JOURNAL OF BASIC AND APPLIED SCIENCES

CRISPR-Cas System: Reversing Antibiotic Resistance in Bacteria

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ARTICLE INFORMATION

Systemic review

Received: Feb 19,2026
Revised: June 16,2026
Accepted: June 21,2026
Published: June 25,2026

Available online:

Citation: Omega M. Immanuel and Atamobebhu I. Isaiah (2026) *CRISPR-Cas System: Reversing Antibiotic Resistance in Bacteria*

Abstract

Antibiotic-resistant bacteria are a phenomenon threatening the efficacy of antimicrobial therapy in modern medicine. To tackle this public health menace, attention is shifting to the inclusion of a genetic approach to fight antimicrobial resistance (AMR), with the target being to effectively alter the genes that confer resistance on bacteria. The use of the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and its associated protein (Cas) holds promise as a genetic technology that can help tackle resistance in bacteria by directly targeting and incapacitating resistance genes or inducing lethal DNA breaks. This review x-rays antibiotic resistance as a menace to modern medicine, surveys the CRISPR system, explains the application for the treatment of infectious diseases, and identifies current challenges, limitations, and future directions for translating the technology into clinical practice. This technology has potential for use in the selective elimination of resistant pathogens, elimination of plasmids harbouring resistance genes, and resensitization of resistant pathogens. Modern medicine urgently needs to adopt this technology to combat antibiotic-resistant infectious diseases. However, with delivery efficiency, off-target effects, immunogenicity, and ethical governance must first be tackled before implantation succeeds.

Keywords: Antimicrobial therapy; CRISPR-Cas; drug-resistant bacteria, gene editing

1. Introduction

The widespread and excessive use of disinfectants and antibiotics has led to an unprecedented increase in the emergence of bacteria that are resistant to a variety of antibiotics, resulting in a routine rise in therapeutic failures, despite the ongoing development of new treatment strategies for infectious diseases (Gholizadeh et al., 2020). The inappropriate use of antibiotics alongside exposure to antibiotic molecules has escalated the antibiotic-resistance problem and, in grave cases, has increased mortality and fatality (Årdal et al., 2017; Jebri et al., 2021; Pendleton et al., 2013). This situation is threatening the gains of using antibiotics in modern medicine.

Bacteria have devised various defence mechanisms to evade the lethal toxic effect of drug molecules, rendering common infections untreatable. Resistance genes can easily spread across bacterial populations from clinical sources to environmental or vice versa (Goh et al., 2024; Vivekanandan et al., 2025). Nowadays, commonly used antibiotics are often ineffective against some targeted pathogens, creating a continuous demand for new antimicrobial therapies to combat previously susceptible pathogens (Pereira et al., 2021). Most notable and frequently reported resistance to antibiotics is caused by a group of bacteria also notorious for nosocomial infections, the “ESKAPE” bacteria (Boucher et al., 2009).

Antibiotic-resistant bacterial strains continue to emerge almost in parallel to the introduction of new antibiotics, owing to evolutionary pressure (Muteeb et al., 2023; Sun, 2025). To address this critical health concern, approaches to mitigate and eliminate Antimicrobial Resistance Genes (ARGs) in pathogens beyond developing new therapies have been proposed. In recent times, scientific investigations have focused on exploring novel genetic editing technologies with high-fidelity target recognition that can be used in the reversal and treatment of antibiotic resistance. The Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated (Cas) system has emerged as a genetic tool that can help tackle antimicrobial resistance (AMR) by directly locating, pairing, and incapacitating resistance genes (Rafiq et al., 2024).

This review provides a tripartite examination: first, a survey of CRISPR-Cas; second, the menace of AMR on modern medicine; and third, the exploitation of the system for neutralization of antibiotic resistance. We also discussed current challenges, limitations, and future directions for translating CRISPR-Cas therapies into clinical practice.

