EuroBuzz Video: Day 1

Watch the full video of EuroBuzz day 1 with Jeff Carroll and Ed Wild at the Euro-HD Network Meeting in Stockholm

By Professor Ed Wild | **September 19, 2012** | **Edited by Dr Jeff Carroll**

Jeff Carroll and Ed Wild present EuroBuzz episode 1 - bringing the European HD Network Meeting direct to you, in plain language. Watch online!

ED: Ladies and Gentlemen, this is EuroBuzz. Please welcome your hosts Jeff Carroll and Ed Wild.

JEFF: Hi everybody, thanks for sticking with us through a long and exciting day of science. You guys are part of an experiment here. What we're hoping to do is bring some of the excitement of the meeting here that we all feel to our audience of HD families and caregivers worldwide. We're recording and will be sharing this with families via our website: HDBuzz, which for those of you who don't know is an information portal online for HD families to get information about both clinical and research news. So we all got a lot of excitement from scientists today and we're hoping via this short session tonight which we promise will end on time to bring this home to families. So thanks for being here.

ED: So what you're saying Jeff is we're going to be offering a combination of science and entertainment, or scientainment. [laughter]

JEFF: Only Ed Wild would say scientainment so no I would not say that

ED: But what we will be doing, whether we refer to it as scientainment or not, is shortly we'll be interviewing some of the top scientists who've been presenting today or will be presenting later on in the meeting so that they can talk directly to the global HD community about their research and share one or two facts about themselves in the process. Later on we'll be giving you an exciting sneak preview of some changes that are coming to HDBuzz in the very near future. But first because it's been a long day and we've all been concentrating very hard we want to wake everybody up with an exciting science quiz. So, everybody please stand up. This is not optional.

JEFF: This is the only exercise part of the whole thing actually.

ED: And in case you're still feeling lethargic and unmotivated the winner of our science quiz will be awarded Alfred - the HDBuzz fluffy neuron. Complete with dendritic spines so what more motivation could you possibly need. So question one Jeff.

JEFF: Here we go, in honor of our host city we're going to have a Nobel question. Yesterday we visited the Nobel museum where they have a really great exhibit you should catch if you can in which laureates are asked to describe their prize winning work in one picture - it's great In honor of that let's think about HD - gene silencing is a therapy we all talk about - don't say it out loud - think in your head and keep silent if you know the name of this person who pioneered gene silencing and won the Nobel prize in 2006.

ED: So everyone should have an answer, don't say it out loud. This quiz is based on an honor system. So you can stay standing if you got it wrong but you're only cheating yourselves. So the correct answer is of course Craig Mello who won the prize in 2006 for his work on RNA interference. If you got that right stay standing if you didn't get it right, and be honest, sit down - wow! That's really sorted the geeks from the chaff. Ok, we may not need all our questions here Jeff. I think we may need to dumb it down a little. We may not need all our questions Jeff. I think we may need to dumb it a little.

JEFF: This is going to be really challenging. This morning Michael Haydn of the University of British Columbia chaired a really important talk suggesting that Huntington disease may be much more prevalent than we thought. This has really important implications so we wanted to make sure you were paying attention. When Michael was speaking was he wearing a shirt that was: checked, striped or plain? Remember answer in your head don't say anything to your neighbors. Remember answer in your head.

ED: And the correct answer is - once again be honest with yourself and each other - it was delightful blue striped shirt - and here he is having some help to recover from his wardrobe malfunction earlier on so if you said striped stay standing, if you said anything else sit down in shame.

JEFF: This is good, we had the right number of questions. Final question: recently on HDBuzz we covered research out of Sweden from Professor Jan Sundquist... suggesting that Huntington's disease patients are about half as likely as non Huntington's disease

patients to get what? Remember - in your head. Everybody ready?

ED: So what condition might HD - the HD mutation - protect you against? The answer is cancer. Large epidemiological study looking at a huge population in Sweden. Huntington's disease patients after correction for age seem to be about 50% less at risk of cancer for a given age. So, if you got that wrong please sit down. We're down to a pool of hardcore geeks. I think it's time for the tie breaker.

JEFF: So this time closest guess wins - what is the official number of attendees at this meeting? Get a very solid, precise number in your head. Everybody ready?

ED: 690. 700. Neil? 200?

