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Poster abstract submission

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Poster title

Chemical Induction of Prophages as an Antimicrobial Strategy

Poster abstract

Bacteriophages frequently integrate their genetic material into bacterial genomes, establishing a lysogenic state as prophages. Small-molecule compounds can trigger prophage induction by activating the lysis-lysogeny switch across diverse bacterial species. While prophage induction may facilitate horizontal transfer of virulence genes, it can also be beneficial when prophages lack virulence or toxin-associated factors, leading to faster cell lysis and bacterial eradication.

Understanding the outcomes of prophage induction in clinically relevant pathogens is crucial for advancing the development and optimization of novel antibacterial strategies while minimizing unintended effects. However, standardized approaches for quantifying prophage induction and identifying ecologically relevant triggers remain largely unexplored.

In this study, we established robust, quantitative methodologies for measuring prophage induction to test the hypothesis that secondary metabolites can function as prophage inducer. We systematically compared six quantitative approaches to evaluate prophage induction in Escherichia coli (λ prophage) following mitomycin C treatment. The assessed methods included double-layer plaque assays, quantitative PCR (qPCR), flow cytometry, fluorescence-based DNA quantification, optical-density based mathematical modelling, and prophage-specific genetic reporter. This comparison provided a framework regarding sensitivity, throughput, and suitability for various experimental designs.

Using these standardized protocols, we screened a library of secondary metabolite extracts for induction activity against laboratory and clinical isolates of key pathogens. Through activity-guided fractionation, followed by compound identification using NMR and mass spectrometry, we identified siderophore pyochelin, produced by Pseudomonas aeruginosa, as a potent prophage inducer in Gram-positive bacteria, including Staphylococcus aureus. Mechanistically, we propose that pyochelin generates reactive oxygen species (ROS) to trigger the bacterial SOS response and subsequent prophage induction thereby giving P.

aeruginosa a competitive advantage over S. aureus in polymicrobial environments such as cystic fibrosis lungs and chronic wounds. These findings establish a methodological standard for studying phage-bacteria interactions and highlight the therapeutic potential of small-molecule prophage inducers as a novel strategy to combat multidrug-resistant pathogens.

Research topic

Phage or phage products