Review Article

Pharmacogenomic strategies and CRISPR-CAS9 Gene Editing: A targeted approach towards HIV cure

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Abstract

HIV/AIDS remains one of the most pressing global health challenges, affecting nearly 39.9 million people worldwide in 2023 alone. Despite the success of antiretroviral therapy (ART) in controlling viral replication and improving patient survival, a complete cure remains out of reach due to the persistence of latent HIV reservoirs. These reservoirs, consisting primarily of resting CD4+ T cells and macrophages, are sequestered in anatomical sanctuary sites such as the brain and lymphoid tissues, where current therapies cannot reach or eradicate the virus. Recent advancements in gene-editing technologies, particularly CRISPR/Cas9, have opened new possibilities for targeting and excising integrated HIV-1 proviral DNA directly from infected cells. Experimental studies have shown that CRISPR/Cas9 can effectively disrupt viral gene sequences, including those hidden within latent reservoirs. However, therapeutic application still faces challenges—one of the most critical being the formation of episomal circular DNA with reformed long terminal repeats (LTRs) after excision. These episomes may remain transcriptionally active, contributing to potential viral rebound. To address this, ongoing research is focused on developing combinatorial strategies that employ multiple guide RNAs (gRNAs) targeting different regions of the HIV genome. This approach aims to reduce the risk of viral escape and enhance editing precision. Additionally, integrating pharmacogenomic insights into treatment planning allows for more personalized and effective intervention by considering individual genetic variability in drug metabolism and response. Combining gene-editing tools with pharmacogenomic strategies represents a promising shift toward a functional or even sterilizing cure for HIV. Continued investigation and refinement are essential to overcome current barriers and move closer to eradicating the virus.

Keywords: CRISPR-CAS9, Pharmacogenomics, Latent reservoirs, HIV-1/AIDS, Gene editing, Host factor, CD4-t, HIV, Latency reversing agent, Provirus

Introduction

Human Immunodeficiency Virus (HIV) remains one of the most persistent global health challenges, despite decades of research and medical advancements. As of 2023, nearly 39.9 million individuals live with HIV worldwide, with a significant portion of cases reported in the WHO African Region (Wang. 2024). HIV-1, the more virulent strain, is the primary cause of Acquired Immunodeficiency Syndrome (AIDS), a condition that compromises the immune system and increases vulnerability to infections and certain cancers (Wang, 2024). HIV is a retrovirus that integrates its RNA genome into the host DNA, establishing both active and latent infections (Hou et al., 2022). While active replication can be suppressed with current therapies, latent reservoirs—particularly in resting CD4+ T cells remain hidden and inaccessible to the immune system and antiretroviral therapy (ART). These reservoirs are the major obstacle to curing HIV, as they allow the virus to persist and rebound if treatment is interrupted.

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The introduction of ART, including highly active antiretroviral therapy (HAART), has significantly reduced HIV-related morbidity and mortality (Xiao et al., 2019). However, it is not curative and requires lifelong adherence. Issues such as drug toxicity, pill burden, resistance, and variable patient responses further complicate long-term treatment. One major factor contributing to resistance is the high mutation rate of HIV, resulting from its error-prone reverse transcriptase enzyme, which creates frequent genetic variants (Cetin et al., 2025). To address these challenges, researchers are increasingly exploring personalized medicine approaches. Pharmacogenomics, the study of how genetic variation affects individual responses to drugs, enables tailored ART regimens that optimize efficacy while minimizing side effects. This strategy holds the potential to improve outcomes by guiding drug selection based on a patient's genetic profile.In parallel, gene-editing technologies have emerged as innovative tools in HIV research. Among them, the CRISPR/Cas9 system stands out due to its precision, efficiency, and adaptability. Originally discovered as part of bacterial immune defense, CRISPR/Cas9 can be programmed to target and disrupt integrated HIV DNA or edit host genes required for viral replication.