2. Overview of CRISPR-Cas

CRISPR was discovered in the genome of *Escherichia coli* (Ishino et al., 1987). CRISPR-Cas is a common feature among prokaryotes (*Makarvo et al., 2015*). Following their discovery, the functions were unknown and were then referred to as "loci of repeated sequence from the iap gene" (Ishino et al., 1987). Despite its discovery in 1987, the system's genomic-editing ability was identified in *Streptococcus thermophilus* in 2007 (Barrangou et al., 2007). It has evolved ever since, from its immunological roles in bacteria (Barrangou et al., 2007) and mammals (Goren et al., 2012), and has now been adapted as a powerful tool for genome editing, particularly when paired with the Cas protein (Silva and Fontes, 2022; Han et al., 2023; Li et al., 2023).

Based on the endonuclease, CRISPR-Cas is grouped into two key classes, Class 1 and Class 2, and six main types (I to VI), having numerous subtypes (*Strich and Chertow, 2019*). The Class 1 CRISPR-Cas systems (types I, III, and IV) operate with a complex of Cas proteins to recognize target DNA through base pairing and cleave it with a different enzyme, while class 2 (types II, V, and VI) employs a single-protein effector protein to recognize and cleave target DNA (Manvati and Dha, 2020; Mohammadzadeh et al., 2020; Strich and Chertow, 2019; Thurtle-Schmidt and Lo, 2018).

The technology has been successfully utilized to reverse resistance to specific antibiotics in bacteria (Aslam et al., 2020; Goren et al., 2017; Wang et al., 2019). This was achieved through multiple strategies, including the degradation of resistant genes (Goren et al., 2017), elimination of resistance plasmids (Tao et al., 2023), silencing regulatory genes (Vivekanandan et al., 2025) and knocking out regulatory gene elements such as efflux pumps (Delgado Ruitón et al., 2025). The field is fast-growing and has evolved from targeting single genes to enabling the systematic reprogramming of bacterial regulatory networks against multidrug resistance.

Precise addition, deletion, or modification of genes via the CRISPR-Cas platform is carried out by specific cleavage of the Cas9 protein directed by the RNA molecules to specific regions of the DNA, making an incision on the target region (Du et al., 2023; Sioson et al., 2021). Further, elimination of foreign nucleic material from the genome targets alien "Protospacers" embedded into the bacterial genome (Asmamaw and Zawdie, 2021).

As an acquired immune system, CRISPR-Cas functions primarily for defense, but it also acts as a storage system in the host bacteria or archaea, fighting against invading genetic material and storing acquired micro-molecules, respectively (Mohammadzadeh et al., 2020; Makarova et al., 2015; Strich and Chertow, 2019). Following horizontal acquisition through either conjugation, transduction, or transformation (Watson et al., 2018), short DNA sequences are integrated into the CRISPR locus of their hosts, where they target and eliminate encroaching genetic material after transcription and endonucleolytic processing into CRISPR RNA (crRNA) (Charpentier and Marraffini, 2014).

3. Antibiotic Resistance: A menace to modern medicine

A promethean event that ushered in the era of modern medicine was the discovery of antibiotics. Selman Waksman first defined antibiotics in the 1930s as "a compound made by a microbe that can destroy other microbes," following his evaluation of edaphic microbes and their ability to synthesize antimicrobial compounds. However, Paul Ehrlich's earlier discovery in 1910 set the pace for the modern antibiotic era with the discovery of salvarsan and neosalvarsan, primarily used in the treatment of syphilis caused by *Treponema Pallidum* (Hutchings et al., 2019). While the discovery of antibiotics in the 20th century was notable for revolutionizing modern medicine,

the concomitant evolution of antibiotic-resistant bacteria is fast becoming a silent pandemic, rendering even last resort antibiotics ineffective (Salam et al., 2023). Antibiotic resistance is developed intrinsically through chromosomal gene mutation or acquired through horizontal gene transfer as an evolutionary response to antibiotics; environmental changes in the subinhibitory antibiotic levels can also result in temporarily adaptive resistance (Salam et al., 2023)

Antibiotic resistance emerged alongside the antibiotic era, although the effects then were minimal and were largely dismissed as a minor concern. However, the phenomenon, once dismissed as a minor concern, has become a menace to modern medicine (Levy and Marshall, 2004). Antimicrobial resistance has risen to one of the leading public health threats, as it accounts for over a million deaths as of 2021 and contributes to about 5 million deaths globally, with a greater fatality rate among older adults (*Antimicrobial Resistance Collaborators, 2024*). The efficacy of common antibiotics is near extinction, with an alarming resistance rate among pathogenic bacteria (WHO, 2025).

