UNIVERSITY OF OXFORD

Nuffield Department of Women's and Reproductive Health

D Phil Open Afternoon

WRH October 18th 2021

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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.

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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.

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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.

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WRH Graduate Studies Team

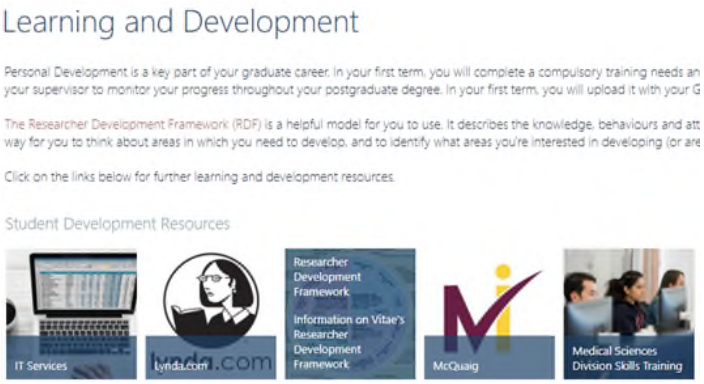
Karl Morten

Principal Investigator
Director of Graduate Studies

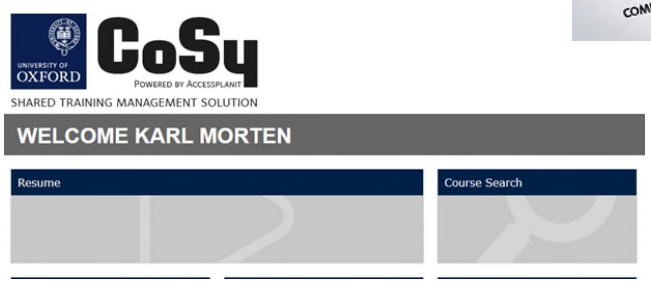
Delphine Vaneecke

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

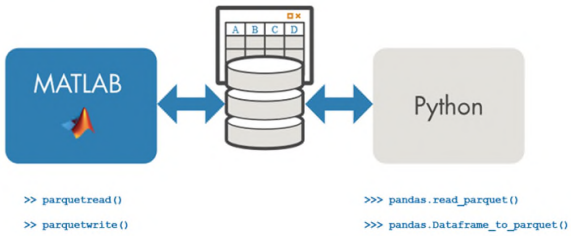
Skills training in NDWRH



The Hub



Online training at the University

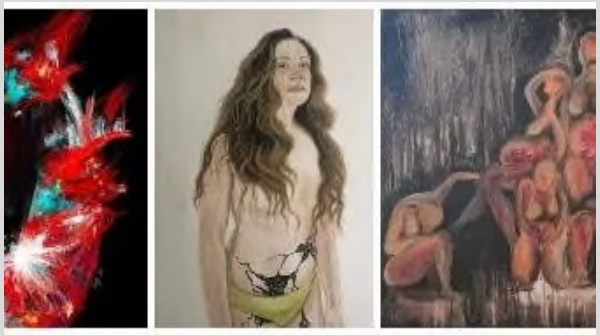


MATLAB training

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

Multimorbidity[3]
Novel methods for temporal phenotyping

Uncertainty estimation[4]
Deep probabilistic modeling provisioning of uncertainty measurements

