

**Nuffield Department of
Women's and Reproductive
Health**

D Phil Open Afternoon

WRH October 18th 2021



Experts in Women's Health



Established in 1937, we have been innovating, teaching, pioneering and evolving women's health for more than 80 years. The Nuffield Department of Women's & Reproductive Health is one of the largest and most successful academic departments in the world in its field. Led by Prof Krina Zondervan, we have over 200 members including senior academic staff, clinicians, research support staff, professional staff and graduate students carrying out research towards a higher degree.



What we do



Our department encompasses multi-disciplinary research across the full spectrum of women's health.

Our work has four overarching themes; Cancer, Global Health, Maternal & Fetal Health and Reproductive Medicine & Genetics.

We focus on genetic studies, the dissection of molecular, biochemical and cellular mechanisms underlying normal and aberrant reproductive tissue function, clinical studies in women's health and pregnancy and growth and development across the first 1000 days of life.



Where we work

Our clinical and laboratory-based research programmes are based in the Women's Centre, the Weatherall Institute of Molecular Medicine (both at the John Radcliffe Hospital, Oxford) and the Institute of Reproductive Sciences (IRS), Begbroke Science Park, Winchester House and the Big Data Institute.

The department's main offices are on level 3 of the Women's Centre (John Radcliffe Hospital, Oxford) which is responsible for the care of over 7,000 pregnant women and over 7,500 new gynaecology patients per year.



Study



We run three world class Postgraduate study programmes: MSc in Clinical Embryology (1 year residential programme) MSc by Research (2 years research degree) and DPhil (3-4 years research degree).

We also teach the fundamentals of Obstetrics & Gynaecology to clinical undergraduate students as part of their medical degree.



WRH Graduate Studies Team



Karl Morten

Principal Investigator
Director of Graduate Studies



Delphine Vanecke

HR & Graduate Studies Administrator
Delphine.Vanecke@wrh.ox.ac.uk



Skills training in NDWRH

Learning and Development

Personal Development is a key part of your graduate career. In your first term, you will complete a compulsory training needs analysis with your supervisor to monitor your progress throughout your postgraduate degree. In your first term, you will upload it with your G

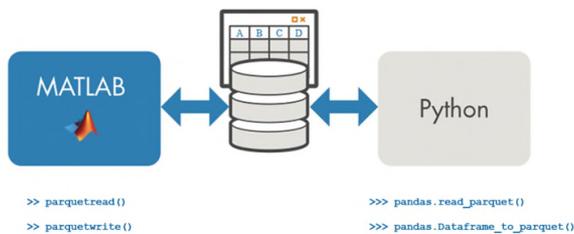
The Researcher Development Framework (RDF) is a helpful model for you to use. It describes the knowledge, behaviours and attitudes for you to think about areas in which you need to develop, and to identify what areas you're interested in developing (or are

Click on the links below for further learning and development resources.

Student Development Resources



The Hub



MATLAB training



SHARED TRAINING MANAGEMENT SOLUTION

WELCOME KARL MORTEN



Online training at the University

Medical Sciences Division Skills Training Programme

The Medical Sciences Division seeks to equip all graduate research students with a comprehensive set of transferable and research skills. The aim is to maximise each researcher's potential, enabling participants to see beyond the day-to-day demands of their own research. Students build the foundation for a successful career through communication, networking and team-building as well as through excelling in their own research area. As a guide, the Research Councils recommend that graduate students spend 10 days a year on additional skills training.

The Division's programme consists of over 60 short courses, ranging in length from just a day to 30 days, as well as luncheon seminars run on the Division's three sites (John Radcliffe Hospital, Churchill Hospital and South Parks Road). The programme supplements departmental training and provides additional networking opportunities across the Division and promoting interdisciplinary collaborations.

Students and their supervisors are strongly encouraged during their first term and throughout the course of their studies to spend time revisiting their individual training requirements, planning a training timetable and developing their CV. In addition both supervisors and students are encouraged to use the facility within GSR to record training requirements which are then fed back to the Training Officer to follow up and offer advice regarding the availability of courses and events which would fulfil their training requirements.