The efficacy of some antibiotics for some clinically significant pathogens can be alarmingly lower than 50% and as low as 35% for methicillin-resistant *S. aureus* (WHO, 2022). The upsurge in antibiotic-resistant *E. coli* has been exacerbated in recent times, with antibiotic efficacy as low as 42% for infections (WHO, 2022). In 2020, 1 in 5 *E. coli* isolates from urinary tract infections showed increased resistance to frequently used antibiotics like co-trimoxazole, ampicillin, and fluoroquinolones, increasing the severity of *E. coli*-related urinary tract infections (WHO, 2022). Furthermore, an increased level of resistance has been reported for *K. pneumonia* isolated from the intestine (Isozumi et al., 2012). The emergence of multidrug-resistant *Neisseria gonorrhoeae*, carrying extended-spectrum β-lactamases (ESBLs), renders many antibiotics ineffective, conferring broad resistance to penicillin and cephalosporins. Other multidrug-resistant organisms of clinical significance include *Mycobacterium tuberculosis, Enterobacteriaceae, P. aeruginosa, A. baumannii,* and *Candida auris* (Kim et al., 2024; Wright, 2010; Wright et al., 2019).

Recently, the use of last-resort antibiotics has been intensified, giving credence to the continuous evolution of antibiotic-resistant bacteria observed across all regions. The compromised effectiveness of last-resort antibiotics, like carbapenems, has prompted the questioning of the continuous reliance on antibiotics in modern medicine (Meletis, 2016). This is so because, if drug regimens deemed a last resort are no longer effective, then we cannot win the war against pathogens. Use of antibiotics without proper medical guidance is the principal cause behind the sharp rise in global microbial resistance (Aslam et al., 2018). Over-the-counter antibiotic availability and customers' limited knowledge are known contributing factors to the escalating resistance patterns observed globally (Aslam et al., 2018; Baquero et al., 2008).

Antibiotic stewardship presents a viable means of mitigating some of these challenges. A particular concern is evident in Low- and Middle-Income Countries (LMICs), where antibiotic stewardship is challenging to implement (Cox et al., 2017). This situation in part accounts for the disproportionate acceleration of the development of resistant bacteria in these settings, making infections harder to treat in these regions (Desai et al., 2025). This situation highlights the urgent need to address health inequity and emphasizes the importance of including underrepresented and at-risk populations in research planning and implementation.

4. CRISPR-Cas: A Precision Tool Against Antibiotic Resistance

CRISPR-Cas is a precise gene editing technique that can be engineered to locate, pair, and neutralize genetic sequences of interest in the bacterial genome, including the problematic AMR genes (Gholizadeh et al., 2020). On one hand, the system can be guided towards plasmids harboring resistance genes to alter the gene and make the pathogen susceptible to antibiotics to which they were resistant (Aqeel and Raza, 2017; Mayorga-Ramos et al., 2023; Tao et al., 2022; Wang et al., 2019). The other approach is to use the system to cause DNA breakage that can be so lethal as to cause cell lysis (Liao et al., 2024; Tavella et al., 2025).

Editing genes using this technology can take the gene-focused approach or the pathogen-focused approach (Bikard et al., 2012; Dong et al., 2019). The delivery system remains a big challenge (Seijas et al., 2025; Tang et al., 2025). Common delivery methods include phagemid and conjugative plasmid techniques (Javed et al., 2023). However, a notable downside of these techniques is the encapsulation of both guide RNA (gRNA) and the protein, which limits their usefulness due to low efficiency and the increased chances of cytotoxicity at high dosage (Du et al., 2023; Sioson et al., 2021). To circumvent these limitations, novel non-viral delivery methods

have been developed. One of such promising techniques uses a nano-sized CRISPR complex to target the mecA gene (Li et al., 2025; Nujoom et al., *2024)*. Here, the polymer-derived Cas9 protein is linked with a cationic polymer to form the stable CRISPR nanocomplex (CrNc), without altering the CRISPR-Cas DNA cleavage function (Li et al., 2025; Nujoom et al., 2024).

