# Keynote Speakers:

## First International GENCODYS Conference

## "Integrative Networks in Intellectual Disabilities"

**Hans van Bokhoven** is head of the research unit Molecular Neurogenetics at the Radboud University Nijmegen Medical Centre. He investigates the genetic and epigenetic networks that are disrupted in intellectual disabilities, using a multi-level strategy that combines neurogenetics, functional genomics and molecular & cellular neurobiological approaches. Recent key publication: **Genetic and Epigenetic Networks in Intellectual Disabilities.** *Annu Rev Genet.* 2011; 45:81-104

Title presentation: **Genetic & Epigenetic Pathways of Disease**

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**Han G. Brunner** is full professor and head of the department of Human Genetics at Nijmegen University Hospital. He has initiated and conducted several research projects that use clinical genetic observations as the starting point for human molecular genetic investigations into such topics as intellectual disability, human behaviour, skeletal development, brain development, neuromuscular disease, congenital malformations, and gonadal development and function. Recent key publication: **De novo mutations in human genetic disease.** *Nat Rev Genet.* 2012; 13(8):565-75

Title presentation: **Is intellectual disability mainly a de novo problem?**

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**Jamel Chelly**, MD, PhD, Professor at Paris Descartes Medical School -Paris Descartes University. Jamel Chelly is a founding member of the European XLMR Consortium that has been instrumental in the remarkable recent progress in the field of X-linked mental retardation and neuronal migration disorders. Current research programs aim to better define and understand disrupted molecular, cellular and neurobiological processes underlying cognitive deficits, neuronal migration defects and malformations of cortical development. Recent key publication: **Mutations in the beta-tubulin gene TUBB2B result in asymmetrical polymicrogyria.** *Nat Genet.* 2009; 41(6):746-52

Title presentation: **Centrosome- and MT-related proteins: the extent of their contributions in the pathogenesis of ID and epilepsy with malformations of cortical development**

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**Mara Dierssen** leads the Neurobehavioral Phenotyping of Mouse Models of Disease research group at the Center for Genomic Regulation in Barcelona. The work of Dierssen has helped to understand the neural plasticity deficits in Down syndrome and establish therapeutic trial. She has demonstrated mechanisms involved in intellectual disability through modifying the activity of brain regions responsible for learning and memory. Dierssen's group has developed novel methods, and experimental and computational tools in behaviour. Her work establishes a novel paradigm to study the behaviour and cognition in model organisms. The work of Mara Dierssen has received numerous awards and recognitions, including the Sisley-Lejeune Award. Dierssen has a very intense activity in the neuroscience community. She teaches neuroscience at the Pompeu Fabra University Master's Course in Biomedicine, and chaired in 2012 the most important neuroscience forum in Europe in 2012 (FENS Forum). She has been president of the International Behavioral, Neural Genetics Society, she is president elect of the Spanish Neuroscience Society and member of the Executive Committee of the Federation of European Neuroscience Societies. Recent key publication: **Cognitive deficits and associated neurological complications in individuals with Down's syndrome.** *Lancet Neurol.* 2010; 9(6):623-33

Title presentation: **The future of cognitive therapy: can we reset the brain with intellectual disability?**

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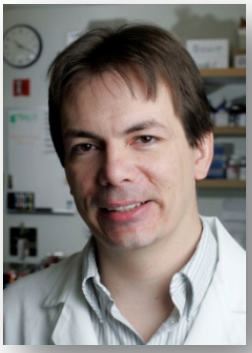

**Evan Eichler,** Ph.D., is a Professor and Howard Hughes Medical Institute Investigator in the Department of Genome Sciences, University of Washington School of Medicine. He graduated with a B.Sc. Honours degree in Biology from the University of Saskatchewan, Canada, in 1990. He received his Ph.D. in 1995 from the Department of Molecular and Human Genetics at Baylor College of Medicine, Houston. After a Hollaender postdoctoral fellowship at Lawrence Livermore National Laboratory, he joined the faculty of Case Western Reserve University in 1997 and later the University of Washington in 2004. He was a March of Dimes Basil O'Connor Scholar (1998-2001), appointed as an HHMI Investigator (2005), awarded an AAAS Fellowship (2006) and the American Society of Human Genetics Curt Stern Award (2008), and elected to the National Academy of Sciences (2012). He is an editor of *Genome Research* and has served on various scientific advisory boards for both NIH and NSF. His research group provided the first genome-wide view of segmental duplications within human and other primate genomes and he is a leader in an effort to identify and sequence normal and disease-causing structural variation in the human genome. The long-term goal of his research is to understand the evolution and mechanisms of recent gene duplication and its relationship to copy number variation and human disease. Recent key publication: **Sporadic autism exomes reveal a highly interconnected protein network of de novo mutations. *Nature*** 2012; 485(7397):246-50

