July 2019 · Issue 37

EHDN *News*

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

Photo: Katrin Barth

Photo: SportOnline.de

Photo: Horst Winkelmann

May is HD Awareness Month, and this year buildings and monuments all over the world were illuminated in blue and purple to draw attention to the disease - blue for HD, purple for juvenile HD. The European Huntington Association raised a team - "HD on the Bike" - to take part in the Škoda Velotour bike race in Frankfurt on 1 May, as illustrated by the top three photos. From top to bottom, and left to right: (1) Dina De Sousa and EHA President Astri Arnesen; (2) Katja Vitkin, Katrin Barth, Anita Zanotti and Heidi Jäger from Ulm; (3) The HD on the Bike team. The sun blazed in Frankfurt, but rain in Florence didn't deter 15 participants from completing the course of another cycling event organised by the Italian League for Research on Huntington's Disease (LIRH) on 18 May. The photo shows (front row, from left to right) LIRH Director and Vice President Barbara d'Alessio with Giuseppe Ursi, Ferdinando Squitieri and Alessia Migliore.

Photo: Loredana Barca

@EHDN_GRANTM
Your Grant & Collaborations Manager has a Twitter account! Follow her for the latest news on EU funding and rare diseases.

www.ehdn.org

Subscribe here to EHDN *News*:
Please go to the URL below and fill out the online form:
http://www.ehdn.org/news-events/
Please send us your comments, suggestions and overall feedback:
newsletter@euro-hd.net

Imprint:
Editorial Board of EHDN News:
Laura Spinney, Editor (Paris, France)
Gabriele Stautner Artifox Communication Design (Ulm, Germany).

Adela is 10

Jan Motlik

Exactly 10 years ago, an international consortium of researchers based in the US, Italy and the Czech Republic, supported by CHDI, announced the birth of the first transgenic HD minipig, Adela.

The consortium was motivated by the realisation that, in future, there would likely be a need for preclinical testing of experimental treatments for HD in large animals. The miniature pig, or minipig, seemed a promising candidate, because of its large brain and long life. Single-celled minipig embryos were therefore engineered via infection with a lentivirus containing the sequence of the promoter of the human huntingtin gene and that of the protein's first 548 amino acids, including 145 glutamine repeats.

Adela was born at the PIGMOD research centre in the Czech town of Liběchov. She subsequently gave birth to several litters of her own, composed of equal numbers of wild-type and transgenic piglets. This meant that transgenic and wild-type piglets with the same genetic background could always be compared in physiological, biochemical and behavioural tests.

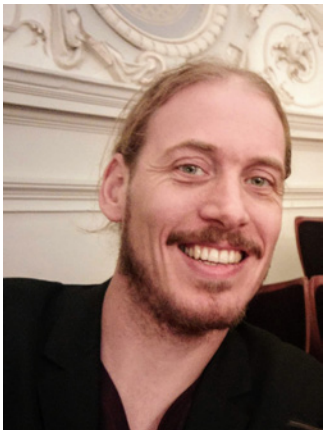
The consortium, of which I am a member, was particularly interested to see how the mutant huntingtin (mHTT) protein was distributed through the bodily tissues of the transgenic minipigs, including the different compartments of the brain and the cerebrospinal fluid (CSF). The US- and Netherlands-based company uniQure, which specialises in gene therapy, expressed interest in the model, after testing some of their experimental therapies in rodents, and this led to trials in the larger-brained minipig.

A viral vector carrying a transgene was injected intracranially. This transgene incorporated an engineered microRNA—that is, a short RNA sequence that can turn a gene on or off—that in this case interfered with the production of human HTT. Widespread, dose-dependent distribution of the vector was detected throughout the minipig brain, that correlated with expression of the transgene. mHTT messenger RNA (mRNA) and protein were found to be significantly reduced in all the same brain areas, as well as in the CSF.

A longitudinal study was subsequently designed in collaboration with uniQure, neurosurgeons from the Na Homolce and Saint Anne Hospitals in Brno, Czech Republic, and the British engineering firm Renishaw—which provided a convection-enhanced delivery system. In this study, a modified vector-transgene combination, containing another microRNA called AMT-130, was injected into the putamen and caudate nucleus of the minipig brain under MRI guidance. Six months later, the vector was reported to have penetrated key brain regions and the CSF, once again mirroring the pattern of reduction of mHTT mRNA and protein, which was again significant. Similar results were reported at one-year follow-up.

