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Development, Phenotypic Characterization, Genomic Analysis, And Virulence Assessment Of A *Francisella tularensis* Panel For Tularemia Vaccine Testing

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Francisella tularensis is one of several biothreat agents for which a licensed vaccine is needed to protect against this pathogen. To aid in vaccine development to protect against pneumonic tularemia and possible genetically engineered strains, we generated and characterized a panel of *F. tularensis* isolates. Our panel consists of both historical and contemporary isolates derived from clinical and environmental sources. Whole genome sequencing was performed to assess the genetic diversity in comparison to the reference genome *F. tularensis* Schu S4. We identified several unique mutations within the *Francisella* Pathogenicity Island across multiple strains in our panel. To determine if any of these mutations would affect virulence, small animal model testing was performed initially in mice by intranasal challenge and then whole body small particle aerosol sprays in Fisher rats. All but one of the strains retained full virulence in mice, and this strain was dropped from this panel. When progressing to aerosol challenges in rats, a wide range in LD50s was determined in this panel. From these *F. tularensis* strains, we are currently down selecting which ones will be transitioned for testing in a non-human primate model. Overall, we provide a well-characterized panel of virulent *F. tularensis* strains that can be utilized in ongoing efforts to develop an effective vaccine against pneumonic tularemia to ensure protection is achieved across a range strains beyond just the prototype Schu S4 strain.

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