



More than 500 participants from 16 European countries came to Lisbon.

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(AM) = Article of the Month

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EHDN
2008
Lisboa

EHDN 5th PLENARY MEETING

By Diana Raffelsbauer, PharmaWrite, Giebelstadt (Germany)

EHDN 2008 Meeting

The 5th Plenary Meeting of the European Huntington's Disease Network (EHDN) was held in conjunction with the 12th Bi-annual Meeting of the European Huntington Association (EHA) in Lisbon (Portugal) on September 5-6, 2008. More than 500 participants from 16 European countries and elsewhere attending the meeting were welcomed by the Organising Committee, represented by the Chair of the EHDN, **Bernhard Landwehrmeyer** (Ulm, Germany), **Joaquim Ferreira** (Lisbon, Portugal) and **Beatrice De Schepper** (Moerbeke-Waas, Belgium). You may download the Proceedings of the Meeting at <http://www.euro-hd.net/html/ehdn2008>.

"Huntington's disease (HD) is an orphan disease", said **Joaquim Ferreira**. "It is our mission to change this perception and to redirect public attention to HD. The EHDN sets an excellent example of how this change can be brought about. Our goal is to find effective treatments for Huntington's disease and improve the quality of life of affected families." **Emilia Nunes** (Lisbon, Portugal), representing the Portuguese Health Minister Ana Jorge, told the audience that Huntington's disease has been included in the National Programme for Rare Diseases in Portugal. As the EHA president, **Beatrice De Schepper** highlighted the close collaboration between EHDN and HD families through different international and national HD lay associations. **Allan Tobin** from the CHDI Foundation (New York, USA) said that "this is the largest gathering of people who are interested specifically in Huntington's disease in the history of this field." As noted by **Bernhard Landwehrmeyer** in his welcome speech, "this is a sign of success for the Network." >>

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Hot Topics

It has become customary to begin the EHDN plenary meeting with a 'hot topics' discussion session. The first hot topic was devoted to Huntington's disease pathology outside of the brain. **Gillian Bates** (London, UK) and **Maria Björkqvist** (Lund, Sweden) led a lively discussion of peripheral symptoms in HD, their possible cause and whether peripheral markers could be used to track disease progression. They were followed by **Jan Kaszubek** (Ulm, Germany) and **Edward Wild** (London, UK), who presented modern imaging techniques being used to track disease progression in HD, highlighting their pros and cons. **Anne Rosser** (Cardiff, UK) and **Stephen Dunnett** (Cardiff, UK) gave an overview of cell replacement therapy as a means of replacing neurones that are lost in HD. There is a pressing need for a renewable source of stem cells suitable for transplantation. Finally, in a soul-stirring speech, **Katharine Moser** (New York, USA) told us the story of HD in her life. This young woman, who works as an occupational therapist caring for HD patients in a nursing home in Manhattan, carries the HD gene. In 2005, at the age of 23, she underwent predictive genetic testing. She is committed to raising awareness of HD and helping people to cope better with the disease. Her story raised many questions regarding predictive testing of a terminal disease without a cure, particularly the challenges of living 'at risk' and the pros and cons of testing at such a young age.

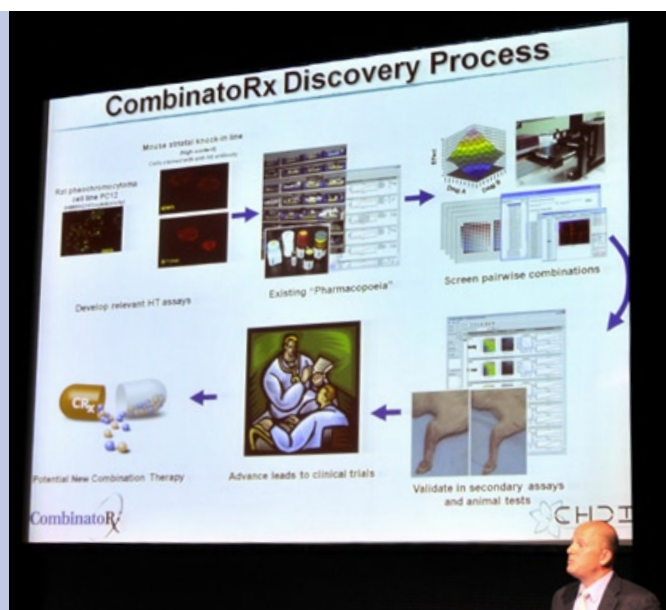
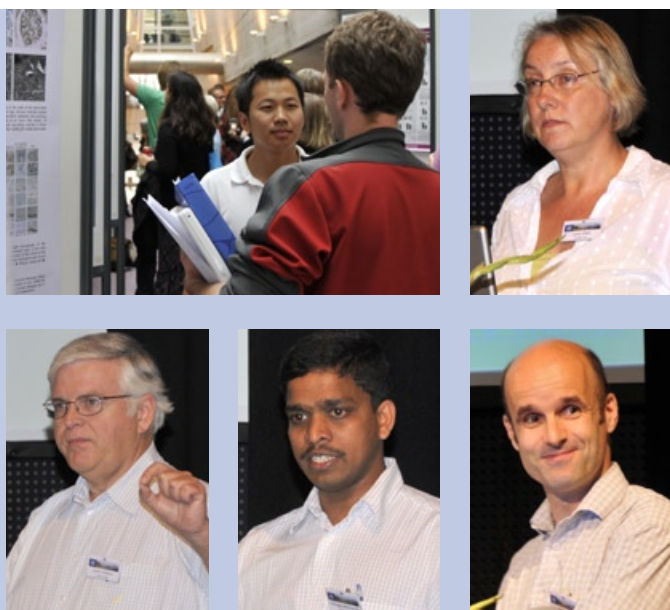
Working Group Summaries

