November 2024 · Issue 53

EHDN *News*

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

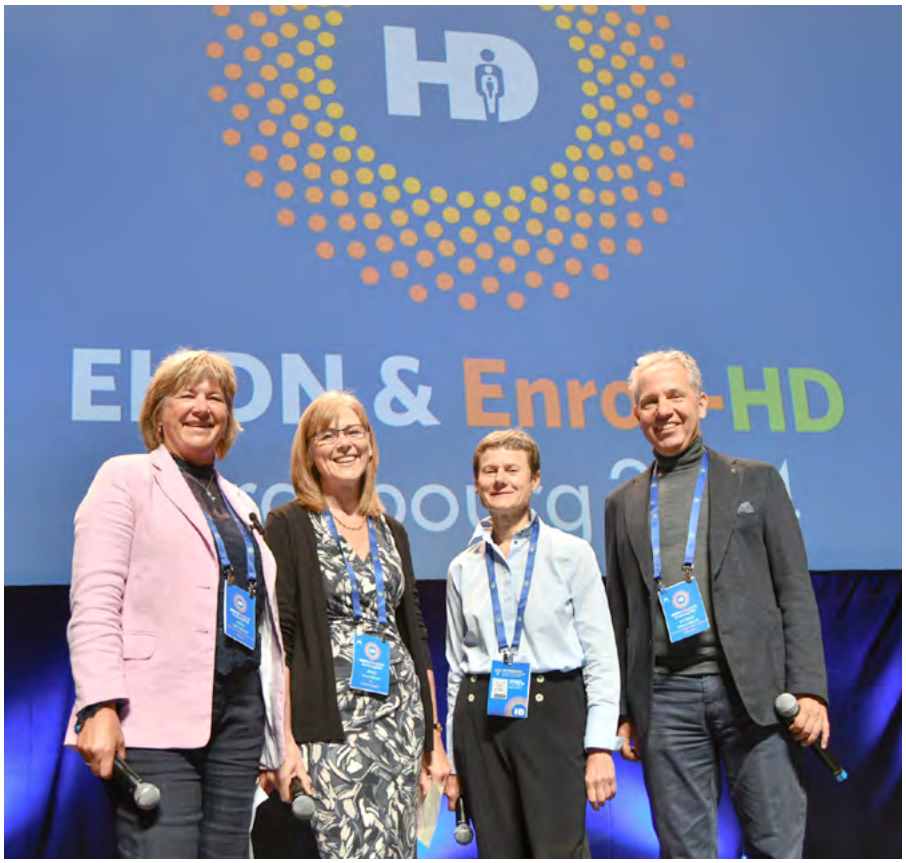

Photo: Gabriele Stautner, artifox.com, for EHDN

Astri Arnesen, Anne Rosser, Christine Tranchant, Patrick Weydt

EHDN & Enroll-HD
Strasbourg 12–14 Sep 2024

PHOTOS RECORDINGS POSTERS

ehdn.org

EHDN & Enroll-HD 2024:

Ce sera un événement mémorable!

Catherine Deeprose

More than 1,100 eager delegates convened in the city of Strasbourg, France, for EHDN & Enroll-HD 2024. This marked 20 years since the founding of EHDN and was also the first collaborative event to combine the bi-annual EHDN Plenary Meeting (Day 1), EHDN and Enroll-HD joint program (Day 2) with the Enroll-HD Congress (Day 3). Delegates were welcomed to a stimulating array of scientific and clinical presentations, special meetings, networking opportunities, and social events, spanning three days. Here is a whistlestop tour of just some of the many event highlights. Further details (including Short Communications and Parallel Sessions) will be provided in a report which will be published online shortly – but in the meantime, presentations from Day 1 and Day 2 can be viewed on our YouTube channel and posters can be viewed at ehdn.org/ehdn2024/#posters. All photos from the event can be viewed at artifox.com/ehdn-enroll-hd-2024-strasbourg.

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Catherine Deeprose, Editor
Gabriele Stautner Artifox Communication Design (Ulm, Germany).

Experiences from HD Family, Clinic, and Laboratory

After a warm welcome from Anne Rosser, Astri Arnesen, Christine Tranchant, and Patrick Weydt, the first session on Day 1 set the stage for the meeting with presentations from experts across different aspects of HD. **Anne Elizabeth Saldarriaga Velez Magnusson** (former caregiver, at-risk, HD representative) shared a moving, personal account of her experiences and her inspiring vision for the future. Alexandra Durr (Sorbonne University) discussed her pioneering work on pre-sypmptomatic genetic testing in France and work with HD families. Finally, Erich Wanker (Max Delbrück Center for Molecular Medicine) discussed his work as a protein scientist, and in particular, the role of Huntingtin protein in HD.

Anne Elizabeth Saldarriaga Velez Magnusson

programmes, much to the appreciation of the captive audience. Key insights across the presentations included the importance of collaboration in the HD field, the necessity of adapting to the changing landscape, and the need to plan for future success.

Jean-Louis Mandel

Sarah Tabrizi

Harry Orr

Keynote Presentations

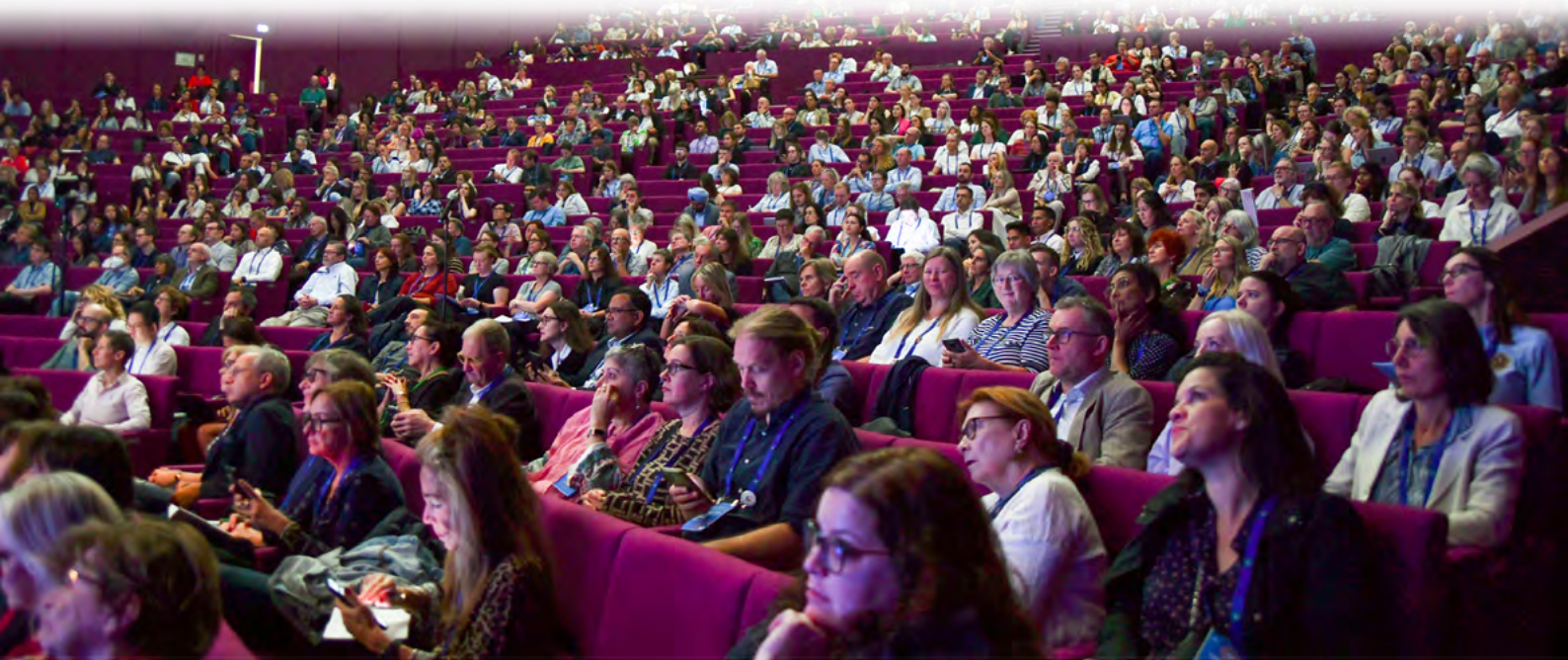
Across Days 1–2 of the meeting, we were treated to three keynote lectures. **Jean-Louis Mandel** (Institute of Genetics and Molecular and Cellular Biology) presented an enthralling history of what we have learnt about unstable repeat expansions across different diseases over the past 30 years. **Sarah Tabrizi** (University College London) discussed mechanisms of pathogenesis, current therapies under development, 'hot off the press' data from HD-YAS (longitudinal study of young adult HD gene expansion carriers) and promising feedback from the