Title presentation: **Neurocognitive Disease and Autism: New Mutations, Genes and Genetic Models**

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**Ype Elgersma,** Prof. Dr. Scientific director *ENCORE* expertise center of developmental disorders, Dept. of Neuroscience, Erasmus MC University Medical Center, Rotterdam, The Netherlands. Genetic disorders present us with the unique knowledge of knowing the causal gene and study the impact of the genetic mutation in mouse models of disease. Because of these mouse models, insight in the molecular and cellular basis of the neurological deficits associated with childhood developmental disorders gains rapid progress. In order to be successful in finding a treatment that can ameliorate the neurological deficits, several hurdles must be taken. First, the mouse model must be a good for the disease, and capture its most distinguishing features. Second, the molecular and cellular mechanism that is underlying the disorder must be identified. It must be ensured that the identified mechanism is directly underlying the pathology, and not the result of a homeostatic compensation mechanism. Third, a suitable drug must be found that targets the identified pathological mechanism, and

demonstrates reversibility of the affected processes. The fourth and ultimate step is of course to test the toxicity and efficacy of the potential drug in a clinical trial. In this presentation, I will describe basal and clinical research performed at the Dutch *ENCORE* center for neurodevelopmental disorders. Specifically, I will present novel insights in the pathophysiology underlying Neurofibromatosis (NF1) and Tuberous Sclerosis Complex (TSC). I will also discuss how these new findings can be translated to clinical trials. Our work is supported by grants from NWO-ZonMW, the Dutch brain foundation (HsN), the ASF, NINA foundation, ORSA and AFSA patient organizations for Angelman syndrome, and by the Children's Tumor Foundation. Recent key publication: **Treatment of neurodevelopmental disorders in adulthood.** *J. Neurosci.* 2012; 32(41):14074-9

Title presentation: **Molecular mechanisms underlying TSC and NF1: from genes to trials**

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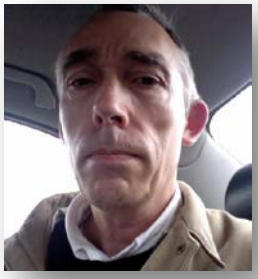

**Jonathan Flint** is a psychiatrist working at the Wellcome Trust Centre for Human Genetics, where he investigates the genetic basis of behavour. He pioneered the use of outbred mice as a way to identify the molecular basis of complex traits. Outbred mouse populations, derived from fully sequenced progenitors, provide a resource for identifying the genes and sequence variants that contribute to complex phenotypes, including cognition. He is currently running a large project based in China to identify the causes of major depression. Recent key publication: **Sequence-based characterization of structural variation in the mouse genome.** *Nature* 2011; 477(7364):326-9

Title presentation: **Genetic dissection of behavioural variation using outbred mice**

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**Seth Grant** has degrees in physiology, medicine and surgery from the University of Sydney and postdoctoral training at Cold Spring Harbor Laboratory with Douglas Hanahan and later with Eric Kandel at Columbia University. He is currently Professor of Molecular Neuroscience at Edinburgh University and Visiting Professor at Cambridge University and Melbourne University. From 2003-11 he was Principal Investigator at the Wellcome Trust Sanger Institute. He is an elected Fellow of the Royal Society of Edinburgh. Recent Key publication: **Synaptopathies: diseases of the synaptome.** *Curr Opin Neurobiol.* 2012; 22(3):522-9

Title presentation: **Genetic dissection of cognition in mice and humans**

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**Yann Herault** is the Director of the Mouse Clinical Institute (MCI-ICS, Illkirch), and the leader of a research group at the IGBMC (Illkirch). He has a strong interest on gene dosage effect and copy number variation in intellectual disabilities such as in Down Syndrome. He is using the mouse as a model organism to better understand the pathophysiology of intellectual disabilities and to propose new therapeutic approaches. Recent Key publication: **Mouse large-scale phenotyping initiatives: overview of the European Mouse Disease Clinic (EUMODIC) and of the Wellcome Trust Sanger Institute Mouse Genetics Project.** *Mamm Genome*. 2012; 23(9-10):600-10

Title presentation: **Mining mouse models to open up new paths for treating Intellectual disabilities**