Plenary session II was devoted to the **EHDN Working Groups**. There are now 18 working groups. New working groups are: 1) Biological Modifiers and Neuropre-

vention, 2) Functional Ability, 3) Genetic Testing and Counselling, and 4) Physiotherapy. The EHDN encourages its members to participate in a working group and actively contribute to HD research. To this end, the [EHDN Working Group Website](#) has been recently updated and improved. Furthermore, the EHDN Newsletters feature two working groups per issue on pages 5 and 6.

Keynote presentation I

Paul Muchowski (San Francisco, USA) presented his results on putative molecular mechanisms to reduce huntingtin (Htt) neurotoxicity. The polyglutamine repeats in mutant Htt may act as zippers to promote protein aggregation into amyloid-like fibrils and oligomers. These assemblies seem to exert different toxic effects on neurones. One aim is to design antibody-based aggregation inhibitors able to neutralise mutant Htt without affecting the normal Htt protein. Muchowski showed that the chaperone Hsp70 can modulate Htt aggregation by suppressing the formation of toxic oligomers and promoting the formation of fibrils, and that Hsp70 plays a critical role in protecting against mutant Htt toxicity *in vivo*. Starting from a genetic screen in yeast cells, Muchowski has studied the role of the kynurenine 3-monooxygenase (KMO) gene in HD. KMO is a mitochondrial enzyme which is expressed in microglia and produces CNS-toxic substances. JM6, a KMO inhibitor developed by Muchowski and his father Joseph, increases the survival of R6/2 mice in a dose-dependent manner, decreases the level of KMO's toxic products, reduces immunoreactivity of microglia, and increases the levels of proteins used as markers for synapses and neuronal activity. This work has revealed KMO as a therapeutic target for HD. >>



Poster Viewing

The first day of the meeting ended with a poster viewing session. More than 100 posters relating to different fields of HD basic and clinical research were presented. The abstracts were published in the *Journal of Neurology, Neurosurgery and Psychiatry*, October 2008, Vol. 79, Supplement 1. The poster award winners were **Ahmad Aziz** (Leiden, The Netherlands, for poster C.30 on weight loss in HD), **Nicola Fearnley/Flaviano Giorgini** (Leicester, UK, for poster A.10 on identification of microglia-specific suppressors of mutant Htt toxicity), and **LaVonne Goodman** (Lake Forest, USA, for poster F.10 on a survey of clinical trial participation and literacy in Huntington support groups).

Endorsed Projects and Scientific Presentations

The second day of the meeting focused on research projects endorsed by the EHDN and on scientific presentations. On behalf of the EHDN Scientific and Bioethics Advisory Committee (SBAC), **Anne Rosser** (Cardiff, UK) provided the audience with an overview of the submission and review process of research projects (see EHDN Newsletter Issue of September 2008). **Lesley Jones** (Cardiff, UK) presented a genome-wide association study searching for genetic modifiers of HD using biological and clinical data collected through REGISTRY (see page 5), to be performed in collaboration with **James Gusella** (Boston, USA), who described this approach further. **Vinayagam Arunachalam** (Berlin, Germany) from Erich Wanker's lab reported on his search for HD modifiers using systems biology approaches. An interactive case vignette discussion session on management of HD was led by **Michael Orth** (Ulm, Germany). Further topics

selected from the abstracts for presentation included: pathogenic mechanisms, experimental therapeutics, genetic aspects/testing, clinical care/management, and clinical characteristics/biomarkers.

