



Clockwise from top left:

**Marina Frontali,
Nayana Lahiri and
Rhona MacLeod,
co-lead facilitators of the
EHDN's genetic counselling
working group**



Spotlight on the genetic counselling working group: The challenge of intermediate alleles

Marina Frontali, Nayana Lahiri and Rhona MacLeod

HD is generally caused by stretches of more than 40 CAG repeats in the HD gene, but the age of onset of the disease is not determined solely by this. Modifier genes and environmental factors can also have an effect. When the gene contains stretches of between 27 and 39 CAG repeats, this can cause some uncertainty with respect to diagnosis. (More information about intermediate (27-35) and reduced penetrance (36-39) alleles can be found [here](#). Intermediate alleles (IAs) are relatively common in the general population, with around 6% of people carrying one.

Neurologists routinely carry out diagnostic genetic testing in individuals who have symptoms of HD, while geneticists carry out predictive testing in those

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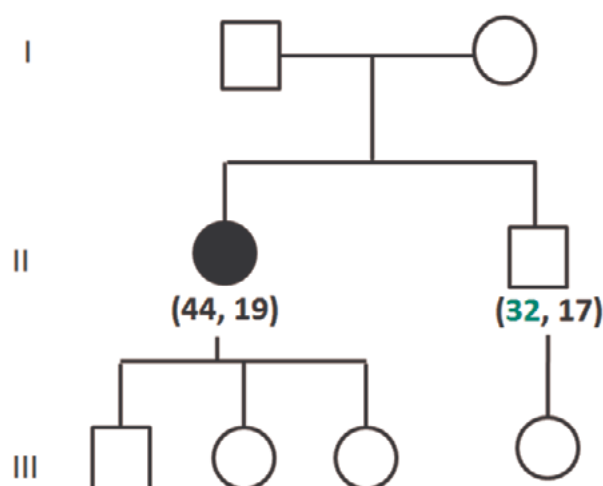
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who don't yet have symptoms. When they identify an IA this can raise some challenging questions. The genetic counselling working group hopes to help address those questions by means of research and by providing practical guidance to clinicians and families.

The two main questions we hope to address are:

Could the IA be the cause of a patient's symptoms?

It is generally believed that only stretches of 36 or more CAG repeats cause the symptoms of HD, but there has been some controversy over the clinical consequences of IAs and some reports of individuals with IAs who have symptoms. Killoran et al (2013) reported more behavioural symptoms in IA carriers compared to healthy controls, but no motor or cognitive differences, while Cubo et al (2016) found no significant differences between IA carriers and controls on a range of assessments at younger ages, but more chorea and faster cognitive decline compared to controls at older ages. Large-scale genetics studies may soon provide useful insights in this area, enabling more accurate information to be given to clinicians and patients alike.



This is the family tree of a woman who has been diagnosed with HD (black circle). She has no family history of the disease. Her brother (white square) decides to have predictive genetic testing and discovers that he carries an intermediate allele with 32 CAG repeats. What advice should he be given?

Is there a risk of an individual having children who may develop HD, as a result of an inter-generational expansion of the IA allele into the disease-causing range?

The overall risk is low but HD has to start somewhere in a family and it starts as a result of an expansion from an IA. This causes difficulties in the clinic because not all IAs are expanding, so what advice can we give patients? The working group has found that genetic counselling practice for IAs is very variable, which reflects the current lack of understanding in this area. There has been some research into potential risks for the offspring of IA carriers (eg Hendricks 2007, Semaka and Hayden 2014), but reported risk figures vary and the reason why some IAs show an intergenerational expansion while others remain stable is unknown. It is possible that genetic modifiers influence intergenerational repeat instability.

It would be so valuable to be able to offer IA carriers more accurate information about the risks to them, their children and grandchildren, and hence a more informed choice about the reproductive options open to them. This will become even more important as treatments for HD move into the clinic, potentially causing more people to come forward for testing and more IA carriers to be identified. With the help of a seed fund grant from the EHDN, the working group plans to explore these questions in greater depth.