This article explores the limitations of current HIV treatments and the promising role of pharmacogenomics and CRISPR/Cas9 gene-editing technologies in advancing the search for a functional cure. These novel approaches represent a major step forward in transforming HIV management from lifelong suppression to potential eradication**.**

HIV Trend Analysis and Global Impact

The retrovirus known as HIV, or Human Immunodeficiency Virus, targets the body's immune system, weakening it and rendering people vulnerable to a variety of illnesses and infections. Even though the human immunodeficiency virus type 1 (HIV-1) was identified as the cause of acquired immunodeficiency syndrome (AIDS) more than 30 years ago, it is still one of the most deadly infectious diseases in the world. Despite a lot of study, there is still no vaccine that prevents HIV infection (Wang, 2019).

Sexual contact, intravenous injection, and vertical transmission are the main ways that HIV-1 is spread. Every HIV-1-positive individual progresses through three stages: acute HIV infection, persistent HIV infection (clinical latency), and clinical illness (AIDS) (Xiao et al., 2019).

Since the Centers for Disease Control and Prevention (CDC) in the United States first reported it in the early 1980s, acquired immunodeficiency syndrome (AIDS), which is brought on by HIV-1 infection, has posed a serious risk to human health worldwide (Hou et al., 2022).

HIV transmission is occurring worldwide. In 2023, there were about 39.9 million people living with HIV, with 65% of them residing in the WHO African Region The Global Fund, the World Health Organization (WHO), and UNAIDS all have international HIV strategies that are consistent with the SDG objective 3.3 of eradicating the HIV epidemic by 2030 (Borrajo, 2025). In 2023, it is predicted that 1.3 million individuals will contract HIV, and 630,000 people will die from AIDS-related causes (Borrajo, 2025).

HIV Virology and Pathogenesis

There are two distinct forms of HIV: HIV-1 and HIV-2. Both share numerous commonalities and have the potential to cause AIDS. HIV-2 is less contagious and less pathogenic than HIV-1. Since HIV-1 is known to be the primary cause of AIDS, it has become the primary target for AIDS prevention and treatment (Xiao et al., 2019).

HIV-1 is a retrovirus with an RNA genome of roughly 9.8 kb. The whole genome is flanked by two long terminal repeat (LTR) sequences, and it codes for ten viral proteins with varied roles in viral invasion and replication, including gag, pol, vif, vpr, vpu, env, tat, rev, nef, and the antisense protein. The three main ways HIV-1 is spread are through vertical transmission, intravenous injection, and sexual contact (Xiao et al., 2019).

The CD4 receptor on the target cell membrane is bound to the HIV1 gp120 envelope protein as the first step in the mechanism by which the virus infects host cells. Depending on the tropism of the viral strain, the virus then interacts with the CCR5 or CXCR4 coreceptor. The majority of the host cells are T cells, monocytes, dendritic cells, and even astrocytes, microglial cells, and perivascular macrophages in the central nervous system. One of the factors contributing to the challenge in eradicating the virus is the complexity of its life cycle (Figure 1). When HIV-1 enters a cell, it will create two types of infections: latent infection and active infection (Xiao et al., 2019).

At the beginning of an illness, a latent infection develops in a few cells, but the majority of cells exhibit an active infection. The provirus is active during an active infection, generating viral particles that cause infected cells to create new progeny virions. Complex mechanisms, such as RNA interference, chromatin environment transcription factors, and HIV-1 provirus integration sites, may contribute to the development of latent infection. Latent reservoirs, which harbor infected dormant CD4+ T cells, macrophages, and microglial cells, are the outcome of latent infection. The latent reservoirs are frequently found in lymphoid tissues, brains, and gastrointestinal tracts, which are hard for antiviral medications to penetrate. After stimuli reactivate

the latently infected cells, newly produced virus will be produced and infect nearby cells, then a new latent reservoir will reestablish itself. The dormant HIV-1 reservoir is, therefore, the biggest barrier to a successful HIV-1/AIDS therapy (Xiao et al., 2019).

