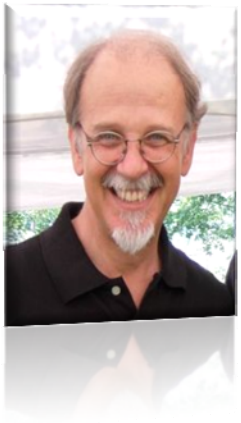
Keynote Speakers:

Second International ENCODYS Conference

"Integrative Networks in Intellectual Disabilities"



Stylianos E. Antonarakis is currently Professor and Chairman of Genetic Medicine at the University of Geneva Medical School, and the founding director of iGE3 (institute of Genetics and Genomics of Geneva). He is a medical, molecular, human geneticist, physician-scientist, who studied extensively the relationship between genomic and phenotypic variation. His research work includes the molecular bases of monogenic disorders and complex genetic disorders including the beta-thalassemias, hemophilias, and trisomy 21. His laboratory participated in the human genome sequence and functional analysis, particularly on chromosome 21. He is an international expert on disorders of chromosome 21, cloning of genes for genetic disorders, development of diagnostic tests, genome structure and function, studies of the genome variability, and conserved non-coding sequences in human DNA. He has published extensively (more than 620 well-cited papers) in the scientific literature, and is co-editor of the current edition of the classic textbook "Genetics in Medicine"; he is listed as one of the highly cited scientists by the ISI institute (more than 45,000 citations; h-index 104). He was the President of the European Society of Human Genetics (2001-2002), and President of HUGO for 2013-2016, foreign member of the Academy of Athens (2003), member of EMBO (2006). He was the co-organizer of the European School of Genetic Medicine, and in the last 28 years taught in the Bar Harbor Genetics Course, Maine. He was awarded the Society of Pediatric Research Young Investigator Award (1984), International Jerome Lejeune Prize (2004), the European Society of Human Genetics Award (2005), and was elected to the Society of Scholars of the Johns Hopkins University (2006), and the American Academy of Physicians (2010). He was awarded the Commander of the Order of Phoenix medal from the Hellenic Democracy (2007). More than 70 talented young scientists were trained in his laboratory (graduate students and postdoctoral fellows); in addition more than 25 young physicians were trained in the Medical Genetics Clinic of his department. With Haig Kazazian he has established one of the first molecular diagnostic laboratories in USA as early as 1982. He is a member of the Swiss National Science Foundation Research Council, and the Chair of the Genetics Review Panel of the EU ERC. His research laboratory was/is supported by grants from the National Institutes of Health, the European Union (including the European Research Council), and the Swiss National Science Foundation and numerous other Foundations including the Gebert and Lejeune Foundations. His is the originator of the World Down Syndrome Day (http://en.wikipedia.org/wiki/World_Down_Syndrome_Day). His current interests and research projects are the functional analysis of the genome, effect of human genetic variation to phenotypic variation, the molecular pathogenesis of trisomy 21 and polygenic phenotypes, the functional characterization of the conserved fraction of the genome, diagnostics and prevention of genetic disorders, and the societal implications of

genetics and genome research. Recent key paper**: Domains of genome-wide gene expression dysregulation in Down's syndrome**. **Nature** 2014; 508(7496): 345-50

Title of presentation : **Transcriptomes, twins, and single cells: delightful liaisons**

Zoltan Asztalos is director of Aktogen Limited, Cambridge, UK. He has received his Ph.D. in biology at the Lorand Eotvos University, Budapest, Hungary. Before he founded Aktogen Ltd., a University of Cambridge start-up company, Zoltan studied the inheritance of innate and learned *Drosophila* behaviour as postdoctoral fellow in Cold Spring Harbor, Tokyo and Cambridge. Aktogen is set up to accelerate the discovery of drug targets and drugs to treat mental (Central Nervous System) disorders employing the fruit fly as model system. Recent Key Publication: **Automated measurement of Drosophila jump reflex habituation and its use for mutant screening**. J. Neurosci. Methods 2009; 182(1): 43-8

