Private & confidential: *Please be aware that the contents of this form may be made public resulting from the "Freedom of information Act". Personal details will not be released.*

G: NON-TECHNICAL SUMMARY (NTS)

Please attach the Non-technical Summary as generated by your application in ASPeL.

Describe the aims and objectives of the project (e.g. the scientific unknowns or scientific/clinical needs being addressed):

Infections by large parasitic worms, particularly those that live in the intestine are extremely common, but often under appreciated. Approaching two billion people are currently infected with at least one type of parasitic worm and these infections have been classified as Great Neglected Tropical Diseases by the World Health Organisation. The most heavily infected individuals that suffer most disease are young children, often from the poorest communities.

Farm and domestic animals are also naturally and extensively infected with worm parasites and without repeated treatment with deworming drugs suffer ill health and poor growth. In animals, drug resistance is high so that in some parts of the world no effective treatments remain and indeed, drug resistance is now developing in humans. No vaccines are available against these infections in humans and few for animals of veterinary importance. New therapies and approaches are urgently required to help control these infections.

In order to develop these, Aim One of the project is to generate a much greater understanding of how worm parasites interact with man and animals, especially how they can survive attack by our body's defence system, the immune system. This will enable us to identify key aspects of the immune response that may be defective and those that need to be enhanced to help clear the parasites from the body.

Aim Two of the project aims to identify particular ways that we can enhance our immune response to worm parasites and what molecules of the parasite we must target to achieve this.

Our work has already identified some of the most important components of the interactions between parasites and the immune system and shown that they operate in a similar way in animal models as in human infections.

What are the potential benefits likely to derive from this project (how science could be advanced or humans or animals could benefit from the project)?

We will generate an in depth academic knowledge for the biomedical and veterinary communities of how different worm parasites survive or are cleared by the body's immune system. This will open up avenues for development of new targets for anti-worm drugs and vaccines by research scientists and pharmaceutical companies. Moreover, there is clear evidence that in areas of the world where parasitic worms infect people extensively, diseases such as allergies (such as asthma) and autoimmune diseases (such as diabetes) are relatively rare, and this is believed to be as a result of being infected by parasites. The information we obtain from Aim One will help us identify parasite molecules involved and mechanisms that may be responsible for this. In Aim Two we will target these molecules and mechanisms to help develop new approaches and treatments that not only have anti-parasitic effects but also beneficial effects for people with allergic and autoimmune disease.

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What types and approximate numbers of animals do you expect to use and over what period of time?

Mice and rats. We will use up to 20000 mice and 250 rats over a five-year period.

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

The majority of animals will undergo infection or treatments associated with infection. Some will be used for studies testing parasite molecules as potential vaccines. For example, mice may be infected with one or more type of parasitic worm, as experienced in the wild and their immune responses to these parasites investigated by taking samples from them at different time points following infection. In some studies, mice will be vaccinated with molecules taken from parasitic worms and then infected with the parasite to see if this will protect them. Some mice and some rats will be infected with parasitic worms to provide parasites for use in our experiments. The majority of infections and treatments lead to mild symptoms that are often transient. The parasites we use are those that naturally infect rodents in the wild and are thus well adapted to laboratory animals, which minimises excessive adverse effects. Animals are monitored closely and after use are humanely killed with the tissues taken for further laboratory research. Any that show adverse effects during the experiment will be humanely killed and again tissue used for further laboratory research.

Application of the 3Rs

Replacement

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

Replacement

The parasites that we use cannot grow, develop or reproduce outside of their mammalian host. They cannot be frozen and thawed to use in the laboratory.

The control of parasite infection, treatment and vaccination requires an intact animal as the response involves many different cell types in the immune system, at many different body sites and occurs over a period of time. This is a very complex response and cannot be accurately analysed by computers or in cell culture in an incubator.

People infected with worm parasites are mostly present in parts of the world with very limited access to very limited resources for research and it is very hard to assess their infection histories. Moreover, only samples such as blood can be taken for analysis, which does not accurately measure changes that go on in the intestine. Also, people are often infected with other infections that make it difficult to determine cause and effect from samples taken from people.

Reduction

Explain how you will ensure the use of minimum numbers of animals

Reduction

In consultation with experienced statisticians we design our studies to utilise the fewest number of animals to ensure trustworthy results. All tissues possible are taken from the animals and used in multiple projects to reduce the numbers used. Where possible we will use cell culture and computer based analysis to help our study design prior to using animals that will also reduce numbers used.

Refinement

Explain the choice of animals 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.

Refinement

We use natural mouse or rat worm parasites that have the same life cycle and infection sites as human and large animal counterparts.

As much as possible, infections, treatments and vaccinations are given via the same route as they would be for humans or large animals.

Extensive use is made of information from previous animal experiments to identify the most informative times to treat animals and take tissues from.

Where possible, information taken from the limited studies carried out in humans and large animals are used in experimental design to work out the most important questions to ask.

Treatments are as minimally invasive as possible.

Animals are usually housed in social groups in a cage with nesting and tubes/shelters to enrich their environment.