There are a wide range of courses offered by the MSD Skills Training Programme which cover both professional skills and personal development. Courses under Research and Study Skills cover research techniques, ethics, data analysis and statistics. The most appropriate timing for you to attend these courses will depend on the nature of your research.

There are a number of courses to assist postgraduate researchers in developing effective communication skills, including a range of Writing and Presentation Skills courses and English language courses for researchers whose first language is not English. The Division also encourages postgraduate students to be proactive in considering their career options, and runs careers workshops and seminars to provide support in this area.

Below is a suggestion for some of the courses that you should think about over the course of your graduate career:

First year	Second year	Third year
<ul style="list-style-type: none"> Avoiding Plagiarism Ethics: Introduction to Research Ethics How To Plan Your PhD Managing Your Supervisor Writing Skills for PhD Students: Reports Presentation Skills 	<ul style="list-style-type: none"> GRAD Challenge 7 secrets of highly successful research students Writing Skills Papers and Theses 	<ul style="list-style-type: none"> Organising Your Research for Publication Viva Preparation Preparation for Academic Practice Get that Job

MSD Skills Training Programme



WORLD OVARIAN CANCER DAY ON TWEETS



Public Engagement - Exploring widespread pain through visual art!



New Endometriosis podcast launched: "Unheard of"



Machine Learning and Electronic Health Records (EHR)

Research at the cross-section of population health and personalised medicine



Rahini Group



- Comprehensive longitudinal UK EHR
- Large-scale research databases

- Statistics / machine learning / deep learning

Representation Learning

Multi-modal EHR-based representation learning

Risk Prediction^{1,2}

State-of-the-art performance on heart failure and subsequent disease prediction

Multimorbidity³

Novel methods for temporal phenotyping

Uncertainty estimation⁴

Deep probabilistic modeling provisioning of uncertainty measurements

Interpretability²

Data-driven risk factor analysis and causal hypothesis generation

Causal inference⁵

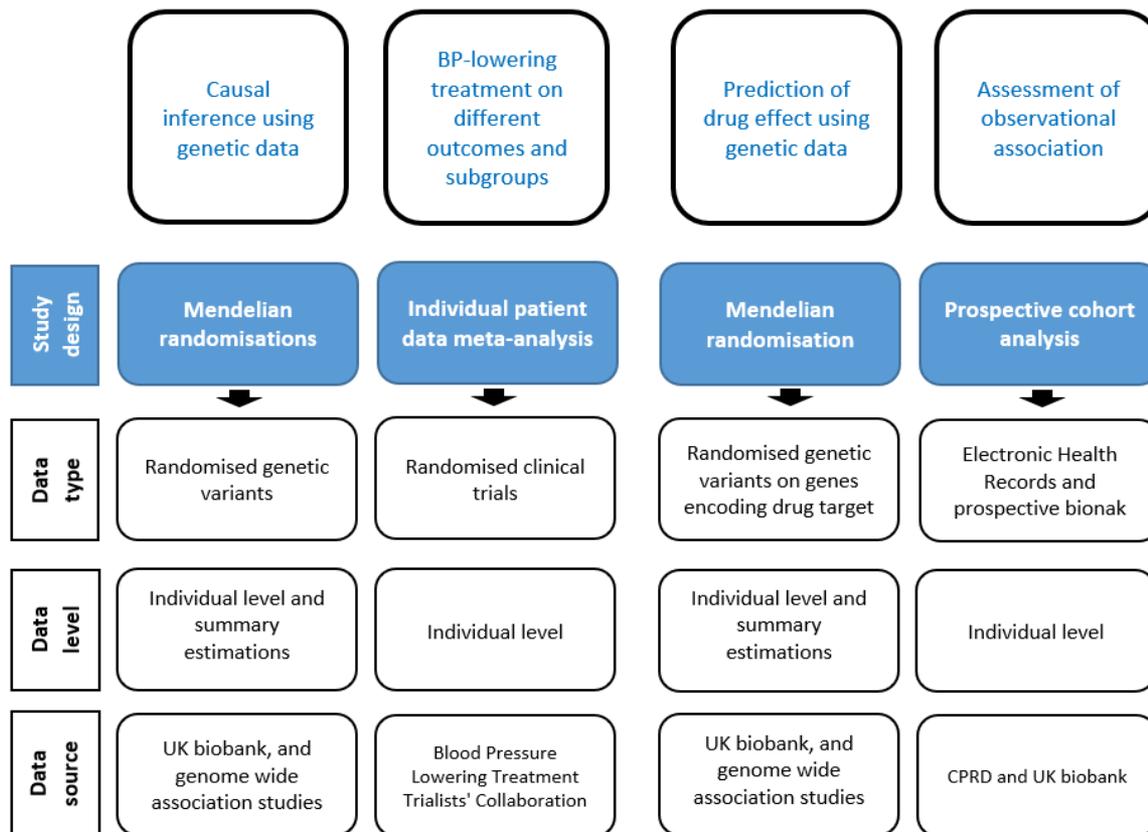
Deep learning methods for population-level causal inference