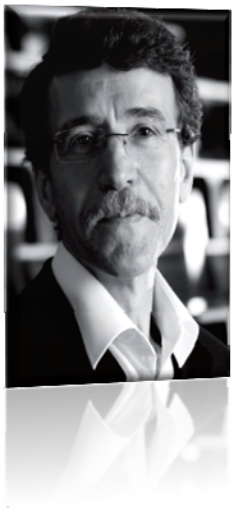
Title of presentation: **Developing a fruit fly neuro-behaviour test battery**

Claudia Bagni is professor at the Faculty of Medicine University of Rome and the KU Leuven and group leader at the Flemish Institute for Biotechnology. Her research focus is on cellular and molecular studies of synaptic plasticity and cancer in the context of intellectual disabilities. Memory formation and cognitive processes that rely on activity-dependent synaptic plasticity are affected by local protein synthesis and shaping of the synapses. Synaptic inputs dictate the time, place and amount of protein synthesis necessary for the single synapses. Dysregulation of these mechanisms leads to spine dysmorphogenesis and to a variety of neuropathological conditions including the most common form of inherited mental retardation, the Fragile X syndrome (FXS), which is due to the absence or mutation of a single protein, FMRP. FMRP is involved in multiple steps of neuronal messenger RNA metabolism. The work of her group, as well as the work of others, has shown that Autistic Spectrum Disorder (ASD), Schizophrenia (SCZ) as well as Alzheimer's Disease (AD) are linked to FMRP function. They aim at identifying molecular pathways that are impaired in FXS and other disabilities such as ASD and SCZ using mouse and fly models as well as cell lines from patients. One of the major goals is to understand the regulation of synaptic protein synthesis and actin remodeling during brain development in physiological and the above-mentioned pathological conditions. Recent key publication: **FMRP regulates multipolar to bipolar transition affecting neuronal migration and cortical circuitry.**. Nat Neurosci. 2014 Dec; 17(12): 1693-700

Title of presentation: **From molecules to behaviour: disentangling FXS and ASD**

Hans van Bokhoven is full Professor of Molecular Neurogenetics at Radboud University Medical Center. His research, embedded at the intersection between the Departments of Human Genetics and the Department of Cognitive Neuroscience, studies the molecular underpinnings of development and functioning of the nervous system and its building blocks, the neurons and other cell types. The research is translational: from patient to the bench and back to the patient. The basis of his multidisciplinary research are genes that are underlying genetic disorders, such as intellectual disability, autism spectrum disorders, and neural migration disorders. Besides innovative genetics and genomics methodologies to identify causative gene mutations in neurodevelopmental disorders, his group applies a range of complementary in vitro and in vivo approaches to get insight into the mechanisms of disease and the normal physiological pathways that are regulated by these genes. Thus behavioral paradigms are studied in genetic animal models such as mouse and Drosophila and linked to neurobiological and neurophysiological pathways in primary neurons. In addition, patient-derived iNeurons derived via induced pluripotent stem cells are used. An important emphasis of his research is placed on the elucidation of epigenetic pathways interfering with learning and memory defects in intellectual disability and autism. Followed by his group's discovery that mutations in EHMT1 give rise to Kleefstra syndrome, which is characterized with intellectual disability, ASD and facial characteristics as leading phenotypic features, the study of the epigenetic network around the *EHMT1* gene has become a leading topic of his research. It is his aim to understand how (haploinsufficient) mutations in this gene lead to neuropathology. In addition, he and his group have the ambition to use this knowledge to develop new strategies for intervention. Recent key publication: **The genetics of cognitive epigenetics.** Neuropharmacology 2014 May; 80: 83-94