5. Mechanism of CRISPR-Cas System Neutralization of ARG

The neutralization of ARG using the CRISPR-Cas system follows a sequence of detection of the specific DNA sequence, cleavage, and then repair, guided and executed by a specially designed Cas protein (Asmamaw and Zawdie, 2021; Yoon et al., 2026). The process begins with the design of gRNA, which is complementary to a recognizable target sequence. The Cas9 enzyme and gRNA are introduced into a mixed microbial community using either conjugable plasmids from bacteria, bacteriophages, or nanocomplexes derived from polymers (Moitra et al., 2024; Ye et al., 2025).

The phagemid and conjugative plasmid techniques for the introduction of Cas9 nuclease into the bacteria were well described by Javed et al. (2023). (Figure 1). The CRISPR_Cas complex recognizes and binds to the target sequence. The Cas enzyme cleaves the DNA to trigger a cellular response to repair the break by the bacteria. The outcome is either an insertion or deletion at the target site that disrupts the antibiotic resistance gene, or it could be a mutation that silences the resistance gene.

Figure 1: Mechanism of the CRISPR-Cas system (Javed et al., 2023).

Selective elimination of single or multiple genes from a population can be done by simultaneous and precise targeting of the genetic locations of interest. The Cas-9 phagemid method was utilized to selectively eliminate resistant *S. aureus* strains from a mixed bacterial population (Ahmed et al., 2024; Huan et al., 2023). A phagemid was engineered with Cas9 and crRNA sourced from a gene that confers methicillin resistance, Mec90 (pDB121: mecA). The pDB121: mecA phagimid targets specific plasmids encoding tetracycline resistance (pUSA01 and pUSA02). A 99.99% tetracycline sensitivity was observed in the previously tetracycline-resistant *S. aureus* USA300Φ, treated with pDB121: mecA phagimid, with no cell death observed in any of the Cas9 plasmids (Citorik et al., 2014). The efficacy of the Cas9 phagemid against the kanamycin resistance gene was assessed, and the therapy involved the application of pDB121:aph on the back of CD1 mice infiltrated with RNK cells; this resulted in a significantly more effective treatment than 2% mupirocin or 200 mg streptomycin per mouse (Javed et al., 2023).

The system delivered the Cas9 nuclease that led to a sharp rise in the community of bacteria that donate genetic material during conjugation in *Salmonella* (Citorik et al., 2014). Although targeting nonessential genes, it pointed to the possibility of using this technology to modify microbial communities and prevent the transmission of undesirable genes. Thus, it is anticipated that the CRISPR-Cas system will facilitate the complete removal of selected genes, reduce unwanted genetic factors that influence bacterial survival, tolerance, pathogenicity, or metabolic activity pathways, and ultimately alter the genetic makeup of various bacterial strains.

6. CRISPR-Cas System Potential for the Treatment of Infectious Diseases

The CRISPR-Cas technology has been successfully used to reverse resistance to specific antibiotics in bacteria (Aslam et al., 2020; Goren et al., 2017; Wang et al., 2019). This was achieved through multiple strategies, including the degradation of resistant genes (Goren et al., 2017), elimination of resistance plasmids (Tao et al., 2023), silencing regulatory genes (Vivekanandan et al., 2025) and knocking out regulatory gene elements such as efflux pumps (Delgado Ruitón et al., 2025). The field is fast-growing and has evolved from targeting single genes to enabling the systematic reprogramming of bacterial regulatory networks against multidrug resistance.

The relevance of CRISPR-Cas technology in the context of reversing antibiotic resistance in bacteria comes primarily in the form of CRISPR-based antimicrobials and resensitisation therapy. New scientific discoveries support the use of this technology in medicine. Its ability to hinder the acquisition of foreign genetic elements that code for antibiotic resistance has been proven, aligning with previous reports of the likelihood of the use of bacterial defence against them in microbiome therapy, as shown in Figure 2. In *E. coli,* the I-F CRISPR-Cas technology has been linked to antibiotic sensitivity. A novel discovery in the therapeutic application of this

technology was reported by Araya et al. (2021), and Javed et al. (2023) eliminated antibiotic-resistant pathogens using CRISPR-Cas after growing specifically titratable antimicrobials. This concept has previously been used by Strich and Chertow (2019) in vitro in a mixed and pure culture experiment to target and selectively eliminate *E. coli* and *Salmonella enterica* strains by means of the I-E CRISPR-Cas Subtypes. Bikard et al. (2014) applied the phagemid to transmit RNA-guided Cas9, which kills virulent bacteria, while avirulent strains remained unharmed. Thus, this approach successfully eliminated the plasmid that carries the mecA gene without harming the host bacteria (Bikard et al., 2014).

