EuroBuzz Video: Day 2

Watch the full video of EuroBuzz day 2 with Jeff Carroll and Ed Wild at the Euro-HD Network Meeting in Stockholm

By Dr Jeff Carroll on September 21, 2012
Edited by Dr Ed Wild

Jeff Carroll and Ed Wild present EuroBuzz episode 2 - 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: Hello again everybody. Thanks for joining us for the second and final installment of EuroBuzz from the European Huntington's Disease Network in Stockholm. It's been another great day of fascinating science. We're here to help share that with the global community of HD affected people via HDBuzz while at the same time hopefully having a bit of fun at the end of the day.

ED: But first, we do need to touch on something serious. It's been brought to our attention that a significant miscarriage of justice occurred during yesterday's EuroBuzz session. We want to take a moment to address that.

JEFF: That's right, a number of people have pointed out to us that the winner of yesterday's science quiz, Dr Michael Hayden, was given an unfair advantage because one of the questions was based on the color of his own shirt. [laughter] In retrospect we could have picked up on that or Michael could have disqualified himself.

ED: We were troubled deeply by this gross injustice. As I'm sure you all are. In fact I've heard

talk of little else all day. [laughter] We brought this to Michael's attention last night, and his response, after the dinner and some post dinner drinks was: [bad South African accent] "I won this neuron fair and square, I love it more than anything else in the world, I will fight to the death anybody that tries to take it away from me"

JEFF: I didn't know Michael was Scottish [laughter]

ED: After some extensive negotiations Michael has agreed to a joint custody arrangement with the true winner. The two individuals who reported that they should have won were Drs Nayana Lahiri and Doug Macdonald. In the hope of avoiding unnecessary bloodshed we turned to that time tested alternative to open combat - rock, paper, scissors. So this afternoon the belligerents reported to the balcony of justice where the game commenced.

JEFF: After a hard fought game it was Dr Lahiri who reined victorious smothering Macdonald's entry level rock with a classic English paper. [laughter] We hope this goes some way towards healing the sorrow caused by this event.

ED: So congratulations to the true winner, Dr Lahiri. [applause] Ok, so now that tawdry episode is laid to rest it's time for today's science quiz. So once again everybody please rise majestically to your feet. Tonight, ladies and gentlemen, we're playing for this charming reindeer, or possibly moose, festooned teatowel. [applause] Yes! As a keen ornithologist I'm a big fan of owls, but my favorite owl of all is the teet owl. [groans and laughter] So, so, sorry.

JEFF: Let's move on. First a bit of local trivia, so remember how this works, think of the answer in your head but don't say it out loud. Last night we had dinner in the fabulous Blue Hall across the water. There is an object in the hall that is the largest of its kind in Scandinavia. What is it?

ED: Don't say it out loud, no cheating, don't do a Hayden. Actually that could mean any one of a number of things… all wonderful. If you have your answer stay standing if you said the magnificent pipe organ. Sit down if you forgot or you didn't know. The pipe organ is the largest of its kind with 10,000 pipes, here it is built into the roof of the room. One reporter shared with us this picture of a typical reaction by some prominent EHDN attendees on first witnessing this magnificent organ. [laughter] I think we all share that reaction. We still have people standing so the next question Jeff.

JEFF: Precisely as predicted by Cristina 'Crystal Ball' Sampaio an observational question about the therapy session from this afternoon. Robert Pacifici of CHDI compared therapeutic development from Huntington's disease to a long distance cycle race rather than a sprint. But what was the length of the New York race that inspired Robert to realize this?

ED: Everybody have an answer? Stay standing if you said 100 miles.

JEFF: Trick question!

ED: Some insiders are shouting that's incorrect, 100 miles was the length disclosed on stage today and therefore the only reasonable answer. Robert is telling some people it was 106 miles, mostly people who've only cycled 100 miles. So 100 miles or 106 miles you may stay standing. He also disclosed to me that after the race he went to check in at the airport wearing the lycra outfit which made for an interesting security pat down. [laughter] We do still have people standing, next question.

JEFF: Another Nobel Prize question. The oldest living Nobel laureate won the prize in 1986 for a topic that was mentioned today which is the discovery of growth factors. Who is this eminent scientist?

ED: This is going to be a tricky one. Stay standing if you got the correct answer: Rita Levi-Montalcini. We have two.