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



Jamel Chelly has degrees in medicine and human genetics. He was appointed as scientist by CNRS (Centre National de Recherche Scientifique, France). In 1991 he was awarded by the Cancer Research foundation (UK) a three year Post-doc fellow position and carried out his research at the Institute of Molecular Medicine in Oxford UK and contributed in the identification of several diseases-related genes. In 1995, he established at the Cochin Institute the Laboratory of Genetics and Pathophysiology of intellectual disability (ID) and neurodevelopmental disorders. He is a founding member of the European XLMR Consortium that has been instrumental in the remarkable progress in the field of ID and neuronal migration disorders. In September 2003, he was appointed as Professor at University Paris Descartes. Since September 2014, Professor Chelly moved to Strasbourg University - Medical School of Strasbourg, joined the IGBMC and established his research group "Genetics and Pathophysiology of neurodevelopmental and epileptogenic disorders". Objectives of his research programs, firmly anchored to genetic discoveries of his group, aim to better define and understand disrupted molecular, cellular and neurobiological processes underlying neuronal migration defects and malformations of cortical

development (MCD), such as lissencephaly/pachygyria and polymicrogyria. Following the identification of Doublecortin (DCX) gene and its implication in large spectrum of neuronal migration disorders (des Portes et al., Cell 1998), his group showed that doublecortin is a protein associated with microtubules (Francis et al., Neuron 1999) that stabilizes oligomers of tubulins (Moores et al., EMBO J. 2006). He recently showed that **mutations in TUBA1A** (collaboration with J Flint's group, Oxford University), **TUBB2B, TUBB3, TUBB5, TUBG1, FIF2A, KIF5C and DYNC1H1**, **are associated with MCD** (recent key publications, Poirier et al., 2013; Kielar et al., 2014). This confirms that microtubule-dependent mitotic and postmitotic processes are major players of cortical development and contributors to the pathogenesis of MCD.

Title of presentation: **Insights from Genomic approach into the understanding of human brain development**

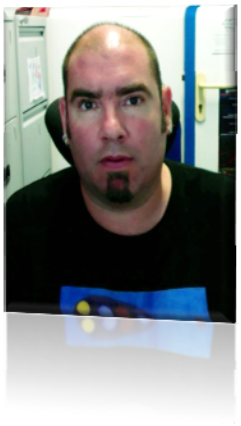
Ype Elgersma is professor in the department of Neuroscience at the Erasmus University Medical Center and Scientific Director of ENCORE expertise Center. His laboratory seeks to get insight in the molecular and cellular basis of cognitive disability, and to use this knowledge to develop treatments. The laboratory is particularly interested in developmental disorders that are associated with intellectual disabilities, with a specific focus in disorders in the RAS-ERK and TSC-MTOR pathways and in Angelman Syndrome. Central to the approach is the use of genetically engineered mice. These mice are studied at the biochemical, cellular and behavioral level. In this way the lab hopes to understand the specific function of these genes and proteins in neuronal function, and to develop therapies. To translate the mouse findings to the clinic, Ype Elgersma was founder of the *ENCORE* expertise center for neuro-developmental disorders, which includes the national referral center for TSC, Angelman Syndrome and Neurofibromatosis. Several clinical trials are currently ongoing in this center. The *ENCORE* expertise center is an inter-departmental collaboration involving 9 departments, but with a particular strong participation of the departments of Pediatrics, Child Neurology, (Child) Psychiatry, Clinical Genetics and Neuroscience. Recent key publication: **TORC1-dependent epilepsy caused by acute biallelic Tsc1 deletion in adult mice**. Ann Neurol. 2013;74(4): 569-79

Title of presentation: **Mouse models for rare disorders: from mechanisms to trials**

Andre Fischer is professor for Epigenetic in Brain Diseases in the Department for Psychiatry and Psychotherapy, University Medical Center, Georg-August University Göttingen and speaker of the German Center for Neurodegenerative Diseases (DZNE) in Göttingen. His group investigates epigenetic mechanisms in neurodegenerative and neuropsychiatric diseases. To this end they pioneered next-generation sequencing approaches to study gene-expression networks in brain plasticity. They combine the analysis of human tissue with mechanistic studies in rodents employing behavioral and molecular approaches. Recent key publication: **K-**

Lysine acetyltransferase 2a regulates a hippocampal gene expression network linked to memory formation. EMBO J. 2014;33(17): 1912-27

Title of presentation: **Reading the code: Epigenetic mechanisms in brain diseases**