Bernhard Landwehrmeyer

Patrik Brundin

Celebrating 20 Years of EHDN

This special session featured insights and reflections from three EHDN members who've been there right from the very start: **Bernhard Landwehrmeyer** (Ulm University), **Patrik Brundin** (Roche) and **Anne Rosser** (Cardiff University). Each shared their personal recollections of the formation of EHDN and the trajectory to where we are now, sharing anecdotes, photographs, correspondence, and even previous meeting



FDA on biomarker integration into the drug development process. **Harry Orr** (University of Minnesota) presented on CAG triplet repeat disorders, and more specifically, his proposal that if we can better understand the pathogenic similarities and differences between HD and other inherited conditions such as spinocerebellar ataxia type 1 (SCA1), we can move closer towards the overarching goal of developing effective treatments.

EHDN Business Meeting

Anne Rosser delivered this session and quickly moved to the results of the Executive Committee (EC) elections. We heard that Anne would be stepping down along with Alzbeta Mühlbäck, Caterina Mariotti, and Jaime Kulisevksy. Newly elected members Ahmad Aziz, Nayana Lahiri, Esther Cubo, and Hoa Nguyen were congratulated and introduced themselves on stage. These new appointments now leave a gap on the Scientific and Bioethics Advisory Committee (SBAC), and new appointments to the SBAC will be announced in the coming months.

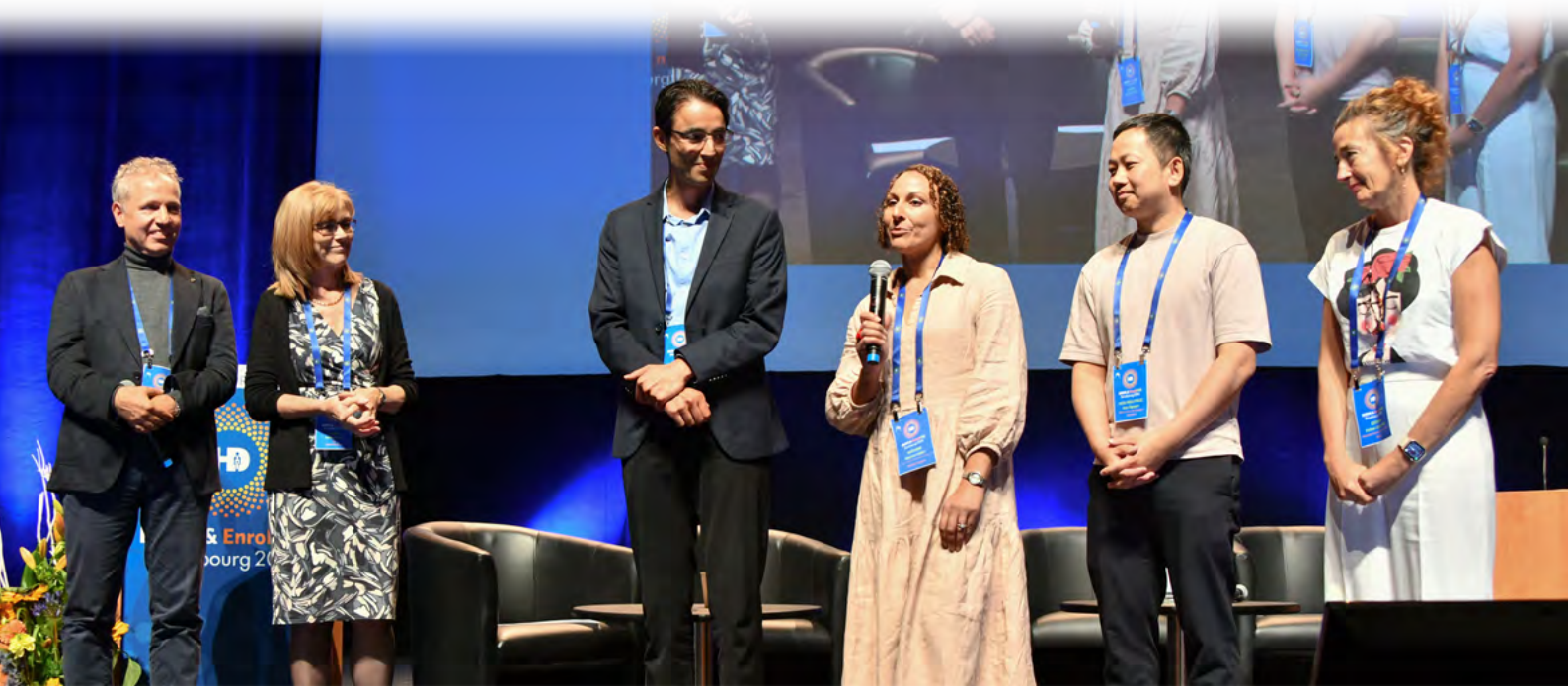
The constitutional amendment to include one person on the EC representing the European community of families with HD as appointed by either the European Huntington's Association or other organisation as determined by the EC was accepted by voters.

Anne recapped on key activities since 2022, including the appointment of joint Science Directors Flaviano Giorgini and Juliana Bronzova. We were reminded of the process for endorsing clinical trials and were shown a snapshot of the studies endorsed since the last plenary

Sandra Durr, Sarah Tabrizi, Bernhard Landwehrmeyer

meeting. We also heard that 10 Lesley Jones Seed Funds have been awarded since 2022, with pilot projects spanning from molecular genetics to much more clinically orientated work.

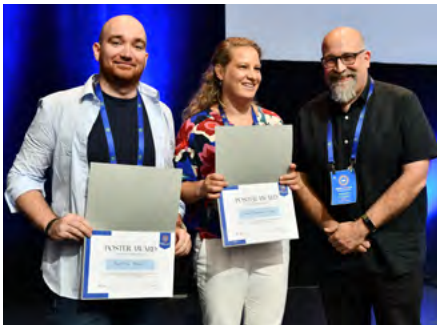
After a summary of current working groups and task forces, we heard how the Fluid Biomarker working group has undergone a shift in focus and ways of working, illustrating how working groups can adapt over time. In terms of outputs, the Neuroimaging working group has recently published a review paper in the Journal of Huntington's Disease, the Physiotherapy working group has published guidelines which have been translated into different languages, and the Incidental Findings task force has published best practice guidelines on reporting incidental findings in genomic studies. The Advanced Therapies working group has been highly active, and several task forces have been set up to address the various challenges in translating advanced therapies to the clinic.



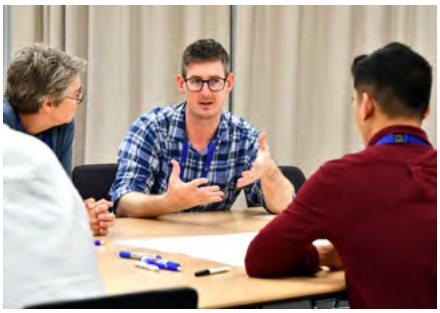
We were reminded about the success of the Working Groups Virtual Forum held in September 2023 and how new collaborations and ideas have emerged from this. One of these is the EHDN Strategic Fund, which will be piloted over the coming year, aiming to support working groups and task forces in meeting their strategic aims (next round in March 2025). Excitingly, EHDN (led by Flaviano Giorgini) has been developing a Marie Curie Doctoral Network grant application (STRIVE-HD) for submission in November.