JEFF: You don't even want the neuron [laughter]

ED: 640. 670. 701. This is going to be close. The correct answer is 694! So by a margin of 1 I think Dr Hayden gets it. He said 690. So he wins a neuron!

ED: Pay very close attention you may need to know about this in your many future carers. And what are you going to sing for us? [laughter] No that was a rhetorical question, well done Michael [applause]

ED: OK, let us move to phase two of our plan. It's time for our interviews. We're going to be interviewing three scientists. So we'll move gently back to the couch area and Jeff will introduce our first guest.

JEFF: We asked everybody for something fun, we want our viewers at home to know the scientists are not just machines but people so we asked for some fun facts about people. First up we're going to talk with Dr Ray Truant from McMaster University in Canada. If you ask around you'll find that Ray is very widely respected in the scientific community, things at home, I don't know! Ray's son, young Max Truant, recently graduated from pre-kindergarten and was asked what he wanted to be when he grew up and he said a scientist: very inspiring. The teacher went on to say well what does a scientist do all day? To which young Max answered: eat cookies and watch YouTube. [laughter] Ray, do you want to come up and make some more YouTube? [applause] So Ray, everybody here heard your scientific talk today but recall that we're trying to make this accessible for everybody. You study the huntingtin protein, the protein that's mutated in everybody who has Huntington's disease. What does the huntingtin protein normally do? Why do we have an huntingtin protein?

RAY: It's a big question, I mean it's a question that we've all been stuck on. It's an unusually large protein. It is about seven times larger than the average protein that we see in every single cell in our bodies. It has many functions. We think one of the most critical functions is the fact that huntingtin is involved in response to stress. When I say stress I don't mean emotional stress of talking on a microphone in front of a large group of people: 690?

JEFF: 4

RAY: 4. I mean metabolic stresses. These are actually chemicals that are frequently been washed into the neurons in the brain on a, boring, daily basis, minute by minute.

JEFF: When you say metabolism you mean…

RAY: I mean burning of sugar and production of energy within the brain. These stresses get different and they increase in the aging brain. That is really what we're focussing on. The thought is that in a younger brain huntingtin has a role but it's a rather minor role and as the brain ages it has to take on more and more of an important role. Of course in those with HD it can't do that. That's the reason why we think we're seeing the loss of brain cells.

JEFF: That's why you think Huntington's disease happens later in life, because there's this aging brain problem?

RAY: One reason yes.

JEFF: So you presented a tonne of data and one of the things that's striking about the work you presented is you have all these beautiful technologies and techniques and they let you basically follow the huntingtin protein around as it goes about its business in the cell. As you watch those movies that your students are producing, maybe you're producing I'm not sure?

RAY: No, it's my students

ED: He's eating cookies!

RAY: I'm eating cookies in my office!

JEFF: What's the most surprising thing to you. What did you see that you didn't expect to see in those kind of movies?

RAY: Well what surprised us was that if we treated ourselves very nicely and gave them lots of nutrients and the proper temperature and proper life situation, which is completely artificial, nothing happened. What was interesting was when we started perturbing the systems and making life difficult for those cells. Either not giving them enough nutrients or shifting the temperature on them. All of sudden we saw huntingtin move from one location of the cell to a completely different location in the cell.

JEFF: And you think these environmental changes might be something like what happens in the aging brain?

RAY: Right, that's exactly what we think might be going on. We think it's the movement of huntingtin from one place to another and shifting in its function from doing something in one place to another that is defective in the disease.

JEFF: OK, do you think this kind of work you're doing on the fundamental "How does huntingtin work?" is useful for the development of therapies for HD?

RAY: If we know the functions of the protein we can understand which of those functions are being changed in the disease and if we know the exact molecular pathways of those functions then we can identify what pharmaceutical industry likes to call targets. For example an optimum target an enzyme that somehow changes huntingtin, and the pharmaceutical industry is extremely is extremely good at inhibiting enzymes or promoting enzymatic activity. In our outline of the scaffolding of what's going on in terms of pathway we can hopefully pull out these targets that then we can send the experts at pharma towards with small molecules.

ED: Just to chip in, an enzyme is a protein that makes a chemical reaction go faster in a cell?

RAY: Yes

ED: As opposed to something that is a building block or a structural protein?