Keynote presentation II

Robert Pacifici (Los Angeles, USA) gave an overview of the Huntington's disease therapeutics programme developed by the CHDI Foundation (New York/Los Angeles, USA). Through collaboration with hundreds of academic and industrial scientists worldwide, CHDI supports a broad portfolio of research aimed at the rapid discovery and development of disease-modifying treatments for HD. Pacifici described various projects, underlining the diversity of their nature. They include the targeting of a number of key enzymes, as well as the reduction of huntingtin RNA and protein levels (antisense oligonucleotide and RNA interference) and trophic factor agonism. Strategies include high-throughput screening, fragment screening, searching for existing ligands and rational structure-based drug design. CHDI has added several steps to optimise the drug development process, which begins with a compound of interest and ends with an HD rodent model for testing drug efficacy. Appropriate *in vitro* and *in vivo* systems need to be developed to test candidate drugs. Specific reagents and tools are needed to prosecute particular targets in biochemical and cell-based assays. Likewise, *in vivo* systems need to be tailored specifically to each programme. Concluding, Pacifici emphasised the role of CHDI in collaborative enablement of HD research, by providing not only funding but also whatever other resources are needed for success in the drug discovery and development process.

EHDN 2008 Business Meeting

EHDN Activities

As the Chair of the EHDN Executive Committee (EC), **Bernhard Landwehrmeyer** (Ulm, Germany) reported the activities of the Network between September 2007 and September 2008. He began by thanking **Justo García de Yébenes** (Madrid, Spain), a key initiator of the EHDN Newsletters, for his contribution to the Network. García de Yébenes is rotating out of the EC and will be replaced by **Joaquim Ferreira** (Lisbon, Portugal).

In 2009, two further EC members will retire. Replacements representing Italy and the Eastern European countries are encouraged. Four SBAC members will also rotate out of office. EHDN members are invited to nominate candidates for these positions via the EHDN Website.

Please nominate candidates for office here:

<https://www.euro-hd.net/html/network/project/voting>

A member login to the EHDN web portal is required.

If you do not have a login, please contact

support@euro-hd.net

EHDN Constitution

The EC had proposed changes to the EHDN Constitution (see article by **Robi Blumenstein** in the EHDN Newsletter Issue of June 2008). These amendments were summarised at the Meeting by **Raymund Roos** (Leiden, The Netherlands) and approved by the vast majority of the membership.

EHDN Membership

The EHDN membership had increased to 694 regular members and 74 associated members by September 2008. The EHDN currently operates in more than 120 study sites in 16 European countries, and an expansion into Russia is planned for 2009. Over the past year, the Network has organised a large number of national and regional meetings, thus providing a platform for communication without language barriers. These meetings also allow fostering of country-specific networks and provide extended training sessions.

EHDN REGISTRY

Since September 2007, the number of subjects in REGISTRY has increased by 1,290 to 3,798 and the number of visits by 3,644 to 8,407. Biosamples were collected from 2,188 participants, an increase of about 1,000. **Landwehrmeyer** reminded the audience that data deposited with REGISTRY are available for

research purposes, and encouraged the membership to submit project proposals. The use of electronic case report forms in REGISTRY allows in-built plausibility checks based on the analysis of rating scores. On-site monitoring by EHDN Language Coordinators ensures the verification of source data. Questionnaires have been developed and improved to assess clinical data. The Network is currently working on a new version of REGISTRY (version 3) which aims to accelerate the development and validation of additional explorative assessment tools. These will include functional ability, behaviour, cognition, physiotherapy, lifestyle and quality of life in HD. The end product will be an extended suite of assessment options that can be applied to all forms of HD, including pre-manifest, late stage and juvenile HD.

EHDN Aims

As aims for 2009, **Landwehrmeyer** listed: 1) Dissemination of the activities of the EHDN Working Groups in the form of publications, 2) Implementation of REGISTRY 3, 3) The availability of the standard of care guidelines for all member countries via the web portal, 4) New web-based services for HD families and the general public, and 5) Easier navigation of the EHDN Website.


WCHD 2009

World Congress on
Huntington's Disease **HD 2009** VANCOUVER
CANADA



The World Congress on Huntington's Disease will take place in Vancouver (Canada) from 12th to 15th of September. Registration will be open from January 2009. Please register here for the WCHD 2009:

<http://www.worldcongress-hd.net>



As the host, **Michael Hayden** (Vancouver, Canada) outlined the focus and programme of the Congress.

There will be no EHDN Plenary Meeting in 2009.

Motor Phenotype Working Group

By Raymund A.C. Roos, Leiden University Medical Centre, Leiden (The Netherlands) and Ralf Reilmann, University of Münster, Münster (Germany)

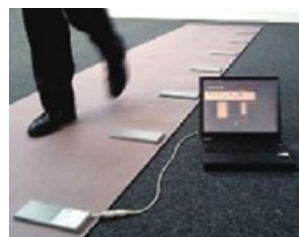
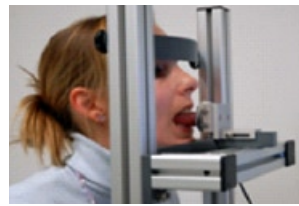
The assessment of motor symptoms is critically important for the diagnosis and follow-up of Huntington's disease (HD). During the last two decades, the Unified Huntington's Disease Rating Scale (UHDRS) has been used for this purpose. However, this assessment scale has several drawbacks. There can be large differences in the scores given by different observers, and both floor and ceiling effects prevent assessment of disease progression, particularly in the advanced stages. The Motor Phenotype Working Group is actively pursuing eight aims to improve the quality of motor assessment in general, many aspects of which have been carried out in collaboration with the Huntington Study Group (HSG, USA).