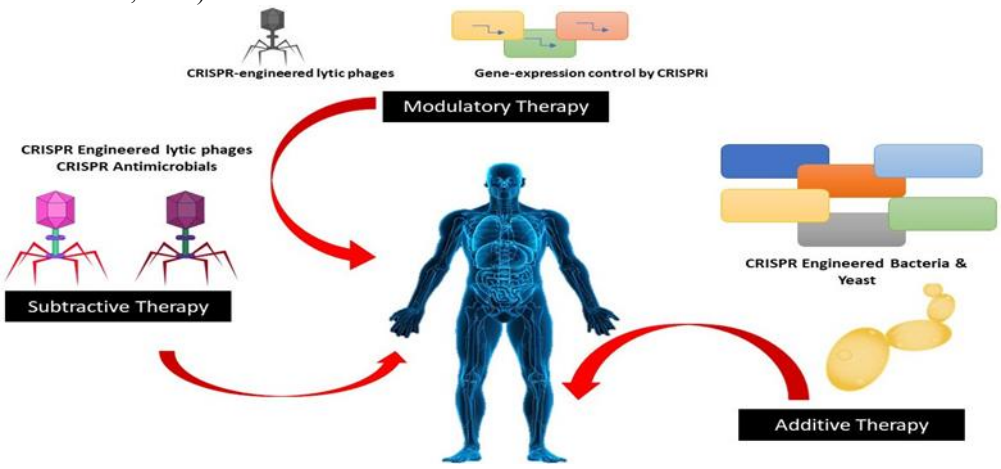

Figure 2: CRISPR approach towards microbiome therapy (*Javed et al., 2023*)

The U.S. FDA approved the first clinical trial for gene therapy using the CRISPR-Cas technology for the treatment of Chronic Granulomatous Diseases in humans in the U.S. on April 29, 2024 (FDA, 2024). This milestone achievement set the stage for the possible treatment of patients with other diseases using permanent gene therapy. The treatment of infectious diseases can be significantly improved through the application of CRISPR-Cas technology in disease diagnostics (Binnie et al., 2021; Dara et al., 2025). Effective treatment of disease is predicated on early detection, determined by a prompt and credible diagnosis. Their high specificity and ability to detect nucleic acid at low concentrations make them valuable in disease diagnosis (Mayorga-Ramos et al., 2023; Qian et al., 2024).

7. Challenges and Limitations of the CRISPR-Cas Technology

CRISPR-Cas has transformative potential for treating antibiotic-resistant infections, but before clinical adoption, we must address several technical, biological, and ethical hurdles. This session explores the limitations of CRISPR-Cas technology and possible strategies for overcoming them.

7.1 Delivery vehicle

Recent advances have enabled engineers to design the system to selectively eliminate AMR genes from pure and mixed microbial communities using CRISPR-Cas technology. The vehicle used for delivering this technology limits its usability, despite the milestone successes recorded with it. Effective in vivo delivery remains a major barrier (*Li et al., 2018; Lino et al., 2018).* As earlier stated in this article, phages are the major delivery vehicle of the CRISPR-Cas system, which is constrained by limited host range for many phagemids, which is a clear drawback when targeting multiple bacterial species (Pursey et al., 2018). Additionally, microbial dysbiosis has been reported when bacteriophages and their bacterial host are used as a delivery vehicle, regardless of the significant role they play in maintaining a healthy human gut microbiome (Manrique et al., 2016).

Addressing this challenge, the incorporation of probiotics can prevent microbial dysbiosis and maintain microflora stability after delivery (Ramachandran and Bikard, 2019). Alternatively, the nanoparticle-based delivery approach, which uses lipid and inorganic nanoparticles, can be utilized as a sustainable alternative due to its proven minimal risk of immunoreactivity, high target specificity, and reduced nuclease exposure (Alton et al., 2015; Chen et al., 2020).

