

Neurobiology Commission

2021 Annual Report

2017 – 2021 Members

Aristea Galanopoulou (USA), chair
Marco de Curtis (Italy, past chair)
Terence O'Brien (Australia)
Kathryn Davis (USA)
Marcio Moraes (Brazil)
Ed Bertram (USA), Management Committee liaison

Purpose

To promote neurobiology research in epilepsy through advocacy, education, training, proposals of optimal methodologies and infrastructure improvements.

Activities

We have had zoom conferences with the members of the Neurobiology Commission and the chairs of its Task Forces (Task Force) regularly to discuss matters pertaining the Neurobiology Commission areas of interest. Among the activities that were discussed during this cycle, the following were worth highlighting:

Proposals and organization of IEC congress sessions with neurobiology research focus. The Neurobiology Commission was invited to organize additional parallel sessions in the virtual 2021 IEC congress increasing the visibility of basic science / translational research sessions in the congress. These included:

- Neurobiology Symposium on “**Neurobiology of SARS-CoV-2 / COVID-19 and relevance to epilepsy**”: Chair: Aristea Galanopoulou; Speakers: Eric Song, Marianna Bugiani, Nicola Marchi, Victor Ferastraoaru.
- “**Kindling Epileptogenesis**”: Chairs Aristea Galanopoulou, David Henshall; Speakers: Jennifer Gelinas, Liset Memendez de la Prida, Esther Krook-Magnuson, Melissa Barker-Haliski, Stephanie Schorge, Sanjay Sisodiya; Honorees: Jerome (Pete) Engel, Gyorgyi Buzsakim Claude Wasterlain, Solomon (Nico) Moshé, Giuliano Avanzini, Astrid Nehlig, Annamaria Vezzani.
- Parallel Session on “**Epigenetics and epilepsy collide: unravelling mechanisms, treatments and diagnostics**”, Chairs: Erwin van Vliet, David Henshall; Speakers: Albert Becker, Karen Conboy, Erwin van Vliet, Michael Johnson.

- Parallel Session on “**Gene therapy for pharmaco-resistant epilepsy – principles, opportunities, and pitfalls**”, Chairs: Simona Balestrini, Premysl Jiruska; Speakers: Merab Kokaia, Stephanie Schorge, Renzo Guerrini.
- Parallel Session on “**Refractory early-life seizures: taking evidence-based insights from basic science into the hands of clinicians**”, Chairs: Shilpa Kadam, Ronit Pressler; Speakers: Wolfgang Loscher, Geraldine Boylan, James Clement.
- Interactive session proposed by the ILAE/AES Joint Translational Task Force on “**Towards an understanding of drug resistance in epilepsy**”. Chairs: Heidrun Potschka, Solomon (Nico) Moshé; Faculty: Ed Bertram, Luisa Rocha, Aristeia Galanopoulou, Matthew Walker, Stephane Auvin.

Bursaries for young investigators. We opened a call for applications for bursaries to support young investigators interested in attending conferences or centers to provide them with specific training. Due to the COVID-19 travel restrictions, the response to our call was limited (4 applicants) and after discussion the Neurobiology Commission decided to defer awarding bursaries and re-open the call in the fall.

Harinarayan Young Neuroscientist Awards 2021. The Neurobiology Commission awards two prizes to the best basic science presentations of young investigators at the IEC congresses. These awards are supported by the Harinarayan donations to Neurobiology Commission / WONOEP Task Force that have been made possible through the efforts of Dr Raman Sankar. In 2021, the prizes were awarded to two talented investigators.

Dr Hyunyong Koh (Boston Childrens Hospital, Boston, MA, USA) and **Dr Gabriele Lignani** (UCL Queen Square Institute of Neurology, London, UK).

Dr Hyunyong Koh’s research was on “Non-cell autonomous hyperexcitability underlies focal epileptogenesis mediated by low-level brain somatic mutations in MTOR”.

Dr Lignani’s research was on “Activity-dependent gene therapy for intractable epilepsy”.

Continuity Plans

During the transfer of leadership to the newly appointed chair of the Neurobiology Commission, the importance of maintaining the presence of neurobiology research in the congresses, advocating for neurobiology research, the continuity of activities that reward and support young investigators like the bursaries and the Harinarayan awards were discussed. In addition, as discussed in the following sections, specific activities organized by the Task Forces of the Neurobiology Commission may benefit from carrying forward to the next cycle.