Videos for training clinicians have been shot in Ulm, Bochum, Manchester, Munich, Münster, Taufkirchen, Cardiff and Leiden, primarily organised by Ralf Reilmann, with Polaris Pictures (Budapest, Hungary) and funded by the CHDI Foundation. A **training video** (Aim 1) and a **video library** (Aim 2) have already been generated and will be available for health professionals soon. The videos have also been used to develop an **annual online certification programme of motor 'raters'** (Aim 3) to improve inter-rater variability and provide a standard for quality control within EHDN. More than 100 raters were certified in 2008, including all those participating in the European ACR-16 trial. From January 2009, all clinicians entering data into the motor portion of UHDRS (UHDRS-M) in REGISTRY must be certified. Please go to <https://www.euro-hd.net/html/certification> where patient's videos can be downloaded or viewed online.

A shortened version of the UHDRS-M was published in 1997 (Raymund Roos et al.), but the scale needs further revision because certain items contribute disproportionately to the total score. Aim 4 is to **apply scientific criteria to adjust the motor portion of the UHDRS**. For this purpose, the CHDI Foundation will fund the analysis of blinded follow-up video assessments of expert rater performance for each of the sub-items of the UHDRS.

Aim 5 is to **identify and validate objective measures of change in motor behaviour**. To address this, four motor assessments are currently being trialed in TRACK-HD (<https://www.track-hd.net/>) in 120 HD patients, 120

pre-manifest gene carriers and 120 control subjects. The four tests are (a) tongue force, (b) grip force, (c) tapping and (d) walking (see figure). The first cross-sectional analysis of these data will be conducted before the end of 2008. Posturography (the measurement of posture and balance) is also a potential objective measure of motor behaviour change. The sensitivity of different gait and posture assessment devices is currently being tested in a cross-sectional study by Heike Beckmann and Ralf Reilmann (Münster, Germany), with the support of EHDN.



New tests of motor function currently being trialed in TRACK-HD:

- (a) Tongue force
- (b) Grip force
- (c) Tapping
- (d) Walking

new techniques and works to develop, test and validate them (Aim 8). These efforts will lead to a series of improved tests of motor function for use in clinical trials of treatments for HD both within EHDN and elsewhere.

Changes in eye movements are frequently reported to be the first manifestation of alterations in motor activity. To explore this further (Aim 6), Stephen Hicks (Oxford, UK) is using a **simple device to monitor eye movements and saccades**. This test is also being assessed through the TRACK-HD protocol.

Aim 7 is to **define the endpoints for physiotherapy interventions** in collaboration with physiotherapists. A systematic trial of physiotherapy interventions supported by EHDN has been set up by Camilla Ekwall and Leif Wiklund (Uppsala, Sweden) and Stefan Bohlen and Ralf Reilmann (Münster, Germany). The first patients have been recruited and first results are expected in 2009.

The practical application of a test is an important issue for the assessment of motor activity, and the assessments must be very simple, reliable and quick. Therefore the Motor Phenotype Working Group **actively searches for**

Genetic Modifiers Working Group

By Lesley Jones, Cardiff University,
Cardiff (United Kingdom)

What are genetic modifiers for HD?

The symptoms of Huntington's disease (HD) are not only variable, but also occur at different ages in different people. We know that having more CAG repeats in the HD gene results in earlier onset of the disease, so CAG repeat length is a genetic modifier of the onset of HD. However, not all of the variation in age of onset can be attributed to the length of the CAG repeat; other factors are involved. This tells us two important things. Firstly, that knowing the length of someone's CAG repeat does not allow accurate prediction of the age at which that person will develop HD. Secondly, other factors must influence the age at which HD symptoms first appear. Among these factors is variation in genes other than the HD gene.

The majority of genes occur in multiple variants, and each of these variants behaves slightly differently in the body. For example, having a particular set of gene variants can predispose people to common diseases, such as heart disease or diabetes. Similarly, there is evidence that multiple genes may influence the age at which people develop HD. Gene variants can act to slow down the onset of disease (a protective effect) or speed it up (a promoting effect).

Why are genetic modifiers useful?

