Culture aeration alters the role of the Pseudomonas aeruginosa PrrF sRNAs in antimicrobial activity against Staphylococcus aureus

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Cystic fibrosis is a hereditary disease characterized by chronic, biofilm-mediated polymicrobial lung infections. These infections typically involve early colonization of the lung by *Staphylococcus aureus,* which is eventually displaced by *Pseudomonas aeruginosa*. This etiological shift is correlated with worsened patient outcomes, but the underlying biology of this shift remains unknown. *P. aeruginosa* secretes several alkyl-quinolone (AQ) metabolites that exhibit antimicrobial activity against *S. aureus* during *in vitro* co-culture and co-infection. This activity contributes to *P. aeruginosa* iron acquisition and may contribute to *P. aeruginosa* predominance in later stages of CF. Previously, our lab has shown AQ production is positively affected by PrrF small regulatory RNAs (sRNAs) in shaking, aerated cultures. Under these conditions, PrrF sRNAs are required for AQ-mediated antimicrobial activity against *S. aureus*. However, PrrF sRNAs are dispensable for both AQ production and antimicrobial activity against *S. aureus* in static conditions, suggesting PrrF regulation is altered by aeration. To test this, we've employed label-free proteomics, using liquid chromatography-tandem mass spectrometry (LC-MS/MS) to characterize iron regulation in *P. aeruginosa* cultures grown in either shaking or static growth conditions. This analysis demonstrated that aeration significantly alters the iron and PrrF regulons of *P. aeruginosa,* including genes involved metabolism, iron uptake, and virulence factor production. Our results suggest oxygen availability dramatically alters the role of PrrF sRNAs in *P. aeruginosa* pathogenesis. This may have implications for studies of chronic CF lung infections of *P. aeruginosa*, a condition in which oxygen availability is greatly diminished due to biofilm formation and decreased lung function.