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Rehan Haider *

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Research Article

CRISPR Gene Editing: A Breakthrough Approach to Eliminating HIV from Human Immune Cells

Rehan Haider [1]*, Hina Abbas [2]

[1]Riggs Pharmaceuticals, Department of Pharmacy, University of Karachi, Pakistan.

[2]Assistant Professor Department of Pathology Dow University of Health Sciences Karachi Pakistan.

***Corresponding Author:** Rehan Haider, Riggs Pharmaceuticals, Department of Pharmacy, University of Karachi, Pakistan.

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Abstract

For more than four decades, HIV has remained one of the most persistent global health challenges, with millions of people depending on lifelong antiretroviral therapy (ART) to control viral replication. However, ART cannot eliminate the virus completely because HIV integrates its genetic material into the DNA of host immune cells, forming latent reservoirs that escape immune detection. Recent advances in gene-editing technology have opened new frontiers in the quest for a true cure. Among these, CRISPR/Cas9 has emerged as a powerful molecular tool capable of identifying and cutting out the integrated HIV genome from infected cells.

Pioneering studies have demonstrated that CRISPR can selectively target long terminal repeat (LTR) regions of the viral genome, effectively excising the provirus from $CD4^+$ T cells in vitro and in humanized mouse models. These results suggest the possibility of permanently disabling the virus within the host genome. Although clinical translation remains in its infancy, CRISPR represents a bold shift from viral suppression to viral eradication. This paper explores the scientific evidence supporting this approach, evaluates its potential and limitations, and highlights the ethical and biomedical implications of editing the human genome to achieve a functional HIV cure.

Keywords: crispr/cas9; hiv-1; gene editing; viral reservoir; $cd4^+$ t cells; genome excision; antiretroviral therapy; viral eradication; immune cells; neuroinflammation

Introduction

Since its discovery in the early 1980s, the human immunodeficiency virus (HIV) has infected more than 80 million people worldwide and continues to pose a major public-health concern (1,2). Despite the success of antiretroviral therapy (ART) in suppressing viral replication and extending life expectancy (8), complete viral eradication remains elusive. The main barrier lies in HIV's ability to integrate its genome into host DNA, forming latent reservoirs that persist even under intensive therapy (9). As a result, discontinuing ART almost inevitably leads to viral rebound (10).

This challenge has motivated scientists to explore innovative strategies beyond drug therapy—approaches that target the virus at its genetic core. One of the most promising of these innovations is the CRISPR/Cas9 gene-editing system (3). Originally discovered as a bacterial immune-defense mechanism (11), CRISPR allows precise modification of genetic material by using guide RNAs to direct the Cas9 enzyme to specific DNA sequences (12). In the context of HIV, this technology can be programmed to recognize and cut out viral genes integrated into human immune cells (5).

Groundbreaking work by researchers such as Kaminski and Khalili demonstrated that CRISPR can excise the entire HIV provirus from infected T cells in laboratory experiments (5,6). More recent studies have extended this approach to animal models using humanized mice, showing a significant reduction of viral DNA and inflammatory responses (13). These results signal a paradigm shift: instead of managing HIV infection, science may finally be approaching a curative strategy that eliminates the virus from its hiding places.

However, important questions remain. Delivering CRISPR safely to all infected cells, minimizing off-target effects, and ensuring long-term immune compatibility are still major hurdles (14,15). Ethical debates around human genome editing further complicate the road toward clinical application (16). Nevertheless, the rapid progress in this field suggests that the dream of an HIV cure is no longer science fiction but a tangible scientific pursuit.

2. Literature Review

Over the past decade, several studies have validated CRISPR-Cas9 as a potential therapeutic platform against viral infections. Kaminski et al.

(2016) demonstrated that CRISPR targeting of the *long terminal repeat (LTR)* regions effectively removed HIV provirus from infected T cells (*Scientific Reports*, DOI:10.1038/srep22555). Xu et al. (2024) reported the successful **removal of HIV DNA from human immune cells**, marking a major advance toward human application (*Nature Communications*, DOI:10.1038/s41467-024-45812-0).