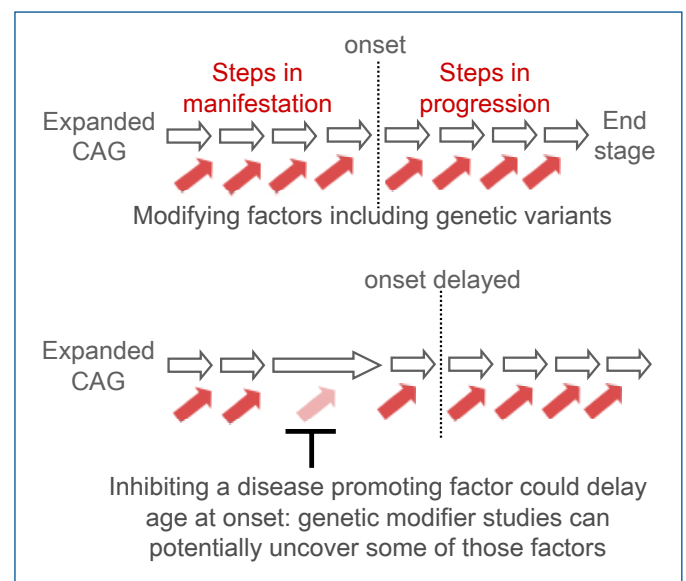
Any gene which contains variations that either slow down or speed up the onset of HD must lie in a biological pathway or network that is important for the disease process. Such pathways are targets for therapies that aim to augment protective pathways and inhibit toxic ones. Looking for genetic modifiers in people (rather than animals) is vital, as it tells us directly about the human disease.

How do we find genetic modifiers?

Recent developments in genetic technology have made it possible to look simultaneously at a million DNA variants throughout the human genome, which enables the analysis of DNA variants in many thousands of people. This approach, called 'genome-wide association' (GWA), has recently revealed new genes involved in many common diseases, such as diabetes. Such findings are illuminating the biology of these diseases, and we wish to harness this potential for HD.

What is the Genetic Modifiers Working Group doing?

The Genetic Modifiers Working Group aims to facilitate genetic studies in HD. Our first priority has been to promote the collection of DNA and appropriate data from HD patients. To carry out GWA to find genes that affect onset, symptoms or progression of HD, we need to analyse DNA from people carrying the HD gene. The first analyses will be done from HD gene carriers who have clinical information in REGISTRY. The CHDI Foundation will fund this work and intends to produce GWA data on the first 1800 DNA samples from REGISTRY over the next year. The Genetic Modifiers Working Group will receive the data for analysis and will make it available via the EHDN so that it can be requested by others who wish to study specific aspects of the disease, either now or later, as the longitudinal clinical data in REGISTRY become richer. We aim to foster links with groups carrying out similar studies in the USA, Europe and elsewhere, as combining these data to yield larger sample numbers will confirm any findings and potentially find more genes. These data will remain a rich resource for research into HD for years to come.

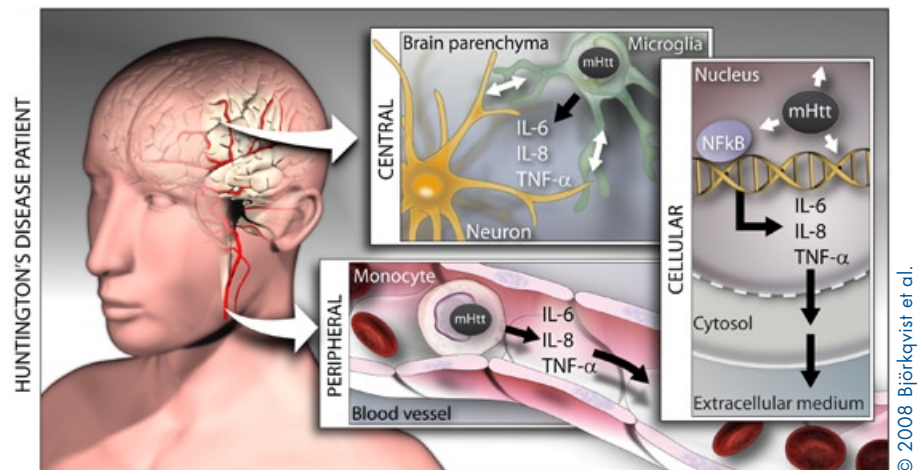


Schematic of the steps in the onset and progression of HD

It is likely that multiple steps are involved in the events that occur in the brain before onset of HD. Each step is likely to involve the actions of multiple genes, and different variants of those genes might alter the way the step occurs, slowing down or speeding up onset. Similarly, the same or other variants in specific genes could alter the symptoms and progression of the disease once it has begun.

A novel pathogenic pathway of immune activation detectable before clinical onset in Huntington's disease

Maria Björkqvist, Edward Wild et al.,
Journal of Experimental Medicine
(2008), 205: 1869-77



The mutant HD protein causes immune cells to become hyperactive in the brain and the blood.