Finally, it is planning a forum for discussing challenging genetic counselling cases, which are by no means limited to IA carriers, and sharing best practice across the network. Information about how to participate in the forum, which the working group believes will benefit the entire community, will be advertised across the network and on the [working group website](#).



Update: Clinical trials

Jenny Townhill and Tim McLean,
Central Coordination

The following trials have been endorsed by the EHDN.



GENERATION HD1: Roche's announcement and initiation of this phase 3 trial of the huntingtin-lowering antisense oligonucleotide (ASO) RG6042 has been greeted with intense enthusiasm by the global HD community. The trial has recently been endorsed by the EHDN and the Huntington Study Group (HSG), meaning that a group of leading HD experts (the EHDN's Scientific and Bioethics Advisory and Executive Committees, and the HSG Clinical Research Advisory Committee) have reviewed and endorsed the study protocol.

GENERATION HD1 aims to gather longer-term safety and efficacy data in a global patient population of 660 participants, in around 15 countries. The trial will last just over two years and patients will be randomised to one of three treatment arms, receiving either RG6042 monthly, or RG6042 every two months, or a placebo monthly, all via intrathecal injection. Further details and a list of participating sites (sites shown when nearly ready to enroll) are available [here](#).

GENERATION HD1 builds on the successful results of the Ionis Pharmaceuticals phase 1/2a trial of IONIS-HTT_{Rx}, now known as RG6042. Patients who completed the Ionis trial have continued participating in an Ionis-sponsored open-label extension trial (responsibility for which has now been taken over by Roche).

In parallel to the GENERATION HD1 study, Roche is recruiting for an observational HD natural history study, whose goal is to improve understanding of the role of mutant huntingtin in disease progression in early manifest HD. This study aims to recruit 100 participants at sites in Canada, Germany, the UK and the US. Further details and a list of participating sites can be found [here](#).

If approved by regulatory authorities and ethics committees, and if trial data support continued



development of RG6042, Roche plans to offer an open-label extension study, GEN-EXTEND, to all participants who complete a clinical trial within the RG6042 research programme.



PRECISION HD1 AND HD2: Recruitment is underway into these two phase 1b/2a trials of allele-specific ASOs sponsored by WAVE Life Sciences. These ASOs target the expanded allele of the huntingtin gene only, via two distinct single nucleotide polymorphisms (SNPs), thereby allowing normal huntingtin to continue to be expressed (a detailed overview of the trials can be found [here](#)).

Participants undergo pre-screening to confirm the presence of at least one of the two SNPs before being included in the study. Trial results are expected towards the end of the year. Participating sites are in Canada, Poland, the UK and the US. Further details can be found [here](#).



HD-DBS: Recruitment continues into this trial of pallidal deep brain stimulation (DBS) for HD, at sites in Austria, France, Germany and Switzerland. The trial aims to demonstrate the safety and efficacy of pallidal DBS for treating chorea, in participants with moderate stage HD for whom existing therapeutic options have been unsuccessful. The trial will enroll approximately 50 participants and recruitment is expected to be completed in 2020. Clinicians in participating countries are encouraged to refer eligible participants to the trial sites shown on the

map. Site contact details can be obtained from Pauline Kleger (pauline.kleger@uniklinik-ulm.de), and further details about the study criteria are available [here](#).



HD-DBS SITE MAP



PACE-HD (Physical Activity and Exercise Outcomes in Huntington's Disease): This activity intervention study, led by Cardiff University, is recruiting at seven sites in Germany, Spain and the US. Recruitment of 120 participants is due to be completed on schedule in the first half of 2019. The study comprises two components: annual evaluation of physical activity and fitness in individuals with HD, which is performed in tandem with annual Enroll-HD assessments, and a randomised control trial of a one-year exercise intervention in HD that will compare structured aerobic exercise training with usual activity.

HD Clinical Trial Site Certification

The HD Clinical Trial Site Certification scheme offers a unique opportunity for sites with the capability to participate in HD trials to register their interest and raise their profile with potential sponsors. While certification does not guarantee participation in approved clinical trials, as this is always a sponsor's decision, it ensures that a site will at least be considered. The majority of Enroll-HD sites, and many non-Enroll-HD sites, have been certified and their details shared with approved (CHDI/EHDN) sponsors. We encourage any sites who have not yet applied to do so as soon as possible.