¹Li et al (2020), ²Rao et al (2020), ³Hassaine et al (2020), ⁴Li et al (2020), ⁵Rao et al (2020)



Large-scale cardiovascular epidemiology and clinical trials

Research across genetic epidemiology, large-scale prospective cohort studies, individual patient data (IPD) meta-analysis, and digital clinical trials



Conrad et al. Lancet (2018)
 BPLTTC, PLOS Medicine (2019)
 Nazarzadeh et al Eur Heart Journal (2020),
 Nazarzadeh et al JAMA Cardiology(2020)
 Rahimi et al. Heart (2020)





The Oxford Centre for Labour Monitoring

Group Lead: Antoniya Georgieva

<https://www.wrh.ox.ac.uk/research/oxfordcentreforlabourmonitoring>



MISSION

The Oxford Centre for Labour Monitoring is committed to preventing injury of babies during labour and delivery, caused by lack of oxygen in utero - rare but devastating events. Our work will potentially benefit families, clinicians and healthcare systems by reducing brain injuries, perinatal deaths and unnecessary interventions.

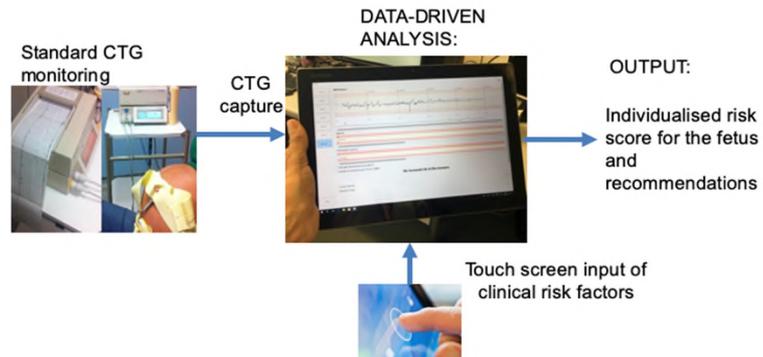
Concept & data

Routine maternity data
since 1993: 100,000
labours at term

Individual risk factors & characteristics

Data-driven risk assessment of the fetus

First research prototype



Multidisciplinary Team & Methods

Obstetrics, Midwifery & Neonatology

Artificial Intelligence & Prognostic models

Signal Processing

Software & Healthcare *App* development

Leading internationally

3rd Signal Processing and Monitoring (SPaM) in Labour Workshop

Porto, Portugal



Mission: To improve endometriosis diagnosis & treatment
 >20 PIs, postdocs, research staff, students

Computational (gen)omic studies

- Genomic discovery
- Molecular phenotyping to identify disease subtypes
- Shared genetics with comorbid traits, e.g. auto-immunity, pain, fat distribution, 'behavioural' traits

