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Targeted Antimicrobial Peptide Discovery and Phage Cocktail Development Against ESKAPE Pathogens

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Treatment options are being limited by the increasing threat of antimicrobial resistance among ESKAPE pathogens, with bacteriophages and phage-derived peptides being regarded as promising alternatives to conventional antibiotics.

Viral tagging, a culture-independent method, was used to identify wastewater-derived phages that selectively infect ESKAPE pathogens. After metagenomic assembly and viral discovery, the resulting viral genomes were screened for potential antimicrobial peptides (AMPs) using three distinct machine learning algorithms. Three candidate AMPs were synthesised and tested against 18 clinical ESKAPE isolates. In parallel, lytic phages were isolated using culture-based methods and formulated into species-specific and broad-spectrum ESKAPE phage cocktails.

Two novel AMPs demonstrated antibacterial activity, with MIC values as low as 4 μM against Enterobacter cloacae (AMP1), 5.3 μM against Enterococcus faecium (AMP1) and 10.6 μM against Acinetobacter baumannii (AMP3). The species-specific phage cocktails covered up to 91% of the tested strains, and the ESKAPE cocktail exhibited comparable or greater bacterial inhibition than the individual phages for most strains.

These findings demonstrate that integrating viral tagging with culture-based phage isolation expands access to host-specific phage diversity and enables the discovery of both phage-derived antimicrobial peptides and therapeutic phages against multidrug-resistant ESKAPE pathogens.

Reference #1

Reference #2

Reference #3

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