

Study of phage resistance emerging during phagotherapy

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Antimicrobial resistance (AMR) remains one of the most pressing challenges in modern medicine. In the fight against multidrug-resistant (MDR) pathogens, phage therapy is considered a promising alternative. Nevertheless, the emergence of bacterial resistance to bacteriophages during treatment significantly limits therapeutic success and requires in-depth analysis.

The presented doctoral research aims to identify and analyze mechanisms of phage resistance using clinical cases of infections caused by *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*, where phage-resistant strains emerged during the course of phage therapy. Fourteen patients have been selected for the study, from whom bacterial strains and phages used in therapy will be analyzed both phenotypically and genotypically. The selection criterion includes cases where bacterial isolates are available from both before and after phage therapy.

The study involves a comparative analysis of the properties of therapeutic phages. This includes phenotypic and genomic characterization of bacterial strains and corresponding phages, such as whole-genome sequencing and bioinformatic analysis. In parallel, detailed clinical case analyses are planned, including infection history, effectiveness of prior antibiotic therapy, duration of phage treatment, and therapeutic outcomes.

The objective of this research is to explore the mechanisms underlying phage resistance in a real clinical context and to relate them to specific bacterial and phage characteristics. The findings are expected to contribute to improved planning of phage therapy and the development of personalized therapeutic strategies, ultimately enhancing the predictability and effectiveness of treatment for MDR infections.