Home Office

NON-TECHNICAL SUMMARY

Understanding persistence and pathology in RNA viral infections

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

Pathogenesis, Virus, Coinfection, Ageing, Integration

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?

One large group of viruses have smaller genomes that are highly variable in nature. Our aim is to understand how these types of viruses are able to stay within cells in the body and cause disease. These types of viruses appear to have multiple ways of hiding from the body's immune system while provoking a response that damages the organs they are in. Examples in humans include the HIV virus and the Hepatitis C virus. These types of viruses are especially important in people who have weakened or improperly functioning immune systems. We now know that highly variable viruses that cause sudden infections in healthy adults can stay hidden in the bodies of newborn or elderly humans or animals. Even the Ebola virus has been found to persist within the body of people who have survived Ebola virus disease. However, the pathways that these viruses affect are not fully known. Because these virus infections affect the immune system they also allow other infections such as a second bacterial infection (so called coinfections) to occur. By allowing these infections to occur, not only does chronic disease develop, but there is also an increased chance for the virus gene to become part of the host genome. If this happens there can be long term negative effects for human health, such as the persistence and recurrence of infection. This research aims to understand how this happens so that it can be prevented.

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?

By understanding the pathways by which this group of viruses cause disease, we may target the damaging responses in ways that can be used as new therapeutic strategies eg specific drugs that block these damaging pathways may be developed. This will help increase healthy ageing and prolong disease free lifestyles in the UK increasingly ageing population.

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?

Mice, all ages
8600 over 5 years

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?

Animals will be infected to study the way in which viruses cause disease. A variety of routes and virus strains may be used that can cause either acute or chronic infection. Animals may develop disease (adverse effects) such as weight loss, ruffled coats, lack of movement. They may show diarrhoea and

some difficulty breathing. Animals may be coinfected with eg parasites to investigate the effect of the virus infection itself and the presence of pre-existing conditions or coinfections. Animals may receive injections of substances that alter the immune system or the microbiome by standard routes such as orally, intramuscularly, or intraperitoneally as well as by more invasive methods eg into the brain of young mouse pups (under anaesthesia).
Animals involved in breeding may undergo surgery eg vasectomy or implantation of embryos. Animals are given anaesthetics and pain relief for surgical procedures.
Older animals may be used to investigate the effect of age on infection and disease susceptibility. However at all times animals will be closely monitored and adverse effects arising related to either age or study effects are taken into account in determining the humane endpoint of the study concerned. All animals are humanely killed at end of study and their tissues, blood, spleen etc used for further analyses.

Replacement

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

The complexity of the interaction between the virus and the immune system cannot be recreated in non protected animal alternatives which do not have living tissue. Whenever possible we will use cells or organs generated from living tissues and cells in a lab setting to answer some of our scientific questions before commencing work in animals

This, in some instances, can provide information to help reduce the number of animals used and to refine the methods to become less harmful.

Reduction

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

Experiments will be carried out in group sizes that are calculated from previous or published data providing solid statistics. Groups will be arranged such that controls can be compared to multiple groups and experimental groups can be compared to each other. This improves the experimental design and also decreases the numbers of animals needed overall in the project.

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 excellent models that reproduce disease uniformly and consistently,thus minimising the likelihood of repeat experiments. Mouse genetic (DNA)make up can be altered such that very specific areas can be changed and this enables study of particular mechanisms involved in disease processes

and immune responses to be studied in greater detail than would otherwise be possible. To aid in the delivery of the experimental work with the minimum adverse effects for animals concerned, animals are carefully monitored for clinical signs of infection and clearly defined humane endpoints applied. Pilot experiments with small group sizes will be carried out when entering new areas of research so that any unexpected adverse effects can be detected and characterised in smaller numbers of mice before deciding whether to move onto a full study with greater numbers of animals.This approach can also lead to an overall reduction in animal numbers based on data from pilot study outcomes.