2015 Huntington's Disease Therapeutics Conference: Day 3

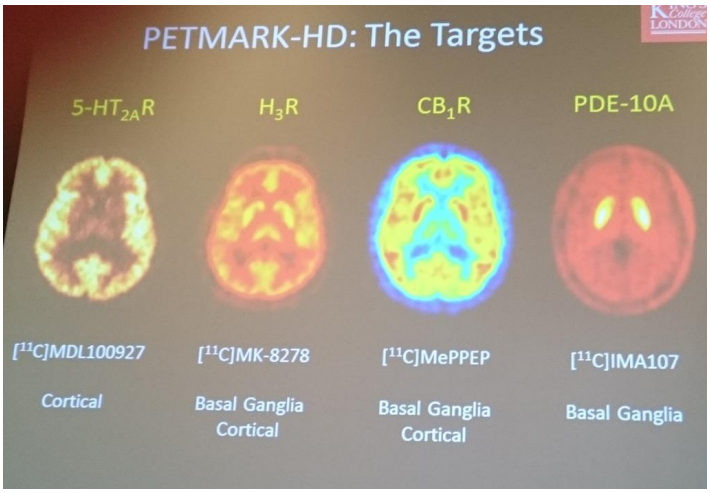
Day 3 of updates from the annual HD Therapeutics Conference in Palm Springs

By Dr Jeff Carroll | **March 03, 2015** | **Edited by Professor Ed Wild**

Our final report from the Annual Huntington's Disease Therapeutics Conference.

Thursday morning: Lessons from clinical research

09:06 - This morning's sessions are focused on findings in people with HD, rather than animal models or cells. Important stuff!



Marios Politis announced his PETMARK-HD study, which will compare multiple molecular scanning methods for the first time in HD.

09:09 - Gil Di Paolo is interested in what scientists call "lipids" and most people call "fats" in the brain. Our brains are about 60% fat.

09:11 - Brain fats come in a bewildering array of types, some abundant and some quite rare. Even rare fat types play important roles in the brain.

09:13 - Di Paolo reminds the audience that thehuntingtin protein likes to stick to "membranes", the fatty sheets that form cell boundaries

09:13 - Also, production of fats is slowed in the HD brain, which could result in changes in the levels of various fats in the brain.

09:15 - Di Paolo's lab specializes is "lipidomics", or the accurate measurement of hundreds (or even thousands!) of different fatty molecules

09:16 - Di Paolo has been working with HD brains to see if it's true that there are reductions in the amounts of important fats.

09:18 - Di Paolo is also studying the fatty molecules found in the blood of HD mutation carriers from the TRACK-HD study

09:24 - Each tissue has a unique fat signature - the brain is very different than the blood in terms of what fats are present

09:28 - Di Paolo observes a number of very specific fat changes in the blood of people carrying the HD mutation

09:30 - These changes are distinct from changes seen in Parkinsons disease, suggesting something specific might be going on in HD

09:36 - Di Paolo just for these results 5 days ago, so watch this space for more a more detailed analysis of this exciting new results.

09:40 - **Disclaimer:** the next guy up is some dude named Dr Ed Wild, so beware our objectivity might be slightly compromised!

09:49 - Wild is working to isolate cerebrospinal fluid from HD mutation carriers, an important way of seeing what's going on in the brain

09:53 - Why is spinal fluid important? We want to learn about brains, but can't sample brain tissue safely. Sampling spinal fluid is much safer.

09:56 - Other diseases, like Alzheimers, have well characterized spinal fluid markers to track disease progression, but HD doesn't

09:58 - Wild has used a fancy machine that lets him measure tiny amounts of thehuntingtin protein in spinal fluid

1000 - Interestingly, the amount of huntingtin protein in the spinal fluid rises with HD progression, and correlates with HD symptoms

1002 - The spinal fluid seems special - blood levels of thehuntingtin protein don't show the same interesting pattern.

