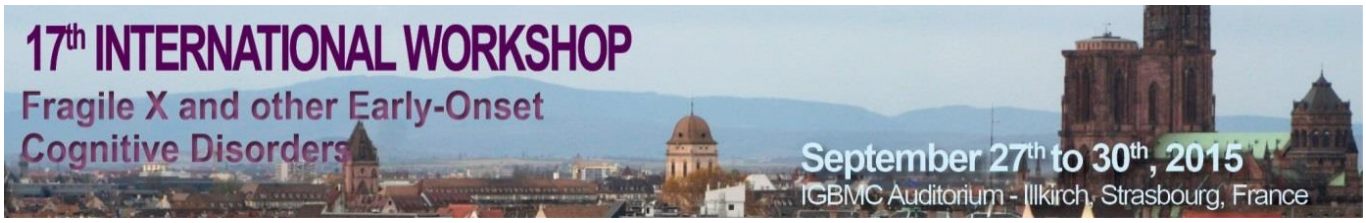


Day 1 - Sunday 27th September

Registration desk open from 9.30 am to 4 pm

10.00 - 12.30 **Visit of Mouse Clinical Institute (ICS) -** Strictly upon prior reservation (3 groups)
Presentation of ICS and visit of the behavior phenotyping platform.

15.00-19.00 **SESSION 1**

15.00 Welcome and general information

15.10 – 17.55 **Session 1A Autism, intellectual disability: Converging or contrasting genetic features ?**

Chairs : **Jozef Gecz and Jean-Louis Mandel**

15.10 **Michael Ronemus** (Cold Spring Harbor Laboratory, USA) The contribution of rare and de novo mutation to autism spectrum disorders

15.50 **Thomas Bourgeron** (Inst. Pasteur Paris, France) Genes and synapses in autisms

16.20 **Sébastien Jacquemont** (U. Montreal, Canada) Sex bias in neuropsychiatric disorders : Clinical and molecular correlates

16.45 **Coffee break**

17.15 **Roberto Toro** (Inst. Pasteur Paris, France) Polygenic contribution to autism and neuroanatomical variation

17.40 **General discussion** ID +/- autism, autism without ID, in males and females : Same genes ? Same pathways ? Same genetic epidemiology ?

17.55 - 19.00 **Session 1B Functional mechanisms**

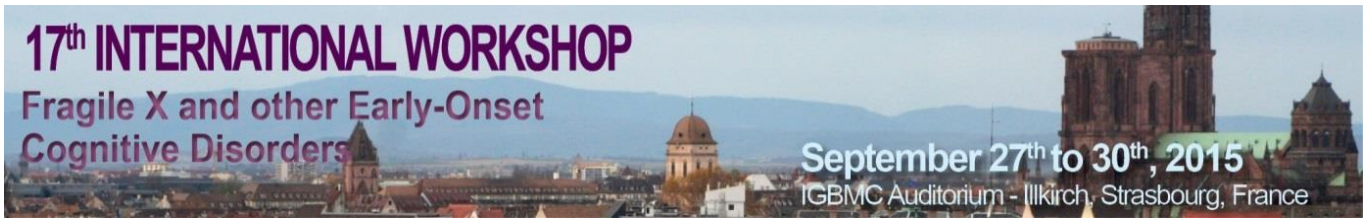
Chairs : **Nicolas Charlet-Berguerand and Lucy Raymond**

17.55 **Jozef Gecz** (U. Adelaide, Australia) Mechanisms of PCDH19 associated female epilepsy & intellectual disability

18.15 **Hans van Bokhoven** (Radboud university medical center, Netherlands) Integrative networks in neurodevelopmental disorders

18.35 **Giuseppe Testa** (IFOM-IEO Milano, Italy) Epigenetic reprogramming in neurodevelopmental disorders : From mechanism to tool and back

19.15 – 21.30 **Welcome party** with gourmet food and special tasting of Alsace white wines
(Wines from and commented by Albert Seltz, the Seltz family's 14th generation owner and winemaker, since 1576, in the same house of the charming Renaissance village of Mittelbergheim.)



