Personalised Medicine in Practice: Advances in Reproductive Science

7th and 8th March 2017

Venue: St Anne's College, Oxford

WidenLife

European Commission | Horizon 2020 European Union funding for Research & Innovation

NUFFIELD DEPARTMENT OF OBSTETRICS & GYNAECOLOGY Medical Sciences Division

St Anne's College University of Oxford

EndometriosisCaRe OXFORD Care & Research

Nuffield Department of Medicine

University of Oxford

Centre for Personalised Medicine

Two days of national and international speakers focussing on methodology development and discoveries in the field of reproductive science

Personalised Medicine in Practice: Advances in Reproductive Science

March 7th: Biomarkers & Model Systems for (Pre)Implantation

09:15 - 09:50 Registration & coffee

09:50 – 10:00 Welcome

Biomarkers in Reproduction: Extra Cellular Vesicles

10:00-10:45 Detection of Extra Cellular Vesicles – Rebecca Dragovic (Oxford)

10:45-11:30 Extra Cellular Vesicle Biomarkers in Reproductive Health – Felipe Vilella (Valencia)

Preimplantation & Screening

11:30-12:15 The evolution of preimplantation genetic diagnosis: karyomapping and beyond – Dagan Wells (Oxford)

12:15-13:00 Methods in Pre-Implantation Screening - Joris Vermeesch (Leuven)

13:00 -14:00 Lunch

Model Systems for Endometrium

14:00-14:30 Decomposing the Cellular Landscape in Endometrium – Karin Hellner (Oxford) & Merli Saare (Tartu)

14:30-15:00 The Immune Cellular Landscape in Endometrium – Jennifer Southcombe (Oxford)

15:00-15:30 Personalised Medicine in endometrial factor evaluation: transcriptomics and machine learning predictors - Patricia Díaz-Gimeno (Valencia)

15:30-15:45 Break

15:45-16:30 Animal Models in Reproductive Health – Erin Greaves (Edinburgh)

16:30-17:15 ***Ethics in Reproductive Science*** (interactive session): Prenatal Assessment of Genome and Exomes – Michael Parker (Oxford)

17:15- 18:00 Copy Number Variants in Reproductive Health – Reedik Mägi (Tartu)

19:30 Pre dinner drinks

20:00 Dinner at St Anne's College

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March 8th: Integrated Genomics in Reproductive Health

09:30 – 10:00 Arrival and Tea/ Coffee

Advances in Genomics of Reproductive Health & Disease

10:00-10:45 Genomics of Reproductive Ageing – John Perry (Cambridge)

10:45-11:30 Genomics of Miscarriage – Triin Laisk-Podar (Tartu)

11:30-12:15 Genomics of PCOS – Cecilia Lindgren (Oxford)

12:15-13:00 Genomics of Endometriosis & Comorbidities – Nilufer Rahmioglu (Oxford)

13:00 -14:00 Lunch

Integrated Genomics in Reproductive Health

14:00 -14:45 Single-cell (multi-omics) sequencing to understand the biology of cellular genetic heterogeneity in early embryo development - Thierry Voet (Leuven)

14:45-15:30 "Gene expression in human granulosa cells – a window into understanding polycystic ovary syndrome"– Stephen Franks (Imperial)

15:30-15:45 Break

15:45 -16:30 Investigation of Socio-Environmental and Genetic Influences on Reproductive Traits – Melinda Mills (Oxford)

16: 30 Close

Speakers:

Rebecca Dragovic

Rebecca Dragovic completed a BSc with first class honours (2003) at the University of Adelaide, followed by a Masters in Medical Science (2006), investigating the role of oocyte-secreted factors in regulating cumulus cell expansion. In 2007 she moved to the Nuffield Department of Obstetrics & Gynaecology, University of Oxford to take on a role as departmental flow cytometer operator. During this time, she obtained her DPhil (2011), investigating the role of extracellular vesicles (exosomes and microvesicles) in normal pregnancy and pre-eclampsia. She continued this work as a post-doctoral researcher in the same laboratory until mid-2015. Following this, she took up a position as a post-doctoral teaching fellow on the MSc Clinical Embryology course at the University of Oxford. Her research interests currently focus on roles of human follicular fluid extracellular vesicles in fertility.