Many Oxford collaborators, e.g.:
 Big Data Institute, Wellcome Centre Human Genetics,
 NDORMS, Target Discovery Institute, Dept of Sociology



Clinical studies

- Data/sample collection
- Deep clinical phenotyping
- Pain characterisation
- Pain sensitivity and 'vulnerability'
- Functional MRI of the brain

Tissue/cellular studies

- Endometrium: functional studies
- Immune cells (macrophages) & fat tissue
- Bulk and 'single-cell' genomics
- Biomarkers

Translation: collaborations with Pharma & Diagnostics companies

e.g. Bayer-Oxford Alliance, Roche Diagnostics, MDNA, Volition

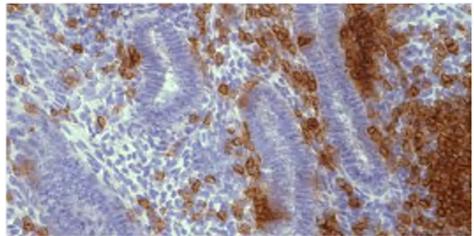
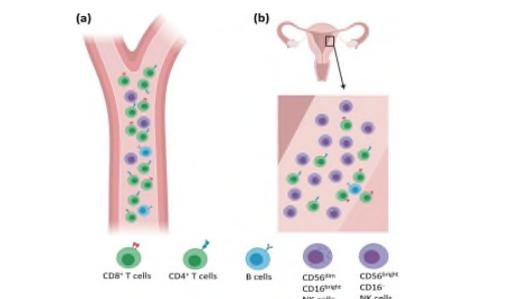
Investigating the endometrium in health and disease



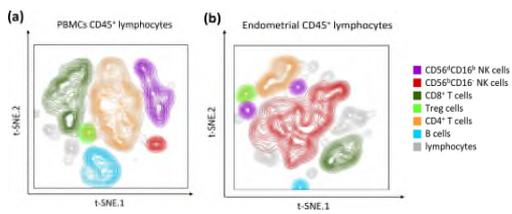
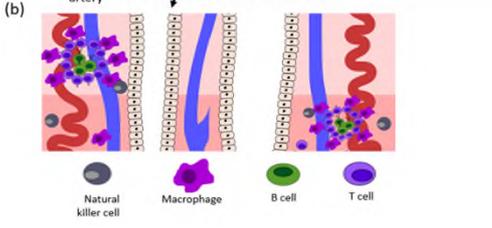
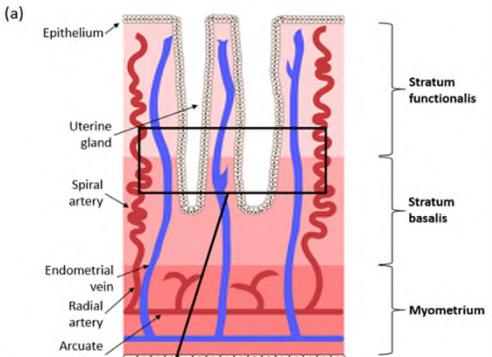
Prof. Ingrid Granne Dr. Jen Southcombe Dr. Rebecca Dragovic

The PIP Study

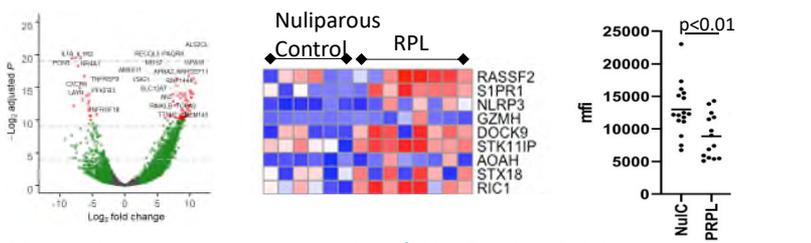
Describe blood and endometrial immune cells in women who are subfertile, have recurrent pregnancy loss or recurrent implantation failure compared to controls.