Day 2 - Monday 28th September

8.30-12.45 SESSION 2

8.30 – 10.15 Session 2A Autism

Chairs : Thomas Bourgeron and Gudrun Rappold

8.30 **Christelle Golzio** (Duke U Durham, NC, USA) In vivo dissection of copy number variants associated with autism spectrum disorders

8.48 **Aia Elise Jønch** (CHUV Lausanne, Switzerland) Converging and diverging phenotypes of the distal and proximal copy number variations at the 16p11.2

9.00 **Nele Cosemans** (KU Leuven, Belgium) Analysis of autosomal CNV profiles in patients and siblings in autism families : The contribution of variants of unknown significance

9.12 **Discussion**

9.15 **John Vincent** (Centre for Addiction & Mental Health Toronto, Canada) PTCHD1 and its role in autism spectrum disorders and intellectual disability

9.30 **Frédéric Laumonnier** (U. Tours, France) GABA/Glutamate synaptic pathways targeted by integrative genomic and electrophysiological explorations distinguish autism from intellectual disability

9.42 **Laura Cancedda** (Istituto Italiano di Tecnologia Genoa, Italy) Autism-associated proteins Negr1 and FGFR2 together regulate cell migration and autism-related behaviors in mice

9.54 **Roger Stevenson** (Greenwood Genetic Center, USA) The metabolomic approach to autism

10.10 **Discussion**

10.15 Coffee break

10.45 – 12.45 Session 2B Fragile X/FMRP functional and preclinical studies

Chairs : Barbara Bardoni and David Nelson

10.45 **Barna Fodor** (Novartis Basel, Switzerland) Dissecting the unmethylated full mutation phenotype in fragile X Syndrome using human induced pluripotent stem cells

10.57 **Olfa Khalfallah** (Institute of Molecular Pharmacology Valbonne, France) Depletion of FMRP (Fragile X Mental Retardation Protein) in embryonic stem cells alters the kinetics of neurogenesis through a pathway involving Amyloid Precursor Protein (APP)

11.09 **Maija Castren** (U. Helsinki, Finland) Activity-dependent mechanisms modulate neuronal differentiation in fragile X syndrome

11.21 **François Bolduc** (U. Alberta, Canada) Acute post-natal treatments targeting camp rescues fragile X learning and memory defects

11.33 **Valeria Specchia** (U. Salento, Italy) The drosophila fragile X mental retardation protein participates in the piRNA pathway

11.45 **Discussion**

11.50 **Stéphane Schmucker** (IGBMC, France) An unexpected role for fragile X-related proteins in mitosis

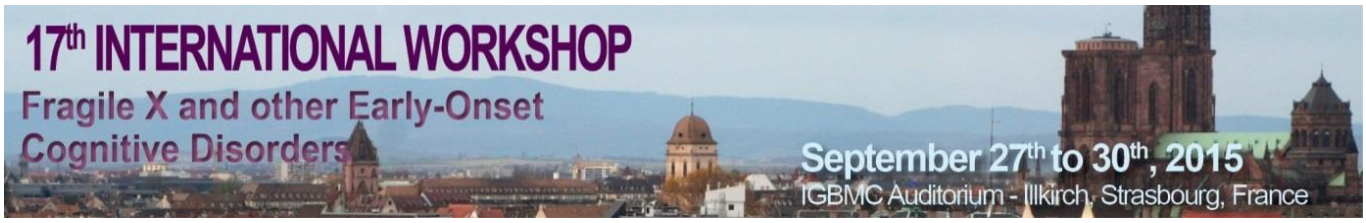
12.02 **Thomas Maurin** (IPMC Valbonne, France) Region specific analysis of FMRP targets highlights new potential therapeutic approaches for FXS

12.14 **Hervé Moine** (IGBMC, France) The fragile X mental retardation protein controls diacylglycerol kinase activity in neurons

12.26 **Iryna Ethell** (U. California Riverside, USA) Role of MMP-9 in auditory deficits associated with FXS

12.38 **Discussion**

12.45 Lunch



13.30-14.25 POSTER SESSION 1

14.30-18.45 SESSION 3

14.30 – 17.40 Session 3A Round table on perspectives of fragile X pharmacotherapies
(with sponsorship by the **Jérôme Lejeune Foundation**)

Chairs : Randi Hagerman and Sébastien Jacquemont

14.30 **Randi Hagerman** (UC Davis Medical Center, USA) General introduction and targeted treatments in early childhood in children with FXS : A controlled trial of sertraline

14.45 **Flora Tassone** (UC Davis Medical Center, USA) Molecular biomarkers for targeted treatments in fragile X syndrome

14.55 **Florian von Raison** (Novartis Basel, Switzerland) Mavoglurant in fragile X syndrome: Results from two phase II randomised, double-blind trials and their extensions

15.05 **Lothar Lindemann** (Roche Pharmaceutical Basel) Comparing mGlu5 NAM treatment effects observed in Fmr1 KO mice and FXS patients

15.15 **Jonathan Rubin** (Alcobra Pharma, USA) A 6-week, randomized, multicenter, double-blind, parallel study of MDX compared with placebo in 62 adolescents and adults with fragile X syndrome

15.25 **Discussion**

15.30 **Elizabeth Berry Kravis** (Rush U. Chicago, USA) Challenges and future outlook for clinical trials of targeted treatments in fragile X syndrome

15.40 **Aurore Curie** (L2C2 CNRS, Hospices Civils de Lyon, France) Can we avoid placebo effect with cognitive outcome measures?