José Luis Gómez Skarmeta is full professor at the Spanish National Research Council and Principal investigator at the Andalucian Centre for Developmental Biology in Seville, Spain. His areas of expertise are Developmental Biology (including *Drosophila*, *Xenopus* and zebrafish as animal models), Molecular Biology, Genetics, Functional Genomics and Epigenomics. In the last years he has been pioneering to combine recently developed molecular and developmental techniques to study the contribution of cis-regulatory elements and chromatin structure to development, evolution and human diseases. In 2009, he created the Aquatic Vertebrate Platform of CABD, an open research laboratory designed to facilitate the study of developmental mechanisms in lower vertebrates within a technological environment in continuous growth. This very successful Platform has been used by more than 50 researchers in the last 5 years from all around the world. Recent key publication: **Obesity-associated variants within FTO form long-range functional connections with IRX3**. Nature 2014 Mar 20; 507(7492): 371-75

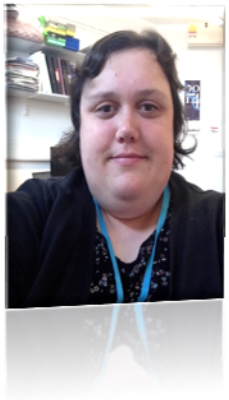
Title of presentation: **Gene regulation dynamics and chromatin architecture during development and evolution**

Seth Grant graduated from Sydney University with a Bachelor of Science (Medicine) in Physiology, Bachelor of Medicine and Bachelor of Surgery. From 1985-1989 he was a Postdoctoral Fellow at Cold Spring Harbor Laboratory with Douglas Hanahan studying transgenic mouse models of cancer. From 1989-94 he studied mouse genetic models of learning and memory with Eric. Kandel at Columbia University. He established his laboratory at the Centre for Genome Research at Edinburgh University in 1994 and in 2000 was appointed Professor of Molecular Neuroscience. In 2003 he was appointed Principal Investigator at the Wellcome Trust Sanger Institute in Cambridge and remained there until 2011, when he returned to Edinburgh University. He has held additional appointments including the John Cade Visiting Professor at Melbourne University, Honorary Professorship at Cambridge University and elected Fellow of the Royal Society of Edinburgh. His work focuses on the molecular basis of synapse function and behaviour. He has characterized synaptic proteome organisation, evolution and function and identified the key role played by supramolecular assemblies of postsynaptic proteins. His synapse proteomic and genetic work has lead to the identification of many diseases impacting on the synapse and the multiprotein complexes that control cognition.. Recent Key publication: **Synaptic scaffold evolution generated components of vertebrate cognitive complexity.** Nat Neurosci. 2013 Jan; 16(1): 16-24

Title of presentation: **How is our behavioural repertoire built?**

Yann Hérault is a Research Director at the CNRS, the French National Centre for Scientific Research, leading the "Institut Clinique de la Souris", ICS (Mouse Clinical Institute, MCI-ICS, Illkirch), and a research group at the IGBMC (Illkirch). His main interest is oriented toward the identification of genes, sensitive to dosage, controlling the neurodevelopment and physiology. He focused on evaluating the consequences of gene dosage effect and copy number variation on cognition. He worked on Down Syndrome (DS, or Trisomy 21) and other intellectual disabilities (ID) attached to copy number variation. His objective is to identify candidate dosage sensitive genes, to further understand the pathophysiological mechanisms and to propose new therapeutic approaches to improve the deficit observed in patients. He developed several preclinical models of DS and other rare diseases causing ID. Using this panel of models he defined the contribution of several genomic regions to DS phenotypes affecting behavior and cognition, the cardiovascular system and the morphology. In addition he worked on DS candidate genes and developed a few therapeutic approaches to tackle down DS learning and memory phenotypes using specific drugs. Recent key publication: **The *App-Runx1* region is critical for birth defects and electrocardiographic dysfunctions observed in a Down syndrome mouse model**. PLoS Genet. (2012) 8, e1002724

Title of presentation: **High throughput standardized investigation of mouse models in Cognitive Dysfunctions: The GENCODYS experience**