WONOEP Task Force

2017 – 2021 Members

Terence O’Brien (Australia), co-chair

Aristeia Galanopoulou (USA), co-chair

Members: Marco de Curtis (Italy, past chair)
Ozlem Akman (Turkey)
Marcia Moraes (Brazil)

Tomonori Ono (Japan)
Raman Sankar (USA)

Aim: Organize the WONOEP meetings prior to the IECs.

The WONOEP Task Force originally discussed the theme for a WONOEP meeting prior to the Paris IEC 2021 and had invited Drs Stephanie Baulac and Stephane Auvin as local co-organizers for this meeting with a main topic of “**Early onset epilepsies: neurobiology and novel therapeutic strategies**”. Due to COVID-19 and the need to transform the IEC into a virtual congress format, the decision was made to postpone the WONOEP till 2022, planning for a pre-EEC WONOEP with the same topic and organizers, and with the support of the new Neurobiology Commission chair.

We selected the Tufts European Center at Talloires, France as the locale of the meeting, due to its vicinity to the congress and experience with such meetings. The call for abstracts was very successful, yielding 64 submissions of which we have selected ~60% for inclusion in the program. The meeting will take place between July 4-8, 2022. We have been fortunate with the support of the congress and ILAE staff in negotiating with the resorts. We are also grateful for the efforts of Dr Raman Sankar in fundraising from donors (\$20,000 donated by the Harinarayan family) and pharma (in progress) to support this meeting as well as for the support of the ILAE in co-sponsoring this meeting.

Continuity plans: The planning and organization of the WONOEP 2022 is being made in collaboration with the current Neurobiology Commission leadership, which will provide a transition plan for the organization of the next WONOEP in 2023. This Neurobiology Commission-supported meeting is highly regarded among neurobiologists and it would be important to continue efforts to support it in the future.

ILAE/AES Joint Translational Task Force

2017 – 2021 Members

AES co-chairs: Aristeia Galanopoulou and Greg Worrell

AES nominees: Richard Staba, Anne Anderson, Manisha Patel, Kevin Kelly

ILAE co-chairs: Terence O’Brien (Australia) and Matthew Walker (UK)

ILAE nominees: Gunther Sperk (Austria), Rudiger Koehling (Germany), Heidrun Potschka (Germany), Steven Petrou (Australia)

Liaison to MC: Ed Bertram (USA)

Project manager: Seonaid Anderson (Belgium)

Activities: Multiple zoom conferences of the main Task Force as well as of the working groups (WGs) have been conducted.

The TASK1-WGs have continued their work towards the creation of an online atlas of rodent EEGs, a system for the interpretation of the rodent EEGs and classification of seizures and

epilepsy models in rodents. There have been significant disruptions aggravated by the COVID-19 impact globally, however there are a number of reports and products that will be coming out:

- Proposal for a nomenclature for the electrode placement used in rodent EEG studies, that compares with the human nomenclature.
- A version of the online Rodent EEG Atlas has been worked by Peter Shen with the guidance of Drs Timofeev, Akman, and Galanopoulou.
- A report on a proposal to rethink the definition of drug resistance in epilepsy in a manner that addresses both clinical and preclinical research needs is being prepared by a TASK1-WG: Drs Galanopoulou, Potschka, Walker, Moshé, Rocha, Auvin, Walker, Bertram.
- A report on whether in vitro studies may aid in the development and use of antiseizure therapies is being finalized by TASK1-WG3, led by Mark Cunningham.
- Interactive session proposed by the ILAE/AES Joint Translational Task Force on “**Towards an understanding of drug resistance in epilepsy**”. Chairs: Heidrun Potschka, Solomon (Nico) Moshé; Faculty: Ed Bertram, Luisa Rocha, Aristeia Galanopoulou, Matthew Walker, Stephane Auvin.