15.50 **Frank Kooy** (U. Antwerp, Belgium) The GABAergic system as a therapeutic target for the fragile X syndrome and related neurodevelopmental disorders

16.00 **Giovanni Neri** (Universita Cattolica Rome, Italy) A cure for the fragile X : How far away?

16.10 **Discussion**

16.15 Coffee break

16.45 **Mara Dierssen** (CRG Barcelona, Spain) Design and early results of clinical trial in Down syndrome

17.05 **Jörg Richstein** (German Fragile X association) The International Fragile X Alliance (IFXA) : An international initiative for improving support for people affected by fragile X around the world

General discussion with above speakers, Vincent Desportes, Sebastien Jacquemont, Jozef Gecz and the audience

17.45 – 18.50 Session 3B Mouse models, general and preclinical aspects

Chairs : Mara Dierssen and Jacques Michaud

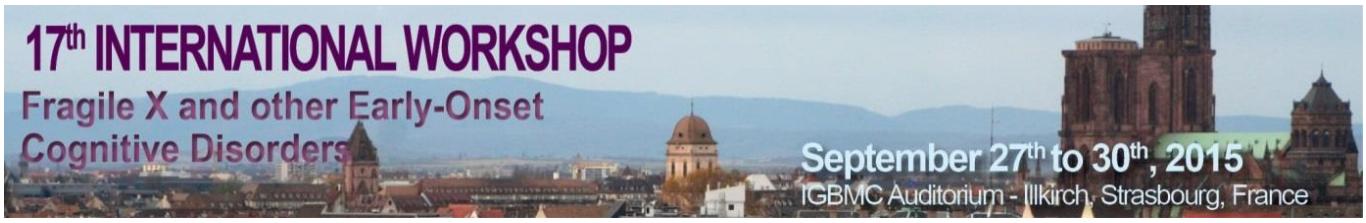
17.45 **Yann Herault** (IGBMC/ICS, France) Standardized exploration of diseases with intellectual disability in the mouse

18.05 **Shimriet Zeidler** (Erasmus U. Rotterdam, Netherlands) Developing targeted treatment for fragile X syndrome : A new robust social behavior paradigm

18.17 **Yann Humeau** (U. Bordeaux, France) Oligophrenin 1 deletion in the medial prefrontal cortex leads to perseveration behaviors by dys-regulating the PKA pathway

18.32 **Binnaz Yalcin** (IGBMC, France) Deciphering the genetic basis of intellectual disability using 1000 knockouts

Free evening and dinner. A list of restaurants of varied cuisine and prices will be provided.



Day 3 - Tuesday 29th September

8.30 – 12.30 SESSION 4

8.30 – 9.30 Session 4A Clinical and diagnostic aspects: fragile X and other conditions
Chairs : Hilger Ropers and Flora Tassone

8.30 **David Godler** (Murdoch Childrens Research Institute Melbourne, Australia) A novel FMR1/SNRPN methylation test for fragile X syndrome and chromosome 15 imprinting disorder screening of symptomatic children and newborns

8.40 **Yvonne Koh** (TNR diagnostic, Singapore) Validation of a commercially available single-tube PCR assay for concurrent determination of FMR1 CGG repeat size and methylation status

8.50 **Solange Aliaga** (Murdoch Childrens Research Institute Melbourne, Australia) Neuropsychological profile and prevalence of pathogenic cryptic fragile X alleles in males, missed using the standard testing protocol

9.00 **Don Bailey** (RTI International, Research Triangle Park, NC, USA) Fragile X newborn pilot study: summary findings and future directions

9.10 **Michael Field** (Hunter Genetics Service Newcastle, NSW, Australia) Twenty years looking in all the wrong places. New insights into Brunner syndrome and potential for targeted therapy

9.20 **Suzanna Frints** (Maastricht University Medical Center, Netherlands) Mutations in RLIM/RNF12 (E3 ubiquitin ligase) lead to a novel X-linked intellectual disability syndrome in which non-random X-inactivation rescues the brain phenotype in carrier females

9.30 – 12.30 Session 4B Genes involved in transcription and epigenetic remodeling
Chairs : Hans van Bokhoven and Hilde van Esch

9.30 **Hilde van Esch** (KU Leuven, Belgium) Altered neuronal network in iPSC derived cortical neurons from patients with MECP2 duplication syndrome

