Home Office

NON-TECHNICAL SUMMARY

Mechanisms controlling cell division, fate and differentiation in the frog embryo

Project duration

5 years 0 months

Project purpose

- (a) Basic research

Key words

Frog, Cell division, Development, Specialisation

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?

Studying how cells know what type of cell to become as embryos develop will help us define the rules that normal cells use when adopting a specific fate like nerve and muscle. When we understand those rules, we should be able to alter genes and proteins to allow cells to change their fate so we can make

new cells more easily for regenerative therapies for diseases where specific cell types are lost such as Parkinsons disease, a disease where special nerves are lost that results in problems with movement, and Type 1 diabetes where the ability to control blood sugar levels is lost. We may also be able to use this knowledge to correct some of the problems of cells failing to maintain normal function, for instance in some cancerous tissues

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?

We are likely to gain important new knowledge about the genes and proteins that are required for cells of the embryo to adopt specific fates including, among others, nerve cells and muscle cells. We are likely to be able to develop better methods to turn one cell type into another.

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?

We expect to use around 500 frogs over a 5 year period

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?

The procedure (injecting hormones, chemicals that usually travel about the body and stimulates fertility, to make the frogs lay eggs) is very mild as we inject just under the skin and frogs have very few nerve endings here. Egg laying is natural and does not cause discomfort. Frogs can be taken through another egg laying cycle by hormone injection after at least a 3 month rest, mimicking the normal reproductive cycle of this South African frog in the wild.
In the vast majority of cases we expect no adverse effects from injecting the female frogs with hormones. However, in 1-2% of cases were we inject hormones, we may see some bloating and lethargy of the frogs due to egg retention in the body cavity. If this doesn't resolve and animals are showing signs of recovery, or the animal's condition deteriorates, the animal will by killed. Sometimes we gently massage the edges of the frog's abdomen to help her expel her eggs, mimicking the massaging normally carried out by the male frog during natural mating. In less than 1% of cases the frog may struggle, which has the potential for causing minor scratches or injuries. These will heal quickly due to the strong antibiotic properties of frog skin. The animals will be killed in the unlikely case of significant abrasions or if they show any signs of distress or injury.

Replacement

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

We are looking at what happens in development in lots of different tissues in the embryos and how those tissues interact with each other so we can't replace embryos with cells growing in a dish.

Reduction

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

Frogs are reused after inducing egg laying, which is standard practise in frog labs all over the world as frogs overwhelmingly exhibit no adverse effects from this procedure. This keeps the numbers of animals we need to a minimum.

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.

Frogs lay lots of eggs that develop outside the mother and are readily available for experimentation. It is the eggs and the embryos that develop from them that we use for our experiments. Using frogs, which share very many of the same mechanisms of control as mammalian embryos, means we can gain valuable scientific understanding of these important processes while our results are still applicable to humans. When not laying eggs, the animals will be housed together in tanks that are specially designed for aquatic animal housing and have cleaned water with appropriate salts to keep the frogs healthy. In our experience, frogs we use for laying eggs can live many healthy years in the lab and indeed, they live considerably longer than the estimated life-span in the wild. We do not observe any suffering on hormone injection; frog skin is known to have very few nerves so it is unlikely that they feel more than mild discomfort even at the time of injection.