We also heard about revisions to EHDN's Scientific Strategy (covering 2023–2028). While EHDN's mission hasn't changed, the aim is to take into account the changing landscape and new opportunities in HD research. Activities related to this include the EHDN Regulatory Science Initiative (EHDN-RSI) seeking to facilitate the implementation of ongoing and future clinical trials on key issues of regulatory importance. The first project is working with the European Medicines Agency on the qualification of the HD Integrated Staging System (HD-ISS). Another initiative is the development of a brain bank for early-stage post-mortem brains. It is also hoped that EHDN Platform Meetings (as held previously with Prilenia and Roche) will continue, and further ideas for this are being discussed by the Think Tank.

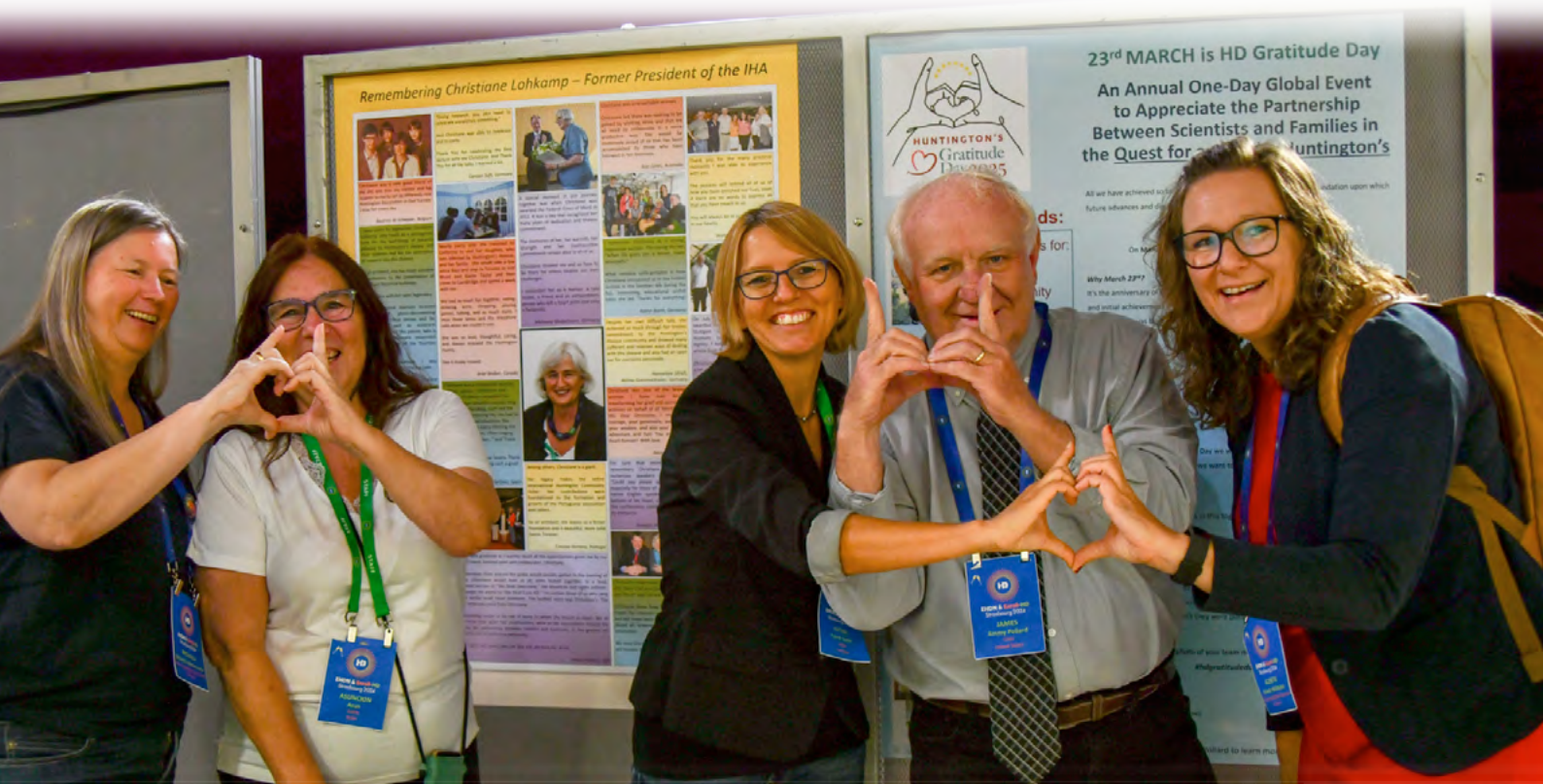
As part of the strategic plan, EHDN continues to focus on communication and education. In addition to the usual activities (e.g., EHDN website, newsletter, social media, and supporting Think Tank projects), new projects for the Communication and Education Group include podcasts, the Fellowship Impact Project, and supporting education initiatives.



Poster awards for Baptiste Brulé and Dorine Boersema-Wijma, presented by Flaviano Giorgini



Grow-HD Workshop



Update: Clinical Trial Developments

Jenny Townhill and Tim McLean, Central Coordination, Catherine Deeprose



Photos: G. Stautner · artifox.com

Day 2 of EHDN and Enroll-HD 2024 opened with exciting updates for ongoing and recently completed clinical trials chaired by Ahmad Aziz (DZNE, Germany) and Tiago Mestre (University of Ottawa, Canada).

First to speak was Raúl Insa of **SOM Biotech**, who described SOM's artificial intelligence platform used to identify known drugs suitable for repurposing in HD. On this basis, the VMAT2 inhibitor bevantolol (SOM3355) was selected and has undergone preclinical studies and a clinical phase 2a proof-of-concept study (completed in 2021), which demonstrated that SOM3355 was safe and reduced chorea. The phase 2b study testing two doses over 12 weeks in a double-blind, placebo-controlled trial started in 2022 and was completed this summer. Results will be released in November 2024.


Raúl Insa

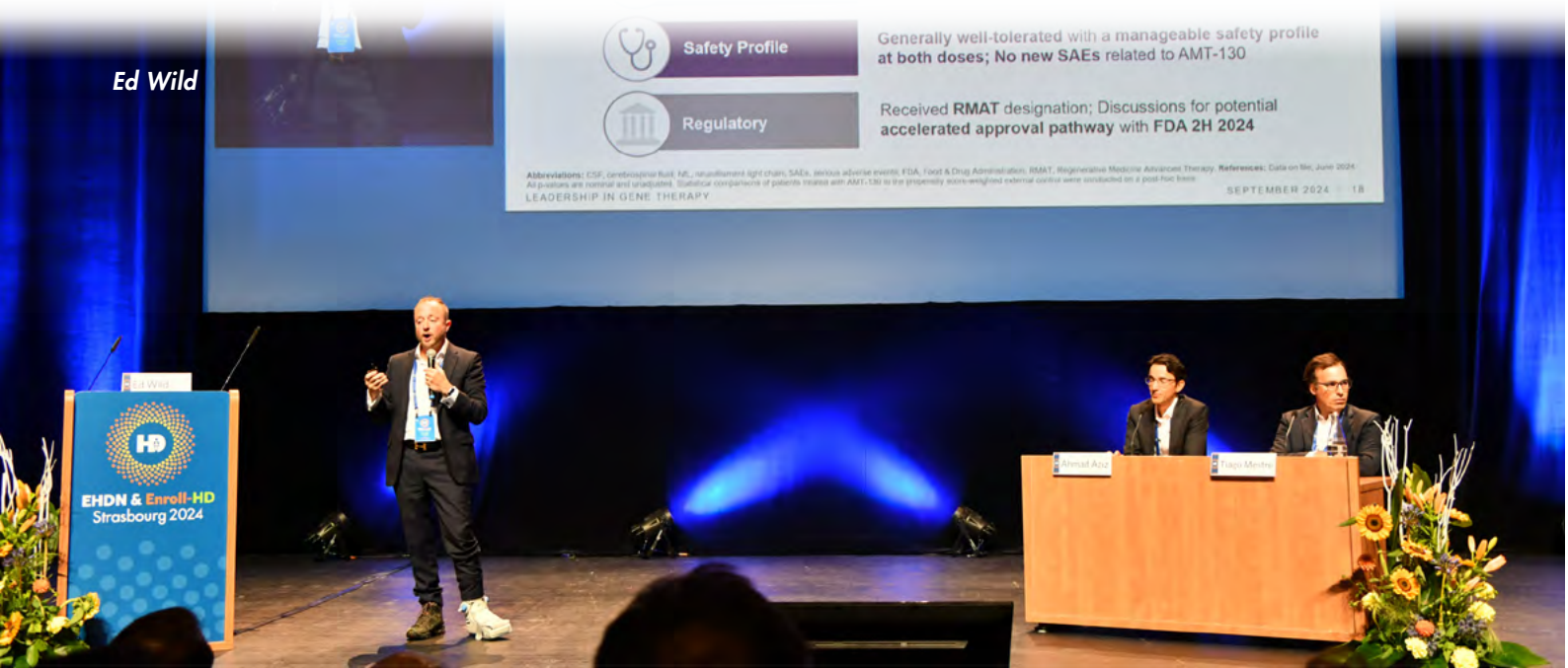
Michael Hayden of **Prilenia** discussed the open-label extension to PROOF-HD, showing the persistence of effects of pridopidine for up to 2 years for the primary efficacy population [off antidopaminergic drugs (ADMs)] across several outcome measures, including the composite Unified Huntington's Disease Rating Scale with -0.54 points over 2 years in comparison to the cUHDRS decline from a propensity-matched historical control with 2-year data from the TRACK-HD longitudinal observational study of -2.2 points. The second message from the presentation was related to the use of ADMs with pridopidine, indicating that pridopidine can be used, without masking its effects, with lower doses of certain ADMs but not with high doses.


