Vaccination against Parasitic Infection

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Introduction
Initial studies on vaccination against Haemonchus contortus in 1997 have shown that total worm protein extracts were able to elicit a partially protective immune response, however attempts to enhance this response with a powerful mucosal adjuvant namely E. coli heat-labile enterotoxin (HLT) failed (Hartina et al., in preparation). Based on our findings and current literature it was suggested that development of anti-parasitic vaccines should emphasize studies on immunostimulants that can enhance the response in the gut rather than selecting protein antigens from gel bands that were not likely to elicit protective immunity. Using rapid cell assay screening methods we have discovered an aqueous extract from Solanum torvum that is strongly mitogenic for splenitic lymphocytes (Israf et al., unpublished data). We have tested this extract several times in a rodent non-replicating antigen model and have shown that it is as effective as cholera enterotoxin in enhancing mucosal immune responses. The results of these trials are presented.

Materials and Methods
Three trials were conducted with outbred female ICR mice. In trial 1, 10 groups of mice were given various doses of Solanum extract as an adjuvant to bovine serum albumin via the intraperitoneal route. Boosters were given and the immune response throughout a 4-month period was analysed. In trial 2 and 3, mice received similar doses as in trial 1 however the route of inoculation was via oral gavage. The main emphasis of these trials was to examine the ability of Solanum extracts to stimulate mucosal immune effector mechanisms towards ovalbumin. Assays used included enzyme immunosassay for detection of antibody isotypes in various tissues and serum. Enzyme immunospot was used to study cytokine responses of lymphoid tissue using monoclonal antibodies towards IFN-γ, IL-2, IL-4 and IL-5.

Results and Discussion
In trial 1, we demonstrated a significant enhancement in anti-BSA IgG titers when the lowest dose of Solanum was used (2 μg). We also demonstrated that following a final booster, the intestinal levels of both anti-BSA IgA and IgG were significantly elevated. Trial 2 demonstrated that an oral booster with ovalbumin/0.5 mg Solanum was able to significantly elevate intestinal and faecal IgA concentration and stimulate both Th1 and Th2 cells as determined by analysis of cytokine production. Trial 3 extended the findings of trial 2 in that it was shown that a very low dose of Solanum (2 μg) administered orally with ovalbumin was far more superior in generating both local and peripheral antibody and cytokine responses. This trial also demonstrated that 2ug of Solanum could enhance immune effector mechanisms in the lung, an example of enhanced mucosal homing. There is no doubt that this extract is truly stimulatory for lymphocytes and has great potential to replace the current mucosal adjuvants that are more toxic in nature. We plan to acquire further data on the mechanism of action and study the enhancing effects in a prototype Haemonchus vaccine.

Conclusions
Solanum extracts are very effective in enhancing local and peripheral effector mechanisms towards model protein antigens. They target lymphocytes by enhancing synthesis and secretion of antibodies and cytokines. However our data suggest that the crude extract contains both immunostimulatory and immunosuppressive factors. This theory is based on the fact that a reduction of the dose to as little as 2 μg leads to enhanced responses. It is therefore necessary to fractionate the components for future studies.

Benefits from the study
We have developed the technology to enhance mucosal immune responses by coadministration of non-replicating antigens with an aqueous plant extract. This technology has the potential to enhance the efficacy of vaccine preparations and allows for oral dosing which is less traumatic and does not require technical skill in administration.

Literature cited in the text
None.

Project Publications in Refereed Journals


Project Publications in Conference Proceedings
10\textsuperscript{th} Veterinary Association of Malaysia Congress, 4-6 September 1998, Shah Alam.


\textbf{Graduate Research}

Azlina Salim. (Ongoing). Immunology [M.S]. Universiti Putra Malaysia.