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# Combating Antimicrobial Resistance: The Role of New Biotechnological Tools

Ms. Priyadarshani A. Patil,

Assistant professor, Krishna Institute of Allied Sciences, Krishna Institute of Medical Sciences “Deemed to be University,” Karad. Email: [pp1655159@gmail.com](mailto:pp1655159@gmail.com)

Dr. Kiran A. Bobde,

Assistant professor, Krishna Institute of Allied Sciences, Krishna Institute of Medical Sciences “Deemed to be University,” Karad. Email: [kiranbobde.7@gmail.com](mailto:kiranbobde.7@gmail.com)

Dr. Snehal A. Masurkar,

Associate professor, Krishna Institute of Allied Sciences, Krishna Institute of Medical Sciences “Deemed to be University,” Karad. Email: [snehalmasurkar2882@gmail.com](mailto:snehalmasurkar2882@gmail.com)

**Abstract.** Antimicrobial resistance (AMR) poses a significant threat to global public health, rendering many conventional antibiotics ineffective against bacterial infections. Addressing this challenge requires innovative approaches, among which biotechnological tools have emerged as promising solutions. This research paper explores the role of new biotechnological tools in combating AMR. It examines various biotechnological interventions such as CRISPR-Cas9 gene editing, phage therapy, antimicrobial peptides, and synthetic biology in the context of AMR mitigation. The paper discusses their mechanisms of action, potential applications, and current challenges. Additionally, it evaluates the implications of these biotechnological tools in clinical settings, agriculture, and environmental contexts. Through a comprehensive review of the literature, this paper aims to highlight the importance of integrating new biotechnological tools into multidisciplinary strategies to address the growing threat of antimicrobial resistance.

**Keywords:** Antimicrobial resistance, Biotechnological tools, CRISPR-Cas9, Phage therapy, Antimicrobial peptides, Synthetic biology.

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## 1. Introduction

Antimicrobial resistance (AMR) stands as one of the most pressing challenges facing global public health in the 21st century. It occurs when microorganisms such as bacteria, viruses, fungi, and parasites evolve to resist the effects of antimicrobial agents, rendering conventional treatments ineffective. The emergence and spread of AMR jeopardize the effectiveness of essential medical interventions, including surgeries, chemotherapy, and organ transplants, as well as the management of common infectious diseases. Consequently, it significantly increases morbidity, mortality, healthcare costs, and undermines sustainable development efforts worldwide.

### 1.1 Antimicrobial Resistance: A Global Health Crisis

The escalation of AMR into a global health crisis is attributed to several factors. Overuse and misuse of antimicrobial agents in human health, agriculture, and animal husbandry have accelerated the development of resistant pathogens. Inadequate infection prevention and control practices in healthcare settings further exacerbate the problem, facilitating the spread of resistant strains among patients. Additionally, globalization and increased international travel contribute to the rapid dissemination of resistant microbes across borders, transcending geographical boundaries.

The World Health Organization (WHO) has recognized AMR as a top priority, emphasizing the urgent need for concerted efforts to mitigate its impact. The WHO's Global Action Plan on Antimicrobial Resistance outlines a multifaceted approach that includes improving surveillance and monitoring, optimizing the use of antimicrobial

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agents, and fostering innovation in the development of new therapeutics. Despite these efforts, the trajectory of AMR continues to escalate, necessitating innovative and interdisciplinary solutions.

### 1.2 The Need for Innovative Solutions

Conventional strategies for combating AMR, such as the development of new antibiotics, have been hampered by scientific, economic, and regulatory challenges. The discovery and development of antibiotics are time-consuming, costly processes, and the emergence of resistance often outpaces the introduction of new drugs. Furthermore, the pharmaceutical industry has largely shifted its focus away from antibiotic research and development due to financial disincentives and low profitability.

Given these challenges, there is a critical need to explore alternative approaches to address AMR effectively. Biotechnological tools offer promising solutions by leveraging advances in molecular biology, genetic engineering, and microbial ecology. These tools enable targeted interventions against resistant pathogens, enhance the efficacy of existing antimicrobial agents, and provide novel strategies for combating AMR across diverse settings.

### 1.3 Role of Biotechnological Tools

Biotechnological tools encompass a diverse array of approaches that harness biological systems and processes to address challenges in healthcare, agriculture, and environmental sustainability. In the context of AMR, these tools offer innovative strategies for understanding, preventing, and treating resistant infections. From precision genome editing techniques like CRISPR-Cas9 to harnessing the therapeutic potential of bacteriophages, biotechnological interventions hold immense promise in the fight against AMR.

