The Presenters

Dr Ron Ronimus (AgResearch)

Dr Ron Ronimus obtained his PhD at the University of Waikato in Hamilton and is now a Principal Scientist at AgResearch in Palmerston North. Ron has worked with archaeal microorganisms, including methanogens which form methane, and their enzymes for over 30 years. Methanogens possess a number of unusual traits such as isoprenoid-based lipid membranes, an unusual cell wall chemistry and a unique energy metabolism (methanogenesis) that requires six methanogen-specific cofactors. Many of the enzymes involved in these key aspects of methanogens have no direct analogues in the host animal. The research team is currently using this knowledge and focusing on developing inhibitors that specifically target methanogens for reducing enteric methane emissions. This has led to multiple *in vitro* techniques (enzyme-based, pure cultures and rumen fluid-based approaches), and *in vivo* experiments being used in a 'pipeline' approach for discovery of novel inhibitors. It has also led to the determination of 30 methanogen enzyme structures which reveal fundamental knowledge about methanogens. The work has involved multiple collaborators at several New Zealand and overseas universities.

Mark Aspin (PGgRc)

Mark Aspin is the General Manager at the Pastoral Greenhouse Gas Research Consortium (PGgRc). Mark's work involves mitigation of greenhouse gas from livestock, developing the science solutions and enhancing their rapid adoption. The PGgRc aims to provide New Zealand livestock farmers with the knowledge and tools to mitigate greenhouse gas emissions from the agricultural sector.

Presentation

Developing methane inhibitors for grazing livestock on New Zealand farms.
YouTube Video link: https://youtu.be/AQAbm2OC4yY

Question & Answers

Thank you all for your participation. Below are the questions which were asked post presentation.

Please note: these answers are provided by the presenters and do not represent the particular views of the NZAGRC or MPI.

Do you see a need to change the ACVM regulations in order to accommodate methane inhibitors, to give processors confidence commercially available inhibitors (when they become available) that they are safe? I understand at present ACVM regs do NOT include any definition for methane inhibitors.

This is not in place but is happening, currently being instigated by the NZ Government and it is a critical part of the pipeline. We see a well-recognised regulatory path as a necessary part of the system to ensure that we keep our high food safety and animal welfare standards front of mind as these are developed and rolled out. We also recognise that a regulated system should provide the opportunity for a consistent way to ensure that the efficacy claims are scientifically sound, understood and can be very clear for the farmers looking to use any products with their livestock.

What is the latest on the practical use of archaeal viruses (bacteriophages?) to manage methanogen's concentration in vivo?

We have trialled some phage in earlier studies with mixed effects, the impacts were minor. Phages are very specific to species and this approach will need further research if its to be a realistic option. There has been a fairly recent study where the lytic enzyme from *Methanobrevibacter ruminantium* (PeiR) has been expressed in polyhydroxyalkanoate nanobeads and shown to be capable of lysing multiple rumen methanogen species (https://pubmed.ncbi.nlm.nih.gov/30356700/). There has also been an excellent review of phage in the rumen (https://pubmed.ncbi.nlm.nih.gov/32273870/) which highlights recent research in this area.

Have you also looked at using it as a feed additive for dairy herds that have in-shed feeding? This would use existing (or future) technologies, making it much simpler to implement. It means that it would only be delivered during milking times over lactation (or prior if dairy farmers run their springers or even dries through the shed to supplement their feeding. Putting the herd through the shed prior to milking also works to train first calvers who haven't been through the dairy shed before, which might be adopted more widely if it reduced GHG) This would make the implementation much more attractive for farmers who have, or are thinking of installing, in-shed feeding.

That is exactly what we are doing by searching for compounds that have very high potency, we have set the bar high by seeking compounds that are potent enough to be in a capsule or bolus and active for greater than 100 days. But these actives could also be used in a feeding situation and if they are active and persist then we are certainly exploring how they might be deployed including as a supplement. It will come down to the characteristics of the active; if they can be used in the rumen environment, how stable they are in the environment, etc. and cost.

Is there any progress possible re dealing to elimination of methanogens? It seems this would be costly and not humanoid but possibly equally beneficial and the RNA sequencing possible? Could a vaccine along these lines be developed?

The PGGRC & NZAGRC are actively pursuing the development of a methane vaccine as well. But to answer the main question, as we learn more it may be possible to have a rumen environment that doesn't produced any methane. However, it is important to note that methane production by methanogens provides a way to manage hydrogen in the rumen (removal of which enhances fibre-degradation) and that impacts the whole microbial community in a very interactive manner.
There are published reports of animal trials at short-term demonstrating >90 % reduction in methane with rumen function remaining stable. How this might be achieved day in, day out with livestock will require a great deal of long-term research to provide understanding of what a methane-free rumen may offer.

Do you have confidence in the ability to include bromoform compounds (e.g., Asparagopsis spp.) as ruminant methane inhibitors from the perspective of milk and carcass residues?
Answered live

Do you know of any feeder/technology that would be able to reliably and consistently deliver the specific doses of an inhibitor? Or is the most likely outcome regularly delivering it via a food pad on farm?
Answered Live

How long do you think it will be before ACVM will have a methane inhibitor category finalised with the parameters necessary to meet the requirements for a methane inhibitor in NZ?
Answered live

Any issue with the build-up of hydrogen in the rumen?
Answered live

Do you see any impact for product (meat/milk) sourced from animals fed with inhibitors i.e., will it need to be declared on a product label in a supermarket?
Answered live

Can you clarify if ovine/bovine cells lines are used to assess toxicity before the mouse bioassay?
Answered live

Have you investigated synergies of different compounds?
Answered live

Can you comment on how vaccine development is progressing?
Answered live

Any estimate as to when there will be a commercially available inhibitor, likely to be led by the sheep sector given the work to date?
Answered live

Once you have identified the preferred inhibitor, how confident can you be of achieving accurate delivery via a bolus?
Answered live

What do you consider would be the gold standard study program required in order to take a compound to market? e.g., which in vitro/in vivo studies
Answered live

ACVM permitting, when might we see first commercial use of inhibitors locally?
Answered live

When suppressing the activity of archaeal bacteria in the rumen could this have other consequences e.g., do methanogens uptake phosphorus as polyphosphate when suppressed/stressed? Could this limit animal assimilation of P?
Answered live

If multiple single action inhibitors are introduced, then surely multi drug resistance could develop one from the other?
Answered Live