9.48 **Chloe Delepine** (Institut Cochin Paris, France) Alteration of microtubule dynamics in Mecp2-deficient astrocytes derived from human iPSC and mouse models : New insight into Rett Syndrome pathophysiology

10.00 **Ilaria Meloni** (U. Siena, Italy) Contribution of excitatory/inhibitory synaptic imbalance to MECP2, CDKL5 and FOXG1 related disorders

10.15-10.45 Coffee break

10.40 **Sponsor presentation : Florent Brun** (Agilent Technologies) NGS solution for simultaneous detection of genome-wide copy number changes, indels, and gene mutations

10.45 **Gholson Lyon** (Cold Spring Harbor Laboratory, USA) Variants in TAF1 are associated with a new syndrome with severe intellectual disability and characteristic dysmorphic features

11.03 **Gudrun Rappold** (U. Heidelberg, Germany) Brain-specific Foxp1 deletion impairs neuronal development and causes autistic-like behavior

11.15 **Maria Giuseppina Miano** (IGB/CNR Naples, Italy) Finding new connections in the regulation of KDM5C path, an epigenetic route damaged in XLID/Epilepsy diseases

11.27 **André Reis** (U. Friedrich-Alexander, Erlangen-Nürnberg, Germany) ARID1B mutations in intellectual disability link chromatin remodeling to neurite outgrowth by depressing Wnt/β-Catenin signaling

11.39 **Discussion**

11.45 **Aline Dubos** (IGBMC/ICS, France) Characterization of the Arx c.428_451dup24 KI mouse line, model of ARX most frequent mutation

11.57 **David Picketts** (Ottawa Hospital Research Institute, Canada) ATRX prevents degradation of stalled replication forks to facilitate progenitor cell expansion and upper layer neuron production

12.10 **Julien Thevenon** (CHU Dijon, France) Loss-of-function mutations of the chromatin modifier MSL3 cause a recognizable syndrome

12.20 **Raman Kumar Sharma** (U. Adelaide, Australia) Increased STAG2 dosage defines a novel cohesinopathy with intellectual disability and behavioural problems

12.30 – 14.00 **Lunch and POSTER SESSION 2**

14.00 - 15.05 SESSION 5 General issues in genome-phenome-pathways correlations

Chairs : **Pietro Chiurazzi and Anita Rauch**

14.00 **Bert de Vries** (Radboud university medical center, Netherlands) Phenotyping novel ID/ASD genes

14.15 **Charles Schwartz** (Greenwood Genetic Center, USA) Phenotype microarray analysis may provide insight for potential therapeutic approaches in human disorders

14.30 **Christiane Zweier** (U. Friedrich-Alexander, Erlangen-Nürnberg, Germany) Systematic phenotype-based deconvolution of intellectual disability disorders into biologically coherent modules

14.45 **Florent Colin** (IGBMC, France) GenIDA : An international registry of individuals affected by monogenic forms of intellectual disability or autism and a families and professionals social network to collect medically relevant information and gene specific natural histories

14.57 **Angélique Quartier** (IGBMC, France) Search for genes regulated by androgens during neurogenesis as possible contributors to the male excess observed in autism and intellectual disability

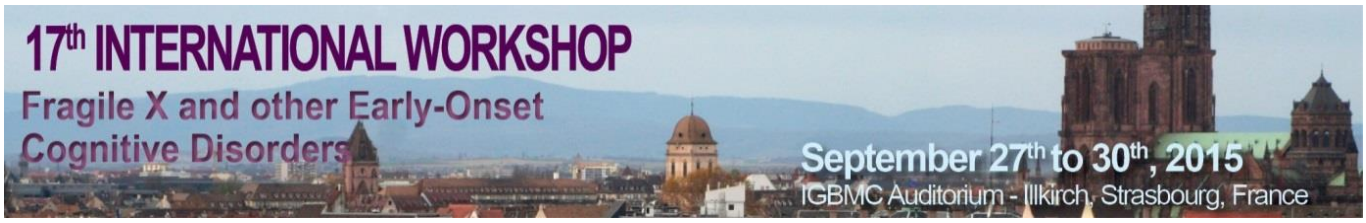
15.15-23.00 SOCIAL PROGRAM

15.15 Visit of Strasbourg. Two proposals : a boat tour on the Ill river or a bus and walk tour.

18.45 Organ concert by Marc Baumann in Strasbourg's gothic cathedral (1015-1439).

20.00 Welcome drink, visit and dinner in the Palais des Rohan (1742). Welcome drink in the courtyard. Short visit of the princely Grands and Petits appartements. Banquet dinner in the Salle du Synode. Upon prior registration. Please, bring name tag and invitation card.