Felipe Vilella Mitjana

I was graduated in Biological Sciences (2002) and Biochemistry (2004) at the University of Navarra. In 2006, I obtained my PhD in Molecular Biology at the Faculty of Medicine of the University of Lleida with the highest degree "Cum Laude". I did the first postdoctoral fellowship in the Clinical Science Centre of the Medical Research Council (MRC) in London. I made a second post-doctoral in CIPF in Valencia. In 2011, I began my career as principal investigator of the Endometrial Receptivity laboratory within the IVI Foundation. My field of work is focused on the study of endometrial receptivity and the cross-talk between the mother and the embryo during implantation. In 2014, I

obtained a Miguel Servet position issued by the Institute of Health Carlos III and became part of the Foundation for Research of the Clinical Hospital of Valencia (INCLIVA).

I have published 30 scientific works in prestigious journals such as Nature Cell Biology, Stem Cells, Endocrine Reviews, Development and Science among others, and I am a regular contributor and reviewer of international journals. I have directed 2 doctoral thesis. I have participated in over 15 international projects so far, being principal investigator in 6 of them. I have participated as invited speaker in over 40 international conferences.

Dagan Wells

Dagan Wells has been actively involved in preimplantation genetic diagnosis (PGD) and the study of human gametes and embryos for almost 25 years. He spent several years at University College London, where he accomplished the first comprehensive chromosome analysis of cells from human embryos in 1998. The following year Dagan moved to the United States and joined Reprogenetics, the world's largest provider of PGD services, initiating their highly successful single gene PGD program. Dagan later joined the faculty of Yale University Medical School, where he set-up a research laboratory, before returning to the UK in 2007. He is now an Associate Professor at the University of Oxford, based at the Nuffield Department of Obstetrics and Gynaecology. After arriving in Oxford, Dagan established Reprogenetics-UK, a laboratory offering state-of-the-art diagnostic services to IVF clinics, which has grown to become the largest provider of PGD services in the UK. Dagan's work has led to the publication of over 150 peer-review publications and in the last decade has been shortlisted for seventeen major conference prizes (ASRM and ESHRE), winning nine of them. Dagan is a Fellow of the Royal College of Pathologists and the Royal Society of Biology and currently serves on the Editorial Boards of several international journals.

Joris Vermeesch

Joris R. Vermeesch, Ph.D. Ir, is Chair of the Department of Human Genetics of the University of Leuven. He is professor Molecular Cytogenetics and genome research, faculty member of the European Genetics foundation, heading the Constitutional Cytogenetics unit of the Center of Human Genetics, and coordinating the genomics core Leuven. He was head of the genomics unit in the basic research division of Aventis CropScience.

The laboratory of molecular cytogenetics and genome research has been pioneering in array development and implementation and is currently developing methods for massive parallel sequencing applications in preimplantation, prenatal and postnatal diagnosis with a focus on structural variation detection. Second, the group is responsible for the cytogenetic diagnostic services of the Center for Human Genetics. Starting from clinical samples, the laboratory aims to understand the mechanisms underlying chromosomal instability and rearrangements. It actively developed methods for single cell CNV detection and will continue to address outstanding questions about instability using single cell genomic approaches. Third, the laboratory actively seeks to define the molecular causes of developmental, mental and behavioural disturbances. The group is partner of the SymbioSys, the systems biology center of excellence in computational biology. Joris Vermeesch has published over 250 papers with an H-index 42.

Merli Saare

Merli Saare has a background in biomedicine, and received her PhD in Medicine at the University of Tartu in 2016. Currently, she is working as a Researcher of Reproductive Medicine at the Department of Obstetrics and Gynecology, Institute of Clinical Medicine, University of Tartu and at the Competence Centre on Health Technologies, Estonia. Her research focuses on molecular profiling of endometriotic lesions and endometrium of endometriosis patients to understand the genetic and

epigenetic background of the disease. Her research interests also include different aspects of genetics of male and female infertility, and molecular basis of endometrial receptivity.

