Home Office

NON-TECHNICAL SUMMARY

Neural regulation of fertility

Project duration

5 years 0 months

Project purpose

- (a) Basic research
- (b) Translational or applied research with one of the following aims:
  - (i) Avoidance, prevention, diagnosis or treatment of disease, ill-health or abnormality, or their effects, in man, animals or plants.

Key words

Fertility, Brain

Retrospective assessment

The Secretary of State has determined that a retrospective assessment of this licence is not required.

Objectives and benefits

Description of the project's objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.

What's the aim of this project?

Up to one quarter of human couples suffer from infertility and require medical help to have children. For most of these couples, the reason they are unable to have children is not known.

The project aims to understand how a specific group of brain cells work together to control fertility. These cells regulate hormone levels in the blood that then control the activity of the ovary and testis.

Previous research in animals and humans suggest that a population of brain cells making a chemical called “kisspeptin” are important for fertility. The studies undertaken in this project aim to determine exactly how two different groups of kisspeptin cells work to control hormone levels necessary for fertility in both male and female mice.

Potential benefits likely to derive from the project, for example how science might be advanced or how humans, animals or the environment might benefit - these could be short-term benefits within the duration of the project or long-term benefits that accrue after the project has finished.

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

The studies in this project are expected to give us a better understanding of how kisspeptin cells in the brain function to control fertility. This information is essential for us to understand how the brain may go wrong when individuals are infertile. The immediate benefit will be increased knowledge of how the brain works to control fertility. Longer-term benefits will be opportunities for making new treatments for controlling fertility in humans.

Species and numbers of animals expected to be used

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

The project will use adult mice, including genetically-modified animals.
We expect to use approximately 8,000 animals over five years for breeding and up to 1,850 for experiments.

Predicted harms

Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.

In the context of what you propose to do to the animals, what are the expected adverse effects and the likely/expected level of severity? What will happen to the animals at the end?

Most of the animals used in this project will be used for breeding and experience no adverse effects.

The next biggest group of animals will receive minor, non-harmful manipulations such as monitoring reproductive cycles (by examining vaginal secretions) and hormone levels (by blood sampling from the tail tip) and being given minor stresses such as being held still for periods of time. These manipulations have no long-lasting effect on the normal behaviour of the animals. Some animals in this group will have surgery to remove their ovaries or testes under anaesthesia followed by injections or implants of sex hormones.

A smaller group of animals will have surgery under anaesthesia involving the placement of thin fibres into the brain with full recovery. These surgeries last 1-2 hours and require small holes to be drilled in the skull to allow very thin fibres (less than 0.5 mm in diameter) and microinfusion tubes to be placed into specific brain areas before everything is sealed. Pain relief medicine is given to all mice undergoing surgery. The fibers allow the activity of brain cells to be monitored while the tubes allow neurochemicals to be given into the brain of awake mice housed by themselves in their normal home conditions. The smallest group of mice in addition have a tiny camera placed on their head for short periods of time to monitor cell activity in great detail. Although complications to such surgery are rare, the animals will be followed closely for signs of ill health, and if such complications were to occur and could not be promptly remedied, the animals would be humanely killed and their tissues collected for analysis.

All animals will be humanely killed at the end of the experiment.

Replacement

State why you need to use animals and why you cannot use non-animal alternatives.

Animals are necessary for these experiments as we want to understand how the kisspeptin brain cells work to control hormone levels and fertility in living animals. It is not ethically justified to use humans for these studies. Also, no computer model is currently available that can mirror the complexity of brain function or hormone control in the living animal. Previous attempts to use cell cultures to investigate how the brain controls fertility have failed but further developments in computer modelling and special culture conditions may hold promise.

Reduction

Explain how you will assure the use of minimum numbers of animals.

We will ensure that the minimum number of animals will be used by making sure that we are using the best experimental design and statistical methods.

Wherever possible, we do experiments on cell lines or brain sections in dishes to reduce the number of experiments to be undertaken on animals.

Refinement

Explain the choice of species and why the animal model(s) you will use are the most refined, having regard to the objectives. Explain the general measures you will take to minimise welfare costs (harms) to the animals.

Mice are an excellent model to study how the brain controls fertility. The hormonal regulation of fertility appears to be similar between mice and humans but it is not understood how this actually works in any

species. Working with mice also allows us to build upon research carried out over the last 40 years. Importantly, studies on kisspeptin brain cells can only realistically be done in genetically-modified mice as this allows their DNA to be manipulated to enable the kisspeptin cells to be seen and modified.

Most experimental animals receive minor procedures such as monitoring of reproductive cycles and blood sampling before being anaesthetised and humanely killed.

For animal experiments requiring surgery, all surgeries are undertaken with great care to avoid infection and complications such as prolonged bleeding and are followed by post-operative monitoring by scientists and animal technicians and given pain relief as recommended by the vet. These mice are accustomed to humans by regular handling with results being collected from mice living in their normal enriched home environment going about their daily activities.