Annual recertification is essential to ensure that site details are up-to-date. Recertification is a simple process that involves confirmation that a site still meets the criteria and that any changes in site circumstances have been recorded in the HD Global Site & Investigator Database. It is important that sites respond promptly to recertification reminders to avoid any interruptions in certification that could result in a site being excluded from the list of certified sites.

For more information, please contact:
hdsite@euro-hd.net

Get in touch with the think tank!

The EHDN's HD Science Think Tank brings together EHDN members staff who are closely involved in supporting scientific research – including members of the Executive Committee, Central Coordination and the working groups – and it engages with the HD research community in three ways:

- Researchers may contact the think tank for help in identifying potential collaborators or funding opportunities, or to discuss scientific ideas
- The think tank welcomes suggestions of research topics, and has provided a contact form on its website via which these can be submitted
- The think tank may occasionally propose specific research topics that could be addressed by a dedicated task force working for a defined period of time



For more information about the [think tank](#), please contact
Leonor Correia Guedes:
leonor@euro-hd.net



Update: Enroll-HD Lite

Olivia Handley, Global Platform Manager, Enroll-HD

Since the Enroll-HD study began seven years ago it has grown exponentially, recruiting its 20,000th participant in December 2018. There are more than 160 sites submitting data and samples on a global population sample of manifest, premanifest, at risk, non-HD gene expansion carriers and community control participants.

In 2017, significant effort was put into evaluating where the study's focus should lie over the next five years and beyond, to ensure that it continues to meet its aims. Statistical models were developed to forecast the composition and size of the cohort required to support the development of therapeutic interventions, and it became clear that sites would need to increase recruitment of premanifest and early manifest participants since this is the cohort most likely to be required for upcoming clinical trials.

A sub-population of participants has progressed into the later manifest stages (currently, HD disease stages III-V represent 15-20% of the cohort). However, the challenge of maintaining annual visits for later manifest participants,

coupled with an assessment battery that includes several tasks with reduced sensitivity for this stage of the disease, can be burdensome for all concerned.

At the same time, Enroll-HD and its predecessor study Registry together provide a robust and rich longitudinal dataset on a range of clinical outcomes, which means it has become possible to consider removing some assessments from the battery.

A strategic decision was taken to plan a parallel longitudinal, observational study of HD specifically aimed at moderate-to-later stage HD: Enroll-HD Lite. This study would maintain annual contact with participants, and ideally also their companions, either via clinic-based or remote visits. Eligible participants would transition from Enroll-HD, and the assessment battery would be adapted to improve the capture of moderate-to-later stage disease milestones, while excluding



those assessments for which there are sufficient existing data, or which are known to have reduced sensitivity in these stages of the disease.

Crucially, Enroll-HD Lite would include two modified instruments for later stage HD: the Unified Huntington's Disease Rating Scale (UHDRS) Structured Interview of Function and the HD Clinical Status Questionnaire. Both instruments build on existing clinical tools (UHDRS Function which includes Total Functional Capacity, Independence Scale, and the Functional Assessment Scale; and the HD

Clinical Characteristics questionnaire), and both will be validated in a smaller study called Later Stage HD Assessments (LSA).

The design of the LSA study will allow for an evaluation of whether these instruments can be successfully administered to a companion in person or via a phone call. The study will recruit 150-170 moderate-to-later stage HD (equivalent to HD stage III) participants and their companions and will be conducted at English-speaking sites only. Between 15 and 20 sites are expected to be included. Site selection is currently underway, and progress is being made with preparing the regulatory and/or ethical submission documents.



Participant enrollment is expected to begin towards the end of 2019, allowing approximately 18 months to complete recruitment and data analysis.

Enroll-HD dataset: bigger and better!

