How genetic background influence phage resistance trade-offs in three different *Pseudomonas aeruginosa* clinical isolates

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Phage steering is an approach to phage therapy leveraging the evolution of phage resistance to steer bacterial evolution toward clinically benign phenotypes. While such phage resistance trade-offs have been demonstrated in a limited number of laboratory reference strains, whether and how trade-offs vary across diverse clinical isolates is not known. Here, we explored how phage resistant trade-offs driven by a lipopolysaccharide-targeting virulent phage varied across three *Pseudomonas aeruginosa* clinical isolates. We first isolated spontaneous phage-resistant mutants from 10 independent cultures per strain and confirmed phage resistance via cross-streaking and EOP. We then compared the performance of mutants relative to their phage-susceptible ancestral strain using microplate growth curves. This revealed that phage resistant mutants from one background showed consistent performance trade-offs, while mutants from the other two strains displayed variable outcomes, with selected mutants exhibiting equal or improved growth compared to their ancestor.
Antibiotic susceptibility against three different antibiotics (ceftazidime, colistin and tobramycin) was also evaluated by standard broth microdilution assay.
Similarly to the growth curves, mutants from a genetic background showed consistent lower MIC values for all drugs compared to the ancestral strain, while the other two displayed cases of lower or higher MIC values of the wild-type bacteria.
Phage resistant mutants will be analyzed through sequencing and additional phenotypic assays.
These findings demonstrate that the outcome of phage steering is variable across clinical isolates, underscoring the importance of characterizing phage-driven trade-offs in a wider set of strains.