Evaluation of a Salmonella Vectored Vaccine Expressing Mycobacterium avium Subsp. paratuberculosis Antigens Against Challenge in a Goat Model.

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Johne's disease (JD), caused by Mycobacterium avium subsp paratuberculosis (MAP), occurs worldwide as chronic granulomatous enteritis of domestic and wild ruminants. To develop a cost effective vaccine, in a previous study we constructed an attenuated Salmonella strain that expressed a fusion product made up of partial fragments of MAP antigens (Ag85A, Ag85B and SOD) that imparted protection against challenge in a mouse model. In the current study we evaluated the differential immune response and protective efficacy of the Sal-Ag vaccine against challenge in a goat model as compared to the live attenuated vaccine MAP316F. PBMCs from goats vaccinated with Sal-Ag and challenged with MAP generated significantly lower levels of IFN-γ, following in vitro stimulation with either Antigen-mix or PPD jhonin, than PBMC from MAP316F vaccinated animals. Flow cytometric analysis showed the increased in IFN-γ correlated with a significantly higher level of proliferation of CD4, CD8 and γδT cells and an increased expression of CD25 and CD45R0 in MAP316F vaccinated animals as compared to control animals. Evaluation of a range of cytokines involved in Th1, Th2, Treg, and Th17 immune responses by quantitative PCR showed low levels of expression of Th1 (IFN-γ, IL-2, IL-12) and proinflammatory cytokines (IL-6, IL-8, IL-18, TNF-α) in the Sal-Ag immunized group. Significant levels of Th2 and anti-inflammatory cytokines transcripts (IL-4, IL-10, IL-13, TGF-β) were expressed but their level was low and with a pattern similar to the control group. Overall, Sal-Ag vaccine imparted partial protection that limited colonization in tissues of some animals upon challenge with wild type MAP but not to the level achieved with MAP316F. In conclusion, the data indicates that Sal-Ag vaccine induced only a low level of protective immunity that failed to limit the colonization of MAP in infected animals. Hence the Sal-Ag vaccine needs further refinement to increase its efficacy.