The demonstration of the safety and efficacy of uniQure's gene therapy strategy for HD in the minipig model provided the grounds for the company's application to the US Food and Drug Administration (FDA) to pass to clinical trials. In April of this year, the FDA granted AMT-130 fast track designation, and uniQure is now preparing for the first trial of AMT-130 in humans, with patient recruitment due to get underway this year. These developments represent a great source of satisfaction for those who work on the minipig model at the PIGMOD research centre, and justify CHDI's unwavering support of the minipig project.

Jan Motlik directs the PIGMOD research centre of the Czech Academy of Sciences' Institute of Animal Physiology and Genetics in Liběchov.
See page 13 for details of an upcoming meeting on animal models.



Giving families a place, a face and a voice

Rob Haselberg

It was summer 2017 when I stumbled on the webpage of the European Huntington Association (EHA). At that time I was taking my first steps in the Huntington world. Having tested positive for the gene a few years earlier, I was now longing to be part of a community. I had attended some national events in the Netherlands, where I come from, and had started to do some volunteer work for the Dutch HD association, but I wanted more. So when I found an announcement for a European patient meeting I was intrigued and registered on the spot.

Flash forward a few months: it's the end of September 2017, and I am at the EHA conference in Sofia, Bulgaria. Having gone there on my own I do not know anybody. The programme starts with a country roll call and I receive two great surprises: first, all the countries in Europe seem to be represented, and second, there are so many Dutch people present! Instantly I feel less alone.

A conference can be judged in many ways. What struck me about the one in Sofia was the deep connections people made there. The presentations were powerful, meaning they automatically sparked discussion. Not long into the proceedings I already felt a part of the Huntington family – hugs included. Being able to share and understand at the same time was such an eye-opener for me. To be honest, I do not fully recall all the talks, but I vividly recall the people. In those three days I made friends for life.

I left Sofia with a lot of energy and the realisation that I wanted to be more involved. I wanted to contribute to the wonderful experience I had just had, so to speak. I volunteered with the EHA and an opportunity to help soon presented itself. The leading HD patient advocacy organisations had just formed a global coalition called HD-COPE (HD Coalition for Patient Engagement), with the aim of giving families affected by HD a voice in clinical research. After a short interview I was selected to join the initiative.

HD-COPE is a group of 24 gene carriers and carers who provide insights, mainly to pharmaceutical companies, on a variety of HD-related topics. The idea is that armed with a clearer understanding of our needs, such companies will be in a better position to tailor therapeutic interventions and clinical trials to those needs. With the research and development process focused on the right things, it will also become more efficient—a win-win situation. In the last year this approach has resulted in fruitful and open discussions with companies including Roche, uniQure and WAVE Life Sciences. Many of our suggestions have already been incorporated into the design of clinical trials.

I know I am lucky that my work provides the flexibility for me to maintain this level of involvement in HD affairs. My boss is very supportive and I am able to plan my own time. Not everyone is so lucky. However, it's important to remember that patient advocacy starts small. It can begin with sharing experiences and being there for people affected by HD, giving a lecture at a local school or sharing a Facebook post to raise awareness. There are so many ways to contribute.

My journey in this Huntington world began after Sofia. Needless to say, when the next EHA conference was announced—in Bucharest, Romania, this coming October (see page 13, Dates for your diary)—I registered immediately. This time, I know that many of my friends will be there, and I hope to make many more. So let's connect and start sharing experiences. Who knows, it could be the beginning of a great new adventure!

Rob Haselberg is an assistant professor in the Department of Chemistry and Pharmaceutical Sciences of the Vrije Universiteit Amsterdam, the Netherlands, and an HD family member. He can be contacted at: rob@huntington.nl


Update: Clinical trials

Jenny Townhill and Tim McLean,
Central Coordination

The following trials have been endorsed by EHDN. EHDN endorsement of a study protocol follows review by the EHDN Scientific Bioethics Advisory Committee, which makes its recommendations to the Executive Committee. A formal letter of endorsement may then be issued to the study sponsor, signalling to the HD community that the study protocol has been reviewed and endorsed by a group of expert HD scientists and clinicians.