Summary

This study reveals that levels of cytokines (key immune system molecules) are increased in HD patients' blood, even many years before disease onset. The mutant HD protein, acting in immune cells in the blood and brain and causing them to become hyperactive, is directly responsible for the increased cytokine levels. This could mean that cells supposed to protect neurons end up harming them instead. These findings suggest possible treatment approaches and open a new window from the blood into the disease's effects in the brain.

Background

This research group previously looked for blood proteins whose levels were altered in HD and found a signature of immune activation. Recent work by others has suggested a possible role for microglia in the pathology of HD. This study examined the immune system in detail and looked for links between immune changes and HD pathogenesis.

Study design

Plasma samples from 194 controls and HD gene carriers at various disease stages, including premanifest subjects, were tested with multiplex ELISA to determine the levels of several different cytokines. Targeted expression profiling was also used to detect activation of inflammatory genes in the HD brain. A series of stimulation experiments was carried out on inflammatory cells from the blood (monocytes and macrophages) and the brain (microglia).

Results

Inflammatory activation in HD plasma and brain.

Increased production of several inflammatory cytokines was detected, which correlated with disease progres-

sion. The most prominent changes were seen in IL-6, IL-8 and TNF-alpha. Strikingly, IL-6 was significantly increased in the premanifest patients, who were very far — 16 years on average — from predicted disease onset. Levels of IL-8 and TNF-alpha correlated with clinical disease rating. Different combinations of cytokines could be used to distinguish between specific subject groups, like controls and HD gene carriers. Similar changes in the profiles of cytokines were seen in plasma from three different HD mouse models. Expression profiling found increased activation of IL-6, IL-8 and TNF-alpha genes in the striatum from HD patient brains, indicating that similar cytokine production also occurs in the HD brain.

The mutant HD protein makes brain and blood inflammatory cells hyperactive. Monocytes from premanifest HD gene carriers produced significantly more IL-6 than control cells when stimulated with the bacterial molecule LPS. This was repeated in macrophages from mouse models carrying either the mutant or normal versions of the HD protein. Only those cells carrying the mutant protein were hyperactive, suggesting that this is a direct effect of the mutant protein in the immune cell. The microglia from an alternative HD mouse model were also hyperactive, suggesting that this effect of the mutant HD protein occurs in the immune cells of both the brain and the periphery.

Possible implications. The authors suggest that immune activation is a key feature of HD, which occurs in the brain and peripherally, and may contribute to neurodegeneration. This raises the possibility of being able to track disease markers in the blood and for developing immune treatments for HD.



In Europe, less than 20% of the at-risk population undergoes predictive testing.

Long-term outcome of presymptomatic testing in Huntington disease

Marcela Gargiulo, Séverine Lejeune et al., *European Journal of Human Genetics* (2008), Epub ahead of print

This study compared the psychological well-being and social adjustment of HD mutation carriers versus non-carriers after predictive genetic testing. It was aimed at identifying determinants to improve support for tested persons. The long-term assessment revealed depression as a frequent symptom in both carriers (58%) and non-carriers (24%). Interestingly, 27% of the non-carriers did not cope well with a favourable result. These findings underscore the need of psychological support following genetic testing, regardless of the test result.

Background

The HD gene with an expanded CAG repeat provides an exact trait marker and enables reliable determination of the genetic status of a person at risk of Huntington's Disease (HD). However, predictive testing cannot ascertain when the disease will begin, how rapidly it will progress, and which symptoms a person will develop. In Europe, less than 20% of the at-risk population undergoes predictive testing. Guidelines for the molecular genetics predictive test in Huntington's disease were developed by the International Huntington Association and the World Federation of Neurology-Research Group on Huntington's disease, and published in 1994. Genetic counselling by a multidisciplinary team, both before and after blood sampling and testing, is mandatory.

Methods

119 persons who had undergone pre-symptomatic genetic testing at the Salpêtrière University Hospital (Paris, France) were interviewed. Of these, 18 showed signs of

HD and were excluded from the study. Thus, the study population consisted of 101 subjects: 62 non-carriers and 39 asymptomatic carriers. The study variables and instruments included depression (Beck Depression Inventory and Mini International Neuropsychiatric Inventory), hopelessness (Beck Hopelessness Scale), anxiety (State and Trait Anxiety Inventory of Spielberger), subjective distress (Impact of Event Scale) and subjective adaptation in work, family, social life, etc (Social Adjustment Scale). Information concerning previous episodes of depression was also collected.

Results

Asymptomatic carriers and non-carriers yielded similar results in the anxiety and social adjustment tests. By contrast, current depression was significantly more frequent in carriers than in non-carriers (58% versus 24%, $P = 0.05$). Before genetic testing, the frequency of depressive episodes was similar in both groups. However after testing, the rate increased in carriers from 42% to 49%, whereas in non-carriers it decreased from 45% to 31%. Nevertheless, the number of suicide attempts was higher in the non-carrier group. Notably, only 15% of the non-carriers were being treated for depression, significantly fewer than the percentage of carriers (36%, $P = 0.01$). It was also noteworthy that more than a quarter of the non-carriers reported difficulty coping despite the favourable results. Previous depressive episodes were identified as the only predictive factor for the occurrence of depression after the test.

