Tick vaccine development

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An integrative approach to the development of a vaccine against the cattle tick, Rhipicephalus microplus.

Fast expansion of tick acaricide resistance in South Africa highlights the need for an improved tick control strategy. Without such a strategy, the spread of acaricide resistant ticks and the associated tick-borne diseases transmitted (e.g. lethal redwater, anaplasmosis, borreliosis) will be crippling for the agricultural industry and food security. To date, only one tick vaccine has been commercialized and was based on a tick gut membrane associated protein Bm86. This vaccine has since been removed from global markets (except for South America), due to variable efficacy in the field. In our laboratory, we were the first to identify 3 proteins that interact with Bm86 inside the tick gut. We therefore expressed these proteins and combined them into a BM86combi vaccine formulation for evaluation.

For the testing of improved vaccine formulations, a cattle trial with 16 Friesian calves was performed. These were subdivided into four groups: two control and two test groups. Whole body infestation was performed with approximately 4,000 R. microplus larvae per calve. Ticks were fed to engorgement, collected, weighed and incubated for ovipositioning. Cattle blood was collected for the obtainment of serum on day before first immunization, after the second and third immunization and before tick infestation to determine antibody titres against the injected proteins. Both vaccine formulations resulted in reduced tick numbers, but the Bm86 combi vaccine (Bm86 and 2 of its interacting partners) showed significance. This vaccine led to a tick reduction of 53%. This is very significant, as the Bm86 antigen alone offered no protection in South African cattle against the South African R. microplus strain. Enzyme-linked immunosorbent assay revealed a several fold increase in antibody titre over time for all antigens used. Further improvement of vaccine formulation, including eukaryotic expression systems to obtain glycosylated proteins (enhanced solubility and antigenicity) and modified adjuvant usage could further improve obtained results. These latter studies will be done in 2015 with funding provided by TIA.

To move the field of tick vaccine development into the next era, more insight into the protective responses from cattle against tick infestation is vital. Currently, available publications focus on skin and blood samples only, which are not a true representation of underlying immune responses. Therefore, the second aim of this study was the comparison of immune responses of three cattle breeds (tick resistant Bos indicus, tick susceptible Bos taurus and South African mixed bred cattle (Bonsmara)) determined by looking at lymph node tissue before and during tick infestation. This will aid in the identification of immunological markers that can lead to improved evaluation and formulation of future vaccines. Three biological repeats per breed were infested with ~7,000 R. microplus larvae. Lymphatic tissues were collected prior to infestation to serve as baseline to be compared to infested cattle (at 2 time points: larvae and adult infestation). RNA from lymph nodes was isolated and yielded very high purity material. Microarray technology was used for the identification of differentially expressed genes between the three cattle breeds allowing the identification of immune pathways influences by the different host immune responses. A total of 8 microarray experiments to determine the gene expression profile of the bovine lymph node tissue have been completed with the remaining 19 microarray experiments currently being underway. For the latter, we will submit a new funding application by mid 2015 to the Red Meat Research Development Trust of South Africa.