IT'S NEW:

Released on 14 December 2018

LARGE NUMBERS:

- 15,301 participants (78% of the total cohort)!
- 50,422 study visits from Enroll-HD, Registry and Ad Hoc*

HIGH QUALITY:

Data are monitored by:

- Centralised statistical monitoring
- Remote data review
- Onsite data monitoring (risk-based monitoring such that only specific data are verified on site)

EASY ACCESS:

- 38 downloads in January 2019 alone

SUPPORTING DOCUMENTS:

Please visit the Enroll-HD [website](#) to find a range of supporting documents including manuals that describe which data are available and how to download and use them

** Ad Hoc data, drawn from a variety of different sources, principally comprise UHDRS data. Typically these were gathered prior to a participant's enrollment in Enroll-HD.*

Review: The Unwanted Inheritance

The Unwanted Inheritance, by Mariska and Bart Beckers, was one of three documentary films screened during the EHDN plenary meeting in Vienna in September 2018, where it was shown for the first time to the global HD community. Here, Gerd De Coster of the Flemish Huntington Association reviews it for us.

The Unwanted Inheritance tells the story of six residents of Home Marjorie, the only nursing home for HD patients in the Flanders region. It is entirely filmed from the perspective of the residents. There is no interviewer, no voice-over, no background music. Mario, Manuela, Marleen, Griet, Yves and Jutta and their loved ones tell their stories in their own words and in their own time.

Home Marjorie is a small, specialised care facility in Belgium that was named for Marjorie Guthrie, the wife of folk singer Woody Guthrie who died from HD. It provides home, respite and day care. The film follows the six residents through their daily lives, revealing how they cope with the disease with the help of staff, how unpredictable HD makes their lives, and what grief it brings them and their families.

Some of the stories recounted in the film are sad, some are hopeful and some are told without words, and are all the more moving for that. Ultimately it is an honest film, and a story of hope, strength and resilience. Mario, Manuela, Marleen, Griet, Yves and Jutta are very pleased with the movie, which they consider an accurate portrait, and the staff of Home Marjorie are proud of the way the film-makers have portrayed their work.

The Unwanted Inheritance can be rented at [Vimeo](#). More information about Home Marjorie can be found [here](#).



Fellowship exchange programme: Crossing continents

Laura Spinney

We describe the experiences of three young clinicians who completed the fellowship exchange programme (FEP) in 2018. The FEP is sponsored by the EHDN and the European section of the International Parkinson and Movement Disorder Society (MDS).



Cinthia Terroba Chambi



Cinthia Terroba Chambi (third from right) and members of the Strasbourg HD care team

Cinthia Terroba Chambi's career to date has been anything but conventional. Peruvian, she completed her medical studies in Cuba and, as a clinical researcher in neurology, is currently working on her doctoral thesis on HD in Argentina. In the late summer of 2018, she spent six weeks in the movement disorders service of the

Hautepierre Hospital in Strasbourg, France, where she was most impressed by the interdisciplinary nature of the assessment and care offered to HD patients.

"The weeks passed in an almost perfect balance between the interesting academic world of Hautepierre Hospital and the dazzling cultural rhythm of Strasbourg," she writes. "I could understand why Hautepierre is the most important neurological reference centre in the Grand-Est of France, and why Strasbourg is one of the most beautiful cities in Europe."

"She was very open and really participated in everything we proposed," says Christine Tranchant, who runs the movement disorders service at Hautepierre Hospital. "For us it was a very positive experience and we would willingly welcome others like Cinthia."

Physiotherapist **Dionatan Costa Rodrigues** of Rio de Janeiro, Brazil, spent his fellowship learning how physiotherapy is tailored for HD patients in a number of Spanish hospitals, though his principal attachment was to the Ramón y Cajal University Hospital in Madrid.



Dionatan Costa Rodrigues (centre, standing)



Dionatan Costa Rodrigues (third from right) and members of the Spanish HD Association (ACHE)

Among other things, he improved his understanding of the scales used to evaluate HD patients, noting that “few people know how to use these scales in Brazil, which hampers research and in particular understanding of how Enroll-HD works”.

He also found time to work with local EHDN language area coordinators and patient associations, even participating in equine therapy sessions organised for patients in Madrid and Barcelona, and he is currently in contact with Lori Quinn – who co-facilitated the EHDN’s physiotherapy working group for a long time – to plan some physiotherapy-related studies in Brazil.