Predictive testing of a fatal disease for which there is no cure involves complex psychological and ethical issues, requiring appropriate genetic counselling and support by experienced professionals. The recently established [EHDN Genetic Testing and Counselling Working Group](#) focuses on methods for delivery of genetic test results and improvement of the existing guidelines (see EHDN Newsletter Issue of September 2008).



Psychological support is needed following genetic testing, regardless of the test result.

Disease-specific induced pluripotent stem cells

In-Hyun Park et al., *Cell* (2008), 134: 877-86

This article describes the generation of induced pluripotent stem cells derived from somatic cells of patients with a variety of genetic diseases, including Huntington's disease. The resulting disease-specific stem cells may recapitulate pathogenesis *in vitro* and provide new methods for disease investigation and drug screening.

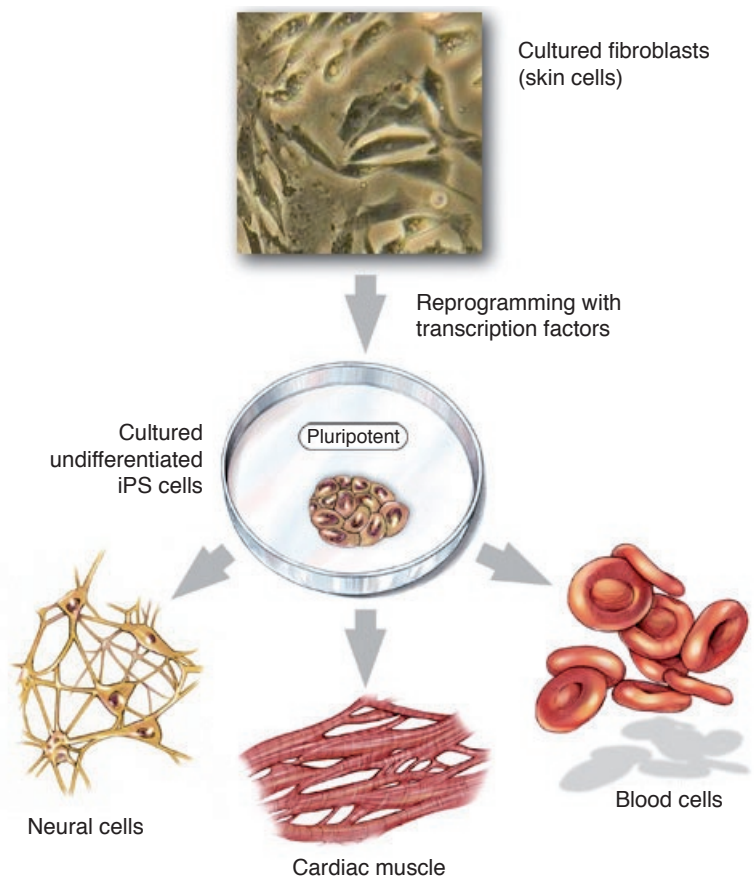
Background

Cell culture models are essential research tools for understanding Huntington's disease (HD) at the molecular and cellular level, and provide platforms for high-throughput drug screening. However, primary human cell lines have a limited lifespan in culture. Most human cell culture models in use are derived from malignant tissues or have been immortalised and carry genetic or epigenetic artefacts. Pluripotent stem (PS) cells are able to renew themselves through cell division and differentiate into all derivatives of the three germ layers. In other words, they can develop into each of the more than 200 cell types of the adult body, and hence give rise to all tissues and organs. PS cells that carry the HD mutation would therefore hold great potential for HD research and drug discovery.

The main source of PS cells is embryonic stem (ES) cells. Mouse ES cells are used extensively for gene manipulation to generate mouse models of disease. Human ES cell lines have also been derived with preimplantation genetic diagnosis (PGD) providing a source of single blastomeres by embryo biopsy for the generation of human ES cell lines carrying the HD mutation. However, the source of these embryos is inevitably limited and the technology challenging.

Results

In 2007, two research groups showed that PS cells could be generated from adult human skin cells. These are known as induced pluripotent stem (iPS) cells. The 'reprogramming' of differentiated somatic cells into an embryonic-like stem cell state was achieved through the ectopic expression of four specific transcription factors (e.g. Oct-4, SOX2, KLF4 and c-Myc). Park et al. have applied this technology to generate iPS cell lines for ten diseases, including HD. They show that the iPS cell lines



Generation of iPS cells and their differentiation into various cell types.

express ES cell markers, and that each can be differentiated into the three embryonic germ layers: endoderm, mesoderm and ectoderm. Therefore, this reprogramming of somatic cells has generated pluripotent stem cell lines that are immortal in culture and can be differentiated into any of a variety of human cell types, e.g. neurones, without using embryos.