CD45+ Immune cells in the human endometrium



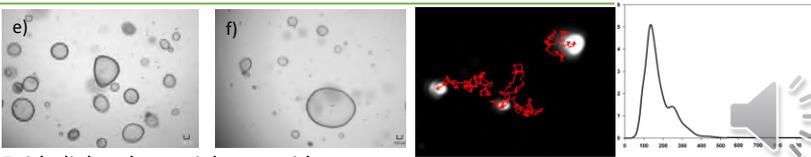
Transcriptomic immune cell analysis – B cells and Treg



[Mucosal Immunology 2021 doi:10.1038/s41385-021-00451-1](https://doi.org/10.1038/s41385-021-00451-1)
[Frontiers in Cell and Developmental Biology 2021 doi:10.3389/fcell.2021.709280](https://doi.org/10.3389/fcell.2021.709280)

New projects : Further endometrial immune cell analysis in pathology

New projects :Developing Endometrial Models to study Epithelial:Stromal:Immune cellular and extracellular vesicular interactions in pathologies.



Epithelial endometrial organoids.

Male infertility and molecular delivery systems for gametes and embryos

Coward Group [kevin.coward@wrh.ox.ac.uk]

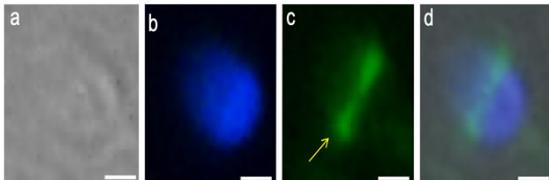


Male infertility, oocyte activation deficiency and phospholipase C zeta

At fertilization, oocytes are activated by a sperm-specific protein (PLCzeta)

PLCzeta deficiencies cause activation failure

1. Diagnostic assays (protein/mutations)
2. Recombinant protein synthesis, storage, and application (therapeutic)
3. Mechanisms controlling the expression of the PLCzeta gene
4. Interacting protein factors in the oocyte

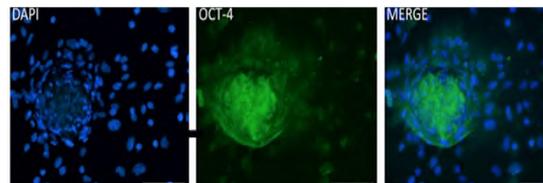


Fertility preservation for prepubertal boys with cancer

Cancer treatments can destroy the future fertility of prepubertal males. We are unable to freeze sperm from these patients.

Instead, we collect testicular biopsies prior to treatment and cryopreserve.

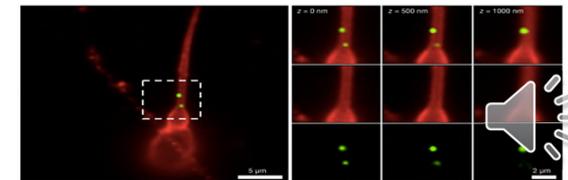
1. In vitro spermatogenesis
2. Generating 3D testicular models
3. Developing methods to test sperm functionality and ability to fertilise



Nanoparticle- and exosome-mediated delivery systems for eggs, sperm and embryos

Developing non-invasive systems to deliver molecular agents to enhance, block, label, or modify specific biopathways

1. Ability to induce functional effects
2. Diversity methodology to other cell types
3. Delivery of protectants to testicular cells prior to cancer treatment





Williams Lab

Developing ovary-focused fertility preservation techniques

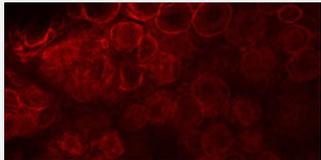


Cancer Patients

Aim: Grow human eggs from ovarian tissue in culture



Ovarian cortical strips



Developing novel imaging techniques to improve accuracy and speed

Fertoprotect

Aim: Protect the ovary from chemotherapy



Human and mouse in vitro and in vivo

Dysfunctional ovaries

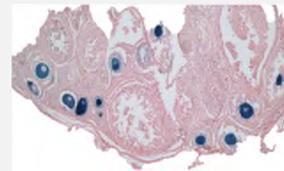
Primary Ovarian Insufficiency (POI)

