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Initiation of an anti-gastrointestinal parasite immune response in sheep by agents that mimic the activity of live gastrointestinal nematodes.

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Gastrointestinal nematode (GIN) parasitism poses a major health and financial cost to livestock production. As GIN resistance to drenches increases, alternative control methods must be developed. Vaccination with live, attenuated parasites established 88-95% protection in sheep (Windon et al 1984; Benitezusher et al. 1977), however commercial production of these vaccines are too expensive. In contrast an effective subunit *haemonchus*-specific vaccine has been developed (LeJambre et. al., 2008), however it requires 5 treatments per season, and does not provide protection against other GIN such as *T. colubriformis* (Tc). Thus a cost effective pan-GIN vaccine is required to protect livestock. In order to establish parasite expulsion, both mucosal barrier and immune responses (e.g. mast cell-induced Th2 response) have been shown to be important. Therefore, we hypothesise that activation of mast cells by agents such as compound 48/80, and the induction of limited parasite-like tissue damage at the site of infection, are necessary to facilitate protective anti-parasite immune responses.

To develop the adjuvant for the vaccine, a cocktail containing compound 48/80, Dextran Sodium Sulphate (DSS), Brij 35 and 10 µm tracer beads was endoscopically injected directly into the abomasum of sheep (site of *H. contortus* (Hc) colonisation). It was hypothesized that this cocktail would induce parasite-like damage down the gastrointestinal tract (GIT).

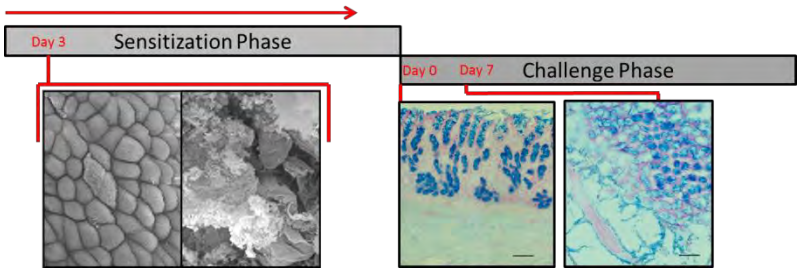

Figure 1: Electron microscopy images showing damage to the abomasal site of injection on day 3 of the vaccine sensitization phase (2000x), and Alcian blue stains showing an increase in goblet cell numbers from day 0 to day 7 of the challenge phase.

Gross histological analysis demonstrated dose-dependent [illegible] site of injection. Microscopic analysis indicated limited damage downstream of the injection site in the duodenum and the jejunum. There was also a dose-dependent increase in leukocyte infiltration into the abomasum (Figure 1), duodenum and jejunum of treated sheep compared to untreated control animals. A significant decrease in IL33 gene expression 3 days after injection was observed indicating tissue damage prior to the mucosal re-epithelisation phase.

Based upon gross and microscopic histology, this adjuvant induced limited parasite-like tissue damage and leukocyte infiltration to the GIT mucosa. The inclusion of recombinant ovine IL33 and Hc and Tc antigens from freeze-dried parasites into this newly developed adjuvant is hypothesized to produce a vaccine that mimics the action of parasites and polarizes the host response towards a protective, anti-GIN Th2 response in sheep.

Benitezusher C., et al. (1977) *Veterinary Parasitology* 3: 327-342.
LeJambre L.F., et al. (2008) *Veterinary Parasitology* 153: 302–312.
Windon R.G., et al. (1984) *Int J Parasitol*. 14:423-8.