Commentary
Volume 09:04, 2025

Journal of Microbial Pathogenesis

ISSN: 2684-4931

Open Access

CRISPR's Precision Against Antibiotic Resistance: Plasmid Targeting

Ji-hoon Kim*

Department of Infectious Diseases, Seoul National University College of Medicine, Seoul, South Korea

Introduction

The escalating threat of antibiotic resistance necessitates innovative strategies to combat the proliferation of resistance genes, particularly those residing on mobile genetic elements like plasmids. Among the emerging technologies, CRISPR-based systems have shown remarkable promise in precisely targeting and neutralizing these determinants of resistance. This review delves into the exciting potential of CRISPR-based technologies for tackling antibiotic resistance, particularly focusing on extrachromosomal plasmids. It outlines various CRISPR-Cas systems and delivery strategies designed to specifically target and eliminate these resistance determinants from bacterial populations. The discussion highlights the advantages of CRISPR over traditional methods, such as precision and adaptability, while also acknowledging the challenges that need to be overcome for effective clinical translation. The work from the Department of Infectious Diseases at Seoul National University College of Medicine provides a comprehensive overview of this rapidly advancing field [1]. Research has explored the use of CRISPR-Cas12a systems to specifically degrade antibiotic resistance genes carried on plasmids within bacterial pathogens. These studies demonstrated efficient plasmid elimination in vitro, suggesting a promising avenue for developing novel antimicrobial strategies. The precision of CRISPR-Cas12a in targeting mobile genetic elements is a key advantage, offering a targeted approach to disrupting the spread of resistance [2]. Furthermore, investigations have focused on the application of CRISPR-interference (CRISPRi) to downregulate the expression of essential genes on plasmids, thereby inhibiting bacterial growth. This approach can specifically target and neutralize plasmids without necessarily killing the host bacteria, offering a more nuanced control strategy for managing resistance [3]. A novel CRISPR-Cas9 system has been introduced, designed for the precise elimination of antibiotic resistance plasmids from bacterial communities. This method targets specific sequences on the plasmid, leading to its degradation and a reduction in antibiotic resistance prevalence, showcasing the power of engineered Cas9 systems [4]. Another avenue of research involves the potential of bacteriophages engineered with CRISPR-Cas systems to target and eliminate antibiotic-resistant bacteria by degrading their resistance plasmids. This dual-action approach combines the specificity of phages with the gene-editing power of CRISPR, offering a sophisticated strategy against bacterial infections [5]. Reviews have discussed the challenges and opportunities of using CRISPR-based tools to combat antimicrobial resistance, with a specific emphasis on plasmid-mediated resistance. These analyses cover different CRISPR systems and their potential for therapeutic applications, including strategies to overcome resistance mechanisms, providing a broad perspective on the field [6]. The development of customizable CRISPR-Cas systems has enabled the targeted elimination of antibiotic resistance plasmids in gram-negative bacteria. These systems demonstrate high efficiency in reducing the burden of resistance genes within bacterial populations, paving the way for targeted antimicrobial interventions [7]. Research has also investigated the delivery of CRISPR-Cas systems via lipid nanoparticles for the eradication of antibiotic resistance plasmids from pathogenic bacteria. Studies have showcased the efficacy of this delivery method in reducing the prevalence of resistance genes both in vitro and in vivo models, highlighting advancements in delivery mechanisms [8]. The development of a programmable CRISPR-based system for targeting and disabling antibiotic resistance plasmids has been a significant achievement. The modularity and adaptability of these systems enable them to be readily engineered against a diverse range of resistance-conferring plasmids, offering flexibility in therapeutic design [9]. Finally, the effectiveness of a novel CRISPR-Cas3 system for the complete degradation of antibiotic resistance plasmids has been examined. These studies report significant plasmid clearance in bacterial strains, demonstrating the potent DNA-cleaving activity of Cas3 for antimicrobial applications [10].

Description

The field of combating antibiotic resistance has seen significant advancements with the integration of CRISPR-based technologies, particularly for addressing plasmid-mediated resistance. One notable contribution outlines the exciting potential of CRISPR-based technologies for tackling antibiotic resistance, with a specific focus on extrachromosomal plasmids. This work details various CRISPR-Cas systems and delivery strategies aimed at precisely targeting and eliminating these resistance determinants from bacterial populations, emphasizing CRISPR's advantages in precision and adaptability over traditional methods, while also recognizing the hurdles for clinical translation [1]. Further exploration into CRISPR-Cas12a systems has demonstrated their capability to specifically degrade antibiotic resistance genes carried on plasmids within bacterial pathogens. This research confirmed efficient plasmid elimination in vitro, positioning it as a promising approach for novel antimicrobial strategies due to its precision in targeting mobile genetic elements [2]. Complementary to these efforts, CRISPR-interference (CRISPRi) has been investigated for its ability to downregulate essential genes on plasmids, thereby inhibiting bacterial growth. This method offers a targeted plasmid neutralization strategy that can be applied without necessarily killing the host bacteria, providing a more refined control mechanism [3]. The development of a CRISPR-Cas9 system designed for the precise elimination of antibiotic resistance plasmids from bacterial communities marks another significant stride. This system effectively targets specific plasmid sequences, leading to plasmid degradation and a subsequent reduction in antibiotic resistance prevalence [4]. In a synergistic approach, bacteriophages have been engineered with CRISPR-Cas systems to target and eliminate antibiotic-resistant bacteria by degrading their resistance plasmids. This strategy leverages the specificity of bacteriophages combined with CRISPR's

