Control of a parasitic nematode in sheep by vaccination with recombinant antigens

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Introduction

o *Teladorsagia circumcincta,* a parasitic nematode that inhabits the abomasum of small ruminants, primarily causes disease in lambs.

o Prolonged exposure is needed to produce protective immunity against *T. circumcincta* suggesting that the worm can manipulate the host immune response over an extended period before protective immunity eventually overcomes this manipulation.

o We have therefore developed a tripartite approach to identifying protective antigens for inclusion in a *T. circumcincta* vaccine (Fig 1):

1. Select L3 and L4 antigen targets of local IgA responses in immune sheep
2. Select putative secreted immunosuppressive molecules
3. Using bioinformatic analysis, identify homologues of known vaccine candidates from other helminth parasites

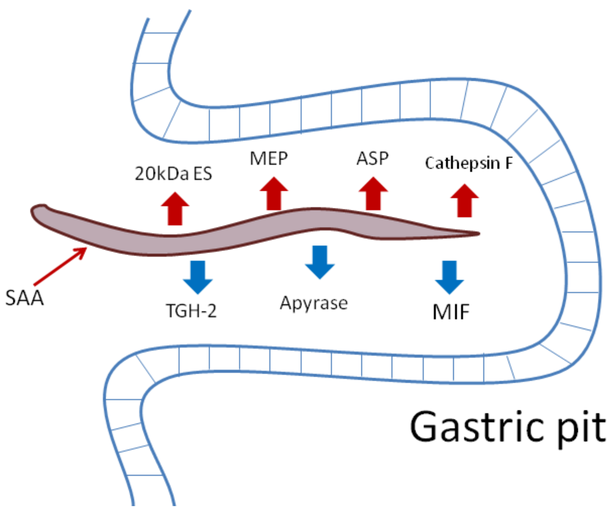

Fig. 1 Vaccine antigens derived from L3/L4 *T. circumcincta*. Red arrows represent ES antigen targets of local IgA responses. Blue arrows represent putative immunomodulatory ES products. SAA is a surface associated antigen homologue of Ac-SAA-1 from *Ancylostoma caninum*

o We generated recombinant versions of 8 molecules selected on this basis and combined them into a sub-unit vaccine which we tested in two independent trials in which sheep were exposed to experimental challenge infection after immunization.

Materials and Methods

o Recombinant proteins were produced in *Escherichia coli* except Cathepsin F (Tci-CF-1) and the 20kDaES protein (Tci-ES20) which were produced in *Pichia pastoris*

o The 8 recombinant proteins were administered as a single vaccine formulation, given 3 times, followed by trickle infection (Fig. 2)

o The entire experiment was performed on two occasions with Trial 1 in 2010 and Trial 2 in 2011

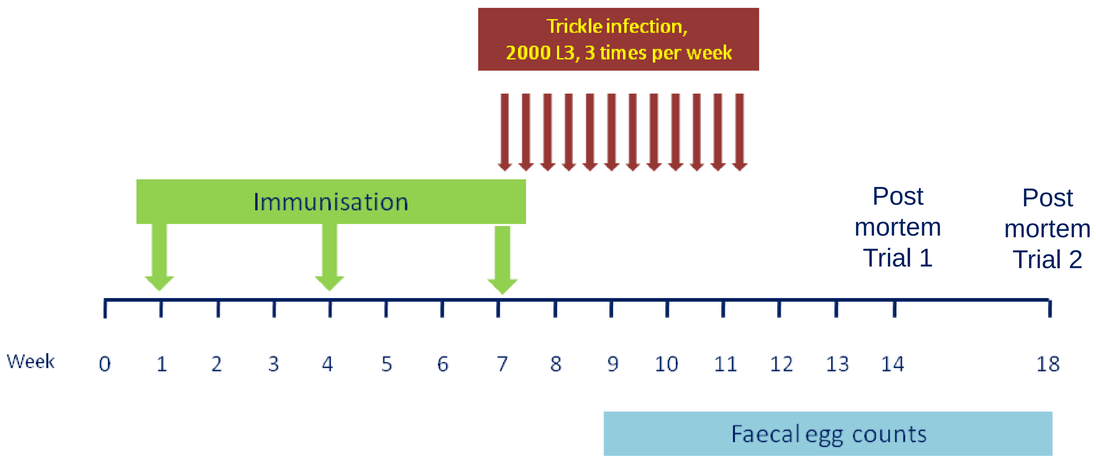

Fig 2. Design of *T. circumcincta* vaccine and challenge trials

Results and Discussion

o In both trials, vaccinates had significantly lower mean faecal worm egg counts (FWECs) over the sampling timeframe, with a mean reduction in egg output of 70% (Trial 1) and 58% (Trial 2)

o During the period of peak worm egg shedding, vaccinates shed 92% and 73% fewer eggs than did controls in Trials 1 and 2, respectively (Fig 3).