Potential of iPS cell technology

In addition to creating cell models of HD, iPS cell technology has the potential to generate patient-specific PS cells that could be grown in cell culture and transformed into specialised cells for use in regenerative medicine without the risk of rejection. However, the current methodology which requires infecting somatic cells with multiple viral vectors precludes their use in transplantation medicine on the grounds of safety. The establishment of alternative reprogramming methods that use chemicals in the absence of the ectopic expression of transcription factors is currently the focus of intense research, and is likely to by-pass some of these hurdles in the near future.

Upcoming Meetings 2009

Jan 17-22	International Conference on Unstable Microsatellites & Human Disease, Guanacaste, Costa Rica http://www.microsatellites.ca/about.html	Jun 7-11	13 th Movement Disorder Society (MDS), Paris, France International Congress of PD and Movement Disorders http://www.movementdisorders.org/congress/congress09/
Feb 15-17	2 nd Asian and Oceanian Parkinson's Disease and Movement Disorders Congress, New Delhi, India http://www.aopmcindia.com/	Jun 20-24	19 th European Neurological Society (ENS), Milan, Italy http://www.akm.ch/ens2009/
Feb 17-22	Neurodegenerative Diseases: New Molecular Mechanisms, Keystone, CO, USA http://www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=1003	Jun 22-26	Spanish Society of Neurology (SEN) and Association of British Neurologists (ABN), Liverpool, UK http://www.theabn.org/meetings/annual-meeting.php
Feb 26-28	Old and New Dopamine Agonists in Parkinson's Disease: a Reappraisal, Pisa, Italy http://www.parkinsonpisa.it/	Jul 11-16	Alzheimer's Association International Conference on Alzheimer's Disease, Vienna, Austria http://www.alz.org/icad/overview.asp
Mar 07-11	40 th Annual Meeting of the American Society for Neurochemistry, Charleston, SC, USA http://asneurochem.org/2009meeting/ASN2009.htm	Aug 27-30	1 st International Congress on Clinical Neuroepidemiology, Munich, Germany http://www.neuro2009.com/
Mar 09-13	Neurological Restoration 2009, Havana, Cuba http://www.ciren.cu/rn2009.pdf	Aug 31-Sep 2	British Society for Human Genetics Conference, University of Warwick, UK www.bshg.org.uk/2009BSHG.htm
Mar 11-15	9 th International Conference on Alzheimer's and Parkinson's Diseases: Advances, Concepts and New Challenges, Prague, Czech Republic http://www.kenes.com/adpd/	Sep 12-15	World Congress on Huntington's Disease, Vancouver, BC, Canada http://www.worldcongress-hd.net
Mar 25	Annual Neuroscience Day 2009, University of Edinburgh, UK	Sep 12-15	13 th European Federation of Neurological Societies (EFNS) Congress, Florence, Italy http://efns2009.efns.org/
Mar 26-28	24 th Conference of Alzheimer's Disease International, Singapore http://www.adi2009.org/	Sep 12-16	22 nd European College of Neuropsychopharmacology (ECNP), Istanbul, Turkey http://www.ecnp.eu/emc.asp?pagelid=1196
Apr 2-4	2 nd International Conference on Psychogenic Movement Disorders and Other Conversion Disorders, Washington, DC, USA http://www.movementdisorders.org/education/pmd/	Sep 23-26	82 nd Congress of the German Society for Neurology (DGN), Nuremberg, Germany http://www.akmcongress.com/dgn2009/
Apr 25-May 2	2009 Annual Meeting of the American Academy of Neurology, Seattle, WA, USA http://www.aan.com/go/am	Oct 17-21	Neuroscience 2009 - 39 th Annual Meeting of the Society for Neuroscience, Chicago, IL, USA http://www.sfn.org/index.cfm?pagename=annualMeeting
Apr 27-30	4 th Annual CHDI Huntington's Disease Therapeutics Conference, Cannes, France http://www.chdifoundation.org	Oct 20-24	American Society of Human Genetics (ASHG), Honolulu, HI, USA http://www.ashg.org/2009meeting/
May 31-Jun 5	Gordon Research Conference on CAG Triplet Repeat Disorders, Waterville Valley, NH, USA http://www.grc.org/programs.aspx?year=2009&program=cag	Oct 24-30	19 th World Congress on Neurology, Bangkok, Thailand http://www.wcn2009bangkok.com/
Jun 5-7	HDSA 24 th Annual Convention, Phoenix, AZ, USA http://www.hdsa.org/index/convention.html	Dec 13-16	XVII World Federation of Neurology Congress on Parkinson's Disease and Related Disorders, Miami Beach, FL, USA http://www2.kenes.com/parkinson/Pages/Home.aspx