TASK3-WGs have been working towards finalizing the reports – companion papers on additional preclinical common data elements (CDEs) and case report forms (CRFs) for general pharmacology studies, pediatric and genetic models, rigor in preclinical epilepsy research, phenotyping seizure models, omics, imaging, pathology. These will be included in a special issue of *Epilepsia Open*. Five of these have been completed and accepted for publication, one is under revision, one has been submitted for approval by the ILAE/AES leadership and two more are being finalized. These manuscripts are as follows:

- “A companion to the preclinical common data elements and case report forms for neuropathology studies in epilepsy research. A report of the TASK3 Neuropathology Working Group of the ILAE/AES Joint Translational Task Force” by Eleonora Aronica, Devin K. Binder, Meinrad Drexel, Chrysanthy Ikonomidou, Shilpa D. Kadam, Guenther Sperk, Christian Steinhäuser. – ACCEPTED
- “A companion to the preclinical common data elements for rodent genetic epilepsy models. A Report of the TASK3-WG1B: Pediatric and Genetic models Working Group of the ILAE/AES Joint Translational Task Force.” By Massimo Mantegazza, Stéphane Auvin, Melissa Barker-Haliski, Anna-Maria Katsarou, Hana Kubova, Aristeia S. Galanopoulou, Bridgette Semple and Christopher A. Reid – ACCEPTED
- “A companion to the preclinical common data elements for rodent models of pediatric acquired epilepsy: A report of the TASK3-WG1B, Pediatric and Genetic Models Working Group of the ILAE/AES Joint Translational Task Force” by Anna-Maria Katsarou, Hana Kubova, Stéphane Auvin, Massimo Mantegazza, Melissa Barker-Haliski, Aristeia S. Galanopoulou, Christopher A. Reid and Bridgette D. Semple. – ACCEPTED
- “A companion to the preclinical common data elements and case report forms for *in vivo* rodent Neuroimaging. A report of the TASK3 Neuroimaging Working Group of the ILAE/AES Joint Translational Task Force” by Erwin A. van Vliet, Riikka Immonen, Ofer Prager, Alon Friedman, Jens P. Bankstahl, David K. Wright, Terence J. O’Brien, Heidrun Potschka, Olli Gröhn, Neil G. Harris – ACCEPTED

- “A companion to the preclinical common data elements for genomics, transcriptomics and epigenomics data in rodent epilepsy models. A Report of the TASK3 Omics Working Group of the ILAE/AES Joint Translational Task Force.” By Erwin A. van Vliet, Michael S. Hildebrand, James D. Mills, Gary P. Brennan, Tore Eid, Susan A. Masino, Vicky Whittemore, Laura Bindila, Kevin K. Wang, Manisha Patel, Piero Perucca, Christopher A. Reid. - ACCEPTED
- “A companion to the preclinical common data elements for phenotyping seizures and epilepsy in rodent models. A Report of the TASK3-WG1C: Phenotyping Working Group of the ILAE/AES Joint Translational Task Force.” By Melissa Barker-Haliski, Julika Pitsch, Aristeia Galanopoulou, Rüdiger Köhling - UNDER REVISION
- Pharmacology CDEs companion paper, TASK1-WG1A led by Lisa Coles and Cameron Metcalfe – BEING FINALIZED
- Rigor CDEs companion paper, TASK1-WG1A led by Brian Klein – BEING FINALIZED

We are also grateful to Lauren Harte-Hargrove, member of the TASK3-WG1A who volunteered to finalize the CDE conversion of the CRFs for the above manuscripts.

In addition, in collaboration with Karen Crawford’s group at LONI (U Southern California) the first electronic CRFs have been created and will be made available to interested investigators. These address core, physiology and EEG CDEs that had been created by the TASK3 group in the previous cycle. This has been made possible with the support of ILAE, AES and CURE Epilepsy through the LONI data analysts group of Karen Crawford (University of Southern California). CURE Epilepsy has co-sponsored these efforts to create electronic modules of the CRFs.

Continuity plans: Largely due to the disruptions posed by COVID-19 upon the WG members, there have been significant delays in the activities of this Task Force. However, the involved members are determined to complete the above tasks which have been progressing. The existing budget of the Task Force will cover any expenses that will be needed.

Areas that have been discussed as worthy of future focused groups include the issue of:

- (a) drug resistance in epilepsies across the lifespan and the importance of setting definitions that would best serve both clinical practice / research and preclinical research
- (b) biomarkers of epilepsy and setting the infrastructure and strategies to enhance such research and discoveries.