RAY: Yes, so for example huntingtin is not an enzyme

ED: So that's why one of the reasons it's so difficult to fix huntingtin directly is because it doesn't have this enzyme activity that's relatively easy to target with a drug.

RAY: In a lot of disease therapies we've had our best success targeting enzymes.

ED: Excellent, thank you Ray. Let's bring on our next guest: Dr Mike Orth from the University of Ulm in Germany. Mike is a neurologist who studies real life human patients to find out more about Huntington's disease. Mike's wife is from Catalonia so there are sort of some gently simmering ethnic tensions in the Orth household it seems. Mike was particularly pleased when he figured out that his young nephew had come up with an affectionate new nickname for him. He calls him Tío Patata. He was disappointed to find out that this means that his nickname is Uncle Potato. So please welcome Uncle Potato. [applause]

MIKE: That's what you have to live with if you are a German marrying into a Spanish family. And not even Spanish it's a Catalan family but I don't want to go into Spanish-Catalan politics…

ED: We'll stop there. So Mike you gave a really interesting talk earlier on about something called the 'default mode network'. What on earth is the default mode network?

MIKE: It's a mouthful. Think about Bernhard telling us about the boats. From the point in time when Bernhard was telling us that we shouldn't miss the boats I kept myself busy with the thought: How can I avoid missing the boats? That's the last thing I want to do today: miss that boat, or one of those three of four boats? So I wasn't doing very much, I couldn't really listen to many of these talks I was sitting thinking how can I possibly make that boat? [laughter]

ED: So the default mode network is the part of the brain that deals with boats?

MIKE: Yes, exactly, well it deals with thinking what's expected of you in terms of behavior, what's going to happen next and how are you expected to perform? In this case you know you have to make one of those boats. You don't want to miss that boat if it can be avoided. I've been thinking about potential obstacles. Obstacles could be me myself, thankfully I haven't put on my high healed shoes today [laughter] so I'll be perfectly mobile, that's reassuring, but I happened to put my stuff in the office which is going to be locked at some stage. I've been thinking how on earth am I going to get out the stuff I've got into the office, come back down and make one of those boats and before I have to sit on one of those sofas.

ED: So question number two, what is the default mode network? [laughter] We get that you're worried about the boats.

MIKE: You see the part of the brain that I tried to use for that purpose: How can I avoid the boat? how can I make sure that I'm ready and have everything in place? I know from past experience that it's a bad idea to miss these things. You play all this out in your brain. Listening you find your legs feel good so you have no problem running, you have to think where are the doors so you have to play out this scene.

ED: We get that you're worried…

MIKE: This mental imagery is something that the default mode network does. The minute that you step into action, making the boat, all of this assessing of mental state, imagery, should stop. Now if I now start thinking, which I was tempted to do, about the boat thing I wouldn't be able to answer your questions. So it's very important to shift between states. Now you have to make the best use of your default mode network in preparing something you expect in the future but you have to be able to focus your attention on your host in the current situation?

ED: And away from the boats?

MIKE: Yes

ED: So in other words the default mode network is the thing that helps you plan the next thing but then you switch it off when action is needed.

MIKE: Yes

ED: You studied it by sticking HD mutation carriers in an MRI scanner? Functional MRI scanner? Which looks at brain activity in different bits of the brain?

MIKE: It does, what you do is contrast two different situations: one in which people have to do a task, have to be active with something specific, in this case pressing a button.

ED: Without going into too much detail because we don't want to miss the boats! [laughter] What functional changes did you find in the mutation carriers?

MIKE: Well you find the same areas are active if the brain is idle, not doing anything, thinking about boats, or whatever they've been thinking about, those same areas. But some of the different players in the network, it's a team that plays together, some of the team players were less capable of switching off. So there was still going on about things…

ED: Going on about boats?

MIKE: Whatever the boat equivalent was in the scanner, but they were still busy, there wasn't a complete switch off which you would have expected and which you had seen in the controls.

ED: So it sounds like they may be trying too hard in patients with the gene?

MIKE: I don't know really what it means but the other interesting thing is we did a simple functional assessment and the reaction time, the time it takes to press that button, was shorter in those who had left more players on the pitch. So the more active the default mode network the better the performance on that task. That may mean it's something they need to optimize function.

ED: To make up for having the mutated gene?

