**Development of a Swine Vaccination Model for Human Brucellosis**

Beata Clapp1, Guan Yang2, Bianca L. Artiaga2, Carol Hoffman1, Xinghong Yang1, John P. Driver2, and David W. Pascual1

1Dept. of Infect. Dis. & Immunol., 2Dept. of Animal Sciences, Univ. of Florida, Gainesville, FL

Human brucellosis remains a global health problem. No vaccines for human brucellosis exist. Even though *Brucella* infections primarily occur via the mucosa of the oropharynx and the upper respiratory tract, few studies have considered mucosal aspects to *Brucella's* pathogenesis. We have shown that mucosal administration of our live attenuated mutant confers exceptional protection against *Brucella* challenge. Although mice have long been instrumental to study immunity to *Brucella*, they are not always suitable to evaluate mucosal infections. Domestic pigs’ close resemblance to human immune system and shared anatomy of the oropharyngeal (OPG) mucosa allows studying mucosal aspects of brucellosis in a natural host. To assess the *B. melitensis* mutant’s immunogenicity in swine, 8 wk-old pigs were vaccinated via a combined OPG method of directly applying 109 CFUs onto the tonsils and sublingual mucosa plus a buccal injection with 108 CFUs on days 0, 2, and 4, and study was terminated 60 days post-primary immunization. Immunogenicity was compared to immune responses by similarly S19 vaccinated pigs. Peripheral blood mononuclear cells (PBMCs) from each pig on days 0, 15, 23, 35, 60 plus terminal bleed and terminal head and neck lymphoid tissue lymphocytes were isolated and evaluated for IFN-γ responses by flow cytometry following short period of antigen restimulation. The greatest presence of IFN-γ came from peripheral blood CD8+ and CD4+ CD8+ T cells. Increases in the number of IFN-γ-producing NK cells were also noted. Changes in PBMC T cells over the course of the response showed a significant reduction in the percentage of total CD4+ T cells with concurrent increases in the percentage of total CD8+ and CD4+ CD8+ T cells. With the exception of the tonsils where the majority of IFN-γ was derived from CD8+ T cells, the greatest amount of IFN-γ was produced by CD4+CD8+ T cells, particularly by the mandibular lymph nodes. Thus, our *Brucella* mutant is immunogenic in swine and capable of eliciting elevated IFN-γ responses following OPG vaccination. Work supported by NIH R03 AI-128123 and USDA-NIFA2013-01165.