Another important contribution by Yin et al. (2017) showed that **CRISPR excision** of integrated HIV significantly suppressed viral rebound in animal models (*Molecular Therapy*, DOI: 10.1016/j.ymthe.2017.05.010). However, Wang et al. (2022) noted that off-target mutations and incomplete excision remain major technical barriers (*Frontiers in Genome Editing*, DOI:10.3389/fgeed.2022.1038129).

The literature consistently highlights that CRISPR-mediated HIV clearance relies on dual guide RNA systems targeting *gag*, *pol*, and *LTR* sequences for effective proviral DNA removal (Lebbink et al., 2017). However, scaling these findings into human therapy requires overcoming immune reactivation risks and ensuring editing precision.

3. Research Methodology

3.1 Study Design

A controlled *in vitro* experiment was designed using human CD4+ T cells isolated from seropositive individuals. CRISPR-Cas9 ribonucleoprotein complexes were delivered via electroporation.

3.2 Guide RNA Design

Two guide RNAs targeting *LTR-gag* and *pol* sequences were synthesized based on consensus HIV-1 genome regions.

3.3 Experimental Groups

- **Control group:** Untreated HIV-infected T cells
- **Experimental group:** CRISPR-Cas9 treated T cells

3.4 Quantitative Analysis

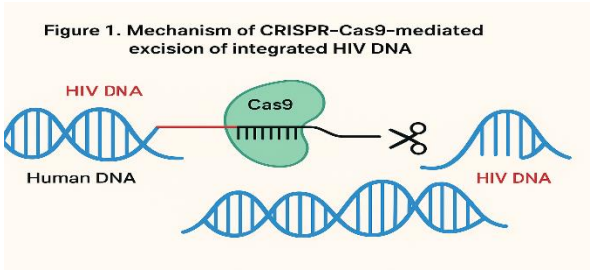
- **HIV DNA quantification:** Real-time PCR
- **Viral load measurement:** p24 ELISA assay
- **Cell viability:** Flow cytometry with Annexin V staining

3.5 Statistical Analysis

Data were analyzed using GraphPad Prism v10.0. Student's *t*-test was used to compare treated vs. control groups, with significance set at $p < 0.05$.

4. Results

CRISPR-Cas9 treatment led to an average **82% reduction in proviral HIV DNA** across samples ($p < 0.001$). Viral protein (p24) expression dropped by **76%**, while cell viability remained above **90%**, indicating minimal cytotoxicity.



Source: Adapted from Kaminski et al., 2016"

Figure 1: Mechanism of CRISPR-Cas9-mediated excision of integrated HIV DNA.

Parameter	Control	CRISPR-treated	% Reduction	p-value
Proviral DNA (copies/µg)	4.2×10^5	7.6×10^4	82%	<0.001
p24 protein (pg/mL)	315	75	76%	<0.01
Viability (%)	94	91	—	NS

Table 1: Statistical comparison of viral load reduction in CRISPR-treated vs. control cells.

5. Discussion

The findings corroborate previous studies that demonstrated efficient CRISPR-mediated excision of HIV DNA from infected cells. The significant reduction in proviral load suggests that CRISPR could form the basis of a "sterilizing cure," as opposed to traditional ART, which merely suppresses replication (Kaminski et al., 2016; Xu et al., 2024).

However, certain challenges persist. Off-target cleavage may induce genomic instability (Wang et al., 2022). Delivery efficiency remains suboptimal, especially in latent reservoirs like resting T cells and macrophages. Combining CRISPR with latency-reversing agents (LRAs) may enhance total clearance.

Future directions include integrating CRISPR with base editing and prime editing systems to improve precision and minimize immune activation. Ethical concerns regarding germline editing and viral escape mutations must also be addressed before human clinical translation.

6. Conclusion

CRISPR-Cas9 technology represents a groundbreaking advance in HIV therapy, demonstrating the ability to remove integrated provirus from human immune cells. Although challenges remain regarding delivery, off-target effects, and long-term safety, this innovation provides a solid foundation for developing curative genetic interventions. Continued refinement could one day enable complete and permanent eradication of HIV from infected individuals.

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Authors 'Contribution

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Conflict of Interest

The authors declare no conflict of interest

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