PACE-HD (Physical ACtivity and Exercise outcomes in HD): Recruitment has been completed into this activity intervention study, with 116 participants enrolled by 14 May 2019. The study, led by Cardiff University, also involves seven sites in Germany, Spain and the US, and makes use of data and resources from Enroll-HD as well as an additional assessment battery. Results are expected in 2020.

GENERATION HD1: Recruitment to this Roche global phase 3 trial of the huntingtin-lowering antisense oligonucleotide (ASO) RG6042, which was described in detail in the last edition of this newsletter, got underway in January 2019. In March, Roche announced that there would be some changes to the study design based on preliminary data from the ongoing phase 1/2a study. As a result, screening would be put on hold to allow for approval of the amended protocol by the relevant authorities. The main proposed changes are detailed in the table below:

Original protocol	
All participants have *monthly* lumbar puncture procedure and are randomised to either:	Group 1: RG6042 every two months (placebo during alternating procedures) Group 2: RG6042 monthly Group 3: Placebo monthly
Amended protocol	
All participants have the lumbar puncture procedure *every two months* and are randomised to either:	Group 1: RG6042 every two months Group 2: RG6042 every four months (placebo during alternating procedures) Group 3: Placebo every two months

Recruitment is being restarted on a site-by-site basis once the amendment has been fully approved. Participants recruited under the original GENERATION HD1 protocol will be offered enrollment into the GEN-EXTEND open-label extension study, as will participants of the open-label extension of the Phase 1/2a study.

PRECISION HD1 AND HD2: Recruitment continues to these two phase 1b/2a trials of allele-specific ASOs, sponsored by WAVE Life Sciences, with the company expecting to report topline clinical data by the end of 2019. These will include clinical safety results and data on the extent to which mutant huntingtin protein is lowered in the CSF. Sites in the US, Canada, Poland and the UK are involved, and an additional site has opened recently in Australia. Further sites in Australia and Europe are expected to be activated soon.

HD-DBS: More than 70% of participants have now been recruited into this trial of pallidal deep brain stimulation (DBS) for HD, at sites in Austria, France, Germany and Switzerland, with recruitment expected to be completed early in 2020. For further information, please contact: dbs@euro-hd.net

Introducing the Enroll-HD Clinicial Trial Committee

The HD Clinical Trials Task Force (HD-CTTF) has been restructured to better serve the current and developing needs of HD clinical trial sponsors, as well as the way in which EHDN supports sponsors and trials at the global level. It has been renamed the Enroll-HD Clinical Trial Committee (CTC) accordingly.

The CTC forms part of the Enroll-HD platform governance structure. It provides advice and support for industry and academic sponsors developing potential therapies for HD, as well as managing the HD Clinical Trial Site Certification scheme. The CTC comprises a management team, chaired by Cristina Sampaio, that has access to a panel of independent members with expertise in all aspects of HD, clinical trial design and methodology. It is responsible for reviewing interventional study protocols, providing advice on various aspects of clinical programmes and trials, and accepting clinical trials whose sponsors wish to access Enroll-HD platform support services (feasibility, site identification or recruitment, for example).

Before a sponsor can access advice or support for a study, the study protocol and associated documents must be reviewed by CTC panel members who are selected for the relevance of their expertise to the study in question. Studies that pass the review process gain access to Enroll-HD platform support services, which are tailored to the study's and sponsor's specific requirements.

For further information about the CTC, please contact: jenny.townhill@enroll-hd.org

Update: Enroll-HD

Here, Enroll-HD's Global Platform Manager Olivia Handley interviews Mette Gilling, the person who knows most about the datasets and biosamples that are available through the Enroll-HD platform.

In her new role as EHDN's Scientific Project Manager, former Danish language area coordinator Mette Gilling manages the specified dataset and biosamples requests for the Enroll-HD platform. This makes her the main point of contact for anyone wishing to access data or biosamples from the Enroll-HD, TRACK-HD or HDClarity studies, that can't be obtained by a simple online application. Her role requires her to work alongside the Scientific Review Committee (SRC), which evaluates and approves such requests, as well as to interact closely with the data management, statistics and biorepository teams that prepare and deliver the requested materials.

