

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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