Phase 3 trial in Alzheimer's.

What about Huntington's disease?

Possible effects of copper in Huntington's disease haven't been studied in as much detail as in Alzheimer's. What we know, though, is that copper deposits have been found in the worst-affected brain regions, and the *huntingtin protein* has several areas that copper atoms can attach to.

At the International Conference on Alzheimer's disease and Related Disorders in 2010, Prof. Robert Cherny of Prana Biotech presented data from a trial of PBT2 in HD model mice. Animals given the drug had improved movement control and lived around 40% longer than untreated mice. This success in the HD mouse model is the basis for Prana's decision to perform a clinical trial in Huntington's disease patients.

PBT2 and copper in context

It's refreshing to see a new player like Prana enter the field of Huntington's disease research, because it's hard to see how we'll find and test treatments to slow HD without pharmaceutical companies.

Because caution is a good seasoning for optimism, it's worth mentioning a couple of things about PBT2.

While the results for PBT2 in the HD mice are encouraging, there's no escaping the fact that, so far, every drug that's worked in an HD mouse has failed to show benefits when tested in humans. Of course, that will be true until the first drug works in patients — and PBT2 might be that drug. But because no mouse is a perfect model of human Huntington's disease, many experienced HD researchers now feel that a new drug should be tested in several different animal models before being taken into human trials.

Bearing in mind our 'ten golden rules' for reading an HD news story, we also note that Prana's HD mouse results were reported at a scientific conference, but haven't yet been published in a peer-reviewed scientific journal — where they'd be scrutinized more closely by independent experts before being accepted.

Finally, we understand that anyone with HD or at risk wants to know what they can do now to give their brain the best fighting chance. But we'd like to point out that if copper is important in HD, it's not because there's too much copper in the brain or body overall. So, there's no reason to believe that restricting copper in the diet, or taking supplements to remove copper, would be beneficial for people with the HD mutation.

With these caveats in mind, we look forward to hearing more details of the trial as they emerge, and we'll keep you posted of any major developments.

INSPIRING DAYS FOR HUNTINGTON'S RESEARCH

Reprinted courtesy of 'Brain Matters' Spring 2011 issue, the Florey Neuroscience Institutes

The Florey Neuroscience Institutes welcomed the Huntington's Disease World Congress to Melbourne in September. This unique conference brought together researchers, clinicians, carers and families who shared the latest in the fight against this crippling genetic disorder.

Having inherited the Huntington's Disease gene from his father, restaurant owner Tony is driven to help researchers like Associate Professor Anthony Hannan to find a cure. Tony sat on a panel at the congress in September, giving a community perspective on life with the gene.

And for researchers like Anthony who helped bid for the congress to come to Melbourne, there was no greater motivator than to mix with patients and families who live with the disease every day.

"To meet people like Tony is utterly inspirational," Anthony says. "The people in my lab and I are passionate about our research and to be face-to-face with people you might help is very inspiring."

Some of the best Huntington's researchers in the world were in Melbourne, sharing their latest results with colleagues. In the evenings, lay people, families and carers received a briefing of the day's progress – without the scientific jargon.

As Tony says: "One of the things the research can provide us is a sense of control."

Huntington's is an inherited single-gene abnormality that causes specific neurons in the brain to become dysfunctional and eventually die. The condition involves cognitive deficits culminating in dementia, psychiatric symptoms like depression and movement disorders.

Tony, a Melburnian living with the Huntington's Disease gene chats with the Florey's Associate Professor Anthony Hannan

Tony has been particularly heartened by Anthony's recent work as it reinforces his own approach to life. He is fit, strong and mentally well thanks to regular exercise, yoga and a healthy diet.

Anthony's research has shown that physical exercise and mental activity are good for the brain and may build a "reserve" to assist those who are asymptomatic.

Anthony's lab has previously shown that increased mental and physical activity can delay onset of Huntington's in mice. At the Florey they are now identifying molecules crucial for the beneficial effects of mental and physical stimulation.

The aim is to use the molecules in 'enviromimetics' – new drugs that will mimic or enhance the therapeutic effects of cognitive stimulation and physical exercise.

Enviromimetics would not only have potential benefits for Huntington's, but also other major brain diseases such as Alzheimer's and Parkinson's.

Drs Thibault Renoir, Terence Pang and Anthony have also recently shown that anxiety and depression in Huntington's are helped through physical exercise. They have identified key molecular pathways in the brain involving the chemical serotonin that may be crucial for exercise-induced antidepressant effects.

But for Tony, life is travelling well.

