PI profile

## Krina Zondervan

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|  | **Prof Krina Zondervan**  **Titles**: Group Leader / PI / Professor of Reproductive and Genomic Epidemiology / Head of Dept (NDWRH)  **Location**: Wellcome Centre for Human Genetics; Oxford Endometriosis CaRe Centre  **Department**: Nuffield Department of Medicine / Nuffield Department of Women’s and Reproductive Health  **Group**: Zondervan  **Webpage**: https://www.wrh.ox.ac.uk/team/krina-zondervan  **Email**: krinaz@well.ox.ac.uk  **PA**: Rebecca Chaplin: rebecca.chaplin@wrh.ox.ac.uk |

### GMS themes:

* Genomic and –omic technologies
* Functional genomics
* Genomics of disease
* Genomic analysis (bioinformatics and statistical genetics)

### Research Overview

Our group focuses on understanding the pathogenesis of common, benign women’s health conditions with large public health impact through genomic, molecular and environmental epidemiological approaches. Current focus is on endometriosis - a common chronic inflammatory disease, causing pelvic pain and reduced fertility in an estimated 5‐10% of pre‐menopausal women (190 million worldwide) - and uterine fibroids (leiomyomata), common extra-uterine growths leading to heavy menstrual bleeding, pelvic pain, and potential pregnancy complications.

We have led the discovery of most genetic variants associated with endometriosis to date through genome‐wide association studies (e.g. Nat Genet, 2011; Nat Genet, 2012; Nat Comm. 2017, NEJM 2020). We are further expanding on this work, in collaboration with academic groups as well as industry globally, with functional ‘omics’ approaches and efforts to understand phenotypic, clinical and biological heterogeneity and translation findings to inform patient-stratified drug target and biomarker investigations.

The work involves samples donated by >1000 women recruited in our ENDOX and FENOX studies and extensive collaboration with groups part of an international data and sample collection standardisation initiative we have founded (endometriosisfoundation.org/ephect), as well as publicly available resources such as the UK Biobank. We also explore direct translation to novel drug targets through a research alliance with Bayer AG, involving scientists across a wide range of disciplines and departments in the Medical Sciences Division: the Big Data Institute, the Botnar Research Centre, Target Discovery Institute, Oxford Centre for Functional Magnetic Resonance Imaging of the Brain, Endometriosis CaRe centre/NDWRH, and Wellcome Centre for Human Genetics (http://www.medsci.ox.ac.uk/news/university‐of‐oxford‐and‐bayer‐healthcare‐join‐forces‐to‐develop‐innovativegynaecological‐treatments).

Project areas: Genetic epidemiology and AI in women’s health, integrated phenotype and omics analyses; deep phenotyping and comorbidity, GWAS, tissue RNAseq, miRNA, metabolomics, proteomics, single cell RNAseq.

We are a multi‐disciplinary, dynamic group, based both at the Wellcome Centre for Human Genetics (WCHG) and the Nuffield Department of Women’s and Reproductive Health (NDWRH), and therefore students will benefit from a strong combination of basic and clinical research environments offered. Projects would be tailored to a candidate’s preferences. They would allow extensive opportunity to gain knowledge and experience of state‐of the‐art computational, statistical, and technological methodologies for the generation and analysis of large‐scale genomic data such as genotyping microarray/sequencing, mRNAseq and miRNA, DNA methylation, metabolomics and proteomics. In NDOG, we are part of the Endometriosis CaRe centre, that focuses on the integration of clinical diagnosis, care and treatment of the disease with clinical and basic research. The group benefits from a strong network of collaborators in the fields of endometriosis, statistical genetics, genomics, bioinformatics, and functional biology locally, nationally and internationally with whom the student will collaborate

### Example project proposal (can be tailored to specific interests):

* Does endometriosis lead to an increased cardiovascular disease risk and (how) is this link genetically/biologically mediated?

Please contact directly for further information.

*These pages were reviewed/updated:* ***19 July 2021***

Project proposal (example)

# **Title**: Does endometriosis lead to an increased cardiovascular disease risk and (how) is this link genetically/biologically mediated?

Supervisors: Dr Nilufer Rahmioglu, Prof Krina Zondervan, and others

Wet/dry lab mix (approx): 100% dry lab

### Description:

Endometriosis is a common chronic inflammatory disease, causing pelvic pain and reduced fertility in an estimated 5‐10% of pre‐menopausal women (190 million worldwide). It features the presence of tissue that resembles endometrium (the lining of the uterus) outside the uterus, mainly on pelvic organs, but causes remain largely unknown. Diagnosis is often delayed for years as it requires surgery, while treatments are limited to surgery and/or hormonal drugs with many side effects. The chronic inflammatory pelvic environment present in women with endometriosis leads to the question whether the disease is associated with more systemic inflammation-association morbidity. Limited data has emerged that there is an elevated post-menopausal risk of cardiovascular disease among women diagnosed with endometriosis pre-menopausally. However, confirmation and specification of this association is required, along with investigation of the biological mechanisms through which the association may act. This project will leverage data from the UK Biobank, which contains data from more than 8,000 women diagnosed with endometriosis to investigate longitudinal cardiovascular (and potential other inflammatory) outcomes and the genetic vs. causal basis for associations. The analysis will include integrated analysis of clinical phenotypic, (gen)omic, inflammatory biomarker and other available data, as well as the analysis of publicly available data resources.

### Training Opportunities:

Training will involve genetic epidemiological research methods including (bivariate) GWAS and LD score regression, Mendelian randomisation and SMR, eQTL and integrated omics analyses, and functional pathway analyses. Opportunities to work with AI/machine learning methodology in analysing multidimensional data and link with other groups working in this methodological space. In addition to a base in WCHG, students will be part of the Oxford Endometriosis CaRe centre, that focuses on the integration of clinical diagnosis, care and treatment of the disease with clinical and basic research. The group benefits from a strong network of national and international collaborators in the fields of endometriosis, statistical genetics, genomics, bioinformatics, and functional biology. Students will be strongly encouraged to publish their work, participate and lead in outreach activities, present at international conferences, attend bi‐weekly group meetings, journal clubs, as well as departmental seminars and training courses.

### Background reading / references:

* Zondervan KT, Becker CM, Missmer SA. Endometriosis. N Engl J Med. 2020;382:1244-1256
* Gallagher CS, Mäkinen N, Harris HR, Rahmioglu N, [....] Chasman DI, Missmer SA, Zondervan KT\*, Morton CC. Genome-wide association and epidemiological analyses reveal common genetic origins between uterine leiomyomata and endometriosis. Nat Commun. 2019; 10: 4857.
* Nilufer Rahmioglu, Karina Banasik, […] Piraye Yurttas Beim, Stacey A Missmer, Grant W Montgomery, Andrew P Morris, Krina T Zondervan. Large-scale genome-wide association meta-analysis of endometriosis reveals 13 novel loci and genetically associated comorbidity with other pain conditions. BioRxiv pre-release, Aug 2018. Under review, Jul 2021.
* Zondervan KT, Becker CM, Koga K, Missmer SA, Taylor RN, Viganò P. Endometriosis. Nat Rev Dis Primers 2018 Jul 19;4(1):9