Ovarian Cancer

Aim: Isolate and grow immature eggs from dysfunctional ovarian tissue



Mouse models of POI and ovarian cancer



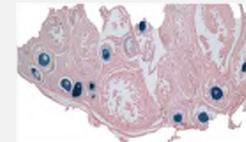
Reaggregated ovaries: blue oocytes from one mouse, somatic cells from another

Age

Aim: Determine how age affects ovarian function



Single cell RNAseq



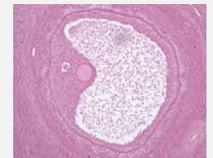
Reaggregated ovaries

Rhino Fertility Project

Aim: Grow rhino eggs from rhino ovaries



Rhino ovary



Rhino ovarian follicle

In vitro and in vivo



Studying Mitochondrial recycling

- To prevent transmission of mtDNA disease
- Important in Mitochondrial replacement therapy (“3 parent babies”)
- As a way of treating mitochondrial disease

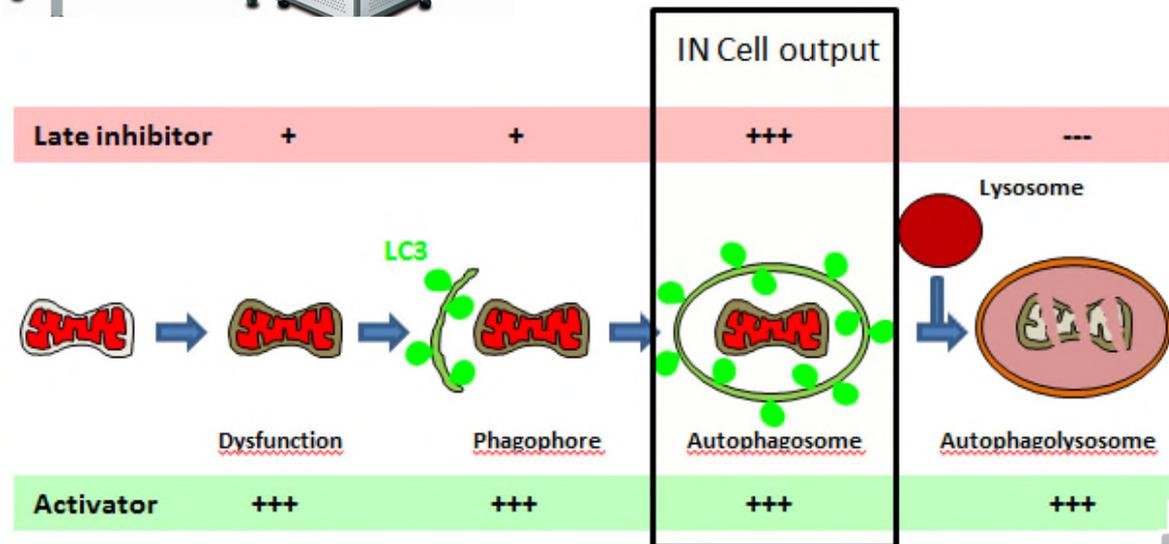
The INCell 1000 Analyser



Objective
High throughput

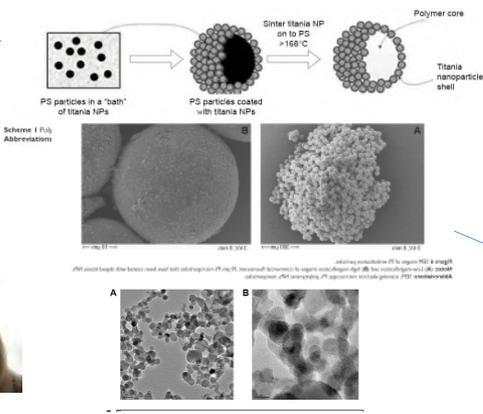


Poulton Group

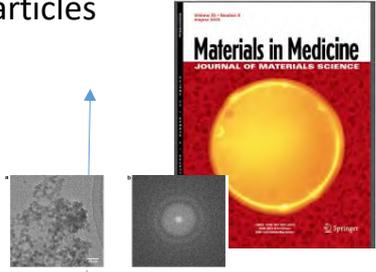


TOWNLEY LAB

Titania & Rare Earths for use as radiosensitizers



Imaging using encapsulated dyes or metals e.g. Tantalum oxide nanoparticles

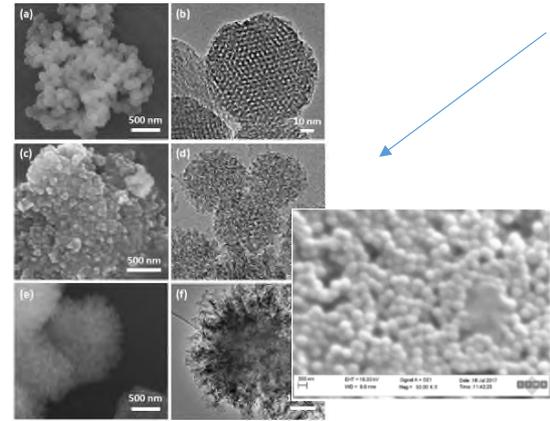


Novel anti-cancer compounds from natural sources