Alexa Horner is the Behavioural Research Manager at Synome Ltd., a Cambridge-based UK biotechnology company.
She is an expert in rodent touchscreen cognitive testing, which utilises a battery of highly standardised and translational tasks, many of which are analogous to those in the human Cambridge Neuropsychological Test Automated Battery (CANTAB). She heads a team of researchers who employ this technology platform to study the effects of mutations, natural genetic variation and drugs on the behaviour and cognition of mice. Recent key publication: **The touchscreen operant platform for testing learning and memory in rats and mice.** *Nat. Protoc.* 2013; 8(10): 1961-84

Title of presentation: **Highly translational touchscreen phenotyping of mice bearing disease-relevant mutations**

Martijn Huynen is a professor in comparative genomics at the Centre for Molecular and Biomolecular Informatics (CMBI), Radboud University Medical Centre.
He develops techniques to extract biomedically relevant information from genomics data to predict the functions of proteins and their interactions in pathways. Using these techniques he predicts new proteins of e.g. the mitochondrion and the cilium. The functions of multiple of his predicted proteins have been confirmed experimentally and the genes have been shown to be involved in intellectual disability. Recent key publication: **Mutations in the UQCC1-interacting protein, UQCC2, cause human complex III deficiency associated with perturbed cytochrome b protein expression.** PLoS Genet. 2013; 9(12): e1004034

Title of presentation: **Identifying the molecular systems disrupted in ID and their genes**

Sebastien Jacquemont is a professor of medical genetics at the University hospital of St. Justine and holds a Swiss national foundation assistant professorship as well as Canadian research chair.
SJ was trained as a clinical geneticist and subsequently completed a research fellowship in developmental pediatrics at the University of California, Davis where he developed expertise in fragile X syndrome (FXS). SJ was instrumental in characterizing a new FMR1-related neurological disorder for which he received in 2003 the clinical research award at the "Annual Meeting of the American Society of Human Genetics". His strong interest in translational research has led him to work, in collaboration with Novartis Pharma, on developing and conducting clinical trials in patients with Fragile X syndrome. SJ developed a second line of research investigating the impact of gene dosage on neurodevelopment, in particular neuropsychiatric and associated energy balance disorders. Recent key publication: **Investigation of memory, executive functions and anatomic, correlates in asymptomatic FMR1 premutation carriers**. Neurobiol Aging. 2014 Aug; 35(8): 1939-46

Title of presentation: **Translating molecular advances into therapy**

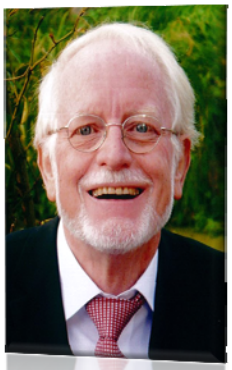
Hossein Najmabadi, PhD, professor of genetics, is the director and founder of the Genetics Research Center (GRC) at the University of Social Welfare and Rehabilitation Sciences in Tehran, Iran. The mandate of the GRC, also designated the National Reference Laboratory for Prenatal Diagnosis in Iran, is to prevent genetic disabilities and disorders by the establishment of a nationwide strategy for the early prenatal diagnosis of genetic disorders. In five areas of preventable genetic disorders, Dr. Najmabadi leads projects that not only apply preventive solutions within the population but also involve nationally and internationally collaborative research in order to improve the quality of life nationwide. The cognitive dysfunction in particular Intellectual

Disability (ID) includes the evaluation of clinical heterogeneity of ID patients either syndromic or non-syndromic and the identification of genetic causes using cytogenetics, molecular genetics techniques. He has identified many novel genes in Autosomal Recessive Intellectual Disability (ARID). In the study of both syndromic and non-syndromic deafness, he has identified the genes or mutations particular to Iran and established diagnostic protocols for them. In order to classify different subtypes of neuromuscular disorders (NMD) in Iran, family DNA studies are guided by the histopathology facilities at the GRC and applied Next Generation Sequencing (NGS). The investigation of hemoglobinopathies has also been conducted by him in a number of projects to identify the mutation spectrum of alpha- and beta-thalassemia, with the establishment of protocols for mutation identification and prenatal diagnosis. Moreover, studies on the potential elements in the induction of gamma globin as well as the molecular mechanism of hydroxyurea aim to improve the treatment of thalassemia. Recent key publication: **Deep sequencing reveals 50 novel genes for recessive cognitive disorders.** Nature 2011 Sep 21; 478(7367): 57-63