Current Treatment Challenges

Antiretroviral therapy (ART), which employs a combination of medicines to combat the virus and protect the immune system from harm, is the mainstay of HIV treatment. Antiretroviral therapy (ART) is the primary treatment for HIV, while highly active antiretroviral therapy (HAART), which is still the main therapeutic strategy for HIV-1 patients, has decreased the morbidity and mortality of HIV-related disease. Modern antiviral medicines can lower the morbidity linked with HIV, lengthen life expectancy, and stop the spread of the virus (Cihlar and Fordyce, 2016).

For long-lasting virologic suppression, combination antiretroviral therapy (cART), ideally consisting of three active medications from two or more classes, is necessary. The factors that influence regimen choice are cost, social situation, comorbid illnesses, resistance test results, drug-drug interaction potential, pill burden and dosage frequency, possible side effects, and virologic effectiveness. Patients will be exposed to antiretroviral drugs for decades as a result of sustained virologic suppression, better clinical results, and increased life expectancy. As a result, it is imperative to prioritize the safety and tolerability of cART. A variety of therapy choices must be available in case individual patients develop resistance and/or intolerance. The development of new medicines concentrates on enhancing safety (e.g., Tenofovir Alafenamide) and/or resistance profiles (e.g., Doravirine) inside the current drug classes, combination therapies with greater adherence (e.g., single-tablet regimens), novel mechanisms of action (e.g., attachment inhibitors, maturation inhibitors, broadly neutralizing antibodies), and treatment simplification within frequent dosing (e.g., long-acting injectable). In conjunction with cART innovations, research and development efforts focused on agents that target persistent HIV reservoirs may lead to prolonged drug-free remission and HIV cure (Cihlar and Fordyce, 2016).

Drug resistance: The initial goal of ARVs was to target viral enzymes or HIV structures, with the expectation that the targeted agents would be curative. The ongoing effectiveness of ARVs was nevertheless threatened by viral drug resistance and other escape strategies. Using reverse transcriptase enzymes and the transcriptional apparatus of the infected host cell, retroviruses such HIV produce cDNA from their genomic (g) RNA template. The error rate of HIV reverse transcriptase is said to be 1/1,700 base pairs, which is quite high even by retroviral standards, and its proofreading capabilities are limited. Consequently, faults go uncorrected and are integrated into the virus's nucleic acid every time the virus replicates and generates fresh DNA strands, leading to new virion variants and gRNA variant copies. The mistake-filled procedure typically results in virions that are replication incompetent, or, less frequently but more significantly, it enables the virus to evade the effects of the initial ARVs. Traditional ARVs attack the natural forms of HIV enzymes, but recently emerging virion variants create nonnative enzymes, which might render ARVs useless (Khan et al., 2023).

But, because HAART and other ART medications are unable to effectively eradicate latent viral reservoirs, viral load rebounds quickly when HAART is stopped, turning HIV-1/AIDS into a chronic and incurable illness. For this reason, it is necessary to create more effective strategies for treating HIV-1/AIDS patients and eliminating latent HIV-1 provirus (Xiaoet al., 2019).

In addition to antiviral medicines, alternative strategies like gene editing have produced positive outcomes and may eventually cure HIV by inactivating the integrated HIV DNA. The clustered regularly interspaced palindromic repeat-Cas (CRISPR-Cas) platform is one of the most promising gene editing methods (Herrera- Carrillo et al.,2023).