Mette Gilling

Olivia Handley

Can you describe the type of data and samples that are available through the Enroll-HD platform?

In Enroll-HD, data and blood are collected at annual visits. More precisely, the biosamples we collect are whole blood and peripheral blood mononuclear cells (PBMCs), which can be used for extracting proteins, DNA and RNA. Previously, we created cell lines for every participant in Enroll-HD. We don't do this

anymore, because the inventory of such cell lines is considered sufficiently large, but it's still the case that cell lines and DNA are available for most participants and can be requested. As a platform, Enroll-HD supports many different types of study and therefore collects different kinds of data. For HDClarity, for example, we collect CSF, plasma and serum. The legacy of TRACK-HD, a study which ended several years ago, is several different types of imaging data, clinical data and biosamples (buccal swabs, plasma, serum and PBMCs) from premanifest, early manifest and control participants.

Who may access the data, and how?

Different types of dataset are available, with different thresholds for access. The threshold for the Enroll-HD periodic dataset (PDS) is fairly low. Any researcher affiliated with an institution may register via the website, where they will be asked to sign an online data use agreement. The PDS doesn't include every single data point from Enroll-HD, however. The most identifying variables are not available but may have been converted (date of birth is converted to age, for example). A researcher who needs data that are not in the PDS should complete a specified dataset application form. This is reviewed by the SRC, and if it is approved, the specified dataset is prepared.

For non-renewable samples, requests also pass via the SRC. The committee considers how rare a sample is and how many aliquots or parts it can be divided into. It then weighs this information against the scientific merit of the proposal to ensure that the samples are used as efficiently as possible.

How long does it take for a data request to be satisfied, on average?

For specified dataset requests, the whole process from application to delivery currently takes about three-to-four months. Where biosamples are concerned, it depends on the sample. For HDClarity samples, for example, the applicant may require the HD and control samples to be matched by age or gender, but there may not be enough samples available to do that yet. If there are, the process takes about six months. If not, it obviously takes longer.

What makes these datasets and sample collections so valuable?

They are each one of a kind! Enroll-HD is unique in that it is a global observational study. Normally, it's very difficult to finance such a study. Enroll-HD offers an invaluable platform for basic research, clinical research and clinical trial support.

What other datasets and collections will become available in future?

A number of platform studies are in the pipeline, including several imaging studies. They build on Enroll-HD, which means that in principle there will be clinical data available from Enroll-HD and imaging data provided by these studies. I should also mention the Origin-HD study, which is a semen collection study, and the Enroll-HD plasma collection. Starting this summer, a number of Enroll-HD sites will start collecting plasma annually.

Finally, when will the next Enroll-HD PDS become available?

All we can say for now is that it will be 2020 at the earliest. The last one, PDS4, was released at the end of 2018 and has already been downloaded by 69 researchers.

The user's view

Geneticist and biostatistician Steve Horvath of the University of California, Los Angeles, answers our questions about his experience of using Enroll-HD resources.

Steve Horvath

Can you give us a little background on your research interests in HD?

I am interested in the molecular basis of biological ageing and its relationship with HD. Our research has demonstrated that, on the epigenetic level, HD can be considered a disease of accelerated ageing. I am intrigued by the idea of potentially delaying the onset or progression of HD by delaying ageing.

How have the Enroll-HD datasets helped you?

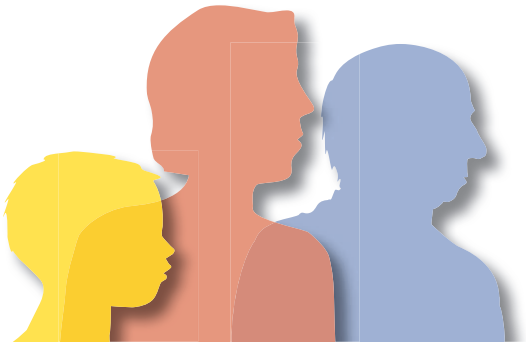
They have been invaluable for carrying out DNA methylation studies in blood. We have shown that HD methylation levels relate to HD status, and that manifest HD is associated with accelerated ageing according to the epigenetic clock.