Genetics / Epigenetics Task Force

2017 – 2021 Members

David Henshall (Ireland), chair
 Katsuhiko Yamakawa (Japan)
 Albert Becker (Germany)
 Chris Reid (Australia)

Alica Goldman (USA)
 Erwin van Vliet (Netherlands)
 Iscia Lopes-Cendes (Brazil)
 Annapurna Poduri (USA)

Michael Johnson (UK)
Hela Mrabet (Tunisia)

Katja Kobow (Germany)
Steven Petrou (Australia)

Aims: Discuss scientific and clinical research priorities of the Task Force and commission review(s) that would focus on promoting the Task Force, promote priority Genetics-Epigenetics topics at key epilepsy meetings, organize training, create infrastructure and promote industry-academia research interactions and developments, and collaborate with the ILAE/AES Joint Translational Task Force on CDEs in genetics-epigenetics.

Activities: During 2021, the Epigenetics-Genetics Task Force continued to meet and progress its original tasks. Meetings occurred during the year by Zoom call. COVID continued to strongly impact on members time and our ability to achieve plans for the year. In particular, the long-planned workshop on epigenetic techniques remained impossible due to campus restrictions at the planned site. Also, the curtailed travel and scientific meetings restricted the scope of members to promote the topic at meetings.

Task I Publications. During 2021, we completed writing our second major publication, focused on how mutations in genes with known epigenetic functions cause epilepsy. However, COVID significantly changed the contributions from Task Force members. Multiple members did not contribute to the article and we had to draft in support from colleagues. Most notably, the first author who drove much of the writing was not a Task Force member. As a result, we have not formerly submitted the work as a Task Force paper.

Under Task II, promoting the topic, Task Force members contributed to various symposia and provided speaker suggestions for various meetings. COVID again impacted activities with some of the 2021 events postponed (e.g. Gordon conference and 14th European Congress on Epileptology). These events will happen in 2022, albeit beyond the term of the Task Force. Nevertheless, key contributions included the Task Force's Workshop "Epigenetics and epilepsy collide: unravelling mechanisms, treatments and diagnostics" at the 34th International Epilepsy Congress (1 Sep 2021). The Chair represented the Task Force at the 2021 "Curing the epilepsies" workshop and contributed to the special workshop hosted by Prof Galanopoulou, "Kindling epileptogenesis: beginnings and future" at the 34th International Epilepsy Congress, (1 Sep 2021). The Chair also co-organized a SfN/FENS webinar to promote the topic ("Noncoding RNAs in nervous system function and disease", May 11th, 2021).

Members of the Task Force were part of the organizing committee for the Epilepsy Climate Change conference, held in November 2021. This was a unique event that brought together climate scientists with clinicians and basic epilepsy researchers as well as patients, industry and advocacy. Sessions focused on climate and health, ranging from water and air quality, disaster-driven healthcare needs, food quality and availability, the spread of infectious disease and resilience to higher temperature. A key focus was on how we can all take action individually as well as within our institutions at different time scales. Importantly, tackling climate change will create a healthier world. A session was dedicated to epilepsy, and how increasing global temperatures can impact patients and the complexity of how genetic variants influence

temperature sensitivity at an individual level where new predictive models are needed. Finally, taking action, how we can perform research in a more sustainable and climate-conscious manner. Under Task IV, activities on resources and infrastructure, two members of the Task Force finalized common data elements for preclinical research. This work is now in revision and includes a specific module for collecting “omics” data.

Continuity plans: The Genetics/Epigenetics Task Force completed its cycle in 2021.

Young Neurobiologists Task Force

2017 – 2021 Members

Premysl Jiruska (Czech), chair

Members: Joseph Raimondo (S. Africa)

Kathryn Davis (USA)

Nigel Jones (Australia)

Liankun Ren (China)

Vadym Gnatkovsky (Italy)

Shilpa Kadam (USA)

Nihan Carcak (Turkey)

Erwin van Vliet (Netherlands)

Christos Panagiotis Lisgaras

Aims: To evaluate the current environment for attracting, sustaining, and advancing talented young neurobiologists in epilepsy research across regions, cultures, and genders, as well as identify areas in need of improvement, challenges and possible solutions. To promote opportunities that will cultivate leadership qualities and identify future young leaders among young epilepsy neurobiologists. To collaborate with the other members of the Neurobiology Commission and its Task Forces so as best to integrate the expertise of this Task Force in the initiatives and goals of the Neurobiology Commission and its Task Forces.

