Home Office

NON-TECHNICAL SUMMARY

The study of epithelial cancer genes

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

Breast, Lung, Cancer, Targeted therapy

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?

We aim to identify the genes responsible for the development of different types of breast cancer and lung cancer.

In particular, the research will focus on an aggressive form of breast cancer which has a high possibility of spreading to other tissues, and patients with this cancer have low rates of survival. Identifying genes that are responsible for the development of breast cancer is essential for the development of treatments in the future.

We will also be studying lung cancer. Nearly 45,000 new cases of lung cancer are diagnosed annually and nearly 35,000 people die from the disease in the UK every year. Broadly speaking there are two major types of lung cancer - small cell lung cancer (12% of cases) and non-small cell lung cancer (NSCLC) (88% of cases). There is an urgent need for the development of more effective treatments for NSCLC as currently only 16% of patients survive for 5 years or more after their initial diagnoses. To improve that, a better understanding of how the various types of lung cancer develop is required.

We will carry out genetic analysis to identify and characterise key factors that drive the development of breast and lung cancers in the hope that, in the future, this knowledge may help in the development of new treatments.

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?

Results from this project could have an impact on the 100,000 breast and lung cancer patients diagnosed every year in the UK.

Our study aims to:

1) Increase the understanding of how types of breast and lung cancers develop;
2) Identify new biological ‘markers’ to enable better cancer diagnosis.

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?

Mouse – 43,180 over 5 years. Out of this number, 20,000 mice will be used for breeding and maintenance of genetically altered animals. 22,000 will be used for breast and lung cancer studies.

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?

[Amended 15 03 19] Under this licence we propose to study the role of candidate genes in driving breast and lung cancers. To achieve this we will use different methods to induce tumours in mice:
1) we will breed and use genetically modified mice carrying mutations found in humans that are known to increase the susceptibility to cancer;
2) we will use chemicals (delivered orally or via injection) to induce tumour development and;
3) in some cases, we will grow human cancer cells in mice, and;
4) in some cases, we will surgically transplant modified breast cells into the cleared breast tissue (Fatpad) of mice to test the effect of the certain genetic mutations on cancer development.
We will also use these different mouse models of cancer to assess the effect of certain drugs on tumour growth. We expect the majority of the animals will have mild adverse effects from our work, indeed about half will only be used for breeding and maintenance of genetically altered animals and not subject to any intervention. For some animals, a moderate severity limit is expected, particularly if the animals develop tumours. Animals that will undergo surgery are expected to recover from the procedure with minimal complications. All surgical procedures will be performed under aseptic conditions therefore, reducing chances of contamination and complications.] However, we have protocols and humane end-points in place to minimise suffering in these animals, and will not allow any animal to suffer more than a moderate level of pain, suffering, distress or lasting harm. Animals expected to develop tumours will be constantly and carefully monitored for any signs of ill health or distress, and no tumour will be allowed to grow beyond 1.2cm2. We expect all tumour bearing mice to exhibit no more than moderate severity levels of distress.

Replacement

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

Cancer is a complex disease that develops in intact tissues. It is necessary to have a realistic model, which is amenable to genetic, and biochemical studies whilst maintaining the tissue architecture. The mouse allows us to perform detailed genetic and biochemical studies whilst maintaining the 3D organisation and normal physiological environment of tumours in the body. We will aim to use human cell lines in culture dishes in the laboratory, whenever possible, to perform some of our studies.

Reduction

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

We will restrict our analysis of genes using mice to those showing potential clinical relevance in large patient datasets.

1) We will use the latest gene editing technology (called CRISPR/Cas9) to perform our experiments which will allow us to reduce the number of animals needed to generate a genetically modified mouse.

2) When possible we will perform pilot studies on human cell lines in the laboratory before moving on to animal experiments.

3) Statisticians have been consulted on experimental design to minimise the number of animals used whilst still obtaining meaningful results.

[Amended 15 03 19: 4) When possible and experimentally appropriate to do so, mice from the core colonies which have not been genetically modified will be used as controls for genetically altered animals. This will mean that we do not need to breed extra mice to use as controls.]

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.

The mouse provides a good model for various human diseases. The genetic and physiological similarities between human and mouse are significant thus the mouse provides a good model to study cancer biology.

We constantly review our surgical procedures to minimize the impact on animal welfare. We have recently changed how we carry out the surgical procedures in this study which will reduce the chances of post-surgical complications and also reduce the amount of time an animal is under general anaesthesia.

We use pain-killers to minimise any discomfort the animals might feel after surgery.

For all tumour experiments no animals will be allowed to suffer unnecessarily. No animal will be allowed to suffer from ulcerated tumours or any effects on movement, vision, eating, excreting or breathing. All animals will be monitored closely for signs of deteriorating health or suffering.

At present, for our surgical procedures, we make a cut in the skin in the shape of a letter ‘T’, but we are currently trying out the use of a single straight cut to see if that minimises scar tissue formation.

We use tissue from ear-clips which are taken for routine animal identification purposes to obtain the DNA we need to carry out genetic analysis. This means that we do not need to take any additional samples, such as from the tail, in order to get samples to carry out genetic analysis.

In addition, the animals will be housed in a facility, which is equipped with world-class equipment, and highly trained staff that regard animal welfare as a priority. The life of every mouse, including its health status, is captured in a bespoke database.