Pharmacogenomics and Gene Therapy

Pharmacogenomics is the study of genes that affect response to drugs. It combines pharmacological and genomics principles, to predict effectiveness and safety of therapeutic agents. The field of pharmacogenomics focuses on the genes that influence how people react to medicines. It forecasts the efficacy and safety of therapeutic agents using a combination of genomics and pharmacological concepts (Zhou et al., 2021). In recent decades, gene therapy has been developed as a new strategy to improve the health of patients with genetic diseases. In the future, gene therapy could be a powerful strategy for HIV-1/AIDS treatment if we can over-come all limitations and ensure on-target efficiency and safety. Changing a patient's immune cells to increase their ability to recognize and eliminate HIV-positive cells is known as gene therapy. Using techniques like CRISPR/Cas9, researchers are attempting to alter the genetic coding of immune cells to render them resistant to HIV infection. Transferring immune cells that have been altered to identify and destroy HIV-infected cells is another possible aspect of gene therapy. Immunomodulators are chemicals that control the immune response by either boosting immune activation or lowering inflammation. Researchers are examining the possibility of employing

substances like interleukins, interferons, and toll-like receptor agonists to increase antiviral immunity in those with HIV. Clutton et al. claim that interleukin-10 promotes the development of CD8+ T lymphocytes (Klinnert et al., 2024).

The goal of these methods is to boost the immune system's ability to suppress HIV replication and prevent the disease from spreading. Gene therapy, with its innovative strategies for addressing the virus, has the potential to revolutionize HIV management. A key gene therapy technique is gene-editing immune cells, such as T cells, to express receptors that are better able to recognize and kill HIV-infected cells. In addition, gene-editing techniques such CRISPR-Cas9 can directly target HIV DNA inside infected cells, perhaps preventing or blocking viral replication. Despite ongoing challenges such as safety concerns and the need for further research, gene therapy is a potential new avenue in the ongoing quest for effective HIV treatment. Gene therapy may ultimately be a viable treatment for the virus (Klinnert et al., 2024).

Gene editing: Gene editing, or genome editing, is a prime illustration of how basic research combined with applied biotechnology can be extremely helpful in treating and preventing human illnesses right at the center (Ref 1). The development of several severe disorders can now be explained by the complex interactions between multiple genes and environmental factors, as well as by the effects of individual gene products, even little changes in the nucleotides of particular genes. This expanding understanding has led to the development of sophisticated genome-editing technologies that enable accurate changes to the human genome. Through the introduction of specific modifications to the human genome, such as the addition, deletion, or modification of human genes, today's powerful tools for targeted genome editing are available to tackle these pathologies (Cetin et al., 2025).

Gene editing as therapeutic innovation: Gene editing is a technique that makes exact changes to the genome sequence in order to introduce insertions, deletions, or base substitutions. Gene-editing technology is anticipated to manage the incidence of diseases at the genetic level, especially certain genetic disorders caused by mutations in a single gene, as many diseases are accompanied by alterations in gene expression in vivo. Stem cell transplantation has successfully treated HIV in six patients: the Berlin patient, the London patient, the New York patient, the "City of Hope patient," the Dusseldorf patient, and the Geneva patient, which is one of the four strategies used to find a potential cure for the virus. These patients received hematopoietic stem cell transplantation in order to treat their malignancies. With the exception of the Geneva patient, all of the patients received a stem cell transplant from a donor homozygous for a 32 base pair deletion in the CCR5 allele (CCR5Δ32) and matched for human leukocyte antigens (HLA). Because of the treatment's violent nature, expense, morbidity, and mortality, and the scarcity of matched unrelated donors with CCR5Δ32, this method cannot be extended to a larger group of people and is thus not a viable generalized strategy (Kitawi et al., 2024).

The second strategy strives for a sterilizing cure by eliminating all viable latent virus from cell reservoirs, thereby achieving an undetectable plasma load without the use of ART. This strategy, known as the "Shock and Kill" method, has been the subject of considerable research in early phase trial. To cover all possible HIV treatment options, gene therapy has been included in this review, even though it is not currently used in this method of treatment. The goal of "Shock and Kill" is to use latency reversing agents to activate the virus in the dormant reservoir, which causes viral transcription to occur, blocks the infection of new cells through the use of concurrent antiretroviral therapy (ART), and then kills the infected cells through CD8+ mediated lysis, apoptosis, or the humoral immune response. Chimeric Antigen Receptor T-cells (CAR-T) cells could be also employed to enhance the killing of infected cells (Kitawi et al., 2024).