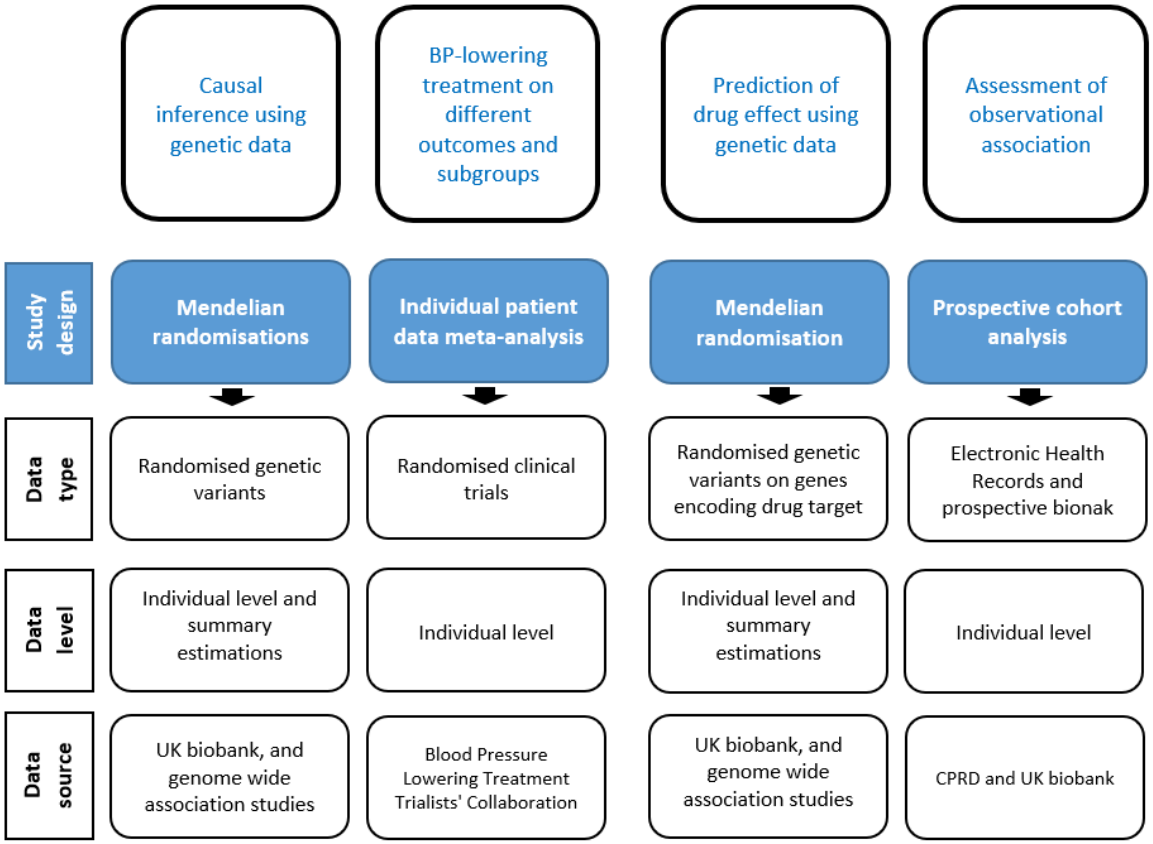
Interpretability[2]
Data-driven risk factor analysis and causal hypothesis generation

Causal inference[5]
Deep learning methods for population-level causal inference

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

BIG DATA INSTITUTE

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.

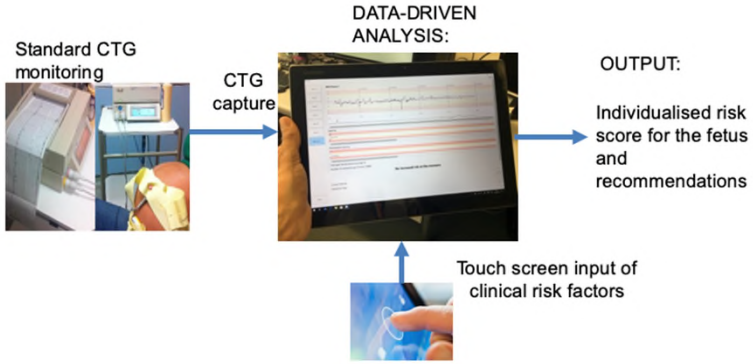
Concept & data

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

EndometriosisCaRe OXFORD Care & Research

PIs:
Prof Christian Becker & Prof Krina Zondervan (Co-Dirs)
Dr Karin Hellner
Prof Katy Vincent

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

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

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

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

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

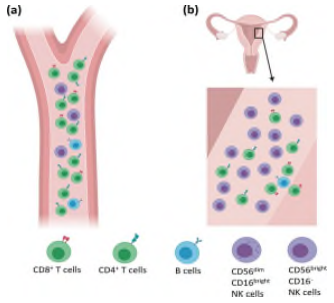
Translation: collaborations with Pharma & Diagnostics companies
e.g. Bayer-Oxford Alliance, Roche Diagnostics, MDNA, Volition

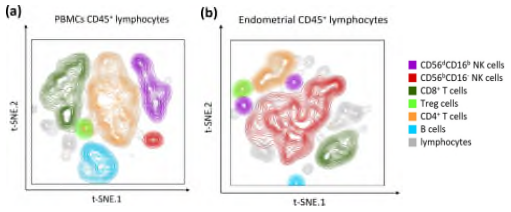
wellcome trust | MRC Medical Research Council | National Institutes of Health | World Endometriosis Research Foundation | WidenLife | European Commission | Wellbeing of Women