MIKE: Possibly I don't know what it means because it's across-sectional study and something we looked at only once. It's something that we looked at only once, we don't know how it evolves and we don't know if this is good or bad, we don't know any of this. But it's an interesting thing you can test in future studies to see how things develop.

ED: Thank you, Mike. Let's bring on our final guest.

JEFF: So finally we'll speak with Ed's boss: Professor Sarah Tabrizi of University College London. As many of you will know Sarah is a woman who gets what she wants often. But what she wants has changed over time. We've been looking for a fun story about Sarah you might not know. According to Sarah's mum she once caught two year old Sarah parading around the house with a clothes peg, or clothes pin for my American friends, strapped firmly to the front of her diaper. When her mum asked Sarah what she was doing young Sarah replied: I want to be a boy so I can have a peg like Kenneth next door. Please welcome Kenneth's favorite neighbor Sarah Tabrizi.

ED: So, Professor Tabrizi what's it like being the most beautiful and intelligent Huntington's disease researcher in the whole world? [laughter]

JEFF: Hang on. On the off chance that Dr Wild has a slight conflict of interest

ED: The very suggestion! [laughter]

JEFF: I might take over at this point.

ED: Sarah, you're the global head of the Track-HD study, a three year long study of exhaustive means of looking at people carrying the HD mutation looking for changes. This has finished in the sense that people have been through the study. What do we know now that we didn't know when the study started?

SARAH: Well the study has studied pre-manifest and early stage subjects so 120 pre-manifest subjects divided into two groups: those who were further from onset, predicted onset, and those closer to predicted onset. And 120 early stage subjects and 120 controls. We've really mapped in ultra fine detail the natural history of change over three years in that group. Looking at, really taking microscopic pictures of the brain, looking at how the brain changes. As Julie told you, really dissecting out thinking changes, movements changes, mood changes. It's like putting a group of people under a very big microscope. We understand much more about - I think in HD we have the advantage of this - we are able to identify people many years before onset - we're really now trying to produce a map of the changes that occur many years before symptom onset though to early stage disease over 36 months. Now we've got the 36 month data we're able to do that.

JEFF: So one of the pieces of data you showed that was striking, or has been shown from Track-HD today is the shrinkage in very specific regions of the brain. It's amazing technology to take a powerful microscopic look at it but it could be a little despairing for people carrying the mutation that gosh my brain is shrinking. Though as was pointed out today everyone's brain is shrinking unfortunately. What's your take home message, what's your feeling about this data and how people might feel about it?

SARAH: I think the point that everyone's brain is shrinking even as we're sitting waiting for the boats [laughter] which I am aware we've got a few minutes. The brain imaging changes are very striking, we're working very hard to try and understand how the brain imaging changes the gray and white matter and the connections between different parts of the brain and what that means. Julie did mention that, she said we really need to try and understand how those brain imaging changes translate, or give us a picture of what's going on and relating it to human's thinking changes and mood changes, and that's what we're trying to do. So the brain imaging changes, they're very clearly associated with aspects of progression but we found in Track-HD - the study's run like a clinical trial, with very clear checking of the data, data monitoring and there's an independent statistical team. We found over 24 months, and now over 36 months, over 24 months the pre-manifest HD cohort didn't change significantly from controls in thinking tests, mood tests, motor tests, motor tests.

JEFF: So they were still performing as well as normal?

SARAH: Exactly, and over 36 months those subjects further from onset did not deteriorate relative to controls so despite those brain imaging changes people's brain are functioning very well. This relates to the data that Nellie mentioned and that Mike talked about which

I'm going to talk a bit more about on Sunday. I think there's more and more evidence for a compensatory network. And so people's brains are able to adapt and change and they have what's called plasticity and change the structure and function.

JEFF: They can recruit new structures to help

SARAH: And grow new neurons and dendrites, theoretically, there is evidence for this and it's a kind of modulating of the brain, we know people can do that and we think symptom onset might be decompensation of those networks, there's an enormous amount to rescue and one day, this is our aim, we can intervene and maintain those neural networks. I think that's we're really understanding, that people are functioning at a good level despite the brain imaging changes so it's not bad news.

JEFF: That's great, thanks very much. So please join us in thanking our interviewees, thanks very much [applause]

ED: Thank you guys, well done.

JEFF: They were good sports.

