Secretion of the Francisella tularensis Protein FTL_1123 by Escherichia coli Containing the ?HlyBD Operon

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Francisella tularensis, a gram-negative bacterium, is the causative agent of tularemia, a severe zoonotic disease which is highly lethal even with minimal exposure. Francisella is recognized by the CDC as a tier one biothreat agent, due to severe potential risk for biological warfare. This volatile bacterium establishes an advantageous environment to thrive within macrophages. Studies demonstrated that Francisella interferes with the innate immune system in a TolC dependent manner. BLAST analysis revealed that the FTL_1123 protein contains a sequence in its C-terminus that shares 72% with an RTX Secretion signal in FrpC, a TolC dependent toxin in Neisseria meningitidis. Further, homologs of the FTL_1123 were present only in virulent Francisella subspecies; characterizing FTL_1123 as a protein of interest. The FTL_1123 protein lacks fully bonafide RTX motifs, typically correlated with T1SS-secreted proteins. This research investigated the secretion mechanism of the FTL_1123 protein in Francisella, and discovered that the FTL_1123 protein is able to secrete through the canonical Type 1 Secretion System (T1SS), located in Escherichia coli. This study established the FTL_1123 as a critical virulence factor for Francisella,and provides insight about secretion mechanisms of F. tularensis. These findings enhance understanding of the pathogenesis of Tularemia and establish a foundation and hope for the creation of therapeutics which disrupt the bacteria’s ability to export virulence factors. This study also expands the knowledge of T1SS’s and their secreted proteins. Current research is being conducted to determine dependence on a predicted ??-helix structure in the C-terminus of the FTL_1123 protein for its secretion.

Awards Won:

Second Award of $2,000