Karin Hellner

I joined the Nuffield Department of Obstetrics & Gynecology in 2011 as clinical lecturer. I trained at the Charite University Hospital in Berlin, Germany, and Oxford University Hospitals NHS Foundation Trust. I now work as Consultant Colposcopist/Gynaecologist in the Women's Center.

As a clinical academic I maintained a strong interest in research throughout my career. Prior to my clinical training I undertook my dissertational research in Neurophysiology at the Humboldt-University Berlin. I also spent 4 years as a postdoctoral research fellow at Harvard Medical School / Brigham & Women's Hospital in Boston, USA, where I worked on the molecular mechanisms of papillomavirus associated carcinogenesis.

After moving to Oxford I worked with Prof. Ahmed A. Ahmed at the Weatherall Institute of Molecular Medicine. My research focused on the role of the stem cell gene SOX2 in ovarian carcinogenesis utilizing whole-genome and targeted sequencing approaches.

In 2015, I joined the EndoCaRe team to apply my expertise in the field of endometriosis. In collaboration with the WTCHG we use single cell genomics technology to gain insights into the cellular landscape of the endometrium and dissect disease evolution in patients with endometriosis.

Jennifer Southcombe

Dr Jennifer Southcombe is a Researcher in Reproductive Science in the Nuffield Department of Obstetrics and Gynaecology, University of Oxford. She has a doctorate researching human immunology, specifically CD4-T cells and MHC class II in HIV infection, and became interested in reproductive immunology working with Prof.'s Ian Sargent and Chris Redman, studying maternal systemic inflammatory changes in pregnancy with specific focus on pre-eclampsia. In recent years she works with Dr Ingrid Granne on peri-implantation uterine immunity, and immunological events that unfold in early pregnancy. Current projects focus on endometrial immune cells and their role in fertility and recurrent miscarriage, the influence of seminal fluid extracellular vesicles on endometrial cells, and embryo factors that enhance implantation.

Patricia Diaz Gimeno

Dr. Patricia Diaz Gimeno is graduated in Biological Science focused on Genetics (2006) with Excellence Award (2007) and a Doctor in Biomedicine by the Department of Pediatrics, Obstetrics and Gynaecology at Valencia University (2011). She achieved her PhD by researching on endometrial receptivity transcriptomics signature as biomarker and its applicability to evaluate human endometrial receptivity in the clinical practice. Dr. Patricia has also worked intensively for the translation of endometrial transcriptomics as a diagnostic method. She reached a deep specialisation in high throughput technologies (microarrays and NGS) and its related functional genomics analysis after her postdoctorate at Príncipe Felipe Research Centre in the Genomics and Bioinformatics department (2011-2013).

Since 2013 she has set up the Bioinformatics Lab at FIVI and has improved the knowledge of Window Of Implantation patient stratification using transcriptomics as gold standard and machine learning predictors. In addition, she has applied a systems genomics perspective for researching the molecular basis of menstrual cycle and endometrial factor subfertilities.

Currently, Dr. Diaz-Gimeno is a Principal Investigator at IVI Foundation in Genomic and Systems Reproductive Medicine for personalizing reproductive treatments in IVI clinics. She also is a lecturer in Valencia University Master's Degrees, and a research supervisor of PhD students.

Erin Greaves

Erin Greaves obtained her PhD in 2009 in Developmental Biology from Leeds University. Erin carried out her postdoctoral training in (what was then) the MRC Human Reproductive Sciences Unit with Professor Philippa Saunders at Edinburgh University during which she developed an innovative mouse model of endometriosis. In 2014 she was awarded a prestigious MRC Career Development Award and in 2015 was appointed as a Principal Investigator at the MRC Centre for Reproductive Health, Edinburgh. Along with Philippa Saunders and Andrew Horne, Erin leads the research at EXPPECT Edinburgh, a Centre focusing on excellence in pelvic pain and endometriosis care and treatment. Erin's research focuses on the pathophysiological processes that lead to endometriosis-associated pain, with a particular focus on the role of macrophages.