1006 - Wild is also using his spinal fluid to investigate ideas scientists have proposed, measuring levels of specific chemicals in spinal fluid

1010 - Wild's collection of spinal fluid is an important resource to provide a window into the HD brain

1012 - Wild is also interested in the flow of spinal fluid throughout the brain - he's launching an imaging study to investigate this

1014 - Wild also announced the launch of his 'HDClarity' consortium, which will collect high quality spinal fluid at a number of centers worldwide

1023 - Guillermo Cecchi, of IBM research, addresses the conference on his teams use of computational techniques in biology and medicine

1024 - In particular, he's studying whether computer analysis of speech can be used to help in psychiatry. Could Siri replace your therapist?

1049 - Awesome to see next generation computer technology and being used to help understand Huntington's disease

11:23 - Diane Stephenson of the Critical Path Institute addresses the conference - her organization works to speed development of therapies.

11:25 - The goal of the Critical Path Outcome is to bring together groups involved in developing drugs - companies, patients and government agencies

11:29 - They try to fill gaps in the drug development process to speed the process of getting drugs approved.

11:30 - A major goal is to get scientists, companies and other stakeholders to share their data from clinical trials

> **"There's a lot of excitement around the upcoming trial of Isis Pharmaceuticals' trial of a 'gene silencing' drug. But we must remember it focuses primarily on safety "**

11:32 - More on the Critical Path Institute here: http://c-path.org/

11:36 - A major problem that exists in drug development is that a large amount of data about patients and drugs is spread across many databases

11:37 - The CPI has been developing techniques to standardize all this data and put it together so everyone can work with standard databases

11:38 - These databases about drug effects and disease progression can help drug companies plan better clinical trials in the future

11:40 - With all this data collected, it's possible to actually simulate a clinical trial before you run it - asking 'what-if' types of questions

11:42 - These computer simulations let people planning trials game out the best way to run efficient trials ahead of time

11:57 - Michal Geva of Teva Pharmaceuticals @tevapharm offers an update on Teva's Huntington's disease drug programs

11:57 - In an unprecedented show of confidence in the HD community, Teva has not one but two drugs in clinical trials for Huntington's disease

11:58 - The first drug is pridopidine, also known as Huntexil. This is aimed at improving movement symptoms in HD http://en.hdbuzz.net/025

12:00 - Teva hopes that their Pride-HD study will provide the evidence needed to get Huntexil licensed for HD patients http://www.huntington-study-group.org/CurrentClinicalTrials/PrideHD/tabid/305/Default.aspx

12:02 - Day 2 of updates from the annual HDTherapeutics Conference in Palm Springs http://en.hdbuzz.net/190

12:08 - While Pride-HD is happening, Teva's scientists have shown some interesting things about the drug...

12:08 - ... including a hint that it could help with the connections between brain cells

12:15 - Teva lso found pridopidine may increase a chemical calledBDNF, which protects brain cells. This may not happen in people though!

12:17 - Teva's second drug is laquinimod, which is being tested in another Huntington's disease trial - LEGATO-HD. http://www.huntington-study-group.org/CurrentClinicalTrials/LEGATOHD/tabid/317/Default.aspx

12:18 - Laquinimod aims to alter the behaviour of the brain's immune cells - calledmicroglia. They're overactive in HD and may be doing harm

12:19 - So Teva hopes that damping down the activity ofmicroglia might help brain cells to survive in HD, or even slow progression.

Thursday afternoon: Clinical trial updates

14:11 - Sarah Tabrizi and Sarah Gregory, UCL, address the conference on the findings of the "TRACKOn-HD" study

14:12 - TRACKOn is designed to follow up the findings of the TRACK-HDobservational study, which found a number of changes in HD mutation carriers

14:16 - Interestingly, in the TRACK-HD study found a number of brain imaging changes that weren't associated with changes in thinking ability.

14:19 - So, how can the brain shrink without causing problems in thinking ability? Tabrizi is interested in how HD brains 'compensate' during HD.

14:20 - Brain imaging from the TRACKOn-HD study is being used to understand how communication between brain regions is altered in HD.

14:23 - There seems to be much less communications between distant brain regions in HD, and more short range communication

14:27 - Tabrizi's team is interested in designing experiments that let them study how brains undergoing damage are coping.

14:33 - They've been able to find patterns of brain activity that are higher in HD mutation carriers doing better on thinking tasks

14:35 - This suggests that brains do have some ability to cope with ongoing damage in HD, at least in some people.

14:36 - But, who cares, can this kind of information help people with HD?

