Non-technical summary: Characterisation of antibodies produced by cattle to rumen methanogens

Project duration
5 years 0 months

Project purpose
(a) Basic research
(d) Protection of the natural environment in the interests of the health or welfare of man or animals

Key words
Methane, climate change, greenhouse gas, global warming, methanogen

Animal types	**Life stages**
Cattle	Juvenile, adult

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

Objectives and benefits
Description of the projects objectives, for example the scientific unknowns or clinical or scientific needs it's addressing.
What's the aim of this project?

The aim of this project is to generate initial, fundamental data, related to the immune response of cattle to methanogens which live in their stomachs and generate methane gas. The ultimate use of which would be to support evidence-based development of vaccines which may help reduce greenhouse gas emissions from cattle (and other ruminants).

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.
Why is it important to undertake this work?
The many effects of climate change are well known, and a primary driver of climate change is the accumulation of greenhouses gasses in the atmosphere themselves a result of human activity. Greenhouse gasses trap heat, and result in increased global temperatures. Livestock account for 14.5% of the global annual greenhouse gas emissions caused by human activities. They impact the climate through various factors such as land use change, feed production, animal production, manure management, transportation, and release of methane - a natural byproduct of their digestive system. The work presented here will provide a proof-of-concept approach to support the development of a vaccine against the methanogen responsible for generating methane in the digestive system of cattle. This information will be used to help generate vaccines which could be used to reduce the production and release of greenhouse gasses from cattle and other ruminants, adding an additional tool for mitigating climate change while supporting food security and healthy protein production.

What outputs do you think you will see at the end of this project?
The outputs expected at the end of this project would be generation of fundamental data establishing if a vaccine approach could be implemented to reduce the growth of the

microorganisms which generate methane in the digestive system of cattle, the methanogens. It is expected this new data would be published in peer reviewed journals and openly shared with the Global Methane Hub that coordinates all types of strategies to reduce the impact of livestock produced methane. This data would also be used to help create vaccines which themselves would aim to reduce methane production from cattle and other ruminants.

Who or what will benefit from these outputs, and how?
The fundamental research data generated from this project will help form part of a wider toolset which will underpin the rational creation and selection of a new generation of vaccines to help combat climate change.

How will you look to maximise the outputs of this work?
This work is part of a larger collaborative project, whereby data generated will be shared and utilized by the partners. The expectation is that the data generated within this project will also be published.

Species and numbers of animals expected to be used
Cattle: 28

Predicted harms
Typical procedures done to animals, for example injections or surgical procedures, including duration of the experiment and number of procedures.
Explain why you are using these types of animals and your choice of life stages.
Cattle, and ruminants more broadly, have a specialised digestive system which enables them to digest long fibre foods such as grass, hay, and other plants. To investigate the immune response to the methanogen organisms living inside the digestive system, cattle provide an optimal platform both based on size, as well as the fact that the pre-existing optimized platforms for interrogating the immune response are already developed for cattle.

Typically, what will be done to an animal used in your project?
This project will examine the immune response of cattle to the methanogen microorganisms present in the digestive system of cattle, and as such, will involve inoculation of cattle with inactivated methanogen organisms by way of injection into the skin or muscle, and collection of blood samples to assess the responses in the blood. Saliva samples may also be taken by way of a non-invasive method.

What are the expected impacts and/or adverse effects for the animals during your project?
Inoculation with inactivated methanogens and the collection of blood samples will require a needle to be introduced through the skin however no additional adverse effects other than the mild and transient effects of the needle penetration are expected. No side effects of inactivated methanogens to the cattle or their digestive systems are expected.

Expected severity categories and the proportion of animals in each category, per species.
What are the expected severities and the proportion of animals in each category (per animal type)?
All animals are expected to experience only mild severity during this study.

What will happen to animals used in this project?
Killed

Replacement

State what non-animal alternatives are available in this field, which alternatives you have considered and why they cannot be used for this purpose.

Why do you need to use animals to achieve the aim of your project?

Only whole animals, and in this case cattle as ruminants, can be used to assess the immune response to methanogens.

Which non-animal alternatives did you consider for use in this project?

There are no non-animal alternatives which can be used in this project.

Why were they not suitable?

As stated, only animal models can be used to assess immune responses.

Reduction

Explain how the numbers of animals for this project were determined. Describe steps that have been taken to reduce animal numbers, and principles used to design studies. Describe practices that are used throughout the project to minimise numbers consistent with scientific objectives, if any. These may include e.g. pilot studies, computer modelling, sharing of tissue and reuse.

How have you estimated the numbers of animals you will use?

The purpose of the pilot study is to characterize the humoral immune response to cattle methanogens, including identification of immune similarities between them. To this end, up to 5 different methanogens will be selected, which are the major methanogen species identified in the rumen. Prior studies analysing B-cell frequencies have suggested that 4 animals would be sufficient to generate the data required in this study, each group of 4 cattle being immunized with one of the 5 methanogen types. In addition, to screen for immune similarities, 2 groups of 4 cattle are planned to be sequentially immunized with different methanogens, based on the data generated from the initial studies.

What steps did you take during the experimental design phase to reduce the number of animals being used in this project?

These numbers are based on similar approaches in cattle using different immunogens and reflect the best evidence-based estimation of the minimum numbers of animals likely to be required for this study.

What measures, apart from good experimental design, will you use to optimise the number of animals you plan to use in your project?

Continual assessment of animal numbers will be made based on the data generated given the humoral immune response to methanogens in cattle using the cutting-edge tools has not been undertaken before.

Refinement

Give examples of the specific measures (e.g., increased monitoring, post-operative care, pain management, training of animals) to be taken, in relation to the procedures, to minimise welfare costs (harms) to the animals. Describe the mechanisms in place to take up emerging refinement techniques during the lifetime of the project.

Which animal models and methods will you use during this project? Explain why these models and methods cause the least pain, suffering, distress, or lasting harm to the animals.

Cattle, as a large animal ruminant model, will be used during his project. There is vast experience and expertise interrogating the humoral immune response of cattle.

Why can't you use animals that are less sentient?
The detailed antibody response of cattle to methanogens will be examined as the overall aim of this project, and therefore cattle are required, and terminal anesthesia / other methods of reducing sentience are not applicable.

How will you refine the procedures you're using to minimise the welfare costs (harms) for the animals?
Most importantly, ongoing review of approaches and results during the project will be undertaken and refinements applied / approaches refined to minimize the harms to the animals.

What published best practice guidance will you follow to ensure experiments are conducted in the most refined way?
Stimulating the humoral responses of cattle using antigens, and subsequent examination of these responses are activities which have been extensively studied at our establishment. The procedures undertaken in this project will be administration of substances and withdrawal of blood, and the LASA published guidance, and other referenced best practice guidance will be adhered to including "A Good Practice Guide to the Administration of Substances and Removal of Blood, Including Routes and Volumes."

How will you stay informed about advances in the 3Rs, and implement these advances effectively, during the project?
There are ongoing national and international links of our establishment with other research groups which enables the sharing of best practice in the fields of shared research. This, combined with extensive experience within the establishment and ongoing review of the scientific literature will assist in using the most refined methods and more widely applying the 3Rs where appropriate.