Title of presentation: **Whole Exome Sequencing in Research and Diagnosis of Intellectual Disability**

Peter Robinson, MD., PD, Msc., is Professor of Medical Genomics at the Charité University Hospital Berlin and Professor of Bioinformatics at the Free University Berlin. He has a BA. In Mathematics from Columbia College, an MD from the University of Pennsylvania, and a Master of Science in Computer Science from Columbia University School of Engineering. After an internship in primary care internal medicine at Yale, he completed a residency in Pediatrics at the Charité, and now leads a computational and wetlab research group at the Institute of Medical and Human Genetics of the Charité. The Robinson lab develops computational and experimental resources for the study of human biology and disease. Recent highlights include the Human Phenotype Ontology (HPO), which is now an international standard for computation over human disease that is used by the Sanger Institute, several NIH-funded groups including the Undiagnosed Diseases Program, Genome Canada, the rare diseases section of the UK's 100,000 Genomes Project, and many others. We develop algorithms and software for the analysis of exome and genome sequences, including most recently the Exomiser, which was developed jointly with the Sanger Institute. The group has used whole-exome sequencing and other methods to identify a number of novel disease genes, including CA8, PIGV, PIGO, PGAP3, IL-21R, PIGT, and PGAP2. We support a range of genomics research projects at the Berlin Brandenburg Center for Regenerative Therapies (BCRT), including ChIP-seq, RNA-seq, T-cell receptor profiling, and deep-sequencing analysis of DNA methylation. We have identified secondary deleterious effects of a class of extracellular matrix fragment containing the motif Gly-x-x-Pro-Gly in Marfan syndrome, and have used this finding to develop a novel therapy in a mouse model of Marfan syndrome. Our focus in the coming decade will be on integrative computational analysis of genomics and clinical data in order to extend our understanding of human disease, personalized and systems medicine. Recent key publication: **Effective diagnosis of genetic disease by computational phenotype analysis of the disease-associated genome**. Sci Transl Med. 2014 Sep 3; 6(252): 252ra123.

Title of presentation: **Human Phenotype Ontology: Algorithms and Applications**



Hans-Hilger Ropers has recently retired as Director at the Max Planck Institute for Molecular Genetics (MPIMG) in Berlin and Professor for Human Genetics at the Free University Berlin (1994-2014), and as Chairman of the Biomedical Section of the (former Prussian) Berlin Brandenburg Academy of Science (BBAW, 2008-2014). From 1983 to 1997 he served as head of the Institute for Human Genetics at the University of Nijmegen, NL. As MD and first-generation Board-Certified Clinical Geneticist, he has a long-standing interest in the molecular elucidation, diagnosis, prevention and treatment of genetic disorders.

In the 1980ies, H.H. Ropers was an active member of the Gene Mapping Community, acting as Chromosome Chair and Co-Chair at all Human Genome Mapping Conferences between 1985 and 1993, and from 2003 to 2011, he served as Council and Program Committee member of the Human Genome Organization. In the early 1990ies, he and his coworkers were among the first to employ positional cloning strategies for systematically identifying the molecular causes of Mendelian disorders, with a focus on X-linked blindness, deafness and mental retardation. As member of the European X-linked Mental Retardation Consortium (*1995) they made seminal contributions to the elucidation and diagnosis of X-linked intellectual disability (XLID); together with their Danish partner, they were involved in the first systematic effort to characterize disease-associated balanced chromosome rearrangements; and they were also one of the first to describe copy number variants in complex disorders other than ID. In 2004, when XLID turned out to be less common than previously thought, H.H.Ropers and his Iranian partner set out to study autosomal recessive forms of ID (ARID) in a systematic manner. By pioneering the use of SNP arrays for large-scale autozygosity mapping in consanguineous ARID families they demonstrated that ARID is extremely heterogeneous. Another milestone was the early adoption of Next Generation Sequencing (NGS) technology in 2007 when the MPIMG became the first Continental European customer of Solexa (now Illumina). This added a new dimension to the molecular elucidation of X-linked and autosomal ID which is still being pursued by his group.

