Developing and testing a live attenuated Johne's disease vaccine as a JD control measure

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Alberta has a high prevalence of Johne's disease, caused by *Mycobacterium avium Subsp. paratuberculosis.* This highlights the need for better JD control to benefit the Alberta dairy industry. A live attenuated vaccine against JD is most promising to protect calves against MAP infections. In this project, we aim to make mutants and fine-tune the attenuation of mutant strains, so that it stimulates protective immune responses without being harmful, persistent or infectious. For this purpose, we will create single and double mutants in MAP genes that were previously identified as being essential for the survival of MAP in the intestinal tissues of dairy calves. We have already created 2 different KO mutants and the reagents (engineered phages) are available to produce any combination of mutations in a single strain. In previous studies we tested these mutants ex vivo in macrophages to measure macrophage viability, MAP viability and cytokines production. These mutants have been also tested in vivo in mice infection model to study histology and size of infected organs. Previous studies showed that mutation in essential genes might result in different pro-inflammatory and anti-inflammatory responses. In the current study these candidate vaccine strains will be tested in our validated calf infection model. We will characterize the protective responses by immune cell and cytokine profiling. This will inform our selection of the best vaccine strain to test in a vaccination/challenge experiment in dairy calves. Implications: As part of an interdisciplinary project, we will contribute to significant new insights on the entirety of JD to the dairy and beef industry and identify control practices that can reduce the massive burden that JD has put on the dairy industry for years.