Stimulating the innate immune system to protect livestock against disease: Vaccine Trial.

A. L. Alexander[A,B,D], B.C. Hine[B], A. B. Ingham[C], I. G. Colditz[B] and E. K. Doyle[A]

[A]The University of New England, Armidale, NSW, 2350, Australia.
[B]CSIRO Livestock & Aquaculture, New England Hwy, Armidale, NSW, 2350, Australia.
[C]CSIRO Livestock & Aquaculture, QBP, 306 Carmody Rd, St Lucia, QLD, 4067, Australia
[D]Email: aalexa22@myune.edu.au

Antibiotics are commonly used to treat many diseases of livestock, yet antibiotic resistance is of increasing concern globally. Therefore, alternatives for the prevention and treatment of disease are required. Compounds that stimulate the innate immune system to 'kick into gear' and enhance its ability to fight off infection have potential to be used as alternatives to antibiotics. Innate immune responses are rapid and broad in their action, whereas adaptive immune responses, like those targeted by vaccination, are slower to develop and are highly specific (Janeway *et al.* 2008). Amplimune® (NovaVive Inc.) is a commercial product based on a mycobacterium cell wall fraction (MCWF) preparation, which is known to activate the innate immune system (Korf *et al.* 2005). The potential of the innate immune stimulant MCWF to provide rapid protection against disease in livestock has been investigated (Nosky *et al*. 2017). Here we hypothesise that co-administration of MCWF at the time of vaccination might enhance responses as a result of heightened stimulation of the innate immune system. We propose to test this by examining the immune response of cattle following treatment with vaccines commonly used by industry to protect against bovine respiratory disease (BRD) either alone or in combination with Amplimune®.

Angus cattle, aged 18 months and of mixed sex, will be randomly allocated to one of six treatment groups (n=9 per group), balanced for sex, weight and sire. Treatment groups one-three will receive Bovilis MH+IBR vaccine (Coopers Animal Health) subcutaneously (BOV), while groups four-six will receive Rhinogard (Zoetis) intranasally as per manufacturer's recommendations (RHINO). Treatment groups one and four will also receive 2mL Amplimune®, groups two and five 5mL Amplimune® and, groups three and six 5mL saline (control). Cattle will be transported for six hours on days –1 and 0 relative to treatment, to simulate transport to a feedlot (see Figure 1). Standard induction procedures, including treatment for internal parasites and vaccination against clostridial disease will be undertaken just prior to treatment. Amplimune® injection sites will be identified and inspected for lesions by clipping a 5cm^2 patch high on the neck.

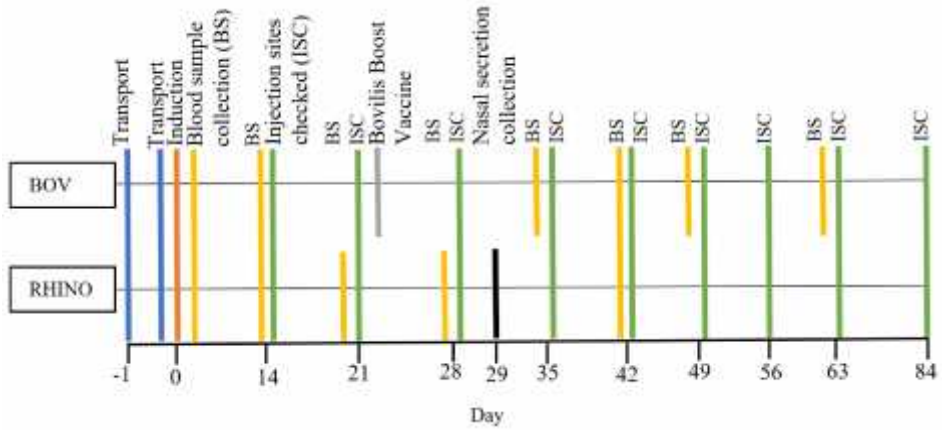

Figure 1. Timeline of vaccination trial

Serum will be prepared from blood and assayed to determine levels of antigen-specific antibodies to Bovilis and Rhinogard vaccine components. Nasal secretion samples will be analysed for IgA antibody and cytokine Interferon gamma (IFNγ) response to vaccination with Rhinogard. Results from an earlier study that investigated the effect of different doses of Amplimune® on immune responses indicated that the product activates the innate immune system (unpublished data) as evidenced by increased circulating concentrations of the pro-inflammatory cytokine Tumour Necrosis Factor alpha (TNFα) and increased core body temperature in treated animals. The innate and adaptive immune responses are intimately linked. As such we hypothesise that Amplimune®, by triggering the innate immune system, will lead to heightened downstream adaptive immune responses to vaccination.

References

Amplimune®, NovaVive Inc., Napanee, Ontario, Canada

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