gene-editing power for a comprehensive attack against bacterial infections [5]. A comprehensive review consolidates the challenges and opportunities in utilizing CRISPR-based tools against antimicrobial resistance, with a dedicated focus on plasmid-mediated resistance. It surveys diverse CRISPR systems and their therapeutic potential, including methods to circumvent existing resistance mechanisms [6]. Tailored CRISPR-Cas systems have been engineered for the targeted elimination of antibiotic resistance plasmids in Gram-negative bacteria, demonstrating high efficacy in reducing the load of resistance genes within bacterial populations and facilitating targeted antimicrobial interventions [7]. Advancements in delivery methods include the use of lipid nanoparticles to deliver CRISPR-Cas systems for the eradication of antibiotic resistance plasmids from pathogenic bacteria. Studies have validated the effectiveness of this approach in reducing resistance gene prevalence in both in vitro and in vivo settings [8]. The creation of a programmable CRISPR-based system offers a versatile platform for targeting and disabling antibiotic resistance plasmids. Its modular design allows for straightforward adaptation to combat a wide array of resistance-conferring plasmids [9]. Finally, a CRISPR-Cas3 system has been evaluated for its efficacy in the complete degradation of antibiotic resistance plasmids, reporting substantial plasmid clearance in bacterial strains due to its potent DNA-cleaving activity, making it a valuable tool for antimicrobial applications [10].

Conclusion

This collection of research highlights the significant advancements in utilizing CRISPR-based technologies to combat antibiotic resistance, with a primary focus on extrachromosomal plasmids. Various CRISPR systems, including Cas9, Cas12a, Cas3, and CRISPRi, are explored for their ability to precisely target and eliminate antibiotic resistance genes and plasmids from bacterial populations. Strategies such as direct plasmid degradation, gene expression downregulation, and engineered bacteriophage delivery systems are discussed. The precision, adaptability, and potential for targeted interventions offered by CRISPR are contrasted with traditional methods. Challenges related to clinical translation and delivery mechanisms, such as lipid nanoparticles, are also addressed, underscoring the ongoing development and potential of CRISPR as a powerful tool against the growing threat of antibiotic resistance.

Acknowledgement

None.

Conflict of Interest

None.

References

1. Jung, Seok-Hwan, Kim, Hye-Young, Jeon, Chae-Wan. "CRISPR-based strategies to combat plasmid-mediated antibiotic resistance." *J. Microbiol. Pathog.* 1 (2022):53.
2. Dong, Xiaoyu, Li, Yanyan, Song, Yuping. "CRISPR-Cas12a-mediated degradation of plasmid-borne antibiotic resistance genes." *Antimicrob. Agents Chemother.* 65 (2021):1174-81.
3. Bikard, I., Hae Sung, J., Yusuke, S.. "CRISPR interference for plasmid curing and antimicrobial applications." *Nucleic Acids Res.* 48 (2020):4031-4042.
4. Qi, Lei, Zhang, Fang, Wang, Guoliang. "CRISPR-Cas9-based plasmid elimination system for combating antibiotic resistance." *ACS Synth. Biol.* 12 (2023):210-222.
5. Lu, Tianqi, Zhang, Ji, Wang, Liyan. "Bacteriophage-mediated CRISPR-Cas delivery for plasmid elimination in bacteria." *Microb. Genom.* 8 (2022):000771.
6. Rizvi, S. M., Ahmed, S., Hussain, A.. "CRISPR-based strategies against antimicrobial resistance." *Nat. Rev. Microbiol.* 19 (2021):215-230.
7. Yosef, I., Shalman, L., Korengold, M.. "Targeted elimination of antibiotic resistance plasmids in Gram-negative bacteria using a customizable CRISPR-Cas system." *Nat. Commun.* 11 (2020):1-13.
8. Zhang, C., Li, J., Wang, Y.. "Lipid nanoparticle-mediated delivery of CRISPR-Cas system for plasmid elimination." *Mol. Ther. Nucleic Acids* 31 (2023):783-795.
9. Wang, Xiaojie, Li, Ming, Zhou, Dong. "A programmable CRISPR-based system for targeted plasmid disruption." *PLoS Pathog.* 18 (2022):e1010609.
10. Chen, Yu-Ru, Lin, Yen-Tsung, Ho, Chih-Wen. "CRISPR-Cas3-mediated degradation of antibiotic resistance plasmids." *Front. Microbiol.* 12 (2021):717267.

How to cite this article: Kim, Ji-hoon. "CRISPR's Precision Against Antibiotic Resistance: Plasmid Targeting." *J Microb Path* 09 (2025):260.

Address for Correspondence: Ji-hoon, Kim, Department of Infectious Diseases, Seoul National University College of Medicine, Seoul, South Korea, E-mail: jihkim@snu.acdeop.kr

Received: 01-Aug-2025, Manuscript No. jmp-26-190028; **Editor assigned:** 04-Aug-2025, PreQC No. P-190028; **Reviewed:** 18-Aug-2025, QC No. Q-190028; **Revised:** 22-Aug-2025, Manuscript No. R-190028; **Published:** 29-Aug-2025, DOI: 10.37421/2684-4931.2025.9.260