This research paper aims to explore the role of new biotechnological tools in combating AMR comprehensively. It will delve into specific interventions such as CRISPR-Cas9 gene editing, phage therapy, antimicrobial peptides, and synthetic biology, elucidating their mechanisms of action, potential applications, and current challenges. Through a multidisciplinary lens, this paper will examine the implications of these biotechnological tools in clinical practice, agricultural settings, and environmental contexts. By synthesizing existing knowledge and identifying future directions, this paper seeks to underscore the importance of integrating biotechnological innovations into holistic strategies to address the growing threat of antimicrobial resistance.

## 2. CRISPR-Cas9 Gene Editing

CRISPR-Cas9 gene editing has revolutionized the field of molecular biology and offers unprecedented precision in genome manipulation. Originally discovered as a bacterial immune system, CRISPR-Cas9 has been adapted into a powerful tool for targeted gene editing in a wide range of organisms, including bacteria, plants, animals, and humans. In the context of combating antimicrobial resistance, CRISPR-Cas9 presents unique opportunities for both understanding the mechanisms of resistance and developing innovative therapeutic strategies.

### 2.1 Mechanism of Action

The CRISPR-Cas9 system consists of two main components: the Cas9 nuclease and a guide RNA (gRNA). The gRNA directs Cas9 to a specific target sequence within the genome, where it induces a double-strand break (DSB). Subsequent repair of the DSB by the cell's DNA repair machinery can lead to gene knockout, insertion, or modification. In the context of antimicrobial resistance, CRISPR-Cas9 can be used to disrupt or modify genes associated with resistance mechanisms, thereby restoring susceptibility to antibiotics.

### 2.2 Applications in Addressing AMR

CRISPR-Cas9 holds immense potential for combating antimicrobial resistance through several key applications:

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**Functional Genomics:** CRISPR-Cas9 enables the systematic knockout or knockdown of genes implicated in antimicrobial resistance, allowing researchers to elucidate the underlying mechanisms and identify novel drug targets.

**Antibiotic Sensitization:** By targeting genes involved in resistance mechanisms, such as efflux pumps or drug-modifying enzymes, CRISPR-Cas9 can restore susceptibility to antibiotics in resistant pathogens.

**Genetic Engineering of Probiotics:** CRISPR-Cas9 facilitates the engineering of probiotic bacteria to deliver antimicrobial agents or antimicrobial peptides directly to sites of infection, thereby enhancing therapeutic efficacy and reducing the risk of resistance development.

**Phage Therapy Enhancement:** CRISPR-Cas9 can be employed to engineer bacteriophages with enhanced specificity and efficacy against specific bacterial pathogens, offering a promising avenue for personalized phage therapy approaches.

### **2.3 Challenges and Future Directions**

Despite its promise, the widespread application of CRISPR-Cas9 in combating antimicrobial resistance faces several challenges:

**Off-Target Effects:** CRISPR-Cas9 may induce unintended genetic modifications at off-target sites, raising concerns about safety and specificity.

**Delivery Methods:** Efficient delivery of CRISPR-Cas9 components to target cells remains a significant hurdle, particularly in clinical applications.

**Resistance Development:** There is a risk that bacteria may evolve resistance to CRISPR-Cas9-mediated interventions, potentially compromising their long-term efficacy.

Addressing these challenges will require continued research to refine CRISPR-Cas9 technology, develop robust delivery systems, and optimize therapeutic strategies. Moreover, ethical and regulatory considerations surrounding the use of gene editing in clinical settings must be carefully addressed to ensure responsible and equitable implementation.

The CRISPR-Cas9 gene editing holds immense promise as a versatile tool for combating antimicrobial resistance. By enabling precise genome manipulation and targeted interventions, CRISPR-Cas9 offers innovative solutions for understanding, preventing, and treating resistant infections. However, realizing the full potential of CRISPR-Cas9 in the fight against AMR will require concerted efforts to overcome technical challenges, address safety concerns, and navigate ethical considerations.

## **3. Phage Therapy**

Phage therapy, harnessing the natural ability of bacteriophages to infect and kill bacteria, has gained renewed interest as a potential strategy for combating antimicrobial resistance. Bacteriophages, or phages, are viruses that specifically target and replicate within bacterial hosts, making them highly selective antimicrobial agents. Phage therapy offers several advantages over conventional antibiotics, including narrow host specificity, self-replication at the site of infection, and the ability to evolve alongside bacteria to overcome resistance. In the context of addressing antimicrobial resistance, phage therapy presents a promising alternative to conventional antibiotics and has shown efficacy in both preclinical and clinical studies.