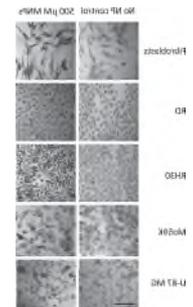


Nanoparticle technology
Find, Fight, Follow
Paediatric cancer

Bio-inspired materials e.g. silica nanoparticles, melanin

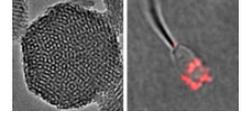


Paediatric cell lines respond differently to adult cancer cell lines



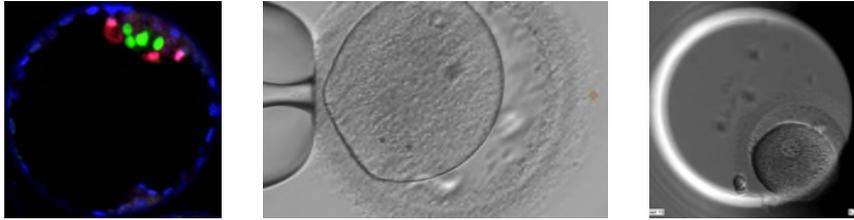
Non-oncology related projects:

- Agricultural
- Reproductive medicine
- Antimicrobial



Wells group

Genome editing – Applying CRISPR to human embryos



- Understanding function of developmental genes
- Investigating genetic stability during early development
- Evaluating potential for correction of serious disease

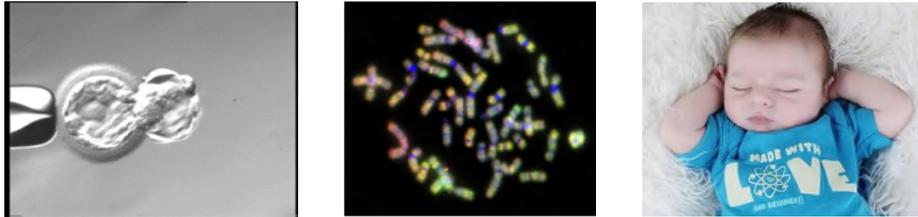
ARTICLE

nature

Genome editing reveals a role for OCT4 in human embryogenesis

Norah M. E. Fogarty¹, Afshan McCarthy¹, Kirsten E. Swijgers², Benjamin E. Powell³, Nada Kubickova⁴, Paul Blakeley¹, Rebecca Leal¹, Kay Elder⁵, Sissy E. Wamailha¹, Daesik Kim⁶, Valdone Machulyte¹, Jens Kleinjung⁷, Jin Soo Kim^{6,8}, Dagan Wells⁴, Ludovic Vallier^{2,9,10}, Alessandro Bertero^{10,1}, James M. A. Turner³ & Kathy K. Niakan¹