Lola Díaz Félix lives and works in the Dominican Republic, where the prevalence of HD is unknown. She suspects it is high, though, because nine Dominican families affected by HD have sought treatment at the Fundación Jiménez Díaz University Hospital (FJDH) in Madrid, Spain, where she took up her fellowship last autumn. Treating such patients in her country is “almost impossible”, she says, due to a lack of resources and specialised knowledge, and the stigmatisation of the disease which discourages many patients from seeking medical care. Diagnosis is further complicated by the fact that genetic testing is done outside the country, in private laboratories that are beyond many Dominicans’ means.



Lola Díaz Félix (second from left) with mentor Pedro García-Ruiz and co-workers

“The most important thing I learned is that there is hope to improve the treatment and management of these patients,” she writes. “Thanks to the fellowship, I will be the first neurologist trained in HD in my country.” She now plans to set up a specialised HD clinic at the hospital where she works, and in collaboration with the FJDH team, to organise genetic and prevalence studies

of HD in the country. “I think Lola can do a lot back home,” says her mentor during the fellowship, neurologist Pedro García-Ruiz of the FJDH. “There may be hundreds of undiagnosed cases of HD in the Dominican Republic.”



Lola Díaz Félix

The 2019 round of the EHDN-MDS Fellowship Exchange Programme is now accepting applications but the deadline is 15 March 2019 so apply NOW! Six places are available this year. Any queries should be addressed to: fep@euro-hd.net

**EHDN
2020
Bologna**

Advance warning!

The next EHDN plenary meeting will be held in Bologna, Italy from 10 to 12 September 2020.

PLEASE NOTE: this is from Thursday to Saturday, not from Friday to Sunday as in previous years.

A web link and registration details will be advertised in future editions of this newsletter.

€4m for HD research

The EHDN is delighted to report that two projects focusing on HD were approved for funding by the Joint Programme – Neurodegenerative Disease Research (JPND) under its 2018 call for multinational, multidisciplinary research projects in the area of health and social care research and innovation, and will receive a total of more than four million euros over the next three years. They are DOMINO-HD (Multi-Domain Lifestyle Targets for Improving Prognosis in HD) and HEALTHE-RND (European eHealth Care Model for Rare Neurodegenerative Diseases). Both the consortia behind the projects, which are described in detail below, are currently negotiating details with national funders and elaborating their consortium agreements. They are expected to get underway in early-to-mid 2019.



DOMINO-HD

Coordinator: Monica Busse, Cardiff University, UK

Partners: Germany (Bernhard Landwehrmeyer), Ireland (Madeleine Lowery), Poland (Grzegorz Witowski), Spain (Esther Cubo) and Switzerland (Hans Jung)

External collaborators: Activinsights, EHA, EHDN and RAND Health Care

Budget: €2,057,969

Duration: 36 months

The ability to assess symptoms in HD in an evidence-based manner is crucial to optimising disease management. The DOMINO-HD study aims to identify key environmental factors that can be successfully targeted in interventions designed to improve disease management for people with HD. The consortium will harness advances in technology to improve understanding of the role of multidomain factors in HD. It will integrate data from physical activity and sleep in everyday contexts, along with nutritional assessment and quality of life and clinical measures used routinely to assess disease severity, to explore how all these factors come together to affect disease progression. It will conduct predictive outcomes modelling in order to identify modifiable factors that influence outcomes in HD. Genetic risk factors, including CAG repeat length and other known modifiers, will be included in this



JPND research

EU Joint Programme – Neurodegenerative Disease Research

analysis. The study will be conducted across a multi-centre European cohort to ensure cross-cultural and social relevance. The information gathered will be used to develop a personalised, multimodal lifestyle intervention for people with HD.



