Two FtsH Proteases Contribute to Fitness and Adaptation of Pseudomonas aeruginosa Clone C Strains

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Abstract

Pseudomonas aeruginosa is an environmental bacterium and a nosocomial pathogen with clone C one of the most prevalent clonal groups. The P. aeruginosa clone C specific genomic island PACGI-1 harbors a xenolog of ftsH encoding a functionally diverse membrane-spanning ATP-dependent metalloprotease on the core genome. In the aquatic isolate P. aeruginosa SG17M, the core genome copy ftsH1 significantly affects growth and dominantly mediates a broad range of phenotypes, such as secretion of secondary metabolites, swimming and twitching motility and resistance to aminoglycosides, while the PACGI-1 xenolog ftsH2 backs up the phenotypes in the ftsH1 mutant background. The two proteins, with conserved motifs for disaggregase and protease activity present in FtsH1 and FtsH2, have the ability to form homo- and hetero-oligomers with ftsH2 distinctively expressed in the late stationary phase of growth. However, mainly FtsH1 degrades a major substrate, the heat shock transcription factor RpoH. Pull-down experiments with substrate trap-variants inactive in proteolytic activity indicate both FtsH1 and FtsH2 to interact with the inhibitory protein HflC, while the phenazine biosynthesis protein PhzC was identified as a substrate of FtsH1. In summary, as an exception in P. aeruginosa, clone C harbors two copies of the ftsH metallo-protease, which cumulatively are required for the expression of a diversity of phenotypes.

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