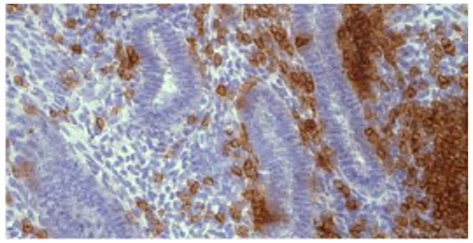
Investigating the endometrium in health and disease

The PIP Study

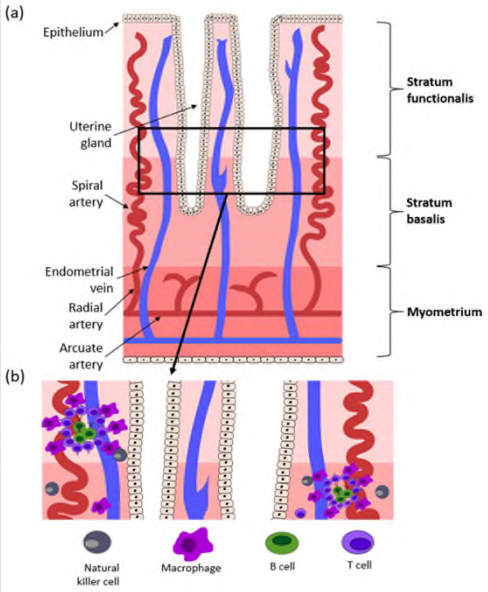
Describe blood and endometrial immune cells in women who are subfertile, have recurrent pregnancy loss or recurrent implantation failure compared to controls.





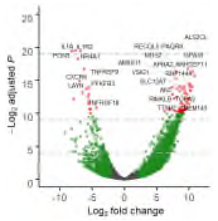


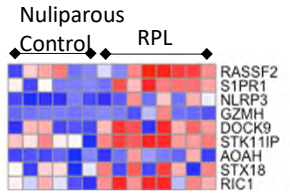
CD45+ Immune cells in the human endometrium

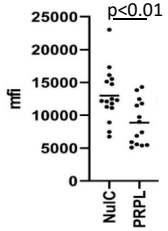


Prof.Ingrid Granne Dr. Jen Southcombe. Dr Rebecca Dragovic

Transcriptomic immune cell analysis – B cells and Treg





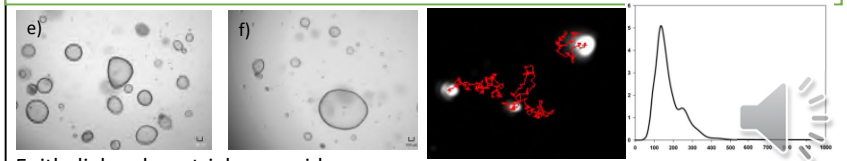


Mucosal Immunology 2021 doi:10.1038/s41385-021-00451-1

Frontiers in Cell and Developmental Biology 2021 doi: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

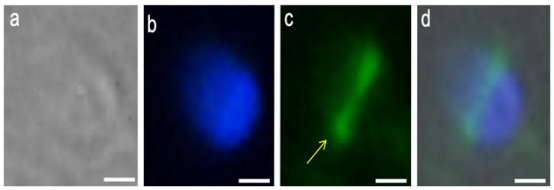
Coward Group [kevin.coward@wrh.ox.ac.uk]

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

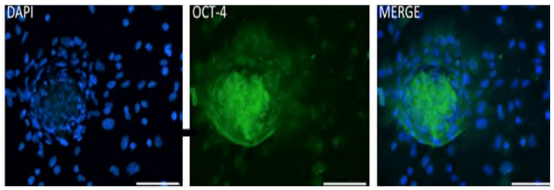


Fertility preservation for prepubertal boys with cancer

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.

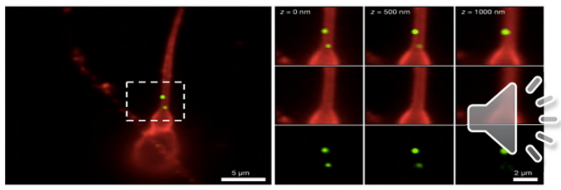
1. In vitro spermatogenesis
2. Generating 3D testicular models
3. Developing methods to test sperm functionality and ability to fertilise



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



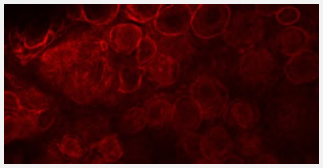
Williams Lab

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

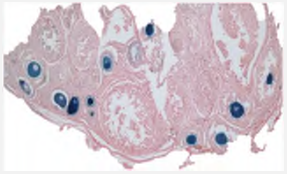
Dysfunctional ovaries

Primary Ovarian Insufficiency (POI)