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**Yann Humeau** is heading a team of neurophysiologists entitled "synapse in cognition" (SynIQ), being part of the interdisciplinary institute for neuroscience (IINS) in Bordeaux, France. Cognitive disorders (CD) mouse models are analyzed using in vivo and in vitro approaches with the aim of understanding the neuronal and synaptic correlates of learning deficits associated with mutations of CD genes. Recent key publication: **Functional roles of synapsin: lessons from invertebrates.** *Semin Cell Dev Biol.* 2011; 22(4):425-33

Title presentation: Pathophysiology of cognitive disorders: **Lessons from multi-scale experimental studies in CD mouse models.**

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**Cor Oosterwijk** is a medical biologist with experience in the field of both molecular and clinical research. Since 2001, he is working as a patient advocate. He is the director of Dutch Genetic Patient Alliance VSOP (director; www.vsop.nl) ) and secretary general of the European Patients' Network for Medical Research and Health EGAN ( www.egan.eu , www.biomedinvo4all.com ). He coordinated the FP7 project PatientPartner project concerning stakeholder relationships in clinical research (www.patientpartner-europe.eu). Reference: **Paediatric Clinical research: The Patients' Perspective**. Kent, A, Oosterwijk, C and Poortman, Y, in: Guide to paediatric drug development and clinical research. Eds: Rose & van den Anker, Karger AG, Basel, 2010

Title presentation: **Patient involvement in genetic and clinical research: practical and ethical challenges.**

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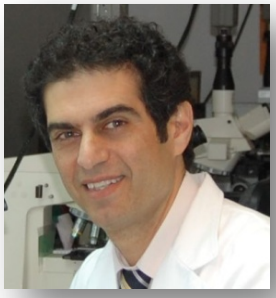

**Philippos C. Patsalis** is the Chief Executive Medical Director of the Cyprus Institute of Neurology & Genetics and Professor and Director of the Cyprus School of Molecular Medicine. He investigates the genetic cause and mechanisms of genetic diseases and syndromes associated with intellectual disability. Furthermore his research is focused on non-invasive prenatal diagnosis of genetic disorders. Recent key publication: **Fetal-specific DNA methylation ratio permits noninvasive prenatal diagnosis of trisomy 21.** *Nat. Med.* 2011; 17(4):510-3

Title presentation: **Non-Invasive Prenatal Diagnosis of Genetic Disorders**

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**Chris Ponting** is Deputy Director of the MRC Functional Genomics Unit and Professor of Genomics at the University of Oxford, UK. His group undertakes biomedical and evolutionary research using genomics data and methods. He recently led a project that provided an online atlas of transcription for cortical cell layers in adult male mice, and is interested in identifying the evolutionary heritage of different brain regions among diverse avian and mammalian species. His group's evolutionary studies on noncoding RNAs provided the justification required for many that these contribute greatly to biological complexity. Recent key publication: **Evolution and functions of long noncoding RNAs.** *Cell* 2009; 136(4):629-41

Title presentation: **Evolution of brain regions and brain-expressed noncoding RNAs in amniotes**

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**Hans-Hilger Ropers**, MD and Professor of Human Genetics, is currently Director at the Max Planck Institute for Molecular Genetics in Berlin. From 1984-1997 he headed the Department of Human Genetics at the University of Nijmegen, The Netherlands.

Hilger Ropers has a long-standing interest in monogenic disorders with a focus on X-linked and autosomal recessive ID. Recent key publication: **Deep sequencing reveals 50 novel genes for recessive cognitive disorders.** *Nature* 2011; 478:57-63

Title presentation: **Intellectual disability: Genetic dissection of a common disorder.**

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**Guy Rouleau** is Director of the Research Centre of the CHU Sainte-Justine, Director of the Laboratory of Molecular Biology of the CHU Sainte-Justine, Tenured professor in the Department of Medicine at Université de Montréal, Chairholder of the Canada Research Chair in Genetics of the Nervous System, Chairholder of the Jeanne-et-J.-Louis-Lévesque Chair in Genetics of Brain Diseases, Director of the Centre for excellence in neuroscience of Université de Montréal, Director of the Réseau de Médecine Génétique Appliquée – FRSQ

Over the last 20 years, Dr. Guy Rouleau and his team have focused on identifying the genes causing several neurological and psychiatric diseases, including autism, amyotrophic lateral sclerosis, hereditary neuropathies, epilepsy and schizophrenia, as well as providing a better understanding of the molecular mechanisms that lead to these disease symptoms. Among Dr. Rouleau's main achievements are his contribution to the identification of over 20 disease-causing genes and his discovery of new mutational mechanisms. Dr. Rouleau has published over 500 articles in peer-reviewed journals and has been quoted more than 20 000 times. He has supervised nearly a hundred students at the Masters, PhD and Post-doctoral levels in addition to receiving numerous awards for his contribution to science and society. Recent key publication: **Mutations in DCC cause congenital mirror movements.** *Science* 2010; 328(5978):592