The third method employs gene editing, utilizing nuclease-based tools or engineered recombinase enzymes, to eliminate the integrated virus. Nuclease-based technologies include TALENs (transcription-activator-like effector nucleases), ZFNs (zinc-finger nucleases), and CRISPR (clustered regularly interspaced short palindromic repeats).Treatment strategies for HIV. CRISPR stands for clustered regularly interspaced short palindromic repeats; ZFN stands for zinc finger nucleases; and TALEN stands for transcription activator-like effector nucleases. Additionally, these nuclease-based methods can be used to target CCR5 and make CD4+ cells resistant to infection, as well as silence CCR5 using short interfering or short hairpin RNA (siRNA or shRNA). The HIV-specific long terminal repeat (LTR) recombinase enzymes, which are targeted site-specific (TRE) recombinase, are an example of the engineered recombinase enzymes through which gene editing can take place. Cre recombinase is modified in this way to target a 34 bp area inside the 5'LTR (termed the loxLTR), which leads to the deletion of integrated proviral DNA in infected cells that express this enzyme (Kitawi et al., 2024).

The 'Block and Lock' strategy is the fourth approach, which seeks to attain a functional cure where the latent virus is kept in its inactive state without being eliminated, with the plasma viral load remaining below detectable levels. This is

accomplished by using latency promoting agents that permanently silence or modify the latent reservoir by repressing epigenetic changes of the viral promoter, thus 'blocking' the transcription of the virus and 'locking' it in a latent state. The ex vivo method is used in the majority of research on HIV gene therapy (Kitawi et al., 2024).

There have been four major approaches to the development of gene-editing technology thus far. The most prevalent third generation gene-editing technique is Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)/CRISPR-associated protein 9 (Cas). In contrast to TALENs and ZFNs, which employ proteins to target DNA strands, CRISPR technology improves the effectiveness of gene editing and extends its applicability by instructing Cas proteins to a particular site in the genome by modifying the base sequence of a tiny portion of guide RNA (Kitawi et al., 2024).

Crispr-Cas9 Technology Overview

The Discovery of CRISPR: The CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technique, developed in 1987, demonstrated that CRISPR repetitive sequences were derived from conjugated plasmids and bacteriophages.CRISPR-Cas was able to induce targeted DNA mutations in these pathogens, resulting in adaptive immunity in bacteria. This was accomplished by using anti-sense RNAs as memory signatures. In 2012, Jinek et al., They conducted groundbreaking research in which they used dual gRNAs to guide Streptococcus pyrogenes Cas9 endonuclease for targeted DNA cleavage in vitro. (1). This discovery suggested that CRISPR-Cas9 may potentially target any specific DNA in any creature (Bhowmik and Chaubey, 2022). CRISPR/Cas9 technology was developed rapidly and achieved great progress in the field of gene therapy in human CD34+ hematopoietic stem and progenitor cells (HSPCs).Invading DNA linked with RNA spacers, a .transcript from the brief segments of host DNA obtained from additional chromosomal elements, can be cleaved by the Cas9 helicase, which is a component of the CRISPR-Cas9 system. In this system, the spacers' transcript is called CRISPR RNA (crRNA), and the transcript of palindromic repeats of DNA is called trans activating CRISPR RNA (tracer RNA). (2). A single guide RNA (sgRNA) that can instruct Cas9 to cause DNA cleavage in the Protospacer adjacent motifs (PAMs) area can be formed by joining the tracer and crRNA.The Cas9 nuclease cleaves distinct DNA strands through its two activity domains, RuvC and histidine-asparagine-histidine (HNH) (Xiao et al., 2019).

