Methane inhibitors – helping to nip a problem greenhouse gas in the bud

Methane inhibitors are shaping up to be a promising element of the toolkit to reduce emissions by belching animals. These compounds can reduce methane production by up to one-third, meaning widespread adoption by local farmers would put national reduction targets within reach.

So what is a methane inhibitor? Your average cow's stomach is basically a vat full of fermenting grass, thick with helpful microbes like methanogens. They use hydrogen gas, a by-product of fermentation, and combine it with carbon dioxide to produce methane and water.

Methane – a problematic greenhouse gas – is then released into the atmosphere when the animal burps. That is unless a farmer uses an inhibitor, a newly discovered chemical compound that stops the methanogens from working, shutting down or slowing the process of methane production.

Commercial production of these inhibitors is likely in the coming years, but New Zealand's pasture-based system poses challenges. Options, such as bolus capsules to slowly dispense the inhibitor in the rumen, are therefore under active investigation.

In 2013, SLMACC supported a project to develop what's called the methane inhibitor 'pipeline', a complex sequence of tests to identify compounds that suppress methanogens without causing unwanted side effects.

Researchers funded from the Pastoral Greenhouse Gas Research Consortium (PGgRc) and New Zealand Agricultural Greenhouse Gas Research Centre concentrated on ways to allow large-scale screening for inhibitors.

Their aim was to enable prediction of inhibitors using computer simulation, testing of inhibitors, and testing early lead inhibitors using rumen simulation in vitro techniques.

Results of the research programme included identification of eight enzyme structures, representing a total of five target enzymes.

"This finding was as successful as the results obtained by large international pharmaceutical companies such as those that develop novel anti-malarial and anti-tuberculosis agents," said PGgRc's Mark Aspin.

These structures each represent "molecular platforms" for the rapid, cost-effective discovery of novel anti-methanogen control agents, he said.

Since 2013, local researchers have screened more than 6,000,000 compounds digitally using these enzyme structures or models developed in-house.

To date, 19 compounds, showing inhibition either in enzyme assays or against pure cultures of methanogens, have been identified.

Three enzymes have been biochemically characterised, with assays developed for screening purposes, with nine more either partially characterised or in assay development.

This means that in excess of 40 “hits” (compounds that inhibit in simple tests), and a number of assays suitable for discovering novel inhibitors, are now available.

“Ultimately, these hits will be tested in enzyme assays, pure culture experiments and/or rumen fluid-based assays,” said Mark. “The research is now nearly ready to accelerate the discovery of novel inhibitors by screening large compound libraries using the developed enzyme assays.”

Synthetic chemistry techniques could be used to enhance the inhibitors and others discovered, and these derivatives could then be tested in animals.

A pipeline to rapidly screen small-molecule chemical inhibitors active against key methanogen enzymes, combined with cost-effective computer-aided design of potential inhibitors, has meanwhile been developed. It has been proven capable of identifying inhibitors that halt the growth of methanogens in vitro.

The next step is to demonstrate methane reductions in animals without significant negative impacts on productivity. Redirection of some of the energy lost as methane (up to 12 percent of feed energy) into useable fermentation products like volatile fatty acids could positively affect productivity with both vaccines and inhibitors. This has to be verified in experiments with animals in which methane formation is dramatically reduced and then all regulatory requirements for these products met.

This project also built on a parallel PGgRc vaccine-development project working in one of the main species of rumen methanogens that had been genome sequenced.