Michael Hayden

Ed Wild (University College London) provided updates on **uniQure**'s AMT-130 (Phase 1/2) programme. This gene therapy candidate may potentially slow the progression of HD in the early to moderate stages of the disease via one-time surgical administration into affected brain areas. He reported 2-year data showing both nominally significant clinical benefits and a reduction in neurodegeneration (based on NfL). Discussions are underway regarding a potentially accelerated approval pathway with the FDA, and updates on the phase 1/2 trials (up to 3 years of data) are anticipated in mid-2025.

Peter McColgan of **Roche** presented new biomarker data from the GENERATION HD1 phase 3 trial of tominersen, including an overview of biomarkers for neuroinflammation (YKL-40), neuronal death (total TAU), and astrocytic reactivity (glial fibrillary acidic protein (GFAP)). In HD, YKL-40, total TAU and GFAP increase compared to healthy controls and in GENERATION HD1, no increases were seen for these biomarkers at the low dose of tominersen.


Peter McColgan



Ed Wild

In the ongoing phase 2 GENERATION HD2 trial, which is more than 80% recruited, current data suggest a favourable safety profile. In August 2024, the Independent Data Monitoring Committee reviewed unblinded safety, clinical, MRI and plasma NfL data and recommended the continuation of GENERATION HD2, which is expected to complete enrollment at the end of 2024.

Maddie Pantoni

Maddie Pantoni of **Sage Therapeutics** shared updates on the ongoing dalzanemdor programme (SAGE-718) for cognition in HD. The phase 2 12-week DIMENSION study has completed enrollment, with results expected at the end of the year, and the PURVIEW long-term open-label safety study is currently enrolling.

Jane Atkins

Jane Atkins of **WAVE Life Sciences** updated on SELECT-HD (a phase 1b/2a study of WVE-003, an antisense oligonucleotide designed to target SNP3). We heard that 30 mg WVE-003 dosed every 8 weeks was generally safe and well-tolerated and that the aim of selective lowering mutant HTT was achieved, whilst wild-type HTT was preserved. This is the first demonstration of mutant HTT lowering being associated with a slowing of degeneration in the brain (as measured by caudate atrophy). Discussions are underway with the FDA, and a path for further development of WVE-003 is expected to be determined by the end of this year.

Scott Schobel

Scott Schobel of **VICO Therapeutics** presented interim data on the ongoing phase 1/2a trial of VO659, an allele-preferential antisense oligonucleotide being investigated for HD, spinocerebellar ataxia type 1 (SCA1) and type 3 (SCA3). Treated HD participants had a reduction of mutant huntingtin protein in CSF and no change in NfL in CSF at day 85 compared with baseline. To date, VO659 appears generally safe and well tolerated and due to the long half-life, may have the potential for infrequent dosing (estimated as 1–2 doses per year).

Amy-Lee Bredlau

Finally, Amy-Lee Bredlau presented on behalf of **PTC Therapeutics** and shared updates on interim data from PIVOT-HD. PTC518, now known by the non-proprietary name of votoplam, is an HTT-lowering small-molecule splicing modifier. She reported that interim data support a dose-dependent and durable lowering of HTT and a trend of dose-dependent delay in clinical progression. PTC518 will continue to be evaluated in PIVOT-HD and the 2-year long-term extension study PIVOT-LTE.

Please refer to Table 1 for a summary of ongoing EHDN-endorsed research. An expanded description of all EHDN-endorsed trials and studies (completed and in progress), as well as details of the EHDN endorsement process, is published on the EHDN website.

