

Role of Gene Editing in Rare Disease Management: Emerging Therapeutic Paradigms

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Abstract: Rare diseases, affecting millions globally despite their individual rarity, represent a major unmet medical challenge due to limited therapeutic options. Advances in gene-editing technologies—particularly CRISPR-Cas systems, base editing, and prime editing—have revolutionized the treatment paradigm from symptomatic management to potential curative interventions. This research paper explores the mechanistic basis, therapeutic applications, clinical progress, quantitative insights, and future directions of gene editing in rare disease management. It highlights emerging paradigms such as personalized gene therapy, in vivo editing, and RNA editing, while addressing ethical, regulatory, and economic challenges. The paper concludes that gene editing holds transformative potential but requires advancements in safety, accessibility, and scalability for widespread clinical adoption.

Keywords: Gene Editing, CRISPR-Cas9, Rare Diseases, Gene Therapy, Personalized Medicine, Base Editing, Prime Editing, Genomic Medicine.

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I. INTRODUCTION

Rare diseases are a group of disorders that affect a small percentage of the population, but collectively they impact millions of people worldwide. Most rare diseases are genetic in origin, caused by mutations or defects in specific genes, which often lead to serious, chronic, and life-threatening conditions. Traditional treatment approaches mainly focus on managing symptoms rather than addressing the root cause of the disease. However, recent advancements in gene-editing technologies, particularly CRISPR-Cas9, have opened new possibilities for directly targeting and correcting the underlying genetic defects.

Gene editing refers to a set of techniques that allow scientists to modify DNA sequences within living cells with high precision. These technologies have revolutionized the field of biomedical research by enabling the correction, replacement, or silencing of faulty genes. As a result, gene editing is emerging as a powerful therapeutic approach for rare disease management, offering the potential for long-term or even permanent cures. In addition, the development of advanced delivery systems and improved editing tools has increased the safety and efficiency of these therapies.

The concept of emerging therapeutic paradigms highlights a shift from conventional treatments to more targeted, personalized, and curative strategies. Gene editing not only helps in understanding disease mechanisms but also plays a crucial role in developing patient-specific treatments based on individual genetic profiles. Despite certain

challenges, such as ethical concerns, high costs, and safety issues, gene editing continues to show great promise in transforming the future of rare disease treatment.

II. REVIEW OF RELATED LITERATURE

The analysis of relevant literature on the application of gene editing to the treatment of rare diseases reveals important advancements in our knowledge of and ability to treat genetically inherited illnesses using cutting-edge molecular techniques. Genome-editing technologies, especially CRISPR-Cas9, have revolutionized the study of rare diseases by enabling precise modification of disease-causing genes, development of disease models, and correction of mutations in patient-derived cells, according to studies like those by Pradhan et al. (2020). Li et al. (2022) reported that CRISPR-based systems have greatly improved the ability to understand disease mechanisms and develop targeted therapies, especially since nearly 80% of rare diseases are genetic in origin. More recent reviews (Israr et al., 2025) underline that gene editing not only supports therapeutic applications but also advances personalized medicine by allowing precise insertion, deletion, or modification of genes.

➤ Objective of the Study

- To examine recent advancements in gene-editing tools and delivery systems.
- To identify the challenges and limitations associated with gene editing therapies.

➤ Overview of Gene Editing Technologies

• CRISPR-Cas Systems

CRISPR-Cas9 is the most widely used gene-editing tool, utilizing guide RNA to target specific DNA sequences and Cas enzymes to introduce precise cuts. These edits enable gene insertion, deletion, or correction.

• Base Editing and Prime Editing

✓ Base Editing: Enables single nucleotide changes without double-strand breaks.

✓ Prime Editing: Offers highly precise edits, including insertions and deletions.

These advanced techniques reduce off-target effects and improve therapeutic accuracy.

• RNA Editing

RNA editing provides temporary, reversible modifications, offering a safer alternative for conditions requiring transient gene regulation .