Any advice for Enroll-HD as to how to improve the user experience?

None. Just keep producing the same high quality data and collecting the samples. We are particularly interested in premanifest samples.

Any advice for HD researchers who have yet to discover the resource?

The data are easy to obtain and to use. Fortunately, there is very little red tape. Wonderful data dictionaries explain the variables and data. I have worked with more than 20 epidemiological cohorts, and I would rank Enroll-HD top.



Registry news

The Registry dataset (RDS) is now accessible. The RDS has been prepared with a format similar to that of the Enroll-HD periodic datasets (PDS), using the same recoded IDs. Also as in the Enroll-HD PDS, some values have been aggregated to further protect the identity of study participants. Those needing disaggregated data or data not provided in the RDS may apply for a specified dataset. Further information is available on the dedicated EHDN webpage.

Photos: Gindel Delgado

A Factor-H volunteer feeds hungry children in Barranquitas, Zulia state, Venezuela.

Bringing hope to HD families in Venezuela

Ignacio Muñoz-Sanjuan, President, Factor-H

Earlier this year, while walking with colleagues through the dusty, garbage-filled streets of Barranquitas in Venezuela's Zulia state, I noticed a small boy following us. Barefoot and dirty, he wore tattered clothes. I asked his name: Brayan. He was 11 or 12 years old, he thought, but he didn't know his birthday or his last name. "My mother died of HD when I was very young," he told us. "My father was killed a few years ago." At first he was too embarrassed to show us where he lived, but after some encouragement he led us to a hot tin shack. There, on a filthy mattress on the ground, he spent his nights alone and afraid.

Barranquitas is typical of many poor towns in Venezuela, but for one thing: hundreds of its inhabitants have either died from HD, are symptomatic or—like Brayan—have been orphaned by the disease and are at risk of developing it. If they are none of these things, they are probably caring for one or more sick relatives. The crisis that has engulfed Venezuela has exacerbated an already dismal situation in Barranquitas, where poverty has eroded family support networks and basic infrastructure is lacking. Power outages are the norm, the local school has stopped functioning, and many children spend their days roaming the streets.

My colleagues and I created Factor-H, a Los Angeles-based non-profit organisation, to try to bring assistance and hope to impoverished communities with a high prevalence of HD, including families from Venezuela's Lake Maracaibo region who contributed to scientific progress. It was tissue samples donated by residents of

Barranquitas and other towns in that region—the parents and grandparents of children like Brayan—that enabled the identification of the HD mutation, yet these same children are likely to be among the last to benefit from any interventions that result from that knowledge. We believe they deserve better.

Factor-H came into existence seven years ago, with the goal of providing food, clothing, medicines, school materials, counselling and social support for HD families living in poverty in Latin America. Our first projects focused on northern Colombia, but two years ago we signed a collaborative agreement with the Hábitat Luz Foundation, a non-governmental organisation associated with the University of Zulia. The foundation is managed by architect Marina González de Kauffman, whose team provides logistical support on behalf of Factor-H, and last February we extended our children's programme to Zulia. A hundred youngsters like Brayan are now being sponsored there.

The institutional breakdown that has accompanied the Venezuelan crisis presents formidable challenges. Few HD specialists remain in the country, and the Maracaibo communities have little or no contact with them. We have therefore established an agreement with Zulia's neurology association and local psychiatrist Rey Varela to provide at least some of the care they need. Thanks to the European neurologists who support us, led by Anna Rita Bentivoglio, we collect medicines in Europe and ship them to Maracaibo, where they are distributed by a local NGO called Primeros Auxilios. We also support local patient associations and local geneticist Lennie Pineda, who aims to survey the populations of Barranquitas and San Luis, to identify those at risk for HD, and to establish counselling and educational programmes for them. Eventually, we hope to establish an exchange programme under which young, local healthcare professionals study in European clinical centres, and then bring back their expertise to improve HD care in their communities. Plans are also afoot to build a community centre in Barranquitas for the care of late-stage and abandoned patients.