7.2 Immunogenicity against Cas9 proteins

The Cas9 protein, as a main component of the CRISPR system, functions fundamentally by attaching dsDNA, guided by the mRNA sequence, and precisely cuts the DNA 3 bases before the PAM sequence (Makarova and Koonin, 2015). However, the Cas9 protein can be identified by the body as a foreign substance, as it is sourced from a common human *Streptococcus pyogenes* (Colque Navarro et al., 2010), even as *S. aureus* has been found to trigger a pre-existing immune response due to homology (SaCas9) (Charlesworth et al., 2019). *S. pyogenes* and *S. aureus* have infected humans for a while; hence, the human defense mechanism has recognized this protein and developed an immune response against them, leading to the rapid Cas9 degradation, rendering it ineffective to perform its intended function (Crudele et al., 2018). Albeit in combating immunogenicity against the Cas9, targeting immune-privileged organs and exposing the protein early in life are considered two major strategies to overcome immunogenicity (*Geurts et al., 2020; Jain et al., 2017; Kotagama et al., 2019*).

7.3 Off-targeting

A notable drawback in the utilization of CRISPR-Cas technology is the off-target side effects. Unintended cleavage at non-target sites as guided by gRNA could lead to mutation (*Kang et al., 2020*). This can be countered using bioinformatics tools (Barman et al., 2020; Kang et al., 2020; Uniyal et al., 2019). Pawluk et al. (2016) demonstrated that the termination of the Cas9 protein function carried out by the anti-CRISPR proteins (Acr), following successful targeting, drastically reduced the number of unintended modifications. This approach has gained wide attention with over 50 anti-CRISPR proteins identified (Zhu et al., 2019).

7.4 Ethical concerns

The alteration of the human genome has been an issue of ethical concern. The CRISPR Cas technology presents appealing applications, but we must conduct an ethical and societal examination of its use. The opinions of various societal members, including the public and religious academics, are fundamental as the current scope of CRISPR-Cas9 applications expands at an incredible rate. One debatable concept of CRISPR-Cas is its use on human subjects to permanently eliminate undesirable mutations and even introduce desired features in offspring (Shinwari et al., 2018); however, this practice is contentious because somatic cell genome modification cannot be transmitted to offspring, while germ cell modification is heritable, raising ethical and moral concerns (Bailey, 2019). Also raised with the morality challenges are three major drawbacks of utmost concern that arose from animal and human models: the lack of target editing efficiency (Peng et al., 2016), incomplete editing mosaicism (Guo and Li, 2015; Tu et al., 2017), and inaccurate off-target and on-target editing (Schaefer et al., 2017; Zischewski et al., 2017). However, the Cas9 enzyme has been modified to limit off-targeting (Ledford, 2016), with the hope of further reducing it with the current improvements made using the technology (Ledford, 2015).

While the CRISPR-Cas system is gaining unparalleled acceptance, serious concerns have been raised about its potential for human germline modification, equity, and possible future backlash. The potential application of the CRISPR-Cas system in germline editing poses great ethical risks, as germline modification can result in incidental genetic alterations across generations, and these alterations result in the alteration of normal genetic functions, leading to irreversible germline changes and the introduction of heritable genes, which contradicts the prohibition on funding human embryo research by the National Institute of Health (NIH) (Ghasemian et al., 2023). Furthermore, its ability to be reprogrammed beyond therapeutic purposes, such as the creation of “designer babies,” has raised serious concerns regarding consent and the preference for genetic inventions over individual rights (Cutter, 2023), stressing the need for the implementation of stringent policies on the use and misuse of CRISPR-Cas technology. Although notable progress has been made using the CRISPR-Cas system to treat diseases such as cystic fibrosis, socioeconomic concerns have been raised regarding its availability and accessibility, which could further deepen the divide in the healthcare system by limiting the benefits of the technology to a specific segment of the population (Lorenzo et al., 2022; Xia, 2023).

The greatest fear for the use of this technology to reverse AMR in bacteria is that it could lead to unintended consequences, such as the spread of modified bacteria with gene-altering machinery, which could lead to bigger public health threats in the future. Currently, there are regulatory hurdles to overcome, as there is no existing framework for the environmental release of gene-edited bacteria. Additionally, while the CRISPR-Cas technology appears to be a promising solution to combat the growing rate of antibiotic resistance, a principled and morally accepted approach to its application is necessary as a cautionary measure to avoid future misuse and ensure total commitment to ethical integrity.

