Project summary

Describe the aims and objectives of the project.

This project aims to understand the physiological mechanisms associated with superovulation and the establishment of pregnancy. Given that these are conserved across species, the results of this project will be of
both clinical and veterinary value. Since the establishment of pregnancy is a rate limiting step associated with many experimental procedures (e.g. the breeding of specific experimental models of human disease), this project will also allow us to improve the methods used to achieve pregnancy and reduce both the numbers of animals used overall but also the severity of the procedures that they are subjected to.

**What are the potential benefits that will derive from this project?**

There are several potential benefits to this research:

(i) For humans: this will highlight the mechanisms associated with superovulation and the establishment of early pregnancy and highlight novel potential interventions for the management of infertility, recurrent miscarriage and preterm labour.

(ii) For animals: the methods developed and optimised as part of this project aim to streamline many laboratory protocols with a view to replacing the use of vasectomised males and reducing the number of females overall in research programmes which use rodents as models (mice and rats). Moreover, it is expected that those that are still used will have refined, milder and less-invasive measures used for establishing pregnancy. This could benefit hundreds of thousands of animals worldwide per year as well as potentially having translational benefits for the farming industry in the longer term.

**What types and approximate numbers of animals will you use over the course of this project?**

**Mice:** 5,300 animals.

**Rats:** 900 animals.

Over 5 years.

**What are the expected adverse effects and endpoints for animals used in this project?**

The adverse effects to these well-established procedures are minimal and the novel ones being developed will present a reduction in severity. The animals will be humanely euthanized at the end of each experiment. Pups generated from experimental females will be used in further experiments wherever possible in order to minimise the numbers of animals used overall.

**Replacement**

**Why can't your project use non-animal alternatives?**

The mechanisms associated with the establishment of pregnancy are highly complex and systemic such that they cannot be studied in alternatives (e.g. cells/organs).

**Reduction**

**How will you ensure that the number of animals used will be kept to a minimum?**

The number of animals will be reduced in two ways: (i) by careful experimental planning with support from a statistician in order to minimise wastage and (ii) by improving existing experimental protocols used for achieving a pregnancy after embryo transfer.

**Refinement**
Why are your choices of animal, model, and method the most refined?

The mouse is used as a model for other rodents as it is the least sentient species, yet remains a representative and useful model. Welfare costs will be reduced by using less invasive procedures (e.g. pessaries instead on injections) as well as ensuring that any animal used in an experimental procedure (none of which are more than moderate severity) is regularly monitored and receives pain control if appropriate. Animals will also be housed in social groups where they can exhibit normal behaviour.