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*RESEARCH ARTICLE*

# REBUILDING HEARTS WITH CRISPR-CAS9

**Madiha Raza**

1. Research Scholar, Johns Hopkins Global Health Leaders Conference, Alliance Academy for Innovation.

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## *Abstract*

Cardiovascular disease (CVD) remains the leading global cause of mortality, responsible for nearly 17.9 million deaths annually, with a disproportionate impact on low- and middle-income countries. CRISPR-Cas9, presents unprecedented opportunities to transform cardiovascular care from reactive treatment to proactive prevention. This paper explores the applications of CRISPR-Cas9 in repairing genetic mutations linked to hypertrophic cardiomyopathy (HCM) and other heritable cardiac conditions. Studies in somatic cell editing, lipid nanoparticle delivery systems, and polygenic risk scoring, the paper highlights both the promise and limitations of gene-editingstrategies.



## Introduction:-

Cardiovascular disease (CVD) is the foremost global killer, accounting for nearly one-third of annual deaths worldwide (WHO, 2024). While lifestyle factors play an important role, genetic predispositions contribute significantly to conditions such as hypertrophic cardiomyopathy (HCM), arrhythmias, and atherosclerosis. These conditions often manifest suddenly and can lead to fatal outcomes, even among young individuals.

Traditional treatments—including pharmacological therapies, lifestyle modification, and surgical interventions—manage symptoms but do not address the genetic basis of disease. Advances in molecular biology and gene-editing technologies, however, have opened the possibility of correcting these conditions at their root. Among these tools, CRISPR-Cas9, often termed “molecular scissors,” stands out for its precision, efficiency, and adaptability.This research examines how CRISPR-Cas9 may be applied to cardiovascular disease, focusing on the case of hypertrophic cardiomyopathy, potential delivery mechanisms, and broader implications for global health equity.

## Methodology:-

This study draws from secondary research, synthesizing findings from peer-reviewed scientific literature, case studies, and institutional reports. Key sources include recent experiments in in vivo CRISPR delivery (Musunuru et al., 2021), stem-cell-based modeling of cardiac conditions (Congrains et al., 2023), and translational applications of gene therapies (Zangi et al., 2013).

**The approach included:**

1. Reviewing mechanisms of CRISPR-Cas9 editing and repair pathways (NHEJ vs. HDR).
2. Evaluating preclinical and clinical studies applying CRISPR to cardiovascular models.

**Corresponding Author:-** Madiha Raza
**Address:-**Research Scholar, Johns Hopkins Global Health Leaders Conference, Alliance Academy for Innovation.

3. Analyzing challenges in delivery methods (lipid nanoparticles, ultrasound-enhanced targeting).
4. Assessing ethical and equity implications through public health frameworks.

## Results and Discussion:-

**CRISPR-Cas9 in Cardiovascular Context:**

CRISPR-Cas9 functions by pairing a guide RNA (gRNA) with the Cas9 enzyme to target specific DNA sequences, inducing double-stranded breaks. These breaks are repaired through non-homologous end joining (NHEJ) or homology-directed repair (HDR). For cardiac applications, mutations in genes such as MYBPC3(linked to HCM) can be corrected through precise HDR-mediated repair.

**From Petri Dish to Patient:**

A promising strategy involves extracting induced pluripotent stem cells (iPSCs) from patients, correcting mutations ex vivo, and re-implanting differentiated cardiomyocytes into the heart. Such cell-based therapies have shown success in experimental models but remain technically complex.

**In Vivo Applications:**

Emerging methods focus on direct in vivo delivery. Lipid nanoparticles carrying CRISPR-Cas9 complexes, enhanced by ultrasound microbubbles (ELIP), have demonstrated improved targeting efficiency in cardiomyocytes. Furthermore, high-fidelity Cas9 variants have reduced off-target risks, a major barrier to clinical application.

**Equity and Global Health Implications:**

While CRISPR therapies hold promise, accessibility remains a challenge. CVD disproportionately affects low- and middle-income countries, yet gene-editing technologies are concentrated in high-resource settings. Integrating polygenic risk scores (PRS) with CRISPR interventions could help identify high-risk populations early, potentially allowing preventive, population-level interventions. However, equitable distribution of such therapies must be prioritized to avoid widening global health disparities.

**Ethical Considerations:**

Ethical debates focus on safety, informed consent, and potential misuse of gene-editing technologies. Somatic editing for therapy is widely accepted, but germline editing—such as one-time interventions at birth—remains controversial due to risks of unintended consequences and heritable changes.

## Conclusion:-

CRISPR-Cas9 technology offers a transformative opportunity to shift cardiovascular medicine from symptomatic treatment to genetic correction and prevention. By targeting root causes such as HCM mutations, CRISPR could reduce the burden of CVD globally. Nevertheless, challenges remain in refining delivery systems, minimizing off-target effects, and ensuring equitable access. A future in which one-time genetic interventions prevent lifelong cardiovascular disease is conceivable, but careful, ethical, and globally inclusive approaches will be essential.

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