### **3.1 Phage Biology and Function**

Bacteriophages are diverse and abundant entities found in various environments, including soil, water, and the human microbiota. They consist of a protein capsid enclosing genetic material, typically DNA or RNA, and may exhibit different morphologies and infection strategies. Upon encountering a susceptible bacterial host,

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phages attach to specific receptors on the bacterial cell surface and inject their genetic material into the host cell. Within the host, phages hijack the bacterial machinery to replicate and produce progeny virions, ultimately leading to host cell lysis and release of new phage particles.

### 3.2 Therapeutic Applications in AMR

Phage therapy holds promise for addressing antimicrobial resistance through several key mechanisms:

**Targeted Killing:** Phages exhibit exquisite specificity for their bacterial hosts, allowing for precise targeting of pathogenic strains while preserving beneficial microbiota. This specificity reduces the selective pressure for resistance development compared to broad-spectrum antibiotics.

**Evolutionary Dynamics:** Phages can co-evolve with bacteria, continually adapting to overcome resistance mechanisms. This dynamic interplay between phages and bacteria, known as "kill the winner" dynamics, can help maintain phage efficacy in the face of evolving resistance.

**Biofilm Disruption:** Bacterial biofilms pose a significant challenge in the treatment of chronic infections due to their inherent resistance to antibiotics. Phages have shown promise in penetrating and disrupting biofilms, making them attractive candidates for the treatment of biofilm-associated infections.

**Combination Therapies:** Phage therapy can be combined with antibiotics or other antimicrobial agents to enhance efficacy and overcome resistance. Synergistic interactions between phages and antibiotics have been observed, leading to improved treatment outcomes in some cases.

### 3.3 Clinical Trials and Implementation Challenges

While phage therapy holds considerable potential, several challenges remain to be addressed:

**Standardization and Quality Control:** Standardizing phage preparations and ensuring quality control are critical for reproducibility and safety. Methods for phage isolation, purification, and characterization vary widely, highlighting the need for standardized protocols and regulatory oversight.

**Phage Pharmacokinetics and Pharmacodynamics:** Understanding the pharmacokinetic and pharmacodynamic properties of phages is essential for optimizing dosing regimens and treatment outcomes. Factors such as phage stability, host range, and immune clearance influence their efficacy in vivo.

**Regulatory Approval and Market Access:** Regulatory frameworks for phage therapy vary between countries, posing challenges for widespread clinical implementation. Streamlining regulatory processes and establishing clear guidelines for phage-based therapeutics are necessary to facilitate market access and commercialization.

Despite these challenges, ongoing clinical trials and case studies have demonstrated the safety and efficacy of phage therapy in treating various bacterial infections, including those caused by multidrug-resistant pathogens. Continued research and innovation in phage biology, formulation, and delivery hold promise for advancing phage therapy as a viable treatment option for combating antimicrobial resistance. By harnessing the natural predatory abilities of bacteriophages, phage therapy offers a targeted and sustainable approach to addressing the global threat of antimicrobial resistance.

## 4. Antimicrobial Peptides

Antimicrobial peptides (AMPs) are naturally occurring molecules found in a wide range of organisms, including humans, animals, plants, and microorganisms. These peptides play a crucial role in the innate immune response, serving as frontline defense mechanisms against microbial pathogens. Antimicrobial peptides exhibit broad-spectrum activity against bacteria, fungi, viruses, and parasites, making them attractive candidates for combating antimicrobial resistance. Their unique mechanism of action, rapid killing kinetics, and low propensity for resistance development distinguish them from conventional antibiotics. In recent years, there has

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been growing interest in harnessing the therapeutic potential of antimicrobial peptides for addressing the global challenge of antimicrobial resistance.

#### 4.1 Nature and Diversity

Antimicrobial peptides display remarkable structural diversity, ranging from linear to cyclic peptides and containing varying amino acid compositions and sequences. Common structural motifs include  $\alpha$ -helices,  $\beta$ -sheets, and extended loops, which contribute to their antimicrobial activity and membrane-disrupting properties. Antimicrobial peptides can be classified based on their sources (e.g., host defense peptides, bacterial peptides, or synthetic peptides) or their mode of action (e.g., membrane-targeting peptides, intracellular-targeting peptides, or immunomodulatory peptides).

