

CRISPR and Phages: A Perfect Pair in Targeting Resistant Bacteria

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Description

The global rise of antibiotic resistance has become a pressing challenge in modern medicine, threatening to render many infections untreatable. As traditional antibiotics lose their effectiveness, researchers are exploring innovative approaches to combat resistant bacteria. Among these, the combination of CRISPR technology and bacteriophages (phages) stands out as a groundbreaking strategy. This synergistic duo leverages the precision of CRISPR systems and the natural bacterial-killing ability of phages to create targeted and effective therapies. By understanding how CRISPR and phages work together, we can unlock new possibilities for addressing antibiotic resistance and improving public health. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) is a genetic editing tool derived from bacterial immune systems. In bacteria, Cas proteins defend against invading phages by recognizing and cutting their DNA. Researchers have repurposed this system to precisely edit genetic material, enabling a wide range of applications in medicine, agriculture, and biotechnology. When combined with phages, CRISPR systems can be tailored to target specific bacterial strains, making them an invaluable tool in phage therapy.

The role of CRISPR in enhancing phage therapy

Phages are viruses that infect and kill bacteria by injecting their genetic material into bacterial cells, leading to their destruction. While phages naturally target specific bacteria, their efficacy can sometimes be limited by bacterial resistance mechanisms. By integrating CRISPR into phage genomes, scientists can enhance the specificity and potency of phage therapy. Engineered CRISPR-Cas systems can be programmed to target antibiotic resistance genes within bacterial populations, effectively neutralizing the resistance traits while leaving beneficial bacteria unharmed. For instance, CRISPR-Cas9 can be used to introduce double-strand breaks in the DNA of resistant bacteria, causing lethal damage. Alternatively, CRISPR interference (CRISPRi) can silence essential bacterial genes, rendering the bacteria non-viable. This targeted approach not only eradicates resistant pathogens but also minimizes the risk of off-target effects, a major concern in conventional antibiotic treatments. Moreover, CRISPR-phage systems can be customized to target multiple resistance genes simultaneously, addressing

the challenge of multidrug-resistant bacteria. One notable example of this technology in action is the development of phages engineered with CRISPR systems to combat *Escherichia coli* and *Klebsiella pneumoniae*, two pathogens frequently associated with drug-resistant infections. These engineered phages have demonstrated the ability to selectively eliminate resistant strains while sparing susceptible bacteria, preserving the natural microbial balance essential for human health.

Advantages and challenges of CRISPR-phage therapy

The combination of CRISPR and phages offers several distinct advantages over traditional antibacterial treatments. First, their specificity reduces the likelihood of collateral damage to beneficial bacteria, which is a common side effect of broad-spectrum antibiotics. This precision helps maintain the host's microbiome, reducing the risk of secondary infections and other complications. Second, CRISPR-phage therapy can be rapidly adapted to emerging resistance patterns, allowing for timely and effective responses to bacterial outbreaks. Finally, the use of phages as delivery vehicles ensures that CRISPR systems reach their bacterial targets efficiently, overcoming many of the challenges associated with gene-editing delivery methods. Despite these advantages, CRISPR-phage therapy faces several challenges that must be addressed before widespread clinical adoption. One significant hurdle is the potential for bacteria to develop resistance to phages themselves. While phages can evolve alongside bacteria, ensuring their continued efficacy, this evolutionary arms race complicates the design of stable and reliable treatments. To mitigate this issue, researchers are exploring the use of phage cocktails mixtures of multiple phages with complementary mechanisms of action to reduce the likelihood of resistance development. Another challenge lies in the delivery and regulation of CRISPR systems. Ensuring that the CRISPR machinery functions as intended within bacterial cells requires precise engineering and thorough testing. Off-target effects, while less common than in traditional antibiotics, remain a concern, particularly in complex microbial communities. Regulatory hurdles also present obstacles, as the approval process for genetically engineered therapies is often lengthy and stringent. Addressing these challenges will require continued collaboration between researchers, clinicians, and policymakers. The ethical and ecological implications of CRISPR-phage therapy also warrant careful consideration. Releasing genetically

modified phages into the environment could have unforeseen consequences, including impacts on non-target microbial populations and ecosystems. Developing robust safety protocols and conducting comprehensive risk assessments will be essential to ensure the responsible use of this technology. The integration of CRISPR technology with phage therapy represents a promising frontier in the fight against antibiotic-resistant bacteria. By combining the precision of CRISPR with the natural bactericidal properties of phages, researchers have created a

powerful tool for selectively targeting resistant pathogens. While challenges remain, including the risk of bacterial resistance to phages and regulatory hurdles, the potential benefits of CRISPR-phage therapy are immense. This innovative approach not only addresses the limitations of traditional antibiotics but also paves the way for a new era of personalized and sustainable antibacterial treatments. As research continues to advance, CRISPR and phages may well become a cornerstone in the global effort to combat antimicrobial resistance.