Characterizing the Secretion Signal in the C-Terminus of the Francisella tularensis Protein FTL_1123: Insights for Type 1 Secretion and Therapeutics

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Francisella tularensis, a gram-negative bacterium, is the causative agent of tularemia, a severe zoonotic disease. The CDC classifies F. tularensis as a tier one biothreat agent, as it is highly lethal at minimal exposures. Understanding its virulence mechanisms is crucial given its potential use in biological warfare. Prior studies have shown that F. tularensis interferes with the host immune system in a TolC-dependent manner. This study focuses on the FTL_1123 protein, identified through BLAST analysis as homologous to a TolC-dependent protein in Neisseria meningitidis. The Type-1 Secretion System (T1SS) is a bacterial mechanism to transport proteins necessary for infection from inside to outside the cell. My previous work demonstrated that the FTL_1123 protein could secrete through the canonical T1SS found in E. coli, confirming its TolC-dependence. This year's research aimed to determine whether the FTL_1123 protein contained other characteristics typical of type-1 secreted proteins, specifically a C-terminus secretion signal. Results demonstrated that while all protein constructs were present at an equal level in the whole-cell lysate, there was a major difference in concentration between the FTL_1123 (?270-300) and FTL_1123 (?280-300) constructs in the cell-free media, suggesting a possible C-terminus secretion signal within these final 20-30 amino acids of the FTL_1123 protein. This knowledge enhances our ability to characterize the T1SS in Francisella tularensis, and our understanding of virulence mechanisms utilized by this bacterium to infect the host, allowing for new avenues for the development of therapeutics to prevent the secretion of this important virulence factor.

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