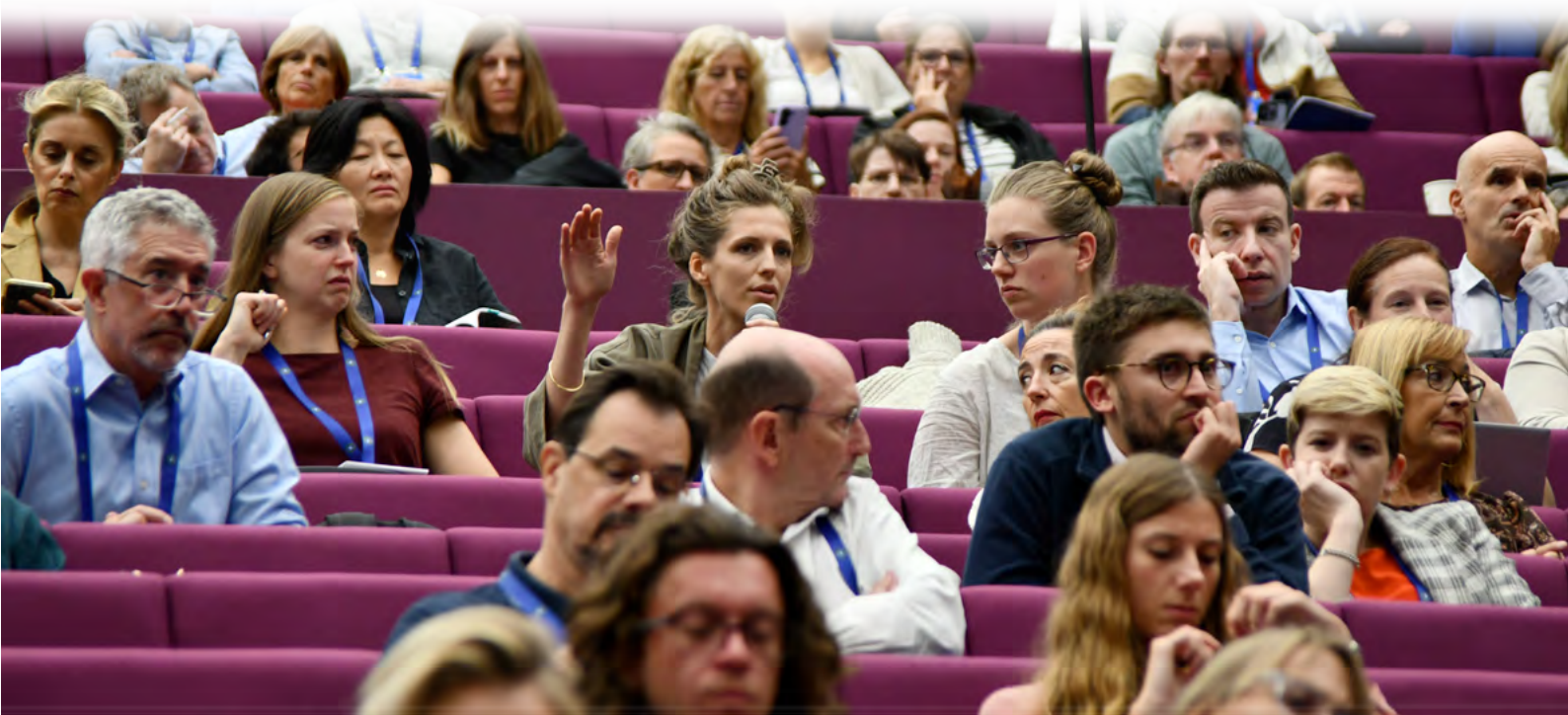


Table 1: Current EHDN Endorsed Trials and Studies

Registration ID	Sponsor	Trial name	Phase	Investigational Product	Mode of Action	Delivery	Treatment Goal	Target Enrollment	Location(s)	Status
NCT06585449	Alnylam Pharmaceuticals	ALN-HTT02-001	1	ALN-HTT02	Htt lowering; siRNA	Intrathecal	Disease modification	54	Canada, Germany, US, UK	Not yet recruiting
NCT05541627	BrainVectis, a subsidiary of AskBio	ASK-HD-01-CS-101	1/2	AB-1001	Restoration of cholesterol metabolism dysfunction (AAV-delivered gene therapy)	Surgical, intrastriatal	Disease modification	18	France	Active, not recruiting
NCT05686551	Hoffmann-La Roche	GENERATION HD2	2	Tominersen	Htt lowering; ASO	Intrathecal	Disease modification	300	Argentina, Australia, Austria, Canada, Denmark, France, Germany, Italy, New Zealand, Poland, Portugal, Spain, Switzerland, UK, USA	Recruiting
NCT05358717	PTC Therapeutics	PIVOT-HD	2	PTC518	Htt lowering; mRNA splicing modifier	Oral	Disease modification	162	Australia, Austria, Canada, France, Germany, Italy, Netherlands, New Zealand, Spain, UK, USA	Active, not recruiting
NCT05655520	Sage Therapeutics	PURVIEW	3/OLE	SAGE-718	NMDA receptor modulator	Oral	Symptomatic	300	Australia, Canada, UK, USA	Recruiting
NCT05243017	UniQure	HD GeneTRX2	1b/2	rAAV5-miHTT	Htt lowering; miRNA AAV delivered gene therapy	Surgical, intrastriatal	Disease modification	15	Germany, Poland, UK	Recruiting

Note. AAV = Adeno-associated virus; ASO = antisense oligonucleotide; Htt = huntingtin; mRNA = messenger ribonucleic acid; NMDA = N-methyl-D-aspartate; OLE = open-label extension; siRNA = small interfering ribonucleic acid

Photos: G. Stautner · artifox.com

Sam Frank, Matt Roche, Erin Koppel, Lauren Byrne

Update: Advances in Enroll-HD – Highlights from Strasbourg (Day 3)

Olivia Handley, Enroll-HD Global Platform Manager, Catherine Deeprose

Although three days into the meeting, Bernhard Landwehrmeyer (Ulm University), Eileen Neacy (CHDI), and Cristina Sampaio (CHDI) nonetheless ensured an enthusiastic start to the day. The first session was dedicated to the practical deployment of the Huntington's Disease Integrated Staging System (HD-ISS) in research, chaired by Chris Ross (Johns Hopkins University) and Sarah Tabrizi (University College London). Cristina Sampaio recapped on the development of the HD-ISS and considered the opportunities and challenges it now offers as a research tool. Jeff Long (University of Iowa) continued on the theme of opportunities in discussing how the HD-ISS can be used in the planning of clinical trials. The session concluded with a stimulating panel discussion involving Abi-Saab Walid (uniQure), Peter McColgan (Roche), Amy-Lee Bredlau (PTC Therapeutics), and Glenn Morrison (Annexon Biosciences).

The first parallel session focused on advances achieved through Enroll-HD, specifically looking at biomarkers and modelling. Speakers included Katrin Barth (EHDN), Jong-Min Lee (Harvard Medical School), Doug Langbehn (University of Iowa), and Jim Mills (University of Iowa). Meanwhile, Sam Frank (Beth Israel Deaconess Medical Center), Matt Roche (CHDI), Erin Koppel (Georgetown University) and Lauren Byrne (University College London) contributed perspectives on the advantages and disadvantages of decentralised visits in HD research.

Katrin Barth

Jong-Min Lee

Doug Langbehn

Jamie Hamilton

A further parallel session showcased the clinical trial and clinical study support offered by Enroll-HD, with speakers including Jenny Townhill (EHDN), Marcelo Boareto (Roche), Jamie Hamilton (CHDI), and Joaquim Ferreira (University of Lisbon). The last parallel session focused on best practices in study coordination, in which speakers Selene Capodarca (EHDN), Jenny Callaghan (EHDN), Bonnie Henning-Trestman (Carilion Clinic), Katie Andresen (University of Cambridge) and Monika Hartmann (King's College London) shared their critical insights.

From left to right: Jamie Levey, Eileen Neacy, Cristina Sampaio, Swati Sathe, Andrew Wood

Michael Panzara

Swati Sathe

Priyantha Herath

Keynote speaker Michael Panzara (Neurvati Neurosciences) delivered a stimulating lecture on the use of innovative trial designs to accelerate drug development, drawing on his extensive experience in developing therapies for neurological disorders.

A particular highlight was the session 'The Next Frontier of Enroll-HD'. CHDI's Swati Sathe introduced Enroll-HD 2.0, explaining important changes to the study that are coming in the future and why. Matt Roche (CHDI) then talked about an upcoming initiative called selfEnroll-HD, a new smartphone-based study and research platform.

The final session on novel approaches to clinical trial design provided exciting insights into the future of HD research. Priyantha Herath (Alnylam) spoke on the need for and practicalities of early clinical trials in HD, and Andrew Wood (CHDI) continued with a discussion on the possibilities for early-stage biomarkers, specifically imaging. Tiago Mestre (University of Ottawa) developed this argument in discussing strategies for more effectively bridging between Phase 2 and Phase 3 studies. Finally, Patrick Weydt (Bonn University and EHDN) presented on how we can best work towards achieving clinical benefit from clinical research – the ultimate but often elusive goal for researchers and participants alike.

Andrew Wood

Tiago Mestre

In summary, these sessions demonstrated how Enroll-HD is making significant strides in advancing and supporting innovative research on HD. The platform's high-quality, high-volume data and biosamples continue to serve as a unique and invaluable resource, promoting new insights into HD and supporting clinical trials. Overall, the meeting highlighted that broad collaboration across the platform's activities is a key element of its ongoing success.

Update: HDClarity

Gail Owen, Clinical Trials Manager,
University College London, UK

HDClarity was designed to: generate a high-quality cerebrospinal fluid (CSF) longitudinal collection and plasma samples (from blood) to evaluate biomarkers and pathways to enable the development of novel treatments for HD.

HDClarity aims to recruit 2,500 participants worldwide. All HDClarity participants must be part of the Enroll-HD study. Since 2016, the study has opened in 38 sites across nine nations worldwide and has recruited an impressive number of 1,035 unique participants.

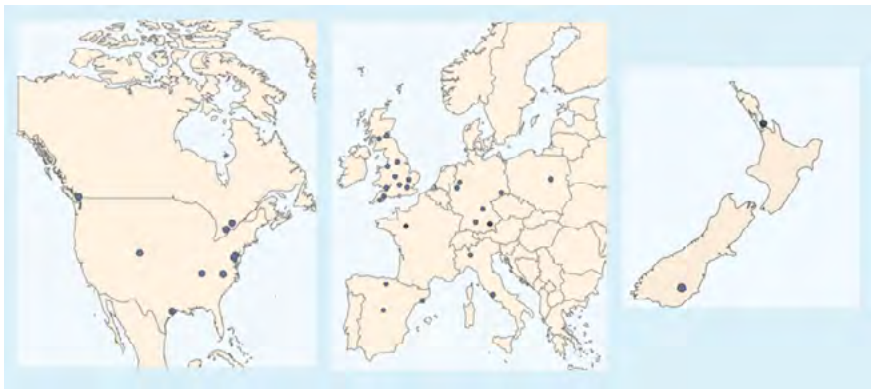


Figure 1: Distribution of HDClarity sites

HDClarity continues to make a vital contribution to HD research. We were thrilled to see these contributions showcased at EHDN & Enroll-HD 2024. Poster presentations included:

Cerebrospinal Fluid Cell Count in the HDClarity Registry Indicates a Transient Inflammatory Response in Late Premanifest Huntington's Disease by Yu Gao and Jan Lewerenz (Ulm University, Germany).