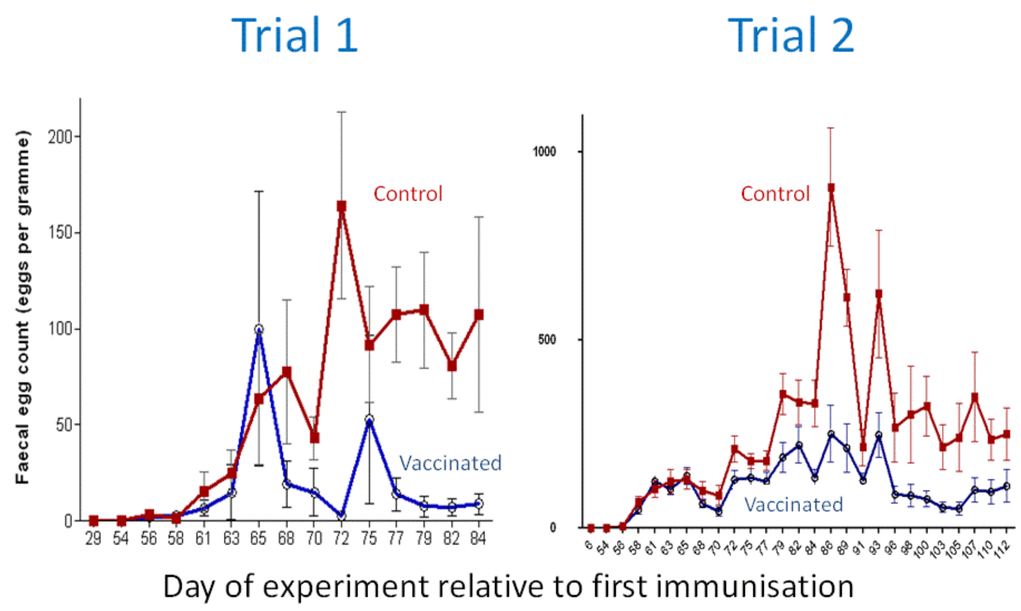

Fig 3. Faecal worm egg counts from sheep vaccinated with a cocktail of recombinant antigens and challenged with a trickle infection of *Teladorsagia circumcincta*

o At post mortem, vaccinates had 75% (Trial 1) and 56% (Trial 2) lower adult nematode burdens in the abomasum than the controls.(Fig 4).

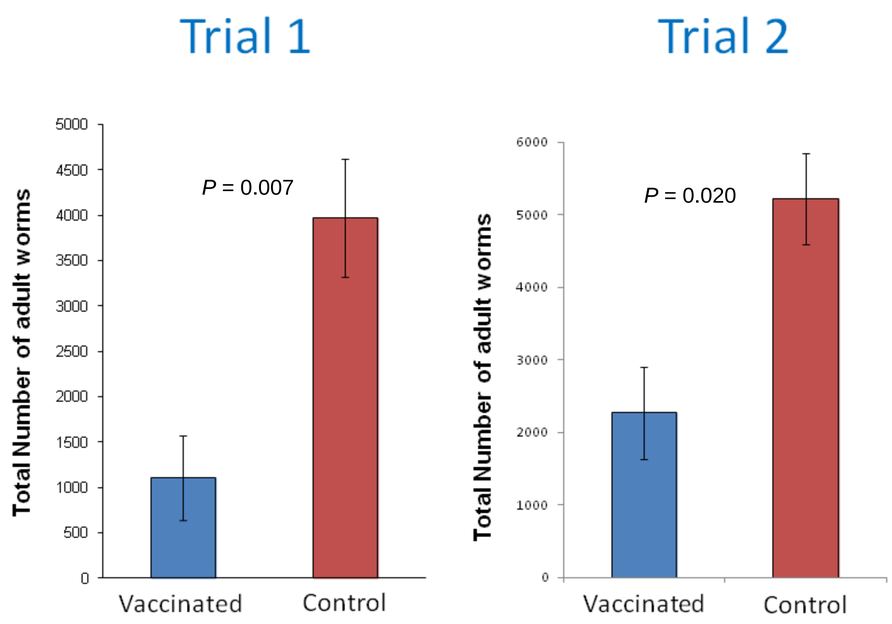

Fig 4. Adult worm counts at post mortem from sheep vaccinated with a cocktail of recombinant antigens and challenged with a trickle infection of *Teladorsagia circumcincta*

Conclusions

These levels of protection are higher than observed in any other system using a recombinant vaccine against a parasitic nematode in the definitive host. Our future studies aim to identify the most effective elements of the recombinant cocktail vaccine.

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