

Poster abstract submission

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Poster title

Systematic Combinatorial Optimization of Three-Phage Cocktails Against Multidrug-Resistant *Pseudomonas aeruginosa*

Poster abstract

Background:

Multidrug-resistant *Pseudomonas aeruginosa* poses a significant global health threat, necessitating alternative therapeutic strategies. Bacteriophage therapy shows promise, but single-phage use is prone to resistance. Bacteriophage cocktails can address this issue, but they are typically formulated empirically without a systematic evaluation of constituent phage interactions.

Methodology:

We employed a comprehensive combinatorial approach to optimize three-phage cocktails against clinical *P. aeruginosa* isolates. From 25 candidate bacteriophages, five were selected based on broad host range ($\geq 60\%$ of 51 MDR *P. aeruginosa* clinical isolates). Ten possible three-phage cocktail combinations were systematically generated and evaluated using real-time Omnilog phenotypic microarray analysis. Phage interactions were quantified using the Highest Single Agent independence model to classify synergistic ($\Delta > +5\%$), neutral ($-5\% \leq \Delta \leq +5\%$), or antagonistic ($\Delta < -5\%$) effects.

Results:

Individual phage inhibition efficiencies ranged from 35.4% to 75.4%. Cocktail performance varied dramatically (16.1–84.1% inhibition). Only one cocktail exhibited synergy, achieving 84.1% inhibition, an 8.7% improvement over the best individual phage. Four cocktails (40%) showed neutral interactions, while five (50%) demonstrated antagonistic effects. The optimal cocktail (Phages 1+3+4) demonstrated efficacy across six of eight diverse clinical isolates in biofilm inhibition assays (29–63% biomass reduction, 2.7–3.6 \log_{10} CFU reduction) and achieved approximately 80% survival in *Galleria mellonella* infection models versus 10% in infected controls.

Conclusions

These findings demonstrate that phage cocktail optimization requires rational validation, as antagonistic interactions can occur, establishing a critical validation step before committing resources to *in vivo*

efficacy studies.

Research topic

Phage or phage products