14:37 - Tabrizi is interested in whether people can be trained to use these compensation techniques.

Dr Ed Wild of UCL (and co-founder of HDBuzz) reported on his work using cerebrospinal fluid in HD. For the first time, Wild and colleagues have detected and measured how much of the mutant huntingtin protein is present in the fluid. Hopefully this will help with forthcoming 'gene silencing' trials.

14:38 - Her group has done a "neurofeedback" study in HD patients, putting them in anMRI machine and training them to modify their brain activity

14:39 - This training led to specific patterns of brain activity, and improved performance on a simple movement task.

14:42 - Tabrizi suggests that this kind of neurofeedback study isn't a treatment for HD, but more like "physical therapy for the brain".

14:53 - Marios Politis from King's College London uses a brain scan technique called PET scanning to study the brain in HD

14:54 - PET uses injections of chemicals called ‘tracers’ to look at changes in specific cell types in the brain.

14:55 - For example, one tracer shows changes in cells that use the signalling molecule dopamine, while another shows the activation of immune cells

15:08 - **Politis:** PET is a powerful tool but so many different methods have been used in the past, it’s difficult to be sure what’s going on in HD

15:11 - Politis announces PETMARK-HD, a CHDI-supported study of PET imaging that aims to overcome these issues

15:19 - Politis illustrates the different chemical brain systems that will be looked at in PETMARK-HD http://t.co/mghXgruyAb

15:23 - Politis will also use PET to study the overlapping brain networks that are involved in HD

16:02 - Ray Dorsey of University of Rochester and the Huntington Study Group gives an overview of previous clinical trials in HD

16:08 - **Dorsey:** 2014 was remarkable for the early halting of 2 huge trials for lack of benefit http://hdbuzz.net/181 http://en.hdbuzz.net/171

16:09 - However, several trials have shown new possible treatments to be at least safe and well tolerated this year, and many more trials planned

16:13 - The Huntington Study Group publishes HD Insights which regularly offers updates on clinical trials in HD http://hdinsights.org

16:17 - The next generation of trials, starting now and soon, will be of drugs specifically aimed at known problems in Huntington’s disease

16:37 - Finally Prof Bernhard Landwehrmeyer closes up with a look ahead to forthcoming clinical trials

16:38 - **Landwehrmeyer:** we are now testing drugs designed specifically for HD

16:40 - Future trials will also be strengthened by the use of biomarkers to give clearer ideas of what works and what doesn’t

16:44 - There’s a lot of excitement around the forthcoming trial of Isis Pharmaceuticals’ trial of a huntingtin lowering / gene silencing drug

16:44 - But we must remember the trial focuses primarily on safety

16:49 - **Landwehrmeyer:** people who don’t take part in the first gene silencing trial aren’t missing the boat

16:50 - If the drug proves safe, future trials will be bigger, and there’ll be other new drugs

too

16:57 - The Amaryllis trial is studying a drug aimed at improving brain signalling by reducing tha activity of an enzyme called PDE10A

16:59 - More on the Amaryllis trial here: http://www.hdsa.org/research/clinical-trials-1/pfizer-pde10a-inhibitor.html

01:04 - In Europe, a trial of deep brain stimulation - giving small electrical shocks to targeted brain areas - is planned to start in 2015

01:05 - Hopefully DBS will provide an additional treatment option for movement problems that don't respond to current drugs

01:08 - In summary: trials are happening - all HD family members should think about taking part so we can get these treatments tested ASAP!

Dr Wild and Dr Carroll have received research support from the Conference organizer, CHDI Foundation. For more information about our disclosure policy see our FAQ...

GLOSSARY

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

CSF A clear fluid produced by the brain, which surrounds and supports the brain and spinal cord.

huntingtin protein The protein produced by the HD gene.

gene silencing An approach to treating HD that uses targeted molecules to tell cells not to produce the harmful huntingtin protein

clinical trial Very carefully planned experiments designed to answer specific questions about how a drug affects human beings

observational A study in which measurements are made in human volunteers but no experimental drug or treatment is given

therapeutics treatments

microglia the brain's immune cells

dopamine A signaling chemical (neurotransmitter) involved in movement control, mood and motivation

BDNF brain-derived neurotrophic factor: a growth factor that may be able to protect neurons in HD

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