22.45 Bus departure to Holiday Inn hotel Illkirch. A second bus may leave later if some people want to stay around.



Day 4 – Wednesday 30th September

Hotel check out

8.45 – 13.00 SESSION 6

8.45 – 11.10 Session 6A Signaling and synaptic defects
Chairs : Jamel Chelly and Roger Stevenson

8.45 **Carlo Sala** (CNR Institute Neuroscience Milano, Italy) The function of the XLID gene IL1RAPL1

9.03 **Dorien Haesen*** (KU Leuven, Belgium) B56delta-related protein phosphatase 2A dysfunction causes intellectual disability **(Isabelle Oberlé prize at ESHG2015)*

9.15 **Jannecke Schuurs-Hoeijmakers** (Radboud university medical center, Netherlands) Phenotypic spectrum of the recurrent de novo c.607C>T mutation in PACS1

9.27 **Loic Broix** (IGBMC, France) Understanding pathophysiological mechanisms underlying KIF2A-related neurodevelopment disorders

9.39 **Cheryl Shoubridge** (U. Adelaide, Australia) Expanding the phenotype due to mutations in IQSEC2 and investigating functional deficits of IQSEC2 on dendritic spine morphogenesis

9.52 **Discussion, short break**

10.00 **Jacques Michaud** (CHU Sainte-Justine Montreal, Canada) SYNGAP1 haploin sufficiency in intellectual disability and neuronal circuit development

10.18 **Nicolas Vitale** (INCI, U. Strasbourg, France) The Coffin-Lowry syndrome-associated protein RSK2 is implicated in calcium-regulated exocytosis and neuronal development through the regulation of phospholipase D1

10.30 **Patrizia d'Adamo** (San Raffaele Scientific Institute Milano, Italy) The RAB39B intellectual disability protein controls AMPAR trafficking and cognitive functions

10.42 3 short talks

Annick Toutain (CHU Tours, France) Intellectual disability associated with spastic paraplegia and glaucoma in an Algerian family is caused by a homozygous mutation in GRID1, a gene encoding a subunit of glutamate receptor channels

Paranchai Boonsawat (U. Zurich, Switzerland) First evidence for viability of a de novo DDX3X missense mutation in a male patient

Gholson Lyon (Cold Spring Harbor Laboratory, USA) The X-linked Ogden Syndrome involving NAA10 and the amino-terminal acetylation of proteins in human biology and disease

11.05 Coffee break

11.30 – 13.00 **Session 6B Gene panels and exomes in cohorts**

Chairs : **Vera Kalscheuer, Michael Ronemus**

11.30 **Vera Kalscheuer** (MPI for Molecular Genetics Berlin, Germany) Update on X-linked intellectual disability

11.40 **Lucy Raymond** (Cambridge Institute for Medical Research, England) Targeted next generation sequence analysis of 1000 individuals with intellectual disability

11.50 **Amélie Piton** (IGBMC, France) Targeted molecular diagnosis of intellectual disability with or without autism : Update from 217 to 275 genes and 100 to 300 patients confirms a 20-25% diagnostic efficiency and highlights genes recently identified or recurrently mutated

12.00 **Richard Rogers** (Greenwood Genetic Center, USA) The search for an etiology of intellectual disability using gene panels and exome sequencing : The Greenwood Genetic Center experience

12.10 **Discussion**

12.15 **Christel Depienne** (UPMC, Hôpital Pitié Salpétrière Paris, France) Unraveling the causes of corpus callosum agenesis with or without intellectual disability using gene panel and exome analyses

12.25 **Miriam Reuter (**U. Friedrich-Alexander, Erlangen-Nürnberg, Germany) Whole exome sequencing in 150 consanguineous families with intellectual disability : High diagnostic yield and identification of novel candidate genes

12.35 **John Vincent** (Centre for Addiction & Mental Health, Toronto, Canada) Gene identification for non-syndromic autosomal recessive intellectual disability in Pakistani families

12.45 **Elizabeth Palmer** (Hunter genetics Newcastle, NSW Australia) “What does this result mean for me?” Experience with changing interpretation of copy number variants on the X chromosome 2008-2015 and challenges in genetic counselling

12.55 **Christian Windpassinger** (U. Graz, Austria) Short talk : A homozygous truncating mutation in the C terminus of KIF1Bß is associated with a novel syndrome with malformations of cortical development and brachycephaly

13.00 **Discussion**

13.05 **Discussion on the location of the 18th Workshop in 2017**

13.30 **Lunch** at Le Show restaurant in Holiday Inn hotel. Upon prior reservation.