JEFF: Doug

ED: Three people, I'm terrible at seeing standing people.

JEFF: Doug in particular.

ED: Three people still standing so we do need a tie-breaker. It's another Sweden related question. Closest answer wins the teatowel. What in 2011 was the population of Sweden? We'll start at the back. 2.5 million [laugher] - apparently a fundamentally risible answer… You were standing, there was someone standing in the middle, yeah you're still in the running, what's your guess for the population of Sweden? Say any number, 5 million, I can tell you you've already done better than Doug. One more at the back, 8.5 million. Well the real answer is 9.453 million and so the gentlemen at the back who I can't see very well, come and collect your teatowel, you are today's winner. [applause] Congratulations, use it wisely.

JEFF: Now we've got that out of the way let's move to the couch to talk to several of the presenters from today. As Ed and I talk with families the two technologies that we hear the most about for sure are gene silencing and stem cells. It just so happens that we had two fantastic presentations on those topics today so we're going to speak with a couple of scientists about this tonight.

ED: Our first guest is Dr Bev Davidson from Iowa. Bev is best know for her pioneering work in huntingtin lowering treatments for HD but she exclusively revealed to us that she was something of a cowboy fan as a kid and one occasion at the age of ten she responded to an advert in the back of National Geographic magazine and unbeknownst to her parents signed up the whole family for a holiday on a cowboy ranch 1000 miles away. So please welcome Bev 'Gunslinger' Davison. [applause] Good evening, have a seat, make yourself at home. I'll take that down, might be a little distracting. So huntingtin lowering treatments - they're something that many people are aware of as one of the most promising possible approaches to treating or even possibly in the future preventing Huntington's. In simple terms what's involved?

BEV: The basic principle is to sort of remove the insult if you will, the mutant huntingtin causes the problem so let's just get rid of it, simple as that.

ED: That's an excellent answer, beautifully simple, so a slightly less simple question: how do you stop cells that have this mutation, it's in every cell in the body, how do you stop cells from producing the harmful protein, or reduce the amount that they produce? How do you do that?

BEV: Right so there's several methods that a number of labs are trying so I tried to present the bulk of those this morning, or this afternoon, and we're trying various methods to reduce the mutant huntingtin from being there, one is to use a mechanism called RNA interference which stops the RNA from becoming a protein and we know that that stops the production of that mutant, toxic protein.

ED: Just stepping back briefly what's RNA? That's like, the way we describe it on HDBuzz is that's like a message molecule between DNA in our genes and the protein which is the thing that does stuff. So the RNA is the message molecule.

BEV: Right, so I guess in a sense we're trying to kill the messenger!

ED: Perfect

BEV: If we can kill that messenger then that protein isn't made - the issue is to either use a delivery vehicle like cerebral spinal fluid that has some DNA in it that will interact with that messenger RNA and induce its degradation or maybe we can take advantage of viruses that have spent millions of years evolving and use those to introduce that molecule into the brain and kill the messenger.

ED: Cool, so the drug in this case is actually an RNA molecule or an DNA molecule itself and that sticks to the messenger molecule inside the cell, right?

BEV: That's exactly right

ED: And then the cell has its own built in mechanisms for getting rid of these messages

BEV: Right, once they pair up they become like something that the cell recognizes as needing to be degraded and so it takes advantage of that process and chews it up

ED: Fantastic, and it's been around for a while, not as long as the Huntington's disease gene itself. Where are we up to as regards these huntingtin lowering techniques for HD?

BEV: So there's, as we heard this morning from some individuals from the CHDI foundation, looks like some of these trials may commence within the next 12-24 months. That's very exciting. These of course of are early stages, we need to progress through testing the safety of these materials in patients and then move on from what those trials tell us.

ED: And in your own lab you've recently published work demonstrating the safety of your particular huntingtin lowering recipe in a monkey brain which is obviously a complicated brain similar to the human brain. Why is it so important to do all of these trials in animals before we

can take it through to patients?

BEV: We don't want to take this horrible disease and make it even more horrible, that's for certain. There's a lot of things we can test in an animal model, or an animal like a monkey that we can't test in rodents, it's a little harder to test in sheep and pigs if want to test for fine motor skills for example, a monkey can tell us wether or not we're causing problems by knocking down or reducing the levels of that huntingtin protein.