Thiamine deficiency in CSF of Huntington's disease presymptomatic carriers evidences etiological relevance and value as a predictive biomarker by Julia Pose-Utrilla (Centro de Biologia Molecular and CIBERNED, Spain), *et al.*

Enroll-HD Platform Biosamples Resources by the Enroll-HD Platform Team.

First HDClarity PI meeting in Strasbourg

10 Years accomplishments in HD research, care and awareness: The LIRH Foundation experience over the period 2014-2024 by Barbara D'Alessio (Fondazione Lega Italiana Ricerca Huntington, Italy), *et al.*

All posters are available to view at: ehdn.org/ehdn2024/#posters

The EHDN & Enroll-HD meeting also provided the first opportunity for PIs from participating sites around the world to meet and share their experiences and recommendations with PIs from potential new study sites. They were also treated to updates from CHDI scientists who have been using the HDClarity samples in their research.

Further information about HDClarity, including the current protocol, is available at www.hdclarity.net, and the Central Coordination team are always happy to answer any questions (hdclarity-cc@enroll-hd.org). Information about the study can also be found on a variety of platforms, as shown here.

Interested in Participating?

Enroll-HD enroll-hd.org

U.S. National Library of Medicine ClinicalTrials.gov clinicaltrials.gov

HDClarity hdclarity.net

@HDClarityStudy

Scan the code for more site information:

Update: Funding Opportunities

Fionnuala Margreiter, Grants & Collaborations Manager

Current Funding Opportunities

An overview of individual and collaborative grant opportunities can be found at ehdn.org/hd-clinicians-researchers/grant-manager/ as well as some information on the grants and collaboration service.

EHDN/MDS Fellowship Update 2024 Fellowship and Future Programme

The six fellows selected in 2024 are currently at various stages in the process of undertaking their fellowships with host clinics, mainly in the UK, Spain, and Portugal (with Norway in discussion). Many thanks to all the hosts and staff at the clinics for their ongoing support of the programme. The next round of the programme is currently under discussion, with publication expected in the coming months.

EHDN and MDS (ES) Fellowship

Past and potential fellows and hosts met up in a session at EHDN & Enroll-HD 2024, chaired by Juliana Bronzova. About 35 people attended this first-of-its-kind session to hear about the results of the Fellowship Impact Project and discuss forming an Alumni group. The EHDN team presented key findings from the Fellowship Impact Project, spurring important discussions on processes and evaluation. Previous fellow Zaruhi Tavadyan (Armenia) presented her experiences working under the supervision of Hugh Rickards (Birmingham and Solihull Mental Health NHS Foundation Trust, UK). We were thrilled to hear about ongoing information exchange activities and workshops arising from this collaboration. A

Photo: Gabriele Stautner · artifox.com

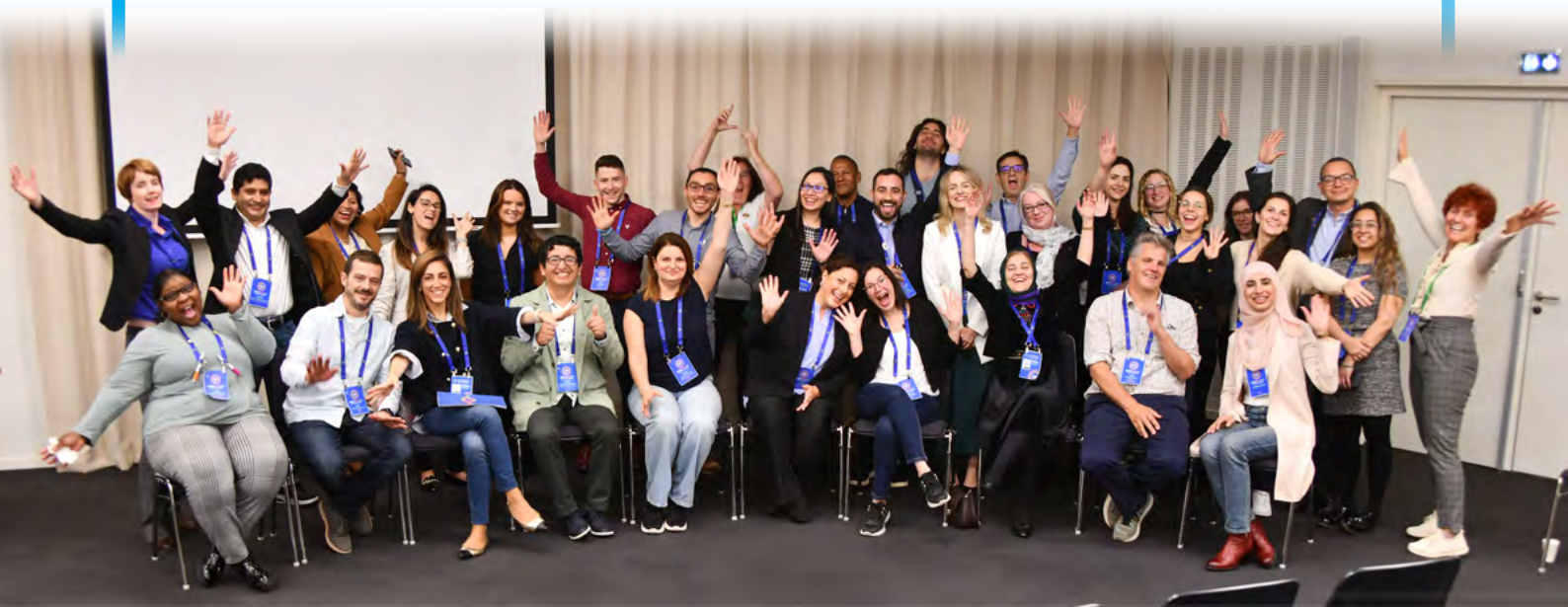
Juliana Bronzova and Fionnuala Margreiter

recent HD workshop sponsored by MDS and EHDN, including international HD experts, was held in Armenia (October 2024) for both Armenian and Georgian audiences. Another HD workshop by a past fellow in Iran is being held in November (sponsored by MDS with UCL HD experts). Hosts and fellows were enthusiastic about ongoing and future opportunities for development and knowledge sharing. The meeting concluded with the agreement to keep in touch and continue to share ideas about the formation of an Alumni fellowship group.

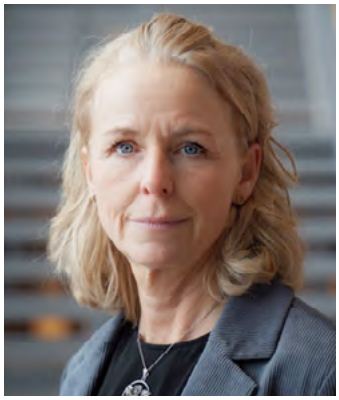
Education and Collaboration

EHDN continues to work closely with various organisations, including the MDS, in the continued implementation of the fellowship programme, as well as organising courses in HD (as previously held in English and Spanish) and with the European Academy of Neurology (promotion activities).

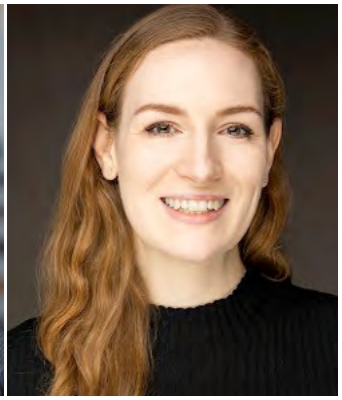
For regular updates about funding opportunities, please see the EHDN website and the Twitter(X) account @EHDN_GRANTM.



