Development of a recombinant multi-stage DIVA vaccine against Johne's disease

Gregers Jungersen[1], Aneesh Thakur[1], Heidi Mikkelsen[1], Claus Aagaard[2], Peter Andersen[2]

[1] Technical University of Denmark, National Veterinary Institute, Frederiksberg, Denmark; [2] Statens Serum Institute, Copenhagen, Denmark

Taking advantage of results from vaccine development against *Mycobacterium tuberculosis*, a new (FET11) vaccine against *M. avium* subsp. *paratuberculosis* (Map) based on recombinant antigens from acute and latent stages of Map infection was developed. A hall-mark in the development of the vaccine was a requirement not to interfere with diagnostic tests for bovine TB and Johne's disease allowing a continued diagnosis of Map infection in vaccinated animals (DIVA vaccine).

In two post-exposure vaccination trials with 28 calves and 15 goats, respectively, animals were orally inoculated with live Map in their third week of life and post-exposure vaccinated at different times after inoculation or with different vaccine constructs. In response to vaccination animals developed vaccine-specific antibody and cell-mediated immune responses, but no measurable antibody responses by ID Screen® ELISA, PPDj-specific IFN-γ responses or positive PPDa or PPDb skin tests. At termination 8 or 12 months of age, relative Map burden was determined in a number of gut tissues by quantitative IS900 PCR and revealed significantly reduced levels of Map and reduced histopathology. Diagnostic tests for antibody responses and cell-mediated immune responses corroborated the observed vaccine efficacy: Five of seven non-vaccinated calves seroconverted in ID Screen® ELISA indicating the progression of infection, while only four of 14 FET11 vaccinated calves seroconverted and a later time point after inoculation. Similarly, increased PPDj-induced IFN-γ responses over time in non-vaccinated calves, while FET11 vaccinated calves had significantly reduced responses in PPDj IFN-γ assay from 40 to 52 weeks compared to non-vaccinated calves. These results indicate the FET11 vaccine can be used to accelerate eradication of paratuberculosis while surveillance or test-and-manage control programs for TB and JD remain in place.