Activities: In 2021, we mainly continued in our educative activities. In collaboration with 4EU+ University Alliance, we have prepared International Elective Course On the Pathogenesis of Epilepsy (<https://4euepilepsy.lf2.cuni.cz/>). The course organizers and faculty are members of the ILAE community and the Neurobiology Commission, Young Neurobiologists Task Force, Young Epilepsy Section, and the Next Generation Task Force. Several other ILAE members and recognized epilepsy research scientists also became faculty members or contributed to the course.

The course is supported by ILAE, ILAE Academy, IBE, YES, national ILAE branches, and other partners. The course is a 15-week lasting event that covers the main topics related to the pathogenesis and pathophysiology of epilepsy. The course is international and open to undergraduate, Ph.D. students, postdocs, and clinicians working in academia or industry. We have received 188 applications, and 40 applicants were selected for the first course round that started on the 24th of February 2022.

The course promotes a strong interaction between participants and between participants and tutors. Apart from the educative content, the course aims to advocate for epilepsy research, attract junior researchers interested in epilepsy research and strengthen the international epileptological community. Due to high demand, we aim to repeat the course annually. We aim

to expand the educative activities in the neurobiology of epilepsy beyond the course. We plan to elaborate foundations for the organization of the micro-credential course, a life-long educative activity composed of five different topics covering various aspects of the pathogenesis of epilepsy and experimental epilepsy research.

Continuity plans: Dr Jiruska has been selected to chair the research training and professional development Task Force of the Neurobiology Commission which will enable to advance and expand the aims of this Task Force.

Advocacy Task Force

2017 – 2021 Members

Raman Sankar (USA), co-chair	Akio Ikeda (Japan)
Solomon (Nico) L. Moshé (USA), co-chair	Janet Mifsud (Malta)
Terence O’Brien (Australia)	Kathryn Davis (USA)
Vicky Whittemore (USA)	Ed Bertram (USA), MC liaison

Aims: To evaluate the current funding environment for neurobiology research in epilepsy. To advocate for the value of neurobiology research in improving knowledge on epilepsy and translating basic science discoveries to better therapies. To advocate for initiatives that will improve research infrastructure and the initiatives of the Neurobiology Commission and its Task Forces, including research, educational and training initiatives. To advise the Neurobiology Commission and the Research Advocacy Task Force on matters related to advocating for neurobiology research.

Activities: Initial work has focused on giving the epilepsy patient and caregiver community access to translational neurobiology research. The Task Force initially decided to work with *Living Well with Epilepsy*, a blog run by Jessica Kennan Smith. Kate Davis has been leading this effort. The Task Force has now been in discussions on how to consistently develop content in lay language to bring new scientific findings to patients and the caregiver community. In 2019, the Task Force had submitted two blogs on the *Living Well with Epilepsy* website. The COVID-19 pandemic and lack of budgetary support halted these efforts as well as the plans to engage a medical writer to assist with the writing of scientific highlights for the general public.

Networks Task Force

2017 – 2021 Members

Christophe Bernard (France), chair	Joao Pereira Leite (Brazil)
Serge Vulliemoz (Switzerland)	Ivan Soltesz (USA)
Liset Menendez de la Prida (Spain)	Patrick Forcelli (USA)
John Terry (UK)	Greg Worrell (USA)
Alon Friedman (Canada / Israel)	Ed Bertram (USA), MC liaison
Chou-ching Lin (Taiwan)	

Aims: To evaluate the current infrastructure, strategies, and advances in knowledge on understanding epilepsies as network disease(s) so as to best integrate them in efforts to accelerate and optimize research towards understanding the neurobiology of epilepsies and comorbidities and the development of better therapies. To collaborate with the other members of the Neurobiology Commission and its Task Forces so as best to integrate the expertise of this Task Force in the initiatives and goals of the Neurobiology Commission and its Task Forces.

Activities: No activities reported in 2021.