CRISPR-Cas was found in prokaryotes as an immune response to bacteriophage infections and invading plasmids. In layman's words, the CRISPR-Cas system consists of a nuclease called Cas, which binds to a short CRISPR RNA (crRNA) and targets complementary viral DNA or RNA sequences, depending on the type of CRISPR-Cas system. The Cas9 and Cas12 endonucleases cut DNA, whereas the Cas13 enzyme cleaves RNA. CRISPR-Cas allows for the simple and efficient site-specific modification of genomes in a wide range of organisms. Successful targeting necessitates sequence complementarity between the crRNA and the target gene. Most CRISPR-Cas systems use a brief crucial 2-6 nucleotide region flanking the target, known as the protospacer 2.adjacent motif (PAM) for Cas9/12 and the protospacer flanking site (PFS) for Cas13 (Herrera- Carrilloet al., 2023).

In addition to the protospacer flanking site (PFS), which is necessary for some Cas13 orthologues, the protospacer adjacent motif (PAM), which is necessary for Cas9 and Cas12 cleavage, is shown in pink. Each CRISPR-Cas system is represented by red-colored crRNAs. Cas9 and Cas12 induce cellular DNA repair mechanisms, either Non-homologous end joining (NHEJ) or homology-directed repair (HDR), when they create double-strand DNA breaks (DSBs). HDR uses a donor DNA template and may produce accurate gene editing, but NHEJ is an error-prone repair process that introduces mutations, insertions, and deletions (INDELS, represented in orange). The Cas13 recognition and cleavage of a target RNA transcript causes its breakdown and, in certain cases, the non-specific breakdown of nearby transcripts (collateral RNA cleavage) (Herrera- Carrillo et al., 2023).

Catalytically active Cas9 and Cas12 nucleases cut both strands of double-stranded DNA (dsDNA), resulting in blunt and staggered ends, respectively, and activating cellular DNA repair mechanism. In the absence of a donor template, DNA ends are repaired by an error-prone method known as non-homologous end joining (NHEJ). NHEJ mainly results in nucleotide insertions and deletions (INDELS), but it can also cause substitutions around the cleavage site. INDELS in a gene's protein-coding region may cause the open reading frame (ORF) to shift. CRISPR-Cas-based techniques have been used as direct antivirals, altering or excising the integrated proviral HIV DNA, or indirectly, by blocking viral receptors for cell entrance (Herrera- Carrillo et al., 2023). The Homology-directed repair (HDR) pathway is frequently used for gene editing carried out by donor templates. Donor templates contain the necessary changes and DNA segments that are identical to the blunt ends of cleaved DNAs. As a result, the cell's inherent HDR DNA repair mechanism can be exploited to precisely modify the genome of another cell. Cas13 causes precise target RNA degradation without altering the genome. It should be understood that a strategy based solely on Cas13 will be unable to interact with the integrated HIV DNA within the viral reservoir. Recently, the

Cas9 and Cas12 enzymes were changed to create "dead Cas" or "deactivated Cas" (dCas) variants. The dCas protein can bind to specific DNA sequences, but it cannot cleave DNA because it lacks endonuclease cleavage capability. Instead, dCas was coupled to several regulatory domains, such as transcriptional activator or repressor domains, in order to impose sequence-specific transcriptional regulation on gene expression. In this study, we looked at the promise of the CRISPR-Cas strategy, which targets host and viral genes, to suppress HIV replication and, ultimately, inactivate the viral reservoir (Herrera- Carrillo et al., 2023).

How CRISPR-Cas9 Works in HIV Eradication

CRISPR-Cas9 is an efficient gene-editing technique that employs guide RNA to target specific DNA sequences. It introduces double-strand breaks, which the cell repairs through natural mechanisms. This technology can be used to:

1. Excise proviral: DNA Targeting conserved regions like LTRs to eliminate latent HIV reservoirs.

2. Disrupt viral genes: Rendering the virus nonfunctional by targeting essential genes.

3. Modify host genes: Conferring resistance to HIV infection by targeting genes like CCR5.

By leveraging these mechanisms, CRISPR-Cas9 holds promise for eradicating latent HIV reservoirs and preventing viral rebound (Moses, 2025).