#### 4.2 Mechanisms of Action Against Resistant Pathogens

Antimicrobial peptides exert their antimicrobial activity through multiple mechanisms, including:

**Disruption of Cell Membranes:** Many AMPs interact with bacterial cell membranes, disrupting membrane integrity and permeability. This leads to leakage of cellular contents, loss of membrane potential, and ultimately cell death. Importantly, the amphipathic nature of AMPs enables them to selectively target bacterial membranes while sparing mammalian cell membranes.

**Inhibition of Intracellular Processes:** Some AMPs target intracellular components of bacteria, such as DNA, RNA, or protein synthesis machinery, leading to inhibition of vital cellular processes. By interfering with multiple cellular targets, AMPs reduce the likelihood of resistance development through target modification or mutation.

**Immunomodulatory Effects:** In addition to their direct antimicrobial activity, AMPs can modulate the host immune response by enhancing chemotaxis, promoting wound healing, or stimulating cytokine production. These immunomodulatory effects contribute to the overall efficacy of AMP-based therapies and may help mitigate inflammatory responses associated with infection.

#### 4.3 Potential Clinical and Agricultural Applications

Antimicrobial peptides hold promise for various clinical and agricultural applications:

**Therapeutic Agents:** AMPs have demonstrated efficacy against a wide range of bacterial pathogens, including multidrug-resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenem-resistant Enterobacteriaceae (CRE). AMP-based therapeutics are being developed for the treatment of skin and wound infections, respiratory tract infections, and systemic infections.

**Biopesticides:** In agriculture, antimicrobial peptides offer eco-friendly alternatives to chemical pesticides for controlling plant pathogens and pests. AMPs can be incorporated into crop protection formulations or applied as biofertilizers to enhance plant growth and resistance to microbial diseases.

**Food Preservation:** Antimicrobial peptides have potential applications in food preservation and safety by inhibiting the growth of spoilage organisms and foodborne pathogens. AMPs may be used as natural preservatives or incorporated into packaging materials to extend the shelf life of perishable foods.

Despite their therapeutic potential, several challenges must be addressed to realize the widespread use of antimicrobial peptides, including optimization of peptide stability, bioavailability, and production scalability. Moreover, understanding the interplay between AMPs and host immune responses is crucial for minimizing potential cytotoxicity or inflammatory effects. Nevertheless, the diverse nature of antimicrobial peptides and their multifaceted mechanisms of action make them promising candidates for combating antimicrobial resistance in diverse settings. Continued research and innovation in peptide design, formulation, and delivery

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hold the key to unlocking the full therapeutic potential of antimicrobial peptides in the fight against resistant pathogens.

## **5. Synthetic Biology Approaches**

Synthetic biology offers innovative strategies for combating antimicrobial resistance by engineering biological systems to address specific challenges associated with resistant pathogens. Through the design and construction of novel genetic circuits, biosensors, and microbial platforms, synthetic biology enables the creation of tailored solutions for understanding, preventing, and treating antimicrobial-resistant infections. By combining principles from engineering, biology, and computer science, synthetic biology approaches hold promise for revolutionizing the development of antimicrobial therapeutics, diagnostics, and surveillance tools.

### **5.1 Engineering Novel Antibiotics**

Synthetic biology provides a powerful platform for the discovery and optimization of novel antimicrobial compounds with enhanced efficacy and reduced susceptibility to resistance. By engineering microbial hosts to produce or modify natural antimicrobial compounds, researchers can overcome limitations associated with traditional antibiotic discovery pipelines. Moreover, synthetic biology techniques such as directed evolution and rational design enable the optimization of antimicrobial peptides, small molecules, and natural products for improved potency, stability, and bioavailability.

### **5.2 Modifying Microbial Communities**

The composition and dynamics of microbial communities play a critical role in shaping resistance phenotypes and infection outcomes. Synthetic biology approaches can be employed to engineer microbial communities, or microbiomes, to promote colonization resistance, modulate host immune responses, and suppress the growth of pathogenic bacteria. By introducing probiotic bacteria or engineering commensal microbes to produce antimicrobial compounds, synthetic biology offers innovative strategies for restoring microbial balance and preventing the emergence and spread of resistant pathogens.

### **5.3 Environmental Remediation**

Antimicrobial resistance is not confined to clinical settings but also extends to environmental reservoirs, such as soil, water, and wastewater. Synthetic biology approaches can be applied to remediate environmental sources of resistance by engineering microbial communities to degrade or sequester antimicrobial contaminants. Engineered microbes equipped with degradative enzymes or biosensors can target specific pollutants and mitigate their impact on environmental resistance reservoirs. Moreover, synthetic biology techniques enable the development of biosensors for rapid detection and monitoring of antimicrobial resistance genes in environmental samples, facilitating surveillance efforts and informing risk assessment strategies.