Earning the trust of a community that has long been ostracised is not easy, which is why Factor-H Vice President Roger Cachope, Gianni Munizza from Italy and I took toys and supplies to Lake Maracaibo last Christmas, and why we helped organise the visit of some Latin American HD families to the Vatican to meet Pope Francis in May 2017. We aim to restore these families' dignity to them, and to fight for the futures of children like Brayan. Please help us if you can.

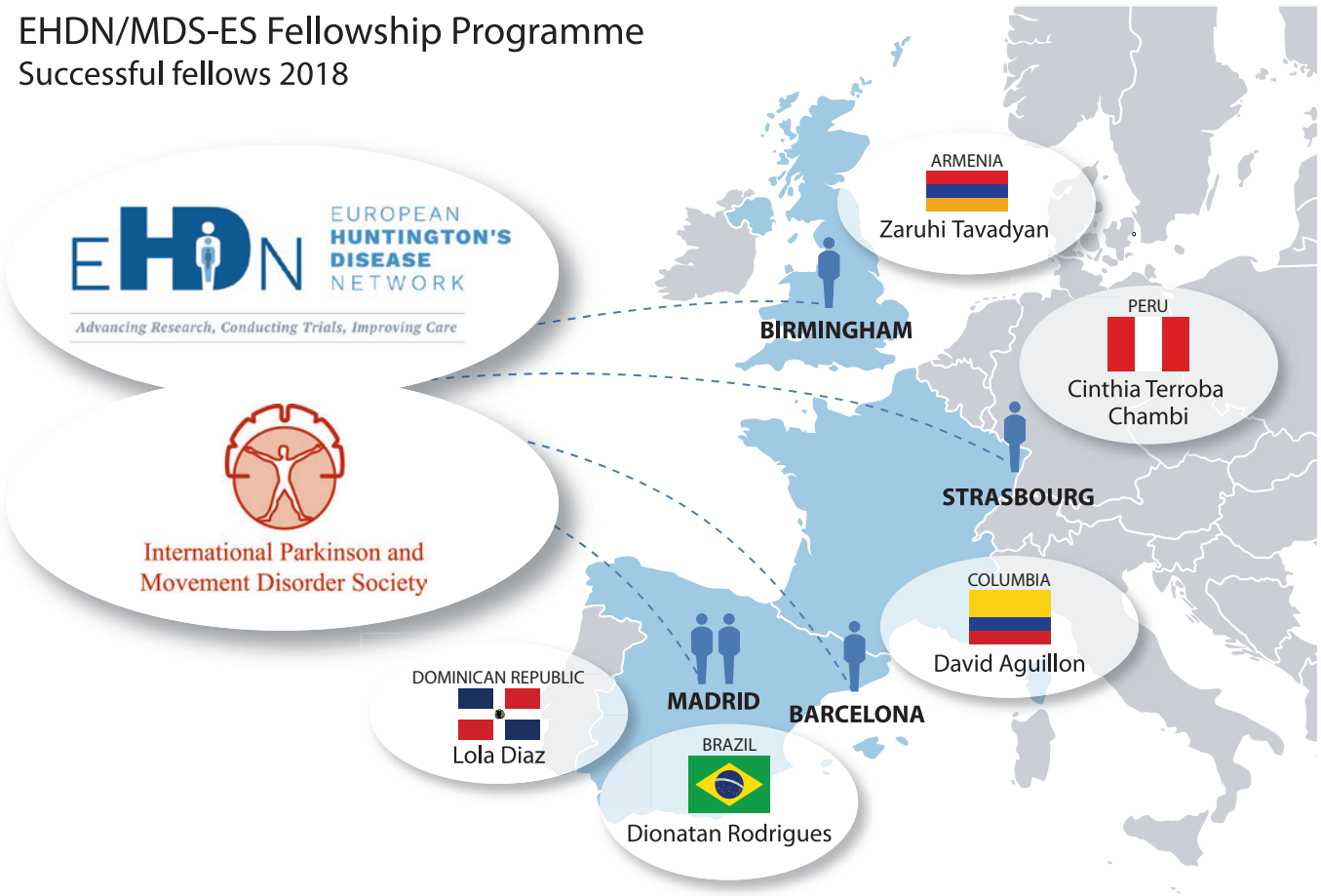
For more information about Factor-H or to make a donation please visit www.factor-h.org. A film about the HD families' visit to the Vatican will premiere in Los Angeles on 27 July.

