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Using structural biology of methanogen enzymes to guide development of inhibitors for mitigating methane emissions and to enhance our understanding of methane formation

A Methane is a potent greenhouse gas (28-fold higher than carbon dioxide), and is a significant factor contributing to climate change. Approximately a billion tons of methane is produced each year. Methane produced by ruminants is generated by methanogenic archaea. Rumen archaea possess a number of unusual traits such as isoprenoid-based lipids linked to glycerol-1-phosphate through ether bonds, and a unique energy metabolism (methanogenesis) that requires six specialized methanogen cofactors. Most of the enzymes involved in these processes have no direct analogues in the host animal. To gain insights into the fundamental biology of rumen methanogens and to aid the development of inhibitors, we have determined crystal structures of key enzymes with archaeal-specific traits. Over 300 enzymes were targeted for structure determination, which produced in excess of one hundred purified soluble enzymes for crystallographic screening. More than 50 different enzymes produced crystals and 30 protein structures have been solved thus far. We have used a subset of these structures for *in-silico* screening, and then have tested these compounds in direct enzyme assays, against pure cultures of methanogens, in rumen fluid-based *in-vitro* assays and/or in animals.

Biography

Ron S Ronimus has completed his PhD in Genetics of a Thermophilic Archaeal Species in 1994 at the University of Waikato, Hamilton, New Zealand. He continued his research at the University of Waikato in two separate Post-doctoral research programs, one for the dairy industry and one with the Royal Society of New Zealand Marsden program. Subsequently, he took up a Senior Scientist Position at AgResearch in 2006, and currently leads a program to develop inhibitors that are specific for methanogenic archaea in an effort to mitigate methane emissions from ruminant animals. This is currently funded by the Pastoral Greenhouse Gas Research Consortium.

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