**Potential Projects in the IfWH. These projects are currently unfunded.**

**Name and contact email of Supervisor:**

**Owen R. Vaughan PhD**

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# Title of Project:

# How does metabolic disease in pregnant women affect health in their children?

**Summary of proposal** :

We want to understand how metabolic disease in mums impacts health in their children. Obesity and gestational diabetes in pregnancy increase obstetric complications and lead to childhood hypertension and obesity. We are investigating the microRNA mechanisms linking maternal obesity with changes in fetal heart and placenta development, funded by the MRC. The project will initially test whether blocking microRNA-142 prevents the adverse effects of obesity on placental and fetal cardiac development. Using a mouse model of maternal obesity combined with knockdown of microRNA-142, you will use imaging to assess placental and fetal cardiac function in mouse embryos e.g. high-resolution ultrasound, MRI, photoacoustics. You will quantify fetal tissue-specific microRNA expression then measure morphological and molecular hallmarks of development in individual fetal tissues e.g. placenta, heart and brain. You will learn skills including preclinical imaging and viral vectors. The project could evolve in several exciting directions: examining the developmental effects of tissue-specific loss of microRNA-142; exploring placenta-fetus exosome signalling; or evaluating prenatal interventions like incretin mimetics and bariatric surgery. We will have biological samples from pregnant women with diabetes and obesity for deeper, hypothesis-generating omics studies of human programming mechanisms. The project is important because it could lead to beneficial new treatments to help mothers and babies.

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# Title of Project:

# Is the placenta a remote control for fetal cardiovascular development?

**Summary of proposal**:

Fetal cardiovascular development is closely linked to placental function. The placenta secretes factors that support heart growth, and placental vascular resistance is a major determinant of haemodynamic load. This project will test the hypothesis that placental signals remotely control fetal cardiac development in response to maternal diet. The project will simultaneously measure placental function and cardiac development in mouse embryos, using advanced imaging, then manipulate gene expression using cutting-edge gene silencing. The findings will help us understand how maternal diet influences development with consequences for lifelong health. In collaboration with biomedical engineers at King’s College London, the initial goal will be to acquire computational imaging skills for analysis of high-resolution in-vivo and ex-vivo imaging of placentas and fetal organs from mice. The first scientific aim will be to simultaneously quantify placental and fetal cardiac function in pregnant mice fed an obesogenic diet, using ultrasound, MRI, microCT and/or PET imaging. Our tissue-specific genetic knock out approach will then allow us to establish the mechanistic role of placental blood flow and signalling factor trafficking on cardiac structure and function. For example, you will knockdown Rab27a or apelin specifically in the mouse placenta by transducing blastocysts with a gene silencing vector. You will then characterize development in these embryos, using the established imaging and analysis pipeline.

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# Title of Project:

# Can we use apelin to treat placental dysfunction?

**Summary of proposal**:

Apelin is a secreted peptide with beneficial cardiometabolic effects via its G-protein coupled receptor. All components of the apelin system are abundant in the placenta but their function there remains unclear. This project tests the hypothesis that the apelin system enhances fetal growth by stimulating placental nutrient transport. The project will be a collaboration with the QMUL Blizard Institute. You will assess transcriptional regulation of placental apelin using epigenomic analyses, measure its expression in human placenta, then determine its function in pregnancy using in vitro and in vivo gene silencing. The results will enhance our basic understanding of prenatal development and pave the way for pregnancy therapeutics, using apelin receptor agonists. The aims of the project could include: (1) Defining the epigenetic and transcriptional regulation of placental apelin system expression and its association with birth weight in humans. You will analyse APLN, ELA and APLNR loci using publicly available datasets, then perform epigenomic and expression analyses in chorionic villus and placenta samples. (2) Determining the effect of apelin receptor knockdown and apelin receptor agonists on nutrient uptake and metabolism in human trophoblast cells. (3) Identifying the mechanistic role of apelin system expression on placental function and fetal growth in vivo. You will use lentiviral vectors to silence APLN and/or APLNR expression specifically in the trophectoderm of mouse blastocysts then quantify fetal growth in pregnant animals.

**Name and contact email of Supervisor:**

**Dr Rajvinder Karda –** r.karda@ucl.ac.uk

**Title of Project:**

**The development of a novel gene therapy viral vector capsid to target neuronal cells or the central nervous system.**

**Summary of proposal:**

Adeno-associated viral vectors (AAV) are widely used in many pre-clinical and clinical studies for neurological disorders. However, there have been reports of liver toxicity and thromobotic microangiopathy in patients who have received AAV9-mediated gene therapy.

Thus, highlighting the need for the development of novel capsids to allow efficient delivery of the viral vector to the appropriate cells to avoid immunotoxicity. Specific neurons of the central nervous system contribute to metabolic support to nearby cells, help maintain the blood brain barrier and regulate extracellular neurotransmitters. We aim to develop a AAV capsid library to generate a specific neuronal AAV capsid, which can be applied to future pre-clinical studies for specific childhood neurological disorders.

**Requirements:** Experience of working in a wet laboratory. This project involves animal research and therefore, will require in vivo work.

**Name and contact email of Supervisor:**

**Bassel H.Al Wattar, Ewelina Rogozinska, Sophie Clarke**

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**Title of Project:**

**Lifestyle interventions to optimise health outcomes of women with PCOS.**

**Summary of proposal:**

Lifestyle interventions have long been proposed as a first line intervention to help women with PCOS manage the impact of this syndrome on their health. Women with PCOS have a well described insulin resistance and metabolic inflexibility. As such, the chosen lifestyle intervention need to be tailored to the address their pathophysiology with features to promote its longterm uptake.

The proposed project will include a series of health technology assessment studies to evaluate the efficacy, feasibility and acceptability of intermittent fasting as key lifestyle intervention to help women with PCOS optimise their health outcomes (metabolic, reproductive, and anthropometric)  including pilot clinical trials, systematic reviews and meta-analysis, Discrete choice experiments, and qualitative evaluation of patient experience.

The PhD candidate will receive mentorship from the EVIE Evidence Synthesis Research Group, the Comprehensive Clinical Trials Unit, and the Institute for Women's health and will gain advanced exposure to applied clinical research in endocrine gynaecology.

**Requirements** Good command in English language!

**Name and contact email of Supervisor:**

**Professor Judith Stephenson -** **judith.stephenson@ucl.ac.uk**

**Title of Project:**

**Use of Contraception Choices Website by Contraception Providers.**

**Summary of proposal:**

 The [contraception choices](https://www.contraceptionchoices.org/) website, which was co-designed by young women and a team of researchers at UCL Institute for Women’s Health, has proved very popular with women and, anecdotally, with contraception providers. The initial evaluation of the website focused on the experiences of young women using the website (Stephenson et al. Digital Heath 2020)1.

The current proposal seeks to evaluate use of the website with contraception providers, at both service and individual level.

The aim is to determine whether use of the website by services (e.g. by signposting women to the website before a clinic visit) or by individuals (e.g. during contraception consultations) has a positive effect on quality and effectiveness of care.

The methodology will depend on the specific research questions formulated to address this aim, but will involve qualitative methods (e.g. interviews) and quantitative methods where relevant data from contraception services data are available.

The project is suitable for clinical and non-clinical researchers.

1Stephenson J, Bailey JV, Gubijev A, et al. An interactive website for informed contraception choice: randomised evaluation of Contraception Choices. *DIGITAL HEALTH*. 2020;6. doi:[10.1177/2055207620936435](https://doi.org/10.1177/2055207620936435)