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# Reverse Antibiotic-Resistance in ESBL *E. coli* using CRISPR technique and programmed bacteriophages

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Antimicrobial resistance of pathogens such as *E. coli* is a growing concern to the health care system. This increased concern of pathogen resistance to current therapies is encouraging the development of new antimicrobial strategies, and is reviving interest in traditional bacteriophage applications. Although therapeutic and prophylactic application of lytic phages has distinct advantages. over conventional medical interventions, bacteria have evolved multiple defense barriers to interfere with nearly every step of phage life cycles. Phages counteract this selection pressure by evolving their genomes to evade bacterial resistance. The antagonistim between bacteria and rapidly mutating viruses promotes the evolution and propagation of phageresistance mechanisms in bacteria. An adaptive microbial immune system, known as Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) provides for acquired immunity against viruses and plasmids. Unlike the restriction–modification anti-phage barrier that cleaves any foreign DNA lacking a protective methyl-tag in the target site, the CRISPR–Cas systems are invader-specific, adaptive, and heritable. In this study, we use bacteriophages for delivering a programmable DNA nuclease, CRISPR-associated (Cas), to reverse antibiotic resistance and to eliminate the transfer of resistance between strains. This novel approach combines CRISPR-Cas delivery with lysogen, lytic phage selection of antibiotic-sensitized bacteria. The strategy uses phages in a unique way that overcomes many of the hurdles encountered by phage therapy, and, therefore, may reduce the prevalence of antibiotic-resistant bacteria in designated facilities that may have concern for MDR strains.

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