"When you're told you have the gene, you go through a range of phases starting with a very emotional period when you consider your own life and what lies ahead. But then, nothing really changes and you develop great hope that work by people like Anthony will come up with a breakthrough cure or treatment."

"You can't let it rule your life and it doesn't seem real while there are no symptoms. But I'm not going to waste my life so I'm out there having fun.

"While I no longer go out disco dancing, I own a café in St Kilda, love cooking and enjoy hanging out with my two-and-a-half year old twins (who do not carry the gene)."

He is yet to experience the early symptoms including a lack of coordination or unsteady gait.

And for Anthony and his team in the neural plasticity lab at the Florey, the work continues at an urgent pace.

GENE SILENCING TAKES A TARGETED STEP FORWARD

This article is reprinted courtesy of the HD Buzz website.

Targeting the mutant Huntington's Disease gene for silencing, while leaving the healthy gene untouched

By Dr Michael Orth on October 07, 2011 Edited by Dr Ed Wild

Most Huntington's Disease researchers agree silencing the huntingtin gene is one of the most promising treatments in the pipeline. But we don't know whether switching off the gene is safe. Now a Canadian team has shown that 'allele-specific' gene silencing - targeting just the mutant copy of the gene, and leaving the healthy copy active - works and is safe in an HD mouse.

Gene silencing recap

Gene silencing is a promising approach to preventing and treating HD. Each step along the way to human patients has to be carefully checked and tested.

Gene silencing is a promising approach to preventing and treating HD. Each step along the way to human patients has to be carefully checked and tested. It's clear what causes Huntington's Disease: a 'spelling mistake' in the gene that tells cells how to make a protein called huntingtin. The mutant gene itself causes no harm: it's the protein built using the gene's instructions that causes problems.

If we could tell cells not to make the harmful protein, in theory the damage it inflicts could be avoided. That's the idea behind ***gene silencing*** therapies, also known as **huntingtin silencing**.

When a cell uses a gene to make a protein, the first step is to make 'working' copies of the gene. They're made from a DNA-like chemical called '*messenger RNA*' or *mRNA*. This *mRNA* message is the target of *gene silencing* treatments.

Scientists can make molecules of DNA, *RNA* and similar chemicals, that are precisely designed to stick to the huntingtin *mRNA* message. When this happens, cells stop reading the message and protein production stops. In fact, cells remove the message. Effectively, this aims to turn off the huntingtin gene, halting production of the harmful protein.

When the drug molecule is made of DNA, it's called an ***anti-sense*** **oligonucleotide**, or ***ASO***.

You can read more background on *gene silencing* in our '*Gene silencing* primer' article at HDBuzz.net.

Allele-specific silencing

Gene silencing therapies sound very attractive in HD. So why not test them in patients straight away? One problem is that we don't know if it's safe to switch off the huntingtin gene.

Each cell has two copies of every gene — one inherited from each parent. A single copy of a gene is called an ***allele***. In the case of the Huntington's disease gene, nearly everyone who has the disease, or who will develop it, has one normal *allele* — called the ***'wild-type' allele*** — and one mutant *allele*. One mutant *allele* is enough to cause all the problems of HD.

"Mutant protein levels fell by 80%, while the wild-type protein fell by only 3%?"

We don't fully understand what the *huntingtin protein* does, but it certainly seems essential for many different aspects of normal cell function. Disabling both alleles of the huntingtin gene entirely might be dangerous — and could cause more harm than good.

So, one option that's being looked at for *gene silencing* in HD is to selectively target the mutant *allele*, without touching the *wild-type allele*.

Work by Prof Michael Hayden's group in Vancouver, Canada, addressed how this might be done. The work was just published in the journal Molecular Therapy. To target the mutant *allele*, Dr Jeff Carroll and Dr Simon Warby from Hayden's lab looked for parts of the mutant *allele* that were different from the *wild-type allele*.

(If the name Jeff Carroll seems familiar — yes, it's the co-founder of HDBuzz. He didn't have any input into this HDBuzz article, though.)

Targeting the mutant allele with SNPs

Hayden's team made use of different patterns of single-letter spelling differences in the mutant and the *wild-type* huntingtin alleles. These single-letter differences are called '*single nucleotide polymorphisms*' or SNPs — pronounced 'snips'.

We each have thousands of SNPs that make our genes different from other people's. Most SNPs are 'silent' — they don't make any difference to the functioning of our genes.

The researchers had a lucky break. It turned out to be quite easy to distinguish between the mutant and *wild-type* huntingtin alleles using SNPs. They found 50 SNPs that were seen more frequently in the mutant *allele* than the *wild-type*.

