Application number/Title: 40560 - Genetic determinants of human reproductive traits

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Keywords provided by the Applicant PI to describe the research project:

endometriosis, infertility, menopause, personalised medicine, polycystic ovary syndrome, reproduction

Application Lay Summary:

Infertility is clinically defined as not achieving pregnancy after 12 months of timed-intercourse at a reproductive age. While most couples achieve pregnancy within 6 months, more than 15% are affected by infertility. Male infertility can usually be easily diagnosed by doing sperm analyses. The complexity of the female reproductive system makes the diagnosis of female infertility more difficult but reproductive conditions such as endometriosis, polycystic ovary syndrome and primary ovarian insufficiency are often identified as the cause of female infertility. In 20% of infertile couples, the cause of the infertility remains unknown.

In both male and female infertility, an important subset of cases could be due to a type of infertility in which both environmental and genetic factors are involved, making the odds of pregnancy lower but not impossible and hence increasing time to conception and/or requiring fertility treatment.

To better understand the pathophysiology of reproductive conditions such as endometriosis, polycystic ovary syndrome, early menopause, miscarriage and infertility, we aim to identify and characterize new variants and genes associated with reproductive phenotypes. We will use the participants survey responses, diagnosis codes, procedure codes and prescription history to ascertain participants case/control status for disease phenotypes. We will first attempt to replicate novel associations between genetic variants and endometriosis, polycystic ovary syndrome and infertility. Second, we will perform genome-wide association studies on age of menopause, age at menarche, number of children,

number of miscarriages, endometriosis, polycystic ovary syndrome, early menopause, nulliparity and twinning. We will also perform gene-based rare variant analysis where we will test for each gene if carrying rare variants predicted to affect the function of the gene is associated with reproductive traits. Finally, we will characterize the variants and genes identified as associated with reproductive traits by performing phenome-wide association studies to test if these genetic variants are also associated with other diseases.

The identification of new variants and/or genes involved in reproductive conditions would provide a better understanding of the biology processes of those diseases and help to identify new targets for treatment. It could also lead to the identification of infertility subtypes, which could result in more personalized treatment of infertility, improving treatment outcomes.