ED: Ok, so just before we close I would like to spend just a couple of minutes giving you an exclusive world first preview of some of the changes that are coming in the next few months to HDBuzz. HDBuzz, as Jeff has said, is our online news portal, at HDBuzz.net where you can get plain language Huntington's disease research news updates. We're supported entirely by donations from patient organizations throughout the world and in addition we were recently given a grant from the Griffin Foundation in the USA which is an independent educational charitable foundation. That's enabled us to embark on a pretty exciting program of redesigning HDBuzz and really making some exciting changes. So this is the sneak preview of the new HDBuzz site, not live yet but coming soon. As you can see it has a new look and feel, it's a lot more sleek, it's a lot more easy to navigate from one story to another and to skip between things that interest you. A couple of things we're excited about that you can see here. The first is the coming soon box at the top of page. Sometimes a story comes out and it takes us a while, a few days, to write a story about it, but we want to let people know that something exciting is happening, and that's what that will do and next to that you can see the start here section of the website. This is something that's been requested by a lot of our visitor who are exited that they can get hold of all this research news but they don't quite know where to begin. The start here page really takes you, if you're someone who's completely new to HD, it takes you right from the very basics to talking about how we do research and why we do it and gradually introduces you to some of the most exciting techniques that are being used so that you're a bit better equipped for browsing your way around the rest of the site. We've completely overhauled the glossary and this is the bit that explains any technical jargon that we have to use. That's much more easy to use, it's searchable, it's a much quicker glossary, hopefully that will be really useful. This is an advance that will hopefully take us beyond the internet. We're aware that not everyone likes using websites or social media. What we can do now is every story

is going to be automatically available for download as a PDF. So you can basically print it as an information leaflet. If you run an HD clinic or a support group or if you have a relative who is interested but doesn't like using the internet you can print these PDFs and then they can just browse them, write notes on them, line the cat litter tray with them, whatever they want to do. This is a relatively small development but it's an important one: on the site we list all of our translators and our writers but you can't find out who's done what so HDBuzz 2.0 launches in a couple of months you'll be able to see who's written what article and who's translated so if you like the way something was written or you're interested to find out more that's one way of going about it. We've chosen Asun here because I hope she's in the audience and she's one of our most enthusiastic and prolific translators into Spanish. The list of articles she's translated couldn't even begin to fit on a single page. These are the twelve languages that HDBuzz is now available in. We launched 18 months ago. We're now getting somewhere between 80,000 and 90,000 visits a month in all of these 12 languages. I can't begin to attempt to say thank you to our translators in each languages but they're there up on the screen, please can we have a round of applause for our volunteer translators. [applause] It really does make such a huge difference to know that, we write in English but then, it rapidly becomes accessible to millions and millions more potential people. I'd just like to briefly thank the Young Adults Working Group, Jamie, Adrien and many other people here and elsewhere who've made HDBuzz possible. We're nearly done, go on we'll have a little ripple. [applause] I'm a big fan of applause One final thing before we go to the boats, I suspect Michael's gone already [laughter], and is swimming across the channel to the city hall. Jeff.

JEFF: One bit of fun just to think about between now and tomorrow night when we're back. For a chance to win a very special prize which we have yet to come up with or buy. We are having the first inaugural EuroBuzz caption contest. Please send your wittiest, dirtiest, most interesting caption for this photo to editors@hdbuzz.net and if you can explain to us what Bernhard is whispering in Alexandra Durr's ear that would be great. Only clean suggestions will be entered in the contest but we'll keep the dirty ones thanks very much. Whoever has the wittiest will win something wonderful tomorrow. Thanks on behalf of Ed and myself, see you tomorrow about the same time for one more round of this and now Bernhard asked me to tell you to get your butts on the boats. Thank you. [applause]

The authors have no conflicts of interest to declare.For more information about our disclosure policy see our FAQ...

GLOSSARY

cross-sectional study A study where each participant is looked at only once - unlike in a longitudinal study, where each participant is looked at several times over a time period

huntingtin protein The protein produced by the HD gene.

RNA interference A type of gene silencing treatment in which specially designed RNA

molecules are used to switch off a 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

metabolism The process of cells taking in nutrients and turning them into energy and building blocks to build and repair cells.

glossary These popups will explain any technical terms we have to use.

manifest after HD diagnosis, or when symptoms are already showing

neuron Brain cells that store and transmit information

cohort a group of participants in a clinical research study

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

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