Title presentation: **Neurodevelopmental disorders: Common Mechanisms**

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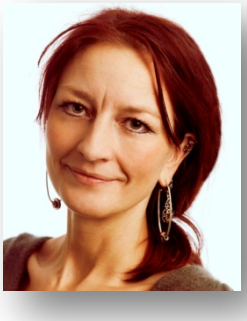

**Annette Schenck** is heading the Drosophila models of brain disorders group at Nijmegen's Human Genetics Department at the Radboud University Medical Centre. Apart from numerous past studies into mechanisms and molecular networks in Intellectual Disability, her group conducts the first large-scale approaches to Intellectual Disability Disorders to systematically map the modular landscape of cognitive genes in health and disease. The goals of her research are to uncover fundamental mechanisms that underlie learning and memory, to integrate Drosophila into Next Generation Genome Diagnostics, and to exploit her model and the identified molecular networks to develop therapeutic strategies to (groups of) cognitive disorders. Recent key publication: **Epigenetic regulation of learning & memory by Drosophila EHMT/G9a.** *PLoS Biol.* 2011, 9(1): e1000569

Title presentation: **Neurodevelopmental disorders: Common Mechanisms**

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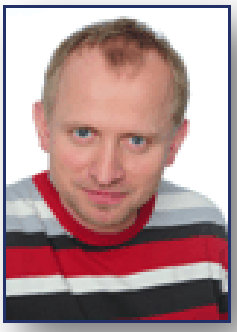

**Stephan Sigrist** is professor for head of neurogenetics in the biological department of Freie Universität Berlin, and affiliated with NeuroCure cluster of excellence at the Charite Medical Campus. He studies synapses in physiological and pathophysiological context in model systems, particularly Drosophila. Genetic analysis is complemented with high-resolution imaging (stimulated emission depletion (STED), biochemical&proteomic analyses as well as physiological methods. Mutations affecting synaptic active zone proteins, associated with autism, are molecularly and functionally characterized. Lately, he started studying mechanisms of synapse plasticity within age-induced memory impairment. Key publication: **RIM-binding protein, a central part of the active zone, is essential for neurotransmitter release**. *Science* 2011; 334(6062):1565-9

Title presentation: **Polyamines protecting from age-induced memory impairment in an autophagy-dependent manner**

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**Dr. Alcino Silva's** laboratory is studying the biology of learning and memory. His research group is also unraveling mechanisms and developing treatments for learning and memory disorders, such as those associated with Neurofibromatosis type I, and Tuberous Sclerosis. He heads the UCLA Integrative Center for Learning and Memory, and he is a professor in the UCLA Departments of Neurobiology, Psychiatry and Psychology. Dr. Silva is also currently a member of the Board of Regents of the University of Minho, Portugal. In 2002 Dr. Silva founded and became the first President of the Molecular and Cellular Cognition Society, an international organization with more than 4000 members and with branches in North America, Asia and Europe. Recent key publication: **Modeling hyperactivity: of mice and men.** *Nature Medicin.* 2011; 17:541-2

Title presentation: **Reversing neurodevelopmental disorders in adults: from mechanisms to treatments**

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**Henk Stunnenberg** is full professor and head of the department of Molecular Biology, coordinator of the EU FP7 High Impact Project BLUEPRINT and co-chair Steering Board of the International Human Epigenome Consortium, member of EMBO. His research aims at unraveling the molecular basis of development and differentiation emanating from the genome and epigenome in the context of health and disease. Key publication: **The transcriptional and epigenomic foundations of ground state pluripotency.** *Cell* 2012; 149(3):590-604

Title presentation: **Epigenome of Embryonal Stem Cells**

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**Li-Huei Tsai** is the Picower Professor of Neuroscience and the Director of the Picower Institute for Learning & Memory at Massachusetts Institute of Technology. Her lab studies brain development and the cellular and molecular mechanisms that contribute to brain disorders associated with cognitive deficits. Recently, she identified a specific epigenetic pathway that regulates learning and memory and demonstrated that targeting a specific chromatin modifying enzyme can ameliorate cognitive deficits in mouse models of memory disorders. Key publication: **An epigenetic blockade of cognitive functions in the neurodegenerating brain**. *Nature* 2012; 483(7388):222-6

Title presentation: **The role of epigenetic gene regulation in cognitive function and dysfunction**