Rashmi et al. (2024) reported growing public concern about the application of the CRISPR-Cas system in human genome editing, accessibility, and its environmental impact. The survey reported an overall 45% increase in public concern about the potential application of the CRISPR-Cas system in human genome editing, a 34% increase in concern about its potential environmental impact, and a 29% increase in concern about its accessibility from 2015 to 2023. This report underscores the current and growing ethical concern of CRISPR-Cas technology. However, the technology, when used properly, holds promise for greatly enhancing health outcomes and overall quality of life (Howard et al., 2018), as it can be applied clinically to avoid the transmission of genetic diseases (Araki and Ishii, 2014; Ishii, 2015). With the development of robust regulation, transparency, public engagement, and ethical frameworks for the use of this technology, as well as strategies to address access disparities, more research funding, and international cooperation for knowledge sharing, most of these ethical challenges can be addressed.

8. Future of CRISPR-Cas

The CRISPR-Cas technology has changed gene therapy and disease diagnosis forever. The first human clinical trial for the treatment of Chronic Granulomatous Diseases was approved in the US (FDA, 2024). This breakthrough established a foundation for the potential treatment of patients with other diseases through permanent gene therapy. This technology is now proposed as a suitable prospect for reversing antibiotic resistance in bacteria without altering the microbial composition and structure of the population. Current advances made on the CRISPR-Cas technology suggest future models with high target efficiency, with the ability to selectively remove individual DNA fragments, enabling them to monitor gene editing and possible consequences (Liu et al., 2025). One important advantage of this system is that the mutations they cause are not spontaneous (Van et al., 2016). This means that researchers can intentionally design CRISPR-Cas to target the resistance gene of interest with reduced risk of inducing unwanted mutations (Wilson et al., 2018). As technology advances, we will also be able to address any resistance that may evolve alongside the use of CRISPR-Cas-based antimicrobials. With improved technology, we can also improve the efficiency and safety of CRISPR-Cas-based antimicrobials to gain public acceptance.

The utility of gene editing technology for the effective treatment of genetic diseases and the enhancement of disease surveillance is critically needed in this region, which is known to be disproportionately burdened by infectious diseases (Kaluvu et al., 2022). While the future of this gene editing technology looks promising globally, concerns persist for LMICs on the grounds of cost, inclusion, and health equity. For instance, the high cost of CRISPR-CAS therapies is a significant barrier to access in these settings (Reuda et al., 2024). To realize the full potential of CRISPR-CAS in LMICs, researchers and policymakers must prioritize developing cost-effective CRISPR-CAS technologies and innovative pricing models. Such research should ensure that clinical trials and research studies include representatives from LMIC populations. In addition, the technologies should be tailored to address local health needs and promote equitable access.

4. Conclusion

This review consolidates current understanding of the use of the CRISPR-Cas system and its possible application for the reengineering of antibiotic resistance genes in bacteria. If the reversal of antimicrobial resistance (AMR) is achievable at a clinically relevant scale, this technology would be a pragmatic way to tackle this global health menace. The CRISPR-Cas system, as a gene editing tool, can become very relevant if we can address some of the current limitations of this technology. The public health benefits will be immense, expectedly from a reduction in morbidity and mortality, reduced healthcare costs, reduced risk of pandemics, improved treatment options, and enhanced infection control, among other benefits. This situation calls for future research in delivery systems, targetable bacterial pathogens, and advancing towards more clinical trials to effectively anchor CRISPR-Cas antimicrobial solutions as the third pillar in the AMR fight, alongside new drug discovery and antimicrobial stewardship.

Author Contributions
Conceptualization, O.M.I.; Methodology, O.M.I; Writing—Original Draft, T.A.I.; Writing—Review & Editing, O.M.I. and T.A.I All authors must confirm that they have read and approved the final version of the manuscript.
Funding: *This research received no external funding*.
Data Availability Statement: *Not applicable*
Conflicts of Interest: The authors declare no conflicts of interest.
Nomenclature: *Not applicable*

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