Update: New Lesley Jones Seed Fund Awarded

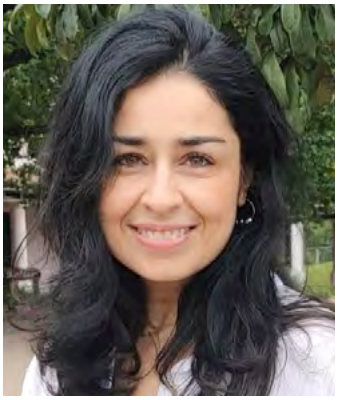


Maria Björkqvist



Alina Blusch

Maria Björkqvist of Lund University has been awarded funding for her project titled 'At the Crossroads of Brain and Body: Exploring the Meninges in HD'. This research will be conducted with her colleague **Alina Blusch** (also of Lund University) and will use an experimental mouse model and flow cytometry to examine changes in meningeal immune cells associated with HD. Importantly, the meninges were previously seen as primarily providing a barrier to support and protect the brain, but have more recently been recognised as playing a key role in brain health, immune surveillance, and inflammation. As such, this work offers an exciting potential to provide new insights into the complex pathology of HD.



Veronica Ines Brito

Veronica Ines Brito (University of Barcelona) has been awarded funding for her project titled 'A Pilot Study of a Novel Molecular Assay to Quantify DNA Repair Synthesis in the HTT Exon 1 as Readout of Somatic Instability'. This study will use a new test that looks for signs of DNA repair and rebuilding in HTT exon1 near the repeats. The idea is that these activities happen more often when the repeats are expanding or contracting, making them easier to spot than the actual changes in the repeats themselves. By measuring the incorporation of a compound similar to DNA's building blocks during the repair activity, this new assay might offer a more sensitive approach to monitor the effect of molecules that affect DNA repair processes and influence the expansion of HTT CAG repeats. It could also help track HD progression in peripheral tissues like blood and skin fibroblasts – even before onset.

It is with heavy hearts that we share the sad news of the passing of

Dr Lorenzo Nanetti

Dr Nanetti, a beloved neurologist at Fondazione IRCCS, Istituto Neurologico Carlo Besta in Milan, left us earlier this month. He provided a beacon of hope and expertise in the field of neurodegenerative diseases, particularly HD, and he was a kind and compassionate presence for all who had the privilege of working with him. Dr Nanetti's contributions to research, practice, and care were profound, and his unwavering commitment to the HD community touched the lives of many. His sudden loss leaves a void that will be deeply felt by colleagues, individuals with HD and their families, and all who knew him. He will be sorely missed, and his memory will continue to inspire those who carry forward his work and his passion.

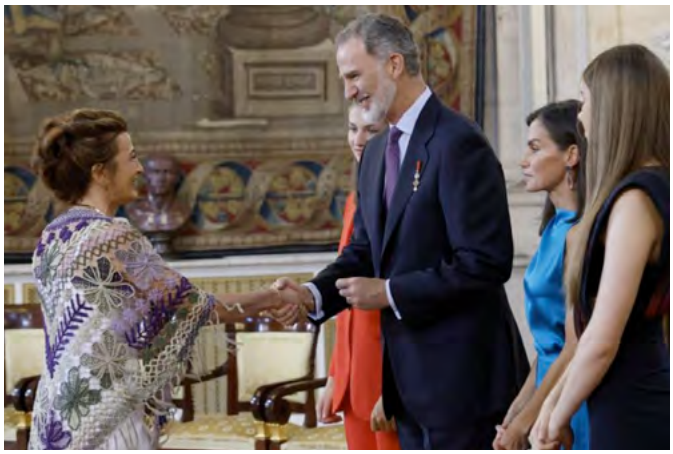
Flaviano Giorgini

Kinga Kolodziej

The Lesley Jones Seed fund programme is intended to support pilot studies that will eventually kickstart larger projects. The next deadline for applications is 1 March 2025.

More information about the programme and how to apply can be found here or you can contact Flaviano Giorgini (flaviano.giorgini@euro-hd.net) or Kinga Kolodziej (kinga.kolodziej@euro-hd.net) for further information.

EHDN Members Receive International Recognition



Esther Cubo with the King of Spain

Congratulations to **Esther Cubo**, Neurologist at the University Hospital of Burgos and Enroll-HD Investigator, who received the Official Cross of Civil Merit from the King of Spain in June this year. This well-deserved recognition of Esther's research on environmental factors impacting HD is a tremendous and hugely deserved accolade.

Sarah Tabrizi

Congratulations also to **Sarah Tabrizi** (University College London) for her election as a Fellow of the Royal Society in May 2024 and election to the US National Academy of Medicine in October 2024 in recognition of her work in HD. The National Academy of Medicine explained that Sarah was elected for 'contributions that have impacted experimental therapeutics of Huntington's disease, leading multidisciplinary research teams to the first randomised clinical trials of nucleic acid therapies, and forging a biological staging approach tethered to fundamental science and patient research for treating neurodegenerative disorders, akin to cancer therapeutics.'

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Working Towards Person-centred Care in HD

Sandra Bartolomeu Pires

Sandra Bartolomeu Pires (University of Southampton) recently published a paper in the Journal of Huntington's Disease looking at experiences of person-centered integrated care. Data for the Integrate-HD survey were collected from across England. Findings showed that people living with HD commonly experience fragmented care, geographical inequalities in care access, and unmet complex needs. This valuable work is part of Sandra's PhD programme and holds important implications for policymakers and the development and implementation of HD care guidelines in the UK and beyond.

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Get in touch with the Think Tank!

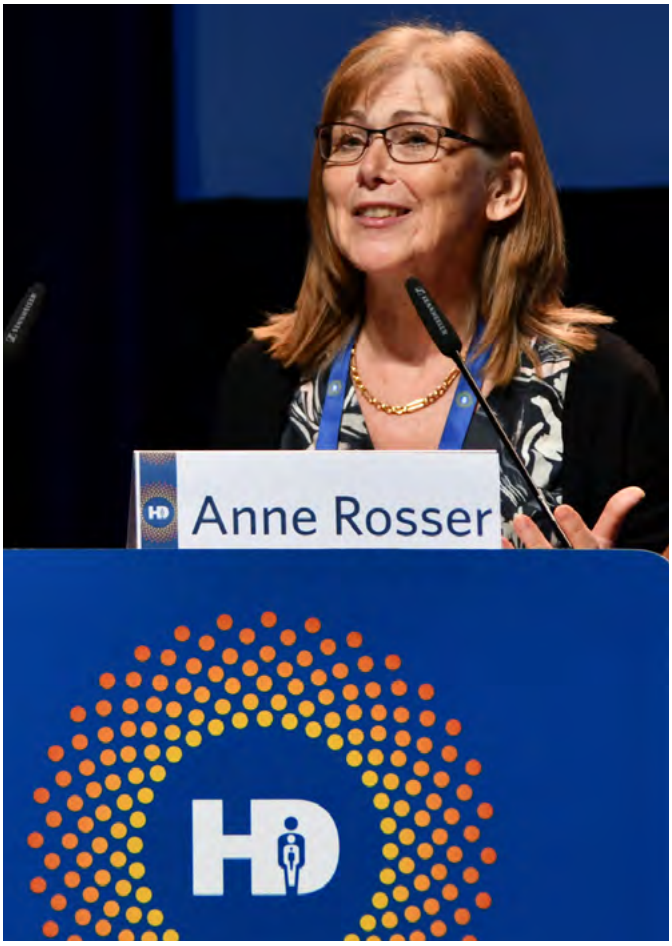
The EHDN's HD Science Think Tank brings together EHDN members and staff who are closely involved in supporting scientific research – including members of the Executive Committee, Central Coordination and the working groups – and it engages with the HD research community in three ways:

- 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 Kinga Kolodziej kmk20@le.ac.uk

Interview with Anne Rosser: A Driving Force in HD Research

Anne Rosser is Professor and Honorary Consultant in the Department of Neurology in the School of Medicine at Cardiff University, where she is the Director of the Cardiff University Brain Repair Group. In addition to her pioneering work on novel therapies for HD, she has undertaken critical roles within EHDN. Notably, Anne was the very first chair of the SBAC and held the position of EHDN Chair and Co-Chair from 2014 to 2024, from which she stepped down in Strasbourg this year.



