Short Note

Advancing AMR Strategies: Integrating Bacteriophages and CRISPR

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Advancing AMR Strategies: Integrating Bacteriophages and CRISPR

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Abstract: Antimicrobial resistance (AMR) threatens global health. In this manuscript, I review recent literature underscoring the promise of engineered bacteriophages and CRISPR-Cas systems as targeted strategies against resistant bacteria. These approaches offer alternatives to broad-spectrum antibiotics by precisely disrupting biofilms and inactivating resistance genes—whether applied independently or in tandem. I also underscore the essential role of public-private partnerships in advancing clinical applications and catalyzing the translation of innovative research into practice

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Antimicrobial resistance (AMR) is one of the most critical health threats, claiming 1.2 million lives each year. Although awareness is rising, this number is projected to rise to 10 million by 2025 [1]. Despite increasing awareness, the battle against AMR is slow to progress. Broad-spectrum antibiotics' accelerated resistance, and the development strategies and design principles used for antibiotic production have led to resistance in pathogens, compromising the long-term efficacy of these drugs [2,3]. Therefore, without fundamental changes in the direction of the EU's current strategy, which focuses on accelerating antibiotic development, the battle against AMR is unlikely to succeed.

The most recent suggested EU strategy on AMR promises a creative approach to antibiotic research and development; yet, reaching progress will need a coordinated, multifarious effort with the creation of new antibiotics only one necessary component. Non antibiotic solutions could be the key in overcoming these challenges. Three recent studies released in 2024 revealed the most recent advances in anti-AMR strategies and bacteriophage technology. In the first study, it was demonstrated that bacteriophages engineered by CRISPR-Cas editing could target and suppress *E. coli* biofilms in mice, which is indeed a powerful new tool against resistant strains without compromising the microbiome [4]. The second paper focused on *Klebsiella pneumoniae* whereby broad host-range phages and last-ditch antibiotics boosted bacterial control by reducing the number of pathogens and resistance in murine models [5]. Finally, CRISPR-Cas9 vectors via engineered phage particles have enabled AMR gene editing at the molecular level: resistance has been diminished by editing gene variants in bacteria [6]. This strategy makes bacterial re-sensitization significantly more accurate and effective by reversing AMR in clinical pathogens.

The use of bacteriophages has been proposed as a potential mechanism to combat AMR in the new pharmaceutical legislation, as discussed by EU Commissioner Stella Kyriakides during a European Parliament debate on AMR [7]. This inclusion is part of an overall effort to strengthen regulatory programs for combating AMR (see Table 1). One might question why the Commission delayed the authorization of bacteriophages for saving human lives, especially given the strong support from its own scientific advisers. Beyond bacteriophages, recent research indicates that CRISPR-phage antibacterials should be included in the legislation. These cutting-edge, non-traditional AMR treatments must be accepted by policymakers as able to provide targeted treatment and prevent the adverse effects of antibiotics.

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Table 1. Summary of Key EU Regulatory Initiatives Against AMR.

Initiative Name	Focus
EU One Health Action Plan	A holistic approach addressing human, animal, and environmental aspects of AMR prevention.
EU Guidelines on the Wise Use of Antibiotics	Provides guidelines to reduce inappropriate antimicrobial use in human healthcare.
HERA (Health Emergency Preparedness and Response)	Focuses on stockpiling critical antibiotics and ensuring preparedness for future AMR threats.
EU4Health Program	Provides grants to support EU member states' efforts in AMR surveillance, prevention, and control.

To address AMR effectively, it is also essential to consider public acceptance of alternative treatments. Farmers have been most resistant to antibiotic control measures, and often unfavorably, and it is time for tougher regulation – including the prohibition of human-use antibiotics in livestock, while at the same time disallowing veterinarians to sell antibiotics [8]. Alongside these measures, there is growing support for alternative solutions like bacteriophage therapy. A 2024 survey of Pakistani farmers found that greater awareness of bacteriophages correlated with stronger support for their use in microbial control in animals [9]. This indicates that education plays an important role in moving toward bacteriophage technology in both healthcare and agriculture to curb AMR.

Public-private partnerships (PPPs) such as The Global Antibiotic Research and Development Partnership (GARDP) are also central to fight against AMR [8]. In low- and middle-income countries, GARDP is involved in developing broad-spectrum antibiotics and advanced diagnostics, addressing the pressing need for equitable solutions to AMR [10]. Table 2 summarizes other PPPs that are crucial for accelerating the development of new drugs and ensuring that new treatments reach those who need them most.

Table 2. Key Public-Private Partnerships in the Fight Against AMR.

Partnership Name	Description
Global Antibiotic Research and Development Partnership (GARDP)	A public-private partnership that accelerates the development of new antibiotics and ensures global access.
CARB-X (Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator)	A global partnership that funds the early development of new antibiotics, vaccines, and rapid diagnostics.
IMI (Innovative Medicines Initiative)	A PPP in Europe that supports the development of new medicines, including those targeting AMR.
REPAIR Impact Fund	Focuses on supporting early-stage AMR-focused companies and developing innovative treatments.

While bacteriophage therapies and other advanced solutions progress through the development and approval phases, a critical component of AMR strategy remains education—not only for healthcare professionals but also for the public [8]. It's also clear that many medical and vets, hospitals, and farmers either lack sufficient training to properly prescribe and/or use antibiotics or fail to recognize that overuse or misuse leads to an endless cycle of resistance [8].

To sum up, we should:

(i) focus on developing new drugs that are less susceptible to resistance.

(ii) promote alternative treatment strategies, such as bacteriophage therapy.

(iii) restrict antibiotic use in animal husbandry while ensuring global access to essential antibiotics.

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(iv) enhance antimicrobial awareness and education; and

(v) leverage the EU's robust regulatory framework and public-private partnerships to lead these initiatives. Without these actions, we may jeopardize the fight against AMR.

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