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Importance of B cells in parenteral murine infection with *Francisella novicida*A. Y. Chou¹, K. L. Elkins¹¹FDA, Center for Biologics Evaluation and Research, Bethesda, United States

Aims: *Francisella tularensis* is an intracellular pathogen that infects macrophages and causes the acute febrile disease tularemia. *Francisella novicida* is a subspecies considerably less virulent in humans but has retained its virulence in mouse models. Previous studies have looked at *in vivo* infection of mice with the attenuated live vaccine strain (LVS). Protection against LVS infection is predominantly achieved through T cell mediated pathways. However, some literature suggests an important role for antibodies as well as B cells. Relatively little is known about protection against *F. novicida*. This study examines the role of B cells and antibody responses to intradermal infection with *F. novicida*, using wild type C57BL/6J and B-cell knock out (BKO) mice. Information from these studies is especially useful for facilitating the characterization and investigation of mutant bacterial strains which have been made on *F. novicida* background.

Methods: C57BL/6J mice and BKO mice were infected intradermally with a sublethal dose of *F. novicida* strain U112 (FnU112) and followed for survival. Mice were sacrificed to determine bacterial dissemination, organ burdens, clearance, and serum analyses. Spleens from surviving mice were harvested for study using an *in vitro* co-culture assay of FnU112 infected bone marrow macrophages to determine ability to control bacterial infection. Other survivors were challenged with a lethal dose of FnU112 intraperitoneally.

Results: FnU112 appeared to be highly virulent in both C57BL/6J and BKO mice. BKO mice were more sensitive to primary infection, and exhibited an estimated LD₅₀ of 25 CFU (compared to LD₅₀ of 100 CFU in C57BL/6J). Bacterial burdens were greater and persisted longer in infected BKO mice compared with wild type mice. Although BKO mice were able to withstand a moderate secondary challenge dose, vaccinated BKO mice were much more susceptible to secondary i.p. challenge with FnU112 than vaccinated C57BL/6J mice.

Conclusions: B cells play an important role in the ability to survive primary i.d. infection with FnU112. Using transfer studies, the relative contributions of immune serum and B cells to protect against *F. novicida* challenge is under active investigation.