ED: Cool, and can you promise me that everyone's working as hard as they possibly can to get this to patients?

BEV: We're in Iowa there's not a lot else to do. [laugher and applause]

ED: Magnificent. Good answer.

JEFF: Our next guest is Dr Lisa Ellerby from The Buck Institute in California. If you've met Lisa one of the things you'll notice is her kind and gentle demeanor but this belies the fact that she's a well known pool shark. It's all brawl.. ball.. bar room brawling, that was a good thing to pick to say on stage [laughter] with Lisa. She tells us she insisted throughout childhood on wearing a tutu at nearly all times. It's not clear if she ever combined the two but we've settled on this artist's rendition to welcome her to the stage. [applause]

ED: No tutu tonight unfortunately. Welcome.

JEFF: As we talk to families, it's probably neck and neck what we hear about most I would say between gene silencing and stem cells. I think stem cells are in a sense maybe the more confusing of the two because as a scientist it seems like there's a lot of different ways you could use them. You talked about several approaches which aren't necessarily directed at therapies - so could you in broad terms talk about the different kinds of things as a scientist you can do with stem cells that are helpful for HD.

LISA: Yes, I think there's a number of things, one is that we have never had human models in a dish that we derived from an actual patient. So number one, we can make models that directly are relevant to the human condition because they come from a patient. The second thing we can do is that we've done a lot of screens for compounds for Huntington's disease but they've been in mouse models…

JEFF: So in the past we've used cells from mice or other organisms and now only just recently we can use them from humans.

LISA: Yes, I mean with the real expression levels that a patient would have and the expansion: the normal and expanded… so you could theoretically find targets that you hadn't anticipated in a human model that didn't come out of a screen from a mouse model.

JEFF: That sounds like a big advance but in this recent work you talked about today you actually corrected the HD mutation in human cells in a dish and so if you said that to a patient the first thing they might say is great, it sounds like the perfect therapeutic option - is that

realistic with this approach?

LISA: I think that it's not realistic in the short term but I don't think that as scientists we shouldn't try to think creatively about how to do that in vivo as an eventual therapy. But it's not something that's going to happen immediately.

JEFF: So for now it's more of a tool to understand the science of what's going wrong with the cells?

LISA: Yeah that's correct

JEFF: I don't want to ask anyone to make a timeline prediction because those are always fraught but can you describe the kinds of work that have to happen before we can use these kinds of new technologies to actually, for example, replace cells in the brains of people with HD.

LISA: I think that in order to use the cells they have to be safe and go through certain controls and so we're quite a way off that. In Parkinson's disease they have made cells that you are able to use in transplantation but for Huntington's disease we don't have those things.

JEFF: So there's still a lot of work in the dish before we get to people?

LISA: Right

ED: But I think it's just worth briefly mentioning this really is a new era in terms of our ability to test and study Huntington's disease and it's the result of a large consortium that's working together on these stem cell technologies.

LISA: That's right, there's a huge team. Leslie gave a beautiful presentation today about gathering cells from different patients and modeling them.

ED: Wonderful, thank you, so please join me in thanking our guests. [applause] Thank you very much.

JEFF: By way of introduction to today's HDBuzz update I'd like to tell you about the recent launch of the Chinese Huntington's disease Network. Last November we were pleased to be invited to Shanghai to attend the launch of this exciting new venture. Jean-Marc Burgunder, long time member of the European Huntington's Disease Network, is working with colleagues in China so they can profit from the experience of the EHDN as they establish their own clinical network. As many of you in the audience know Huntington's disease has been classically described as rare in China and other Asian countries. Recently with improvements in Chinese health care suspected cases of Huntington's disease are actually being confirmed with genetic testing. Many of Jean-Marc's Chinese collaborators are establishing clinics in hospitals in China to confirm and treat patients with Huntington's disease. Even if the prevalence is indeed lower in China there's an awful lot of Chinese people. So there's likely to be a significant number of families in China afflicted with Huntington's disease. What you're seeing behind me is a recent TV special shown on national TV in China about a family undergoing predictive testing for Huntington's disease. A young family member being tested and going through the predictive

process in China to see wether she carries the mutation that's made her father and sister ill. So wherever HD families live, an HD family is an HD family and we think it's important to reach out to community members.

