Genomics of Rare Disease
27-29 March 2019
Wellcome Genome Campus,
Hinxton, Cambridge, UK

Conference Programme

Wednesday 27 March 2019

12:00-13:30  Registration with lunch

13:30-13:40  Welcome and introduction
Programme Committee: Matthew Hurles, Wellcome Sanger Institute, UK

13:40-14:40  Lupski lecture
Chair: Matthew Hurles, Wellcome Sanger Institute, UK
Exploring the “between” spaces: the continuum from mendelian to common disease, and the continuum from polygenic to multifactorial disease
Nancy Cox
Vanderbilt University Medical Center, USA

14:40-16:00  Session 1: Solving the unsolved
Chair: Kym Boycott, Children’s Hospital of Eastern Ontario – Research Institute, Canada

14:40  The NIH undiagnosed diseases program: expansion to a national and international networks
William Gahl
NIH, USA

15:20  Epigenetic dysregulation underpins tumourigenesis in a cutaneous tumour syndrome
Neil Rajan
Newcastle University, UK

15:35  Regulatory de novo mutations play significant role in severe intellectual disability
Santosh Atanur
Imperial College London, UK

15:50-16:30  Afternoon tea
16:30-17:00  
**Session 1 continued: Solving the unsolved**  
Chair: Kym Boycott, Children’s Hospital of Eastern Ontario – Research Institute, Canada

16:30  
Exome sequencing for the diagnosis of ultrasound detected fetal abnormalities: a year’s experience at St George’s Hospital in partnership with Congenica Ltd  
Andrea Haworth  
Congenica Limited, UK

16:45  
A bottom-up predictive approach to identify oligogenic disease causes  
Tom Lenaerts  
Université Libre de Bruxelles, Belgium

17:00-17:30  
**Lightning talks**  
Chair: Matthew Hurles, Wellcome Sanger Institute, UK

17:30-19:00  
**Poster session 1 (odd numbers) with drinks reception**

19:00  
Dinner

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**Thursday 28 March 2019**

09:00-10:30  
**Session 2: Informatics**  
Chair: Kaitlin Samocha, Wellcome Sanger Institute, UK

09:00  
Regulatory variant in rare disease: causal and modifier effects  
Tuuli Lappalainen  
New York Genome Center and Columbia University, USA

09:40  
Tools and evaluation for RNA-seq splicing quantification for suspected Mendelian disorders across tissues  
Joseph Aicher  
University of Pennsylvania, USA

09:55  
Relative expression levels of protein complex subunits is a major determinant of haploinsufficiency in human genes  
Joseph Marsh  
MRC Human Genetics Unit, UK

10.10  
Cross-species data on gene essentiality to identify candidate developmental disorder genes  
Pilar Cacheiro  
Queen Mary University of London, UK

10.25  
Determining the sensitivity of detection of pathogenic CNVs from exome sequencing  
Petr Danecek  
Wellcome Sanger Institute, UK
10:25-11:00  
**Morning coffee**

11:00-12:25  
**Session 3: Developmental genetics**  
Chair: Lisenka Vissers, Radboudumc, Netherlands

11:00 Rare disorders caused by mutations in genes encoding epigenetic regulators: novel diagnostic opportunities  
Rosanna Weksberg  
The Hospital for Sick Children, Canada

11:40 Identifying disorder-specific methylation signatures in patients with severe developmental disorders  
Juliet Handsaker  
Wellcome Sanger Institute, UK

11:55 De novo variants disturbing the transactivation capacity of POU3F3 cause a characteristic neurodevelopmental disorder  
Lot Snijders Blok  
Radboudumc, The Netherlands

12:10 Molecular analysis of syndromic craniofacial patients identifies several novel disorders, including targeted treatments for TBCK-, H3.3-, and MAP4K4-associated syndromes  
Elizabeth Bhoj  
Children's Hospital of Philadelphia, USA

12:25-14:00  
**Lunch**

14:00-15:30  
**Session 4: New therapeutic approaches**  
Chair: Caroline Wright, University of Exeter, UK