Despite the potential of synthetic biology approaches, several challenges must be addressed to realize their impact in combating antimicrobial resistance. These include optimizing genetic circuit design for robust performance, ensuring safety and containment of engineered organisms, and addressing ethical and regulatory considerations associated with the release of genetically modified organisms into the environment. Moreover, interdisciplinary collaboration between synthetic biologists, microbiologists, clinicians, and environmental scientists is essential for translating synthetic biology innovations into practical solutions for addressing antimicrobial resistance across diverse contexts.

The synthetic biology holds promise for revolutionizing our approach to combating antimicrobial resistance by providing innovative strategies for antibiotic discovery, microbiome engineering, and environmental remediation. By harnessing the power of genetic engineering and biological design principles, synthetic biology approaches offer tailored solutions for understanding, preventing, and treating resistant infections, thereby advancing efforts to safeguard public health and promote sustainable antimicrobial use. Continued research and

collaboration in synthetic biology will be essential for realizing the full potential of these approaches in addressing the global challenge of antimicrobial resistance.

6. Integration of Biotechnological Tools into Multidisciplinary Strategies

The effective management of antimicrobial resistance requires a multidisciplinary approach that integrates biotechnological tools with conventional interventions, public health initiatives, and policy measures. By combining the strengths of different disciplines, such as microbiology, molecular biology, clinical medicine, epidemiology, and bioinformatics, multidisciplinary strategies can address the complex and multifaceted nature of antimicrobial resistance comprehensively. The integration of biotechnological tools into such strategies offers unique opportunities for synergistic interventions across various domains.

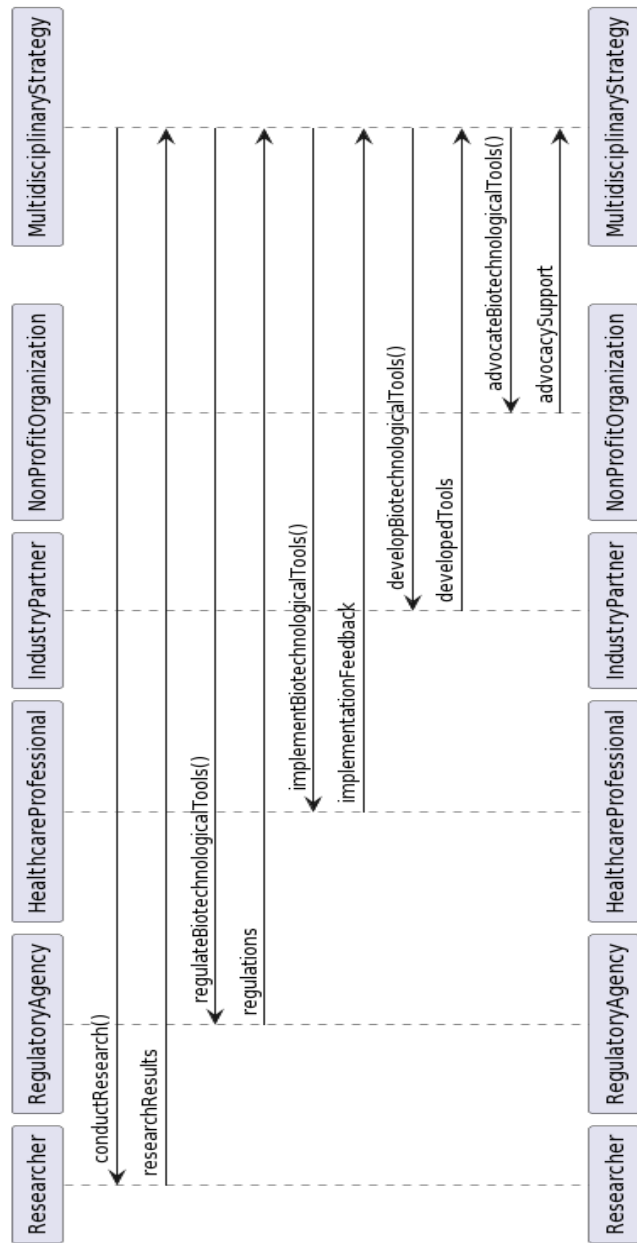


Figure 1. Integration of Biotechnological Tools into Multidisciplinary Strategies

