Evaluation of Mycobacterium avium subsp. paratuberculosis leuD mutant as vaccine candidate against challenge in a caprine model.

Faisal SM, Chen JW, Yan F, Chen TT, Useh NM, Yan W, Guo S, Wang SJ, Glaser AL, McDonough SP, Singh B, Davis WC, Akey BL, Chang YF.

Department of Population Medicine and Diagnostic Sciences.

Abstract

Johne's disease (JD) is prevalent worldwide and has a significant impact on the global agricultural economy. In the present study we evaluated the protective efficacy of a leuD (ΔleuD) mutant and gained insight into differential immune responses after challenge with virulent MAP in a caprine colonization model. The immune response and protective efficacy was compared with the killed vaccine Mycopar. In-vitro stimulation of PBMCs with PPDj showed that Mycopar and ΔleuD generated similar levels of IFN-γ but significantly higher levels than unvaccinated and challenged PBS controls. However only ΔleuD was able to maintain the IFN-γ response. Flow cytometric analysis showed the increase in IFN-γ correlated with proliferation and activation (increased expression of CD25) of CD4, CD8 and γδT cells but this response was significantly higher in ΔleuD vaccinated animals at some time points after challenge. Both Mycopar and ΔleuD vaccines upregulated Th1, proinflammatory and Th17 cytokines and downregulated Th2/anti-inflammatory and regulatory cytokines at similar levels at almost all time points. However, significantly higher levels of IFN-γ (at weeks 26 and 30), IL-2 (week 18) IL-1β (weeks 14 and 22), IL-17 (weeks 18 and 22), IL-23 (week 18) and a significantly lower level of IL-10 (weeks 14 and 18) and TGF-b (week 18) were detected in the ΔleuD vaccinated group. Most importantly, ΔleuD elicited an immune response that significantly limited colonization of tissues compared to Mycopar upon challenge with wild type MAP. In conclusion, ΔleuD mutant is a promising vaccine candidate for development of a live attenuated vaccine for JD in ruminants.