HEALTHE-RND

Coordinators: Jiří Klempíř, Charles University, Czech Republic, and Bernhard Landwehrmeyer, Ulm University, Germany

Partners: Czech Republic (Jiří Klempíř and Alžběta Mühlböck), Germany (Bernhard Landwehrmeyer), Ireland (Jennifer Hoblyn), Italy (Ferdinando Squitieri), Netherlands (Wilco Achterberg; Niels Chavannes and Eline Meijer), UK (Stephen McKenna)

External collaborators: EHA, EHDN, Griffin Foundation, German Huntington's Association (DHH), Italian League for Huntington's Research (LIRH), Scottish Huntington's Association (SHA)

Budget: €1,979,110

Duration: 36 months

Rare neurodegenerative disorders such as HD require multidisciplinary care teams which are in short supply across Europe. There is an urgent need to develop innovative ways to ensure access to best practices and established care pathways, so that patients are not subjected to a "postcode lottery" when it comes to care. The goal of the HEALTHE-RND project is to contribute to this ambitious goal with the motto, "The knowledge travels, not the patient". The multinational and multidisciplinary consortium will use the power of e-health care models for rare neurodegenerative diseases to contribute to the development of need-based patient value assessments, and to conduct an exploratory proof of concept study in HD that will serve as a pilot project for e-health care interventions for RNDs more broadly.

Three new seed funds awarded

In a project the EHDN approved for seed funding in 2017, **Hoa Nguyen** of the Ruhr University Bochum in Germany and colleagues will address the ongoing challenge of delivering huntingtin-lowering antisense oligonucleotides (ASOs) to the brain. They will test a new class, tricyclo-DNA-ASOs, which are reported to have efficient uptake in many tissues. Specifically, they will evaluate three novel members of this drug class in a rat model of HD, and compare their efficiencies in lowering mutant huntingtin.

Knut Stieger of the Justus Liebig University Giessen in Germany and colleagues will also focus on a delivery problem, in their project which was approved for funding in 2018, but in their case it is the safe delivery of the components of the CRISPR/Cas gene editing system to the brain that they would like to make more efficient. They will test nanoparticles as a vehicle, *in vitro* in mouse and pig cell lines and human induced pluripotent stem cells, and *in vivo* in a mouse model of HD. The results of the project will inform subsequent trials of the nanoparticles in a pig model of HD.

Last but by no means least, **Liana Veneziano** of the Italian National Research Council's Institute of Translational Pharmacology in Rome, and colleagues, will explore a potential new biomarker for HD in the form of leucocyte telomere length (LTL). Telomeres are repetitive sequences at the ends of chromosomes that are important for maintaining genomic stability, and a reduction in the length of these in leucocytes, or white blood cells, is known to be associated with neuroinflammation and neurodegeneration in ageing and Alzheimer's disease. The Italian group, whose project was also approved last year, will investigate whether a correlation exists between LTL reduction and disease onset and progression in a large sample of HD patients.

Seed funds are intended to support pilot studies that will eventually kickstart larger projects. The next deadline for applications is 1 November 2019. More information about the programme and how to apply can be found [here](#).



Hoa Nguyen



Knut Stieger



Liana Veneziano



A new era:

Interview with Anne Rosser

Anne Rosser was elected EHDN Chair at the network's plenary meeting in Vienna in September 2018. She co-directs the Brain Repair Group at the Cardiff University School of Biosciences in the UK, and is the clinical director of the Cardiff Fetal Tissue Bank. She also heads the South Wales clinical neurology service for HD.

You've taken the lead of the EHDN at a critical moment in terms of the development of new therapies. How do you see this moment?

I think it's very likely we're moving into a new era. I've been working with HD patients since 1994, not long after the discovery of the gene, and seeing how the momentum has built up thanks to an enormous collective effort over the years has been incredibly exciting. At the same time it's important that we don't get ahead of ourselves, because even very promising treatments can take time to reach the clinic – if they ever do.

What are the particular challenges you face as EHDN Chair?

I feel very privileged to be taking over at this stage. I'll be building on the hard work and vision of my predecessors, Bernhard Landwehrmeyer and Jean-Marc Burgunder, to prepare for this new era. My impression is

that patients and carers have become more aware of HD research over the last decade, and this is reflected in an increase in referrals – at least in our practice. There's a sense of hope. In general it's a good thing that the community is better informed, but we also have to manage expectations.