Highlights

- The Neurobiology Commission, the Genetics / Epigenetics Task Force, the Young Neurobiologists Task Force, and the ILAE/AES Joint Translational Task Force organized 6 sessions with neurobiology theme at the 2021 International Epilepsy Congress.
- The ILAE/AEs Joint Translational Task Force has published several reports for a special issue on preclinical common data elements in *Epilepsia Open*.
- The Young Neurobiologists Task Force, in collaboration with 4EU+ University Alliance, has prepared an International Elective Course On the Pathogenesis of Epilepsy (<https://4euepilepsy.lf2.cuni.cz/>).
- The Genetics / Epigenetics Task Force has organized several scientific sessions in collaboration with SfN/FENS, Epilepsy Climate Change conference, Gordon conference, and IEC/EEC conference organizers.
- The WONOEP Task Force has been organizing the XVII WONOEP that will be held in Talloires, France on “Early onset epilepsies: neurobiology and novel therapeutic strategies” (7/4-7/2022).

Submitted by Aristeia Galanopoulou MD PhD

Neurobiology Commission

2021 Annual Report

2021 – 2025 Members

David C Henshall (Ireland), chair
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Kathryn Davis (USA)
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Terence O’Brien (Australia)
Nico Moshé (USA), special advisor
Raman Sankar (USA), special advisor
Marco de Curtis (EUR) special advisor
Ed Bertram (USA), MC liaison

Purpose

To promote neurobiology research in epilepsy through advocacy, education, training, proposals of optimal methodologies and infrastructure improvements.

Activities

We held our first meeting, by video-conference with the members of the Neurobiology Commission and the chairs of its Task Forces (Task Force). This focused on matters pertaining the Neurobiology Commission areas of interest. Among the activities that were discussed, the following were worth highlighting:

Re-organisation of the Neurobiology Commission committee. At the start of the new cycle we re-structured the Neurobiology Commission to re-focus on key priorities. As a result, the new cycle Neurobiology Commission commission activities fall into the following structure:

- 1. Research & Innovation**, to include the topical Task Forces, and led by Kathryn Davis.
- 2. Research training & professional development**, to include educational activities, led by Premysl Jiruska including the training program on epileptogenesis.
- 3. WONOEP committee**, led by the Chairs Aristea Galanopoulou and Terence O’Brien.
- 4. Advocacy & Dissemination**, which replaces the original “Advocacy Task Force” and includes a greater focus on the external visibility of the Neurobiology Commission.

The Advocacy Task Force was discontinued and the Young Neurobiologists Task Force was discontinued.

Topic-specific Task Forces. The Epigenetics/Genetics Task Force ended its term. The Networks Task Force would begin a new term and two new Topic-specific Task Forces would be launched in early 2022.

Selection and awarding of workshop and travel bursaries. We reviewed and approved two applications for support from the Neurobiology Commission workshop and conference program. This included a neurobiology-focused meeting based at Shiraz University in Iran (\$2000) and the Gordon Research Conference “Mechanisms of epilepsy and neuronal synchronisation” (\$10,000). Both are to be held in 2022. The Neurobiology Commission also reviewed 7 applications for travel bursaries, recommending one for support.

WONOEP Task Force

Meetings were held to support the planning and organization of the WONOEP XVI 2022 progressed with the site selected and the call for Abstracts being launched. The date will be July 4 – 8th 2022 and the venue is Talloires, France. The meeting is entitled “Early onset epilepsies: neurobiology and novel therapeutic strategies”. The overall purpose of WONOEP XVI will be to provide novel insights on early onset epilepsies, underlying neurobiology and strategies towards the development of new treatments. The meeting will have an estimated 40 participants.

ILAE/AES Joint Translational Task Force

Discussions were held during meetings and outside, around the completion of the existing tasks of the Joint Translational Task Force and the focus of any future Task Force. The decision is to retain the leadership of those groups where activities can be concluded in 2022. The focus and composition of any new Joint Translational Task Force will be discussed in 2022 and decisions made based on the focus and the role of the AES.

Highlights

- Awarding of workshop/conference and travel bursaries
- Organizing the XVI WONOEP meeting, held in Talloires, France on “Early onset epilepsies: neurobiology and novel therapeutic strategies”
- Supporting the International Elective Course On the Pathogenesis of Epilepsy (<https://4euepilepsy.lf2.cuni.cz/>).
- Re-design of the Neurobiology Commission to create a revised structure on priority areas for the new cycle

Submitted by David C Henshall PhD