Application of CRISPR/Cas System In Hiv-1/Aids Treatment

Researchers first applied CRISPR/Cas9 to HIV-1 treatment in 2013, targeting specific regions of the virus to suppress gene expression and replication. This pioneering work showed promise in eliminating integrated viral sequences from host cells (Borrajo, 2025).

Subsequent studies in 2014 further explored CRISPR/Cas9's potential, demonstrating successful suppression of viral activity and reduced replication in various cell types. These findings highlighted the precision and safety of the CRISPR/Cas9 system, paving the way for its potential use as a novel HIV-1 therapy (Borrajo, 2025).

The CRISPR/Cas9 technology has been employed to investigate virus-host interactions by whole-genome screening, discovering host factors critical for viral replication (Teng et al., 2021).

Researchers used CRISPR-Cas9 technology in two studies to potentially eliminate HIV from infected hosts. They employed different approaches, including: Using lentivirus to deliver CRISPR-Cas9 therapy to target HIV DNA in infected human cells & Combining CRISPR-Cas9 with antiretroviral therapy to suppress viral replication and target HIV DNA in a humanized mouse model. Both approaches showed promise in eliminating or reducing HIV DNA, highlighting the potential of CRISPR-Cas9 as a treatment strategy (Gendelman et al., 2022).

Limitation and Outlook

CRISPR-Cas9 shows promise in HIV treatment, several challenges limit its practical application. HIV's high mutation rate can render CRISPR-Cas9 ineffective over time. Additionally, off-target effects, where the Cas9 enzyme cleaves unintended genome regions, can cause damage or instability. Immune responses against CRISPR-Cas9 components are also a concern. Ethical concerns surrounding human gene editing, particularly regarding long-term impacts and safety, need to be addressed (Moses, 2025).

Future Research Directions

Ongoing research aims to optimize sgRNA selection and Cas9 variants to minimize off-target effects, enhance vector design and delivery methods, and conduct thorough safety and efficacy assessments. Despite these challenges, CRISPR-Cas9 holds potential for treating HIV and other genetic diseases (Moses, 2025).

Conclusion

Despite the remarkable progress made in HIV treatment over the past few decades, a complete cure remains elusive due to the persistence of latent viral reservoirs and the virus's high mutation rate. While antiretroviral therapy (ART), especially highly active antiretroviral therapy (HAART), has significantly improved patient survival and quality of life, it is not curative and must be continued lifelong. Challenges such as drug resistance, toxicity, adherence issues, and the inability of ART to eradicate integrated HIV provirus highlight the urgent need for alternative therapeutic approaches.

Pharmacogenomics has emerged as a critical tool in enhancing HIV therapy by allowing treatment to be tailored to individual genetic profiles. This approach improves drug efficacy, minimizes adverse effects, and helps in managing resistance, thereby optimizing long-term treatment outcomes. Personalized medicine through pharmacogenomics can guide the selection of antiretroviral drugs based on a patient's genetic makeup, making HIV management more effective and tolerable.

Gene-editing technologies, particularly CRISPR/Cas9, offer a transformative strategy with the potential to target and eliminate latent HIV proviral DNA from host cells. CRISPR/Cas9's ability to precisely cut specific sequences within the HIV genome or host genes essential for viral

replication opens new avenues for a functional or sterilizing cure. Early studies have demonstrated the potential of CRISPR/Cas9 to suppress viral expression, inhibit replication, and even excise integrated HIV DNA with minimal off-target effects.

The integration of pharmacogenomic insights with CRISPR/Cas9 gene-editing technology represents a promising future direction in HIV research. While further studies are needed to address safety, delivery, and scalability challenges, these innovative approaches offer hope for overcoming the limitations of current therapies and achieving a long-term cure for HIV/AIDS.

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