Next, they made *ASO* drugs that would target the SNPs they'd found. Using skin cells grown in the lab, they evaluated how well they recognized their targets and how well they suppressed the mutant huntingtin message, while preserving the message from the *wild-type allele*. More than half of the candidate *ASOs* failed at this stage.

The next question was how many HD patients carried each target *SNP*. That's really important, because if a *SNP* is rare, not many patients will benefit from an *ASO* treatment that targets it.

By asking this question, Hayden's team narrowed the search down to four *ASOs*.

Testing the ASOs in neurons

The next step involved evaluating how well those four *ASOs* would reduce the production of mutant huntingtin in *neurons*.

They used *neurons* from HD mice, grown in the lab, to select the best-performing *ASO*.

After making some chemical changes to maximize the *ASO*'s effects, they went on to test how well the treatment worked in living HD mice, when injected into the brain areas that are worst affected in HD.

They found that their *ASO* was effective in selectively blocking the message from the mutant *HTT allele*. It caused levels of mutant protein to be reduced by 80%, while levels of the *wild-type* protein dropped by only 3%. In the mice, the *ASO* treatment was safe and well tolerated. In these mice, at least, this *ASO* looks like a good treatment.

Allele-specific gene silencing targets the mutant huntingtin allele, while aiming to leave the healthy, or 'wild-type' allele

What's next?

The obvious question is whether such a treatment may be an option in people. Hayden's team claims that if their original list of SNPs was whittled down to the top three, they would be able to target the mutant *allele* selectively in 85% of HD patients. The best *SNP* they tested is present in about half of HD patients.

Obviously, mice are still quite different from human beings. One of the challenges that remains is how to give the treatment in human beings, with their large brains. In addition, treatment may need to be given repeatedly, because humans live much longer than mice and the effects may wear off. There may be side effects in humans that the HD mice just didn't predict — for example, switching off other important genes by mistake that humans have but mice don't. Another issue is how tell whether this treatment is working — you can't go chopping out bits of people's brains to look at under the microscope. Finally, there's the question of the 15% of patients who aren't lucky enough to have the SNPs that these *ASOs* target.

So, there's lots of work to be done, but this is an exciting proof that *allele*-specific *gene silencing* can work safely in HD mice and that, in theory at least, a small number of SNPs could treat the majority of patients.

We try to avoid being too specific when it comes to timelines, because we know there's lots that can go wrong along the way. So, we might look back and kick ourselves for saying this, but HDBuzz predicts that the first trial of *gene silencing* in human patients will begin in the next two years. Needless to say, whenever it happens, you'll read about on http://hdbuzz.net/

FINANCIAL ASSISTANCE TO HUNTINGTONS QUEENSLAND

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Our sincere thanks continue to **Beecham Holden Caboolture** who has kindly nominated Huntingtons Queensland as the beneficiary for a charitable donation by way of CTP on first time registered vehicles sold through them.

You can contact them on:

Ph: 1300 154 876
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If you would like to donate to Huntingtons Queensland and have internet access, go to our website www.huntingtonsqld.com. Scroll down to the 'Please Make a Donation' section on the bottom left, click on the button <CLICK HERE> and follow the instructions. All donations over $2 are tax deductible and we will send you a receipt for taxation purposes.

POTENTIAL SUPPORT FROM MACQUARIE & THEIR STAFF

The Macquarie Group Foundation, one of Australia's oldest and largest corporate benefactors, supports Macquarie staff personal donations and fundraising activities by matching staff contributions to community organisations. Huntingtons Queensland is registered with the Foundation so if you know anyone who works for Macquarie please request and / or encourage them to nominate Huntingtons Queensland as their chosen community organisation.

SUNNYBANK COMMUNITY & SPORTS CLUB

The Club has recently made a second payment to Huntingtons Queensland of $10,000. This is part two of a three-year $30,000 grant to support the Huntingtons Queensland Youth Support Program. The main focus of the program is to provide support and opportunities to young family members.

We sincerely thank the Club once again for their wonderful generosity and kind support.

CAN YOU HELP REDUCE OUR RUNNING COSTS?

At Huntingtons Queensland we are constantly seeking ways to keep our costs down so that we can put more money into providing assistance to our families. You can help us by opting to receive your Huntington's Newsletter by email rather than by post.

If you wish to help us, please send an email to admin@huntingtonsqld.com with your name and contact details. If you are a health professional, please include the name of your organisation.

Alternatively, please let us know if you DO NOT wish to receive our Newsletter, by EMAIL OR POST.

We also look forward to our members renewing their annual memberships for 2011-2012 and we welcome new members.

HUNTINGTONS QUEENSLAND

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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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