Michael Parker

Professor Michael Parker is the Director of the Ethox Centre and of the newly established Wellcome Centre for Ethics, Innovation, Globalisation and Medicine. Both Centres are located in the Big Data Institute Building at the University of Oxford's Old Road Campus. Michael is also the Chair of the Genomics England Ethics Advisory Committee and one of the Directors of the 100,000 Genomes Project. His main research interest is in the ethical issues arising in the clinical and research uses of genomics. Together with partners at the Wellcome Major Overseas Programmes in Kenya, Malawi, South Africa, Thailand and Vietnam, Ethox has a Wellcome Strategic Award to build ethics capacity and conduct research on the ethical issues arising in global health research. This collaboration also has a focus on the ethics of global health research involving genomics and data-sharing.

Reedik Mägi

After defending his PhD degree in bioinformatics in 2007 at University of Tartu, dr. Reedik Mägi spent three years as a postdoctoral researcher in Wellcome Trust Centre for Human Genetics in University of Oxford as a member of the genetic and genomic epidemiology working team. In 2009, he received a European Commission's Marie Curie's Intra-European Fellowship for his research in method development for genome-wide association studies, rare-variant analysis and meta-analysis. Reedik has developed methodologies and software for the analysis of genome-wide association studies. These include GWAMA - a software tool to perform meta-analysis of whole genome association data, GRANVIL - a method to perform rare-variant analysis of binary and quantitative phenotypes, SCOPA and META-SCOPA for the analysis and aggregation of genome-wide association studies of multiple correlated phenotypes, and most recently, MR-MEGA for detecting and fine-mapping complex trait association signals via trans-ethnic meta-regression. Reedik is an active participant in several international consortia including GIANT (dealing with anthropometric traits), MAGIC (glycemic traits), DIAGRAM (type 2 diabetes) and several others. Since 2012 he has been leading the bioinformatics group in Estonian Genome Center.

John Perry

John is a Senior Investigator Scientist at the MRC Epidemiology unit, University of Cambridge. He has a research interest in understanding the aetiology of human growth and reproduction, achieved primarily using large-scale population genetics approaches. Prior to his current appointment he was a Sir Henry Wellcome fellow, holding positions at the University of Exeter Medical School, Wellcome Trust Centre for Human Genetics (University of Oxford), Department of Twin Research (Kings College London) and the Center for Statistical Genetics at the University of Michigan

Triin Laisk-Podar

Triin has a background in biology and biomedicine, and received her PhD in medicine from the University of Tartu in 2015. She now works as a researcher and lecturer at the Department of Obstetrics and Gynecology, Institute of Clinical Medicine, University of Tartu and at the Competence Centre on Health Technologies, Estonia. In parallel, she is doing a joint post-doc under the supervision of Dr. Reedik Mägi, prof. Andres Salumets and prof. Cecilia Lindgren. Her research interests include the genetics of female reproductive health and associated pathologies, endometrial receptivity and embryo implantation, and early pregnancy complications.

Cecilia Lindgren

Prof. Cecilia Lindgren is a Senior Group Leader at the Big Data Institute (BDI), Li Ka Shing Centre for Health Information and Discovery at University of Oxford. She received a Ph.D. in Molecular Genetics from Lund University and continued her career as a visiting researcher at the Whitehead Institute, MIT, USA where she trained in statistical genetics. After post-doctoral work at the Karolinska Institute, she joined the Wellcome Trust Centre for Human Genetics at Oxford University, followed by three years as a Scholar in Residence at the Broad Institute of Harvard/MIT. She has previously been awarded the “Rising Star Award” from EASD (2010), the “ASO's Obesity and Cardiovascular Health Award” (2011) and the “Leena Peltonen Prize for Excellence in Human Genetics” (2013). The last three years she has been listed amongst Thomson Reuters 100 “most highly cited researchers” in Molecular Biology and Genetics. Her research focuses on applying genomics to dissect the etiology of obesity related traits and their relationship with (female) reproductive health. She has recently also received the Khwarizmi International Award (KIA) for her work on "Dissection of the Molecular Pathogenesis of Obesity and Fat distribution".

