transcriptome Bacteriophage P. aeruginosa

Impact of phage predation on bacterial transcriptome under simulated human airway conditions

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Bacteriophages have been proven to be efficient in the combat of bacterial multidrug-resistant infections, including those caused by *Pseudomonas aeruginosa*. Nevertheless, the interactions of phages with bacteria in the human body remains unexplained and its disclosure could lead to advance research and development in phage-based therapies.

In this work, RNA-sequencing of phage-infected *P. aeruginosa* PAO1 adhered to a human epithelial cell monolayer (Nuli-1 ATCC® CRL-4011™) was performed to assess bacterial transcriptional processes occurring in phage–bacteria–human cells, i.e., mimicking phage predation under more realistic settings. To achieve that, adhered bacteria were infected with phage LUZ19, and total RNA was extracted from the complex cell mixture. Thereafter, bacterial rRNA/human RNA was depleted and cDNA libraries were prepared to sequence. The differentially expressed genes (DEGs) were quantified using uninfected bacteria as control.

In human airway-simulated conditions, there were 21, 39, and 129 bacterial DEGs after 5, 10, and 15 min-post infection, respectively. From DEGs, some genes were identified as part of LUZ19 typical induced responses (prophage, glycerol metabolism, and spermidine synthesis genes). However, unique responses were also captured including upregulation of pyochelin syntheses, LPS modification, sulfate starvation, exopolysaccharide-related genes, and downregulation of bacterial global regulators. These changes are associated with starvation-like conditions (iron and sulfate) and bacteria adaptation to the host, but its role in phage infection progression is still unknown. The study of its impact on bacterial virulence or phage efficient infectivity under human physiology is of most importance.

This comprehensive study allows the comparison of bacterial and phage transcripts in the presence of host cells, contributing to a better understanding of phage-bacteria-host interactions, which are relevant in a phage therapy context.