How did you get involved in HD research?

I first got involved in HD back in 1994 – about a year after the gene was discovered. I had just started as an MRC Clinician Scientist Fellow in Cambridge, working on stem cell therapies for neurodegenerative diseases. John Hodges (famous behavioural neurologist and now retired) had recently set up a Huntington's clinic and asked if I'd help out. We started a new clinic together, but as John's main interest was understanding the underpinnings of neuropsychological deficits more broadly, he eventually stepped back a little, whereas the clinic became the mainstay of my work. I rapidly became increasingly interested in HD – and it's been my key interest ever since.

What does it mean to be a 'clinical scientist' in the study of a rare disease like HD?

Basically, being a clinical scientist means undertaking research while also continuing clinical practice. The ways in which people do this vary hugely, including how they dedicate different proportions of their time to clinical work and research. This research could be anything from the basics of molecular and cellular research right through to very clinically orientated work, using human participants or working on a specific disease population, for example.

In my lab, the key theme is regenerative medicine, which means that we use stem cells, cell cultures, and animal studies. We think a lot about why a stem cell becomes a more specialist sort of cell (e.g., a brain cell). I'm particularly interested in how stem cells can become medium spiny neurons. Medium spiny neurons are a specific focus in understanding the pathophysiology of HD, given that they comprise 80-90% of neurons in the brain's striatum, and that their degeneration results in deficits of movement, behaviour, and mood.

I also direct some more clinically orientated research, where we focus on how we can take these emerging therapies through to clinical application. In collaborative work with Duncan McLauchlan, I've been looking at the behavioural aspects of HD, and I've supported Monica Busse in developing rehabilitation strategies for individuals with HD.

Cardiff University is a recognised leader in HD research. How did this come about?

Cardiff has a long history of involvement with HD. I moved to Cardiff in 2001, and by that time, Sir Peter Harper was already well known for his work in clinical

Anne Rosser with Patrick Weydt

genetics and for being part of the team involved in the discovery of the HD gene in 1993.

Peter had already made great strides in terms of the epidemiology of HD and had set up a clinic primarily focused on diagnosis (representing where the field was, in general, at that time). He had also done a lot of work raising awareness of HD in Wales, which I think we still see the benefits of to this day. Professor Leslie Jones was also already in Cardiff, and she had been working on various aspects of neurodegeneration, including Alzheimer's disease, but her work gradually moved more towards HD. She was a great person to talk to and share ideas with. I took over Peter's clinic and then developed it into a follow-up clinic, in line with how the field was shifting, and the focus differed as well because I was a neurologist rather than a geneticist. Then from that point, we developed clinical trials – including Enroll-HD. Sadly, Leslie unexpectedly passed away in 2022. As with Peter only the year before, we were struck by the profound significance of losing pioneering scientists who had devoted so much to the field.

Yet we remain resilient, and Cardiff continues to go from strength to strength. Over the last 20 years we've built up a critical mass of people working in the HD field. We have people working on the molecular basis of HD, like Tom Massey and Vincent Dion, and people working on stem cells, like Meng Li and Nick Allen. Mariah Lelos (my close collaborator) is focused on behavioural and animal models, while Duncan McLauchlan and Cheney Drew work more on the clinical side. We are also lucky to have our colleagues, Peter Holmans, a statistician, and Liam Gray who is a neurosurgeon with an interest in HD.

Cardiff University Brain Imaging Centre possesses really cutting-edge imaging hardware and we've got people like Derek Jones and Claudia Metzler-Baddeley who work on brain imaging and cognitive rehabilitation. And finally, in May this year, we launched the HD Centre in Wales to bring together all this expertise!

We were all thrilled to see so many faces, familiar and new, at EHDN & Enroll-HD 2024. What stands out for you about these bi-annual meetings?

I always think the HD community is really special – it stands out across different research fields as being very collaborative and supportive. It's amazing to see all these people from across Europe who you've been working alongside for several decades and, at the same time, all these energetic young people who are just coming into the field.

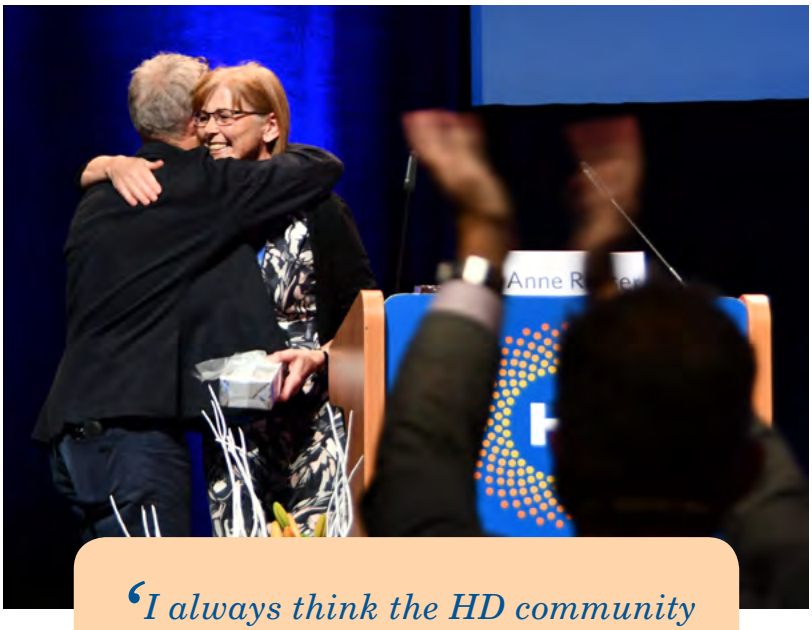
The interdisciplinary aspect is also critical. We can hear all about cutting edge molecular genetics, clinical trials and care, and meet up with the HD-affected families, all within the same meeting. There is a real sense that we are working together towards a common set of aims.

At the Strasbourg meeting, a key theme was '20 years of EHDN'. What did that mean for you?

A lot has changed over the last 20 years. I spent some time recently looking back at some of the programmes from the early conference – around 2005 – and at that point, we knew relatively little about the trajectory of HD, never mind having any realistic possibility of treatment. But now we have clinical trials that offer the potential for meaningful treatment – and that is absolutely amazing. It's incredible to see how the HD field

has developed over the years and to have the prospect of meaningful treatments possibly within our grasp.

Of course, at EHDN, we will also have to continue evolving. I think it has been a hugely important entity and has genuinely brought people together across Europe (and beyond). I'm personally very grateful because EHDN has resulted in me having amazing colleagues across Germany, France, Spain, and further afield – who I almost certainly would not have come across otherwise. EHDN now has influence globally and has opened up many new and exciting collaborations.



We know that the search for treatments for HD will continue, and most likely, we will need to look at the role of personalised medicine in HD in due course. But without doubt, for EHDN and for the HD field, there are many exciting things on the horizon.

> *'I always think the HD community is really special – it stands out across different research fields as being very collaborative and supportive.'*
>
> ***Anne Rosser***

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Dates for your diary

- **7–9 November:** HSG 2024, the 31st annual meeting of the Huntington Study Group, takes place in Cincinnati, Ohio
- **18–20 November:** Huntington's Disease Association online course for professionals will include topics such as genetics, neuropsychology, psychiatry, physiotherapy, occupational therapy, speech therapy, and palliative care. Register here
- **28 November 2024:** Update on Huntington's Disease workshop will be held in Iran (facilitated by the Iranian Neurological Association and supported by MDS)
- **31 January 2025:** North of England NHS Huntington's Disease Conference –
- **24–27 February 2025: CHDI's 20th Annual HD Therapeutics Conference** takes place in Palm Springs, California. Registration will open in mid-November.
- **14–16 March 2024:** HDYO's International Young Adults Congress takes place in Prague, Czech Republic. Registration is now open, and scholarships are available to help young people attend
- **26–28 June 2025:** The 40th Annual HDSA Convention takes place in Indianapolis, Indiana

Would you like to share an upcoming event with our readers?
Please email the details to newsletter@euro-hd.net

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