Nilufer Rahmioglu

Nilufer Rahmioglu is a senior post-doctoral research scientist at the Wellcome Trust Centre for Human Genetics, University of Oxford. She received her PhD in genetic epidemiology from King's College London in 2011; her MSc in Environmental Health from Cyprus International Institute in association with Harvard School of Public Health in 2007; her BA in Biology with a focus on cancer biology from Clark University in 2006. Her current research focus is on investigation of the genetic and environmental risk factors of endometriosis and related conditions. She has a strong epidemiological, biological and computational background, with extensive experience in analysis of large-scale phenotypic and genotypic datasets. She is currently working on integrated analysis of RNAseq, miRNA, genotype data to understand the underlying genetic mechanisms of endometriosis in endometrium, endometrial disease tissue and subcutaneous fat. She is the co-lead post-doc in the World Endometriosis Phenome and Biobanking Harmonization Project (EPHect). She is also the lead post-doc in design and maintenance of Endometriosis Oxford (ENDOX) cohort. She has recently founded the Cyprus Women's Health Research (COHERE) Initiative with aims to understand the regional women's health and disease patterns, investigate the influence of 'Mediterranean lifestyle' and genetic factors for common women's conditions in this Eastern-Mediterranean population.

Thierry Voet

Thierry Voet holds a Master of Science in Engineering: Cell- and Gene Biotechnology from the University of Leuven (KU Leuven, Belgium), and an inter-university post-graduate in Human Genetics. He obtained a PhD from the department of Human Genetics (KU Leuven), and performed postdoctoral research within the VIB (Flemish Institute for Biotechnology) and SymBioSys – pioneering single-cell microarray analyses. Subsequently, he joined the Cancer Genome Project at the Wellcome Trust Sanger Institute (WTSI, UK) to explore next-generation sequencing technologies for single-cell genomics. Since 2011, he is an Associate Faculty member at WTSI, and a founding member of the Sanger-EBI Single-Cell Genomics Centre. Since 2014, he is also associate professor at KU Leuven. His

research focuses on (1) the development of wet-lab and computational methods for single-cell (epi)genomics and transcriptomics. (2) The application of these methods to study the biology of cellular heterogeneity, including DNA-mutational processes, in normal development and in disease.

Stephen Franks

Stephen Franks trained in Internal Medicine and Endocrinology. He is Professor of Reproductive Endocrinology at Imperial College Faculty of Medicine (University of London) and Consultant Endocrinologist at St Mary's and Hammersmith Hospitals, London. He is a former Chairman of the Society for Endocrinology (UK). He is a Fellow of the Academy of Medical Sciences and holds an honorary doctorate from the University of Uppsala, Sweden. He has both clinic and laboratory based programmes of research in the field of normal and disordered function of the hypothalamic-pituitary-ovarian axis. He has published more than 200 papers on the subject. He has a major interest in polycystic ovary syndrome, which is not only the commonest cause of anovulatory infertility but is also a major risk factor for development of type 2 diabetes. His research includes investigation of the mechanism(s) of anovulation, and of the characteristic metabolic abnormalities; it focuses particularly on the interaction between genetic and environmental factors in the aetiology of the syndrome.

Melinda Mills

Melinda Mills is the Head of the Department of Sociology, University of Oxford and Nuffield College. She works in the area of combining a social science and molecular genetic approach to the study of human fertility and socioeconomic differentials. She is the PI of the ERC SOCIOGENOME project and the ESRC NCRM SOCGEN project. Her work includes a genome-wide association study of human reproductive behaviour (e.g., Nature Genetics 2016), genes, environment and educational attainment, genetic overlap in traits, assortative mating, the impact of labour market uncertainty and schedules. She recently published a book on survival and event history analysis in R.