Funding news

Fionnuala Margreiter,
Grant & Collaborations Manager

- The 2019 Marie Skłodowska-Curie Actions call for individual fellowships is now open, with a deadline of 11 September 2019.
- Calls are open for individual grant applications to the European Research Council, with various deadlines.
- The next deadline for European Cooperation in Science & Technology (COST) Actions is 5 September 2019. COST funds research and innovation networks and COST Actions are bottom-up networks designed to do just that, growing ideas and careers across Europe and beyond over a four-year period. Those not yet familiar with COST might consider joining an existing Action first.
- The European Union's Joint Programme—Neurodegenerative Disease Research (JPND) has updated its research and innovation strategy . JPND usually launches one annual call each January.
- Horizon 2020 will hold an Open Info Day in Brussels on 3 July 2019, on the theme of health, demographic change and wellbeing. The Horizon 2020 Societal Challenge 1 work programme for 2020 (2020 Health calls) is expected to offer calls for proposals with an overall budget of about €650 million, and funding opportunities will be presented that day. The proceedings will be webstreamed. Information and a registration link are available here.
- EHDN will have a stand at the upcoming International Congress of Parkinson's Disease and Movement Disorders in Nice (see page 13, Dates for your diary). Drop by to find out more about our current activities.
- The EHDN/International Parkinson and Movement Disorder Society (MDS) fellowship programme received 14 applications in its 2019 round, of which seven were selected. More information about the programme can be found here. The map below illustrates the 2018 fellows and their destinations. The call for applications for the 2020 round is expected to be announced in the autumn.

EHDN/MDS-ES Fellowship Programme
Successful fellows 2018



Ana Cristina Rego

New seed fund awarded

EHDN has approved seed funding for a project proposed by Ana Cristina Rego, of the University of Coimbra in Portugal, to investigate the role of a post-synaptic scaffolding protein at excitatory synapses called SAP90/PSD95-associated protein 3 (SAPAP3). SAPAP3 is of interest because it is highly expressed in the striatum, a brain area that is affected early on in HD, and modified SAPAP3 is known to be associated with obsessive-compulsive disorder—whose symptoms overlap with those of early HD. The role of SAPAP3 in HD has never been properly explored, however. Rego and her colleagues plan to monitor changes in SAPAP3 in striatal versus cortical postsynaptic density. They will also investigate how SAPAP3 affects glutamatergic dendrites, and related mitochondrial function and dynamics. For this purpose they will use animal and cell models of HD, and postmortem HD brain samples.

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.

Postcard from Palm Springs

The scientific presentations from the 14th Annual HD Therapeutics Conference held from 25 to 28 February in Palm Springs, California are available to view online. A "Postcard from Palm Springs" video, that outlines some of the major themes of the conference for HD families, is also available. If you would like to embed this video on your own website, please contact: info@chdifoundation.org

EHDN congratulates Lauren Byrne

Lauren Byrne

Congratulations to HD researcher and family member Lauren Byrne of University College London, who has been awarded a Huntington's Disease Society of America Berman-Topper Family HD Career Development Fellowship for 2019. She will use the funding—USD80,000 a year for three years—to continue her PhD work on neurofilament light protein as a biomarker of neuronal injury in HD, investigating it in well-described cohorts such as PREDICT-HD and TRACK-ON. Her aim is to better understand the natural fluctuations of the marker across the full lifespan of HD gene expansion carriers, with a view to designing more efficient clinical trials and improving disease monitoring. Byrne features in a short video about HD and her research, produced in collaboration with pharmaceutical company Roche.

All photos kindly provided by Jenny Callaghan

Inside the machine:

Interview with Jenny Callaghan

Jenny Callaghan is EHDN's training and compliance manager, but behind that title she has a number of roles within the organisation and the Enroll-HD global observational study. Here she tells us who she is and what she does.

Tell us a bit about your life before EHDN.

I come from Leeds in Yorkshire, in the UK, and I have a degree in psychology. Initially I worked as a healthcare assistant on a neurosurgical ward, looking after patients, and while I found that very fulfilling, I struggled with the shiftwork. I also realised I needed to do something more intellectually challenging. In 2008 I got a job in Manchester, working with David Craufurd's group on HD.