Ovarian Cancer

Aim: Isolate and grow immature eggs from dysfunctional ovarian tissue

Mouse models of POI and ovarian cancer

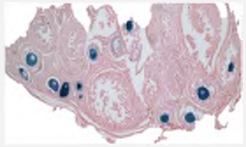


Reaggregated ovaries: blue oocytes from one mouse, somatic cells from another

Age

Aim: Determine how age affects ovarian function

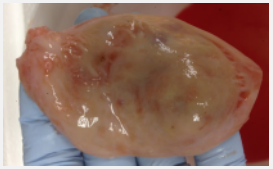
Single cell RNAseq



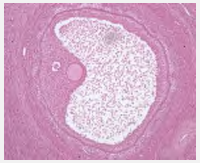
Reaggregated ovaries

Rhino Fertility Project

Aim: Grow rhino eggs from rhino ovaries



Rhino ovary



Rhino ovarian follicle

In vitro and in vivo

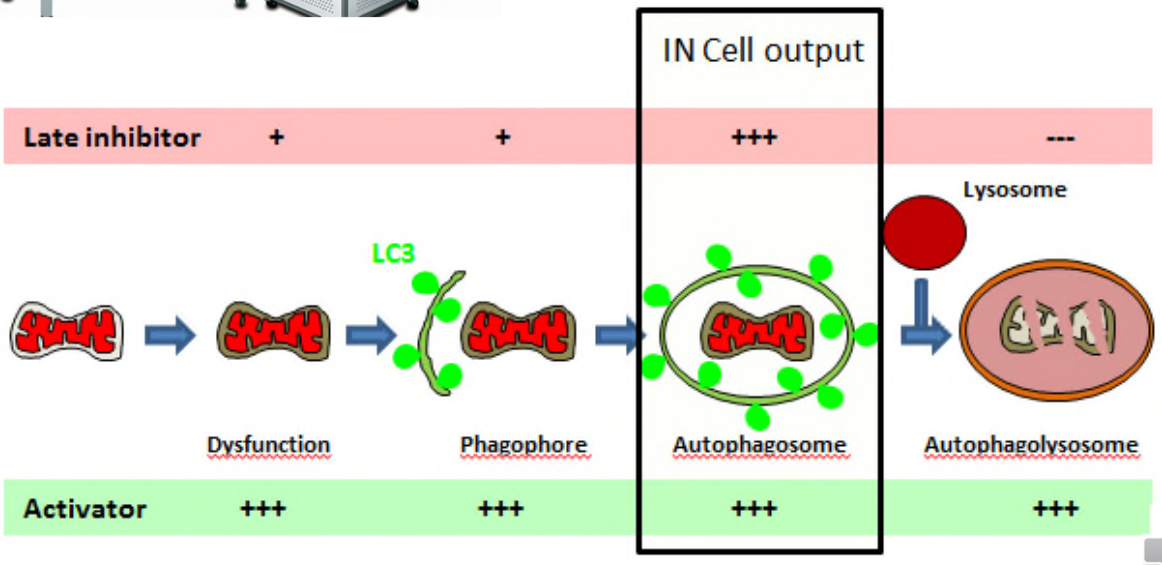
The INCell 1000 Analyser

Studying Mitochondrial recycling

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

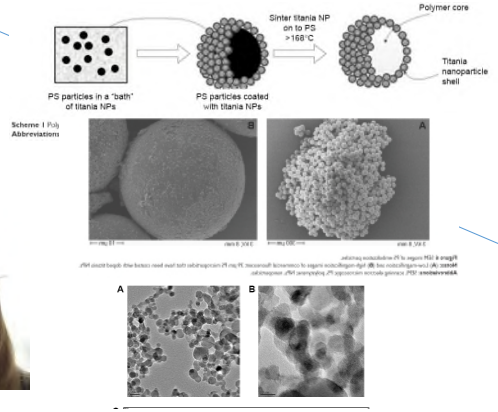
Objective
High throughput

Poulton Group

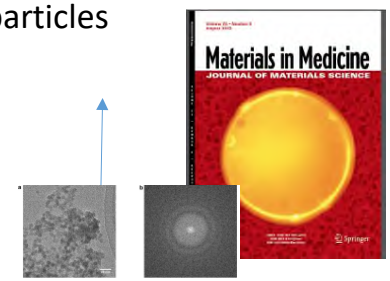


TOWNLEY LAB

Titania & Rare Earths for use as radiosensitizers



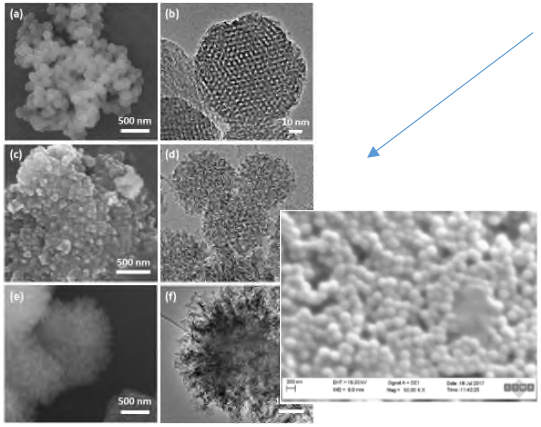
Imaging using encapsulated dyes or metals e.g. Tantalum oxide nanoparticles



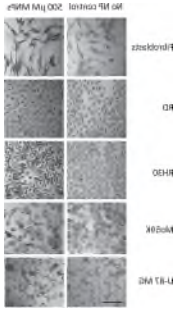
Novel anti-cancer compounds from natural sources

Nanoparticle technology
Find, Fight, Follow
Paediatric cancer

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

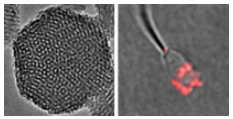


Paediatric cell lines respond differently to adult cancer cell lines



Non-oncology related projects:

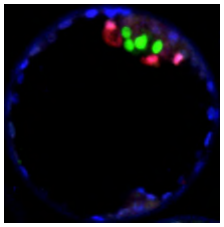
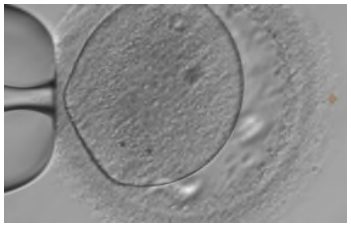
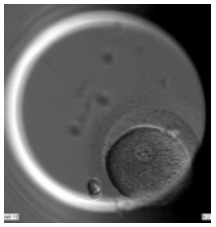
- Agricultural
- Reproductive medicine



- Antimicrobial

Wells group

Genome editing – Applying CRISPR to human embryos

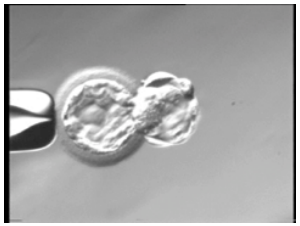
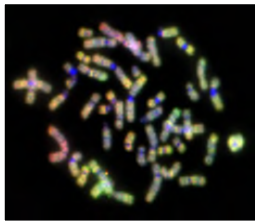
- Understanding function of developmental genes