Technologies for preimplantation genetic diagnosis



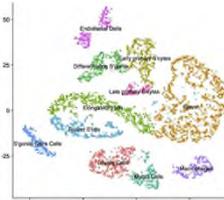
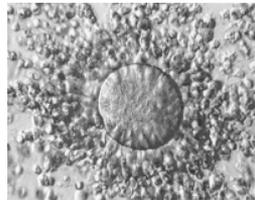
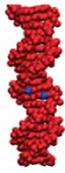
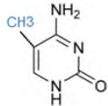
ORIGINAL ARTICLE

JMG
Journal of Medical Genetics

Clinical utilisation of a rapid low-pass whole genome sequencing technique for the diagnosis of aneuploidy in human embryos prior to implantation

Dagan Wells,¹ Kulvinder Kaur,² Jamie Grifo,³ Michael Glassner,⁴ Jenny C Taylor,² Elpida Fragouli,⁵ Santiago Munne⁶

Gamete and embryo biology



Mitochondria

Transcriptomics

Epigenetics

Non-invasive PGT

LETTER

nature

Towards clinical application of pronuclear transfer to prevent mitochondrial DNA disease

Louise A. Hyslop^{1,2}, Paul Blakeley³, Lyndsey Craven⁴, Jessica Richardson¹, Norah M. E. Fogarty³, Elpida Fragouli⁵, Mahdi Lamb¹, Sissy E. Wamailha¹, Nilendran Prathalingam^{1,2}, Qi Zhang¹, Hannah O'Keefe¹, Yuko Takeda¹, Lucia Arizzi^{1,2}, Samer Alfarawati¹, Helen A. Tuppen¹, Laura Irving¹, Dimitrios Kallous¹, Meemakshi Choudhary², Dagan Wells⁴, Alison F. Murdoch¹, Douglass M. Turnbull⁴, Kathy K. Niakan³ & Mary Herbert^{1,2}



Global maternal health and diabetes in pregnancy

PI: Prof Jane Hirst

jane.hirst@wrh.ox.ac.uk



SMART Health Pregnancy

Cluster randomised trial to improve high-risk screening during pregnancy and in the first 12 months after birth in rural India

Projects available*

mental health, health systems, implementation science

*unfunded



Digital advances in GDM

Big data to improve outcomes for women with Gestational diabetes

Projects available

iCase studentship 2022
See MSD website for details



Global Perinatal Health

Viet Nam Preterm Birth biomarker study

Maternal sepsis and AMR in Viet Nam (George Institute, OUCRU, Tu Du)

Projects available*

open to discussions



Digital Health in pregnancy

Developing a digital birth register for Malawi (Colab)

Digital health to improve care in the first 1000 days of life (George Institute, China)

Projects available*

open to discussions

Also interested in other clinical global maternal health projects, so if you have a good idea please get in touch



Next steps

- Contact a supervisor to discuss possible D Phil projects. NB: Not all D Phil projects are advertised on the WRH website.
- Application deadline 3rd Dec 2021
- Personal statement is really important this year for Oxford Scholarships
- Medical Sciences Division 356 new D Phil students per year, 35 scholarships in the competition



Interview process and offers

- Interviews will be in early January 2022 and run over 2 weeks. Interviews last 25-30 minutes with a panel of 5 people.
- WRH are looking to make around 25 offers
- We have a quota of 13 new D Phil students per year. In 2021 WRH took on 17 new D Phil students.
- To make an offer the supervisor must have the running costs in place to run the project
- The student does not need personal funding (i.e. fees and stipend) in place to be given an offer but will need to make the financial commitments to start on the D Phil programme.



Any questions?