What did the job involve?

Coordinating the TRACK-HD project in Manchester. In particular I was rescoring interviews for the short version of the problem behaviours assessment (PBA-s) for HD, to make sure raters were conducting it correctly. Through that I became involved with the EHDN's behavioural working group. I quickly became very familiar with the PBA-s, because I was watching four or five hours of interviews a week and conducting assessments myself in David's clinic. There was a need for other people to be trained on the PBA-s, and the working group was also acutely aware that there was no certification scheme for behavioural assessment, as there was for motor assessment—even though behavioural symptoms are often more distressing for patients and families. There still isn't, by the way, though we've moved a long way towards it—for example in terms of the standardisation of training materials, a project that I eventually took over on the working group's behalf.

How did you standardise training materials?

In Manchester we filmed our PBA-s interviews to create a library of examples, but since those were obviously in English, there was a lot of discussion in the working group about how to standardise the examples across language areas. The solution we came up with was to use a single set of training videos, but to translate the transcripts into the other European languages.

What was your next role within the network?

I agreed to cover for a member of the UK language area coordinator (LanCo) team during her maternity leave, and that experience opened my eyes. Having worked inside the Manchester "bubble" for a little over three years, I was now helping to manage 30 sites across the UK. I saw that, while all the sites were running the Registry study in broadly the same way, there was also some variability in how they applied the protocols. I found that fascinating—that view of how research could be done and how it was actually done. I also realised the importance of EHDN's network function.

> *"LanCos are in many ways the glue that holds EHDN together."*

I felt that a really important part of my job was to connect people—a doctor or research assistant who was

new to the network to an experienced member in the same language area, for example. By helping newcomers understand HD better, we could make sure that they conducted Registry better, and ultimately deliver better care to their patients.

With respect to Registry, and later its successor Enroll-HD, was the ultimate goal once again to standardise procedures?

Yes, and the way to do that was through monitoring. I became involved in monitoring as a LanCo, first for Registry and then for Enroll-HD. After five years of monitoring our UK sites, I was looking for a new challenge again, and in 2018 I joined Ruth Fullam, Selene Capodarca and others on the Enroll-HD project management team. Now I'm leading that team's effort to improve and standardise monitoring procedures for Enroll-HD, which can sometimes be a bit like herding cats.

How so?

Enroll-HD is a big global study. Every country has its own regulations and requirements, and most of the time monitors are making decisions alone, so naturally enough they develop their own ways of doing things. Getting them to adapt so that overall monitoring procedures converge towards a standard can be a challenge, but I'm also aware of the need to listen to monitors. Only by listening will we learn if someone has hit on a better way of doing things, and so improve as a group.

What is your role now, as EHDN's training and compliance manager?

With Katrin Barth I try to come up with ways of making monitoring procedures more efficient. This is vital now that Enroll-HD has over 20,000 participants and data are flooding in. I help the Enroll-HD project management team roll out those improvements globally, and I also train new monitors. As a member of the project management team I'm involved in all strategic and operational activities for Enroll-HD, and I also manage provision of PBA-s training for EHDN and the behavioural working group, of which I remain a member.

It sounds like a lot of work. What keeps you going?

Seeing progress. You really do with Enroll-HD: in six years we've become one of the biggest global registries. Also, feeling part of a strong team in the EHDN. That's true even though we're spread out geographically. I'm based in Cardiff now, and I connect with colleagues mainly via conference calls. Of course, the excitement over the gene therapy trials has given us all a sense of new possibilities in the last few years.

Dates for your diary

Save the dates for:

- The 5th Animal Models of Neurodegenerative Diseases, Liblice, Czech Republic, 15-17 September 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
- WCN 2019 – 24th World Congress of Neurology, Dubai, United Arab Emirates, 27-31 October 2019
- Huntington's Disease Youth Organization's 1st International Young Adults Conference, Glasgow, UK, 9-11 May 2020

Liblice, Czech Republic

Photo: Wikipedia

- EHDN2020 Plenary Meeting, Bologna, Italy, 10-12 September 2020 (NB: the meeting will be held over Thursday to Saturday, not Friday to Sunday as in the past). Details to follow.