Investigating the Regulation of bS21 Homologs in *Francisella tularensis*

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Francisella tularensis is a highly infectious, intracellular human pathogen that can cause fatal disease. The *F. tularensis* type VI secretion system is an essential virulence factor required for survival in host cells, including survival in what are considered a key niche, macrophage. We have determined that ribosome composition influences production of the *F. tularensis* type VI secretion system and virulence. Ribosomes containing one of the three homologs for the small ribosomal subunit protein bS21, bS21-2, positively control key virulence genes and intramacrophage replication. However, the mechanisms that control and coordinate production of bS21-2 and the other bS21 homologs, bS21-1 and bS21-3, are unknown. We have found that bS21-2 negatively regulates its own production, as the presence of bS21-2 leads to significant reductions in abundance of its transcript, *rpsU2*. Further, we have found that the 5′ untranslated region (UTR) of *rpsU2* is sufficient for this bS21-2-mediated repression. Production of bS21-2 appears to be tightly controlled by bS21 levels in the cell, as both bS21-1 and bS21-3 also negatively regulate bS21-2 transcript abundance. In contrast, bS21-1 and bS21-3 do not affect their own production. Thus, the bS21-mediated regulation of bS21-2 appears to be unique among the three homologs. This suggests that *F. tularensis* integrates multiple signals into a regulatory network to control the appropriate production of each bS21 homolog. This regulatory network in turn may control ribosomal heterogeneity and virulence gene expression.