### 6.1 Collaborative Approaches

Multidisciplinary collaboration is essential for harnessing the full potential of biotechnological tools in combating antimicrobial resistance. Collaborative research efforts involving academia, industry, government agencies, and non-profit organizations facilitate knowledge exchange, resource sharing, and technology transfer. By fostering interdisciplinary partnerships, researchers can leverage complementary expertise and infrastructure to accelerate the development and implementation of biotechnological interventions. Moreover, collaborative networks enable the pooling of data, samples, and resources for large-scale studies, clinical trials, and surveillance initiatives, enhancing the robustness and generalizability of research findings.

### 6.2 Regulatory and Ethical Considerations

The integration of biotechnological tools into antimicrobial resistance management requires careful consideration of regulatory and ethical issues. Regulatory frameworks governing the use of biotechnological interventions, such as gene editing technologies and genetically modified organisms, vary between countries and regions. Harmonizing regulatory standards and streamlining approval processes are essential for facilitating the translation of biotechnological innovations from the laboratory to clinical practice. Additionally, ethical considerations surrounding the equitable access, affordability, and safety of biotechnological interventions must be addressed to ensure responsible and sustainable implementation. Transparency, inclusivity, and stakeholder engagement are critical for building public trust and confidence in biotechnological approaches to antimicrobial resistance.

### 6.3 Capacity Building and Knowledge Transfer

Capacity building and knowledge transfer are essential components of multidisciplinary strategies for combating antimicrobial resistance. Training programs, workshops, and educational initiatives play a crucial role in equipping healthcare professionals, researchers, policymakers, and community stakeholders with the knowledge and skills needed to understand, prevent, and manage antimicrobial resistance effectively. Moreover, efforts to disseminate best practices, guidelines, and evidence-based recommendations facilitate the adoption and implementation of biotechnological tools in diverse settings. By investing in human capital development and knowledge dissemination, multidisciplinary strategies can empower individuals and institutions to contribute to the global effort against antimicrobial resistance.

The integration of biotechnological tools into multidisciplinary strategies represents a promising approach to combating antimicrobial resistance. By leveraging the collective expertise and resources of diverse disciplines, such strategies can address the complex challenges posed by resistant pathogens comprehensively. Through collaborative research, regulatory alignment, and capacity-building initiatives, multidisciplinary approaches can harness the full potential of biotechnological innovations to safeguard public health, promote antimicrobial stewardship, and preserve the effectiveness of antimicrobial agents for future generations.

## 7. Conclusion

Antimicrobial resistance (AMR) poses a significant threat to global public health, necessitating urgent and coordinated action across multiple fronts. In this context, biotechnological tools have emerged as promising solutions for understanding, preventing, and treating resistant infections. Through innovative approaches such as CRISPR-Cas9 gene editing, phage therapy, antimicrobial peptides, synthetic biology, and multidisciplinary strategies, researchers are advancing our capabilities to combat AMR and safeguard the effectiveness of antimicrobial agents. Biotechnological interventions offer unique advantages in addressing the complex challenges posed by AMR. CRISPR-Cas9 gene editing enables precise manipulation of bacterial genomes to reverse resistance mechanisms and enhance susceptibility to antibiotics. Phage therapy harnesses the natural predatory abilities of bacteriophages to selectively target and kill bacterial pathogens, offering a targeted and sustainable alternative to conventional antibiotics. Antimicrobial peptides exhibit broad-spectrum activity against resistant pathogens and can be engineered for enhanced potency and specificity. Synthetic biology



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approaches enable the design and construction of tailored solutions for antibiotic discovery, microbiome engineering, and environmental remediation. The integration of biotechnological tools into multidisciplinary strategies is essential for maximizing their impact in combating AMR. Collaborative research efforts, regulatory harmonization, and capacity-building initiatives are necessary to translate biotechnological innovations from the laboratory to clinical practice effectively. Moreover, ethical considerations surrounding the responsible use of biotechnological interventions must be addressed to ensure equitable access, safety, and sustainability. As we confront the growing threat of antimicrobial resistance, it is imperative to prioritize investments in research, innovation, and collaboration. By leveraging the power of biotechnology alongside conventional interventions and public health measures, we can develop comprehensive strategies to mitigate the impact of AMR and preserve the efficacy of antimicrobial agents for future generations. Through collective action and global cooperation, we can turn the tide against antimicrobial resistance and secure a healthier and more resilient future for all.

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