14:00 P4 medicine for intellectual disabilities: integrated -omics the way forward?  
Clara van Karnebeek  
Amsterdam University Medical Centres, The Netherlands

14:40 Hope for escape from a prison of bone  
Frederick Kaplan  
University of Pennsylvania, USA

15:20 Landscape of treatable rare diseases in a founder population  
Alison Eaton  
Children's Hospital of Eastern Ontario, Canada

15:35 Towards treatment of Cantú syndrome  
Gijs van Haaften  
UMC Utrecht, The Netherlands

15:50-16:30  
**Afternoon tea**
16:30-17:30  **Session 5: Electronic health records**  
*Chair: Nancy Cox, Vanderbilt University Medical Center, USA*

16:00  Assessing the pathogenicity, penetrance and expressivity of apparently monogenic disease variants in UK Biobank  
*Caroline Wright*  
*University of Exeter, UK*

16:40  Genomic disorders in the general population. What can we learn and how can we help?  
*Katrin Mannik*  
*University of Lausanne, Switzerland*

17:20  Leveraging genetic relatedness in a large population cohort to identify de novo, rare, and clinically actionable disease-causing variants in reconstructed pedigrees  
*Claudia Gonzaga Jauregui*  
*Regeneron Genetics Center, USA*

17:35  Whole-genome sequencing of rare disease patients in a national healthcare system  
*Hana Lango Allen*  
*University of Cambridge, UK*

17:50-18:20  **Lightning talks**  
*Chair: Kym Boycott, Children’s Hospital of Eastern Ontario – Research Institute, Canada*

18:20-19:50  **Poster session 2 (even numbers) with drinks reception**

19:50  **Conference dinner**

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**Friday 29 March 2019**

08:30-10:20  **Session 6: Data sharing – legal and ethical issues**  
*Chair: Matthew Hurles, Wellcome Sanger Institute, UK*

08:30  Advancing medicine through data sharing and collaboration on a global scale  
*Heidi Rehm*  
*Broad Institute, USA*

09:10  Big data in health and research, opportunities and challenges  
*Ewan Birney*  
*EMBL-EBI, UK*

09:50  Using Exomiser for rare disease variant interpretation at scale in the UK 100,000 Genomes Project  
*Valentina Cipriani*  
*Queen Mary University of London, UK*
10:05 Characterising the loss-of-function impact of 5' untranslated region
variants in 15,708 whole-genomes
Nicola Whiffin
Imperial College London, UK

10:20-11:00 Morning coffee

11:00-12:50 Session 7: Intersection of polygenic and monogenic
Chair: Tuuli Lappalainen, New York Genome Center and Columbia University, USA

11:00 The Finnish population isolate: examples of polygenic and rare
variants in brain diseases
Aarno Palotie
FIMM, University of Helsinki, Finland

11:40 Using polygenic scores to define lifetime trajectories of disease
Michael Inouye
University of Cambridge, UK

12:20 Harnessing transmission genetics to build models of complex disease
from the ground up
Jennifer Posey
Baylor College of Medicine, USA

12:50-14:15 Lunch

14:15-16:05 Session 8: Functional genomics
Chair: Lisenka Vissers, Radboudumc, Netherlands

14:15 Functional characterization and therapeutic targeting of gene
regulatory elements
Nadav Ahituv
UCSF, USA

14:55 Saturation mutagenesis of disease-associated regulatory elements
Martin Kircher
University of Washington, USA

15:10 Epigenetic revertant mosaicism in congenital melanocytic naevi –
proof of concept for allele-specific silencing
Melissa Riachi
UCL Institute of Child Health, UK

15:25 Development and disease at single cell resolution
Malte Spielmann
Max Planck Institute for Molecular Genetics, Germany

16:05-16:15 Closing remarks
Programme Committee: Lisenka Vissers, Radboudumc, Netherlands

16:20 Coaches depart to Cambridge city centre via train station, and
Heathrow airport via Stansted airport