ED: Inspired by this we wanted to do whatever we could through HDBuzz to support this new Chinese organization and the Chinese HD community. Thanks to supreme efforts from a number of Chinese volunteers we're thrilled to be in a position to launch the Chinese language version of HDBuzz here, tonight! [applause] Expanding our potential audience by a cool 1 billion I'm not saying they'll all visit it immediately. Just before we do that I want to mention that this could not have happened without the individuals named here so please join me in acknowledging their support. [applause] Ok, so, I'm English, I'm from the home of pantomime and in true pantomime fashion to launch a new version of HDBuzz the site has to be woken up in it's own language. I'm assured by Marc, our technical guy, that this is the case. We're going to need to count down from 5 in Chinese. Here's how to do it. You can use any of these reference tables that you like except the one on the left. The pronunciation you need are on the right in parenthesis. So it's woo, see, san, aah, ee. We'll do a practice run because if it goes wrong the whole thing will be a disaster. Are you with me? Here we go.

ALL: Woo, see, san, aah, ee

JEFF: That was nice.

ED: I think I can hear it stirring [laughter] Here we go, brace yourselves, the official launch of HDBuzz in Chinese.

ALL: Woo, see, san, aah, ee [music and applause]

ED: Thank you very much for your help with that and in case any of you suspect for a moment that that was merely Powerpoint trickery point your web browsers on your mobile devices to zh.hdbuzz.net which is now live.

JEFF: Before we leave we need to pick a winner for last night's EuroBuzz caption competition. The picture, you recall, reveals a really tender moment between Alexandra Durr and Bernhard Landwehrmeyer. From our barrage of suggestions Ed and I have very unscientifically chosen three finalists. So everybody wants to get to the bar, we don't have time to go through this twice. Your initial reaction to the caption suggestions will determine the winner so the more funny you think it is the louder you clap.

ED: What's that you say children? What's the prize? Oh dear I'm on a slippery pantomime slope. The prize is this, magnificent trophy with built in super accurate thermometer and as you all know it is of course in the shape of a Moomin which is a traditional, fictional hippopotamus creature worshiped throughout Scandinavia. First we have to give an honorable mention for a competitor who wish to remain unnamed who suggested "Gill just told me she wants a clothes peg like Sarah Tabrizi". [laughter]

JEFF: Pretty good.

ED: So our three finalists who were prepared to be named. First, Chris Shirbin, with the following: “For the last time, Alexandra… the boats leave for the Town Hall at 18:30”. [applause and laughter] Good reaction. This is going to be difficult I think, careful you don’t reach ceiling too soon. Next then Martin Delatycki: “Alexandra, have I told you about my expansion?”. [applause and laughter] And finally, around lunchtime I was handed an extremely grubby piece of paper containing approaching a dozen obscene suggestions from one Bill Crowder, this is unsurprising, Bill is from Liverpool, that’s how they do things there. This is only one that was even close to being publishable: Gill says “That’s an interesting mouse model she’s holding…” - to which, wait for it - Bernhard replies “Mmm, yes, don’t you just love multiple organisms” [applause and laughter]

JEFF: I think that’s pretty clear.

ED: Well it was close but I think in the end the winner is obvious, is Bill here? Bill, you are declared the winner, come and collect your Moomin. Here he comes. Come into the spotlight Bill. Congratulations, Bill official representative of the UK Huntington’s Disease Association. [laughter and applause] Your home city would be proud of you. And so as the Moomin of time snuggles up to the Snork Maiden of eternity, one for the locals there, it’s over to Jeff for some final remarks.

JEFF: We’d like to close, finally, by thanking the audience and guests for being good sports in a fairly ridiculous evening. It’s been good fun for us, more importantly we hope that we’re able to bring the excitement that we brought today with all the great science to our audience of affected families at home via HDBuzz. Without further ado thank you, goodnight and get your butts to the bar. [applause]

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

Glossary

Parkinson's Disease A neurodegenerative disease that, like HD, involves motor coordination problems

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

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

messenger RNA A message molecule, based on DNA, used by cells as the final set of instructions for making a protein.

prevalence A figure estimating how many people there are in a particular population who have a certain medical condition.

stem cells Cells that can divide into cells of different types

neuron Brain cells that store and transmit information

RNA the chemical, similar to DNA, that makes up the 'message' molecules that cells use as working copies of genes, when manufacturing proteins.