“As far as clinicians are concerned, the existence of a disease-modifying treatment is going to change the way they work,”

if and when one becomes available. We need to be thinking now about how we get those drugs into practice, for example, and how we ensure they're reasonably priced. And we also have to keep training upcoming generations of clinicians and scientists in how best to manage and investigate HD.

How did you come to work on HD in the first place?

I've always been interested in human brain function. I did a PhD in neuroscience at the University of Cambridge before training as a medic, and then specialised as a neurologist. I got a position as a Medical Research Council clinician-scientist at the Brain Repair Group in Cambridge, where I became very interested in neurodegeneration. An opportunity arose to work with John Hodges, who ran the HD clinic in Cambridge. At that time HD was very much a neglected disease, so I leapt at it, and that was really my introduction. My research, on stem cell therapies, became more and more focused on HD after that.

You went to Cardiff in 2001. How did the Welsh capital become such an important reference centre for HD?

Cardiff has always been strong in neuroscience, and Peter Harper, who worked here for many years as a clinical geneticist, did much of the original epidemiology of HD. Both he and geneticist Lesley Jones, who is also in Cardiff, were part of the consortium that discovered the HD gene.

What is the status of transplantation therapies for HD?

We've been working on these for a long time. The goal is to replace the medium spiny neurons of the striatum that are lost to the disease process. There's a long history of obtaining precursors to these cells from fetal tissue,

and that comprises one, ongoing strand of our research. We're planning a pilot study this year, involving transplantation of fetal cells into a small number of HD patients. Another research strand involves transplantation of stem cell-derived neurons. This approach presents both practical and ethical advantages over fetal tissue, and we are part of a consortium called Repair-HD that has made quite a lot of progress with it. We're not yet ready to transplant stem cell-derived neurons into patients, however, and we're currently looking for funding to prolong the consortium's life.



Anne Rosser, Steve Dunnett and co-workers, 2017

How would such therapies be combined with a potential disease-modifying treatment in future?

I think it's extremely likely that we will end up with an array of treatments. If the huntingtin-lowering treatments work perfectly, with no side effects, one could imagine that's all the patient would need, but that's unlikely to be the case and their efficacy will also depend on the ability

to treat the patient early and for a long time. It's not yet clear whether huntingtin-lowering drugs will be able to affect the disease process once it has got underway, and they won't be able to replace cells once they are damaged or dead. So you could imagine transplantation therapies being useful in patients who can't tolerate the huntingtin-lowering drugs, or to replace lost cells in patients who can.

The HD disease process has turned out to be more complicated than was anticipated at the time the gene was identified. Do you still consider it an important model for neurodegenerative diseases in general?

I do. The powerful thing about HD is that we know that the gene's penetrance is close to full, and we have a test for that gene. The complexities aren't necessarily a drawback, either. For example, we can study the psychiatric component of HD, knowing it to be caused by a single mutation, and that is potentially informative about psychiatric disorders that aren't.



HD on the bike

On **1 May 2019** the European Huntington Association (EHA) in collaboration with the German Huntington's Association (DHH) will furnish a team to take part in the ŠKODA Velotour bike race in Frankfurt, Germany. In last year's edition of the race, 40 people rode on behalf of the EHA in Liège, Belgium, and this year the association would like to better that, so roll up! Fun is guaranteed, and no skill or experience is required. "Our only criteria is that you want to tear down the stigma surrounding Huntington's Disease," writes the EHA. More information about the race and details of how to register can be found [here](#).



Ralf Roletschek - Wikipedia

Dates for your diary

Save the dates for:

- [Neural stem cells in development and brain repair course](#), Venice, Italy, 18 – 25 May 2019
- [5th Congress of the European Academy of Neurology](#), Oslo, Norway, 29 June – 2 July 2019
- [International Congress of Parkinson's Disease and Movement Disorders](#), Nice, France, 22 – 26 September 2019
- European Huntington Association Conference, Bucharest, Romania, 4 – 6 October 2019 (registration opens 1 March; details to go live then)