More recently, H. H. Ropers has been promoting the adoption of NGS techniques to improve genetic health care in Germany. After having analyzed his own genome, he believes that the time has come for introducing whole genome sequencing (WGS) as a first line diagnostic test for selected pediatric patients. At the same time, he is convinced that medical genome sequencing should be confined to experienced, suitably manned and equipped Competence Centers for Rare Diseases.

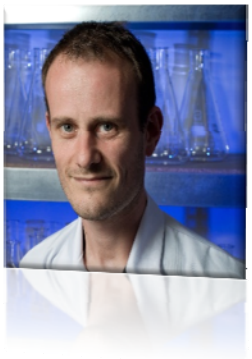
He is member of the Royal Dutch Academy of Sciences (since 2002) and the BBAW (since 2003), Honorary Member of the German Society of Human Genetics and recipient of its Medal of Honor (2009), and in 2014 he received the Scientific Award of the European Organization for Rare Diseases. Recent key publications: **De novo truncating mutations in ASXL3 are associated with a novel clinical phenotype with similarities to Bohring-Opitz syndrome.** Genome Med. 2013 Feb 5; 5(2): 11**; Integrated sequence analysis pipeline provides one-stop solution for identifying disease-causing mutations.** Hum Mutat. 2014 Dec; 35(12) 1427-35

Title of presentation**: Intellectual disability and related disorders: genetic progress and remaining challenges**

Joris A. Veltman is professor in Translational Genomics and head of the Genome Research division at the Department of Human Genetics, Radboud University Medical Centre in Nijmegen and the Department of Clinical Genetics, Maastricht University Medical Centre in Maastricht, The Netherlands.
His research focuses on the identification and interpretation of genomic variation, with a particular interest in the role of rare *de novo* mutations and copy number variations in severe neurodevelopmental and psychiatric diseases such as intellectual disability and rare genetic diseases. With his research group he studies the genomes of patients using next generation sequencing technology and combines laboratory experiments with novel bioinformatic approaches. In addition, he is actively involved in the implementation of these novel genomics approaches in routine clinical diagnosis, aiming to improve the diagnostic yield, reduce the turn-around-time and make personalized medicine a reality. Recent key publication: **Genome sequencing identifies major causes of severe intellectual disability**. Nature 2014; 511(7509): 344-7

Title of presentation**: De novo mutations in intellectual disability**

Patrik Verstreken is professor at the KU Leuven and group leader at the VIB Center for the Biology of Disease in Belgium.
He uses fruit flies and mammalian cells to study neuronal and synaptic function and he creates and analyzes new disease models. His studies combine genetics with electrophysiology, imaging and electrophysiology. Recent key publication: **Mutations in the X-linked intellectual disability gene Ube2a cause neuronal dysfunction and impair Parkin-dependent mitophagy**. Molecular Cell 2013; 50: 831-43



Title of presentation: **Mitochondrial Dysfunction in Intellectual Disability**

Caleb Webber is programme leader in Neurological Disease Genomics at the Medical Research Council (MRC) Functional Genomics Unit at the University of Oxford. He obtained his PhD in 2003 from the European Bioinformatics Institute, The Wellcome Trust Genome Campus, Hinxton Cambridge and from the Department of Genetics, Cambridge University. Afterwards he returned to Oxford to work with Prof. Chris Ponting on most of the major large-scale genome projects of the last decade. Through CNVs, he became interested in the role of genetic variation in disease, applying novel functional genomics approaches to uncover the pathways and process disrupted in neurodevelopmental disorders, including intellectual disability, ADHD and autism. Over the last few years, his lab has been drawn increasingly

into elucidating the role of synergistic interactions in disease. Recent key publications: **The roles of FMRP-regulated genes in autism spectrum disorder: single- and multiple-hit genetic etiologies**. AJHG 2013; 93(5):825-39. **Unbiased functional clustering of gene variants with a phenotypic-linkage network**. PLoS CompBio 2014; 10(8):e1003815,

Title of presentation: **Developmental disorders, genetic interactions and a functionally-clustered genome**