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Type IV pilin-like proteins of *Francisella tularensis* contribute to virulence in a context-dependent manner

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Aims: To discern a role for the type IV pilus in virulence of *Francisella tularensis* ssp. *tularensis* (Schu S4) and a derivative of *F. tularensis* ssp. *holarctica* (LVS).
Methods: In *Francisella* spp. there are six proteins with significant homology to type IV pilins and the potential to encode the major subunit of a type IV pilus. In LVS, only three of these genes encode full length proteins. We used homologous recombination to generate independent deletions of these three genes in Schu S4 (designated FTT0861c, FTT0230c, and FTT1314c), as well as their counterparts in LVS, and performed transmission electron microscopy (TEM) to determine whether these mutations altered the production of extracellular fibrous appendages. To determine the potential role of these genes in adherence and invasion to host cells, all knockout strains were subjected to *in vitro* adherence assays to compare adherence and invasion phenotypes relative to their wild-type parent strains. *In vivo* mouse studies are ongoing to characterize what, if any, roles these proteins have in virulence.
Results: TEM data suggests that two of the type IV pilin homologs are not involved in the production of pili, while the third protein is indispensible and participates either as the major structural subunit or part of the assembly apparatus. Counterpart mutations in Schu S4 and LVS exhibited similar piliated phenotypes. However, *in vitro* adherence and *in vivo* virulence studies indicate the three proteins may play different roles in these processes in their respective strains.
Conclusions: Taken together, the data suggest that subtle contextual differences in type IV pilin systems contribute to the different infectious capacities of virulent and avirulent *Francisella* strains.