

Immune Modeling for Vaccine Development

Influence of Sex on Protection Conferred by Vaccination with Attenuated Strains of *Francisella tularensis* in the Rabbit Model.

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Francisella tularensis (Ft) is the causative agent of tularemia, which has a 30% fatality rate in humans. It can be spread through arthropods, direct contact, ingestion, and inhalation, resulting in different forms of disease, of which the pneumonic form is the most severe. Due to the low infectious dose, ease of dissemination, and potential for severe disease, Ft is considered a category A select agent by the CDC. We have previously shown in the rabbit model that derivatives of virulent Ft strain SCHU S4 (S4) can serve as vaccines, protecting against aerosol challenge with S4. The level of protection depends upon the vaccination route, number of vaccinations, and vaccine strain used. Two aerosol doses of S4 Δ aroD achieved 83% survival. Serum IgG and IgM levels pre-challenge correspond with protection. Previous experiments had been done only in female rabbits so we assessed whether sex would influence protection. Nine of ten male rabbits vaccinated twice by aerosol with S4aroD survived aerosol challenge with a moderate dose of S4 (~100 LD₅₀) although at a higher challenge dose survival was no better than female rabbits. Analysis of all the data, however, suggest sex does influence protection against tularemia. Ongoing analysis of humoral and cellular immune responses will be presented and discussed in the context of the observed differences in protection by sex along with other clinical findings (CBC, ESR, bacteremia, bacterial tissue titration).