- Investigating genetic stability during early development
- Evaluating potential for correction of serious disease

ARTICLE nature

Genome editing reveals a role for OCT4 in human embryogenesis

Norah M. E. Fogarty[1], Afshan McCarthy[1], Kirsten E. Snijders[2], Benjamin E. Powell[3], Nada Kubikova[4], Paul Blakeley[1], Rebecca Lea[1], Kay Elder[5], Sissy E. Wamaitha[1], Daesik Kim[6], Valdone Maciulyte[3], Jens Kleinjung[7], Jin-Soo Kim[6,8], Dagan Wells[4], Ludovic Vallier[2,9,10], Alessandro Bertero[10]†, James M. A. Turner[3] & Kathy K. Niakan[1]

Technologies for preimplantation genetic diagnosis

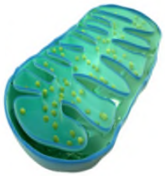
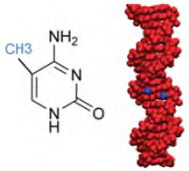



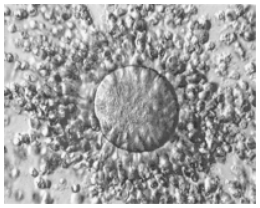
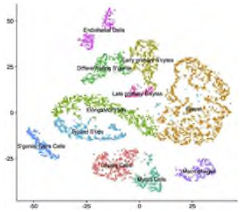
ORIGINAL ARTICLE JMG

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 Munne[6]

Gamete and embryo biology

Mitochondria Epigenetics Non-invasive PGT

Transcriptomics

LETTER nature

Towards clinical application of pronuclear transfer to prevent mitochondrial DNA disease

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Global maternal health and diabetes in pregnancy

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SMART Health Pregnancy

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

Projects available*
mental health, health systems, implementation science
**unfunded*

Sensyne Health

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

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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

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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.

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Any questions?