III. THERAPEUTIC STRATEGIES IN RARE DISEASE MANAGEMENT

Gene editing helps in treating rare diseases through three main therapeutic strategies in a simple and understandable way:

Gene correction means fixing the faulty gene directly. In this method, scientists use tools like CRISPR-Cas9 to repair the mutation in the DNA so that the gene can function normally again. For example, in some types of inherited blindness, the damaged gene (like CEP290) can be corrected to restore vision.

Gene replacement involves adding a healthy copy of a gene into the patient's cells. Instead of fixing the damaged gene, a new working gene is inserted so the body can produce the correct protein. This is often done using harmless viruses such as AAV (Adeno-Associated Virus) to carry the gene into cells. This method has shown success in diseases like Spinal Muscular Atrophy.

Gene silencing is used when a harmful gene is overactive or producing a toxic protein. In this approach, the gene is "turned off" or its activity is reduced. Scientists use techniques like CRISPR interference or RNA-based methods to stop the gene from making harmful proteins, which helps in controlling the disease.

These strategies together provide different ways to treat genetic disorders by either fixing, replacing, or controlling faulty genes.

IV. EMERGING THERAPEUTIC PARADIGMS

➤ Personalized Gene Therapy

Recent breakthroughs demonstrate the feasibility of designing patient-specific CRISPR therapies within months, as seen in rare metabolic disorders . This represents a shift toward ultra-personalized medicine.

➤ In Vivo vs Ex Vivo Editing

• Ex vivo editing: Cells are modified outside the body and reinfused (e.g., hematopoietic stem cells).

• In vivo editing: Direct delivery of editing tools into the patient.

Both approaches are being explored, with in vivo editing offering less invasive treatment options.

➤ Base and Prime Editing Expansion

New editing systems may address ~60% of genetic diseases involving point mutations .

➤ AI-Integrated Gene Editing

Artificial intelligence is increasingly used for:

- Guide RNA design
- Target prediction
- Off-target risk minimization

V. CLINICAL PROGRESS AND CASE STUDIES

➤ Hemoglobinopathies

CRISPR-based therapies have shown success in treating:

- Sickle cell disease
- Beta-thalassemia

A CRISPR therapy (Casgevy) has been approved in some regions, demonstrating clinical translation.

➤ Ophthalmological Disorders

Clinical trials in inherited retinal diseases show:

- ~79% of patients experienced measurable vision improvement in early trials (community-reported summary of NEJM study) .

➤ Metabolic Disorders

A personalized CRISPR therapy improved outcomes in a patient with CPS1 deficiency, highlighting rapid therapeutic development potential.

VI. QUANTITATIVE INSIGHTS

Table 1: - Parameter and Value

Parameter	Value
Global rare disease prevalence	~5% (1 in 20 individuals)
Total rare diseases identified	>10,000
Approved treatments available	<900
Potential coverage by gene editing	Up to ~60% of genetic disorders
Clinical trial success indicators	Up to 79% improvement in some studies

These illustrate both the scale of the problem and the transformative potential of gene editing.

VII. CHALLENGES AND LIMITATIONS

Gene editing offers great hope for treating rare diseases, but it still has many challenges and limitations. One major problem is accuracy. Tools like CRISPR-Cas9 can sometimes cut the wrong part of DNA, which may cause unwanted changes and lead to new health problems. Another difficulty is delivering the gene-editing tools safely into the correct cells of the body. Scientists often use viruses to carry these tools, but this can sometimes trigger immune reactions or may not reach all the target cells. The long-term effects of gene editing are also not fully known, so there is uncertainty about how safe these treatments are over time. In addition, these therapies are very expensive, making them hard to access for many patients. Ethical concerns, especially about changing genes that can be passed to future generations, also create debates. Moreover, since rare diseases are often caused by different genetic changes in different patients, it is difficult to design one common treatment for all. Because of these reasons, more research and careful testing are needed before gene editing can be widely and safely used in treating rare diseases.

VIII. FUTURE PERSPECTIVES

The future of gene editing in rare illness care looks very promising, thanks to rapid advances in technologies like CRISPR-Cas9, base editing, and prime editing. By directly fixing disease-causing mutations at the genetic level, these advancements are anticipated to change therapeutic approaches from symptomatic management to precise, one-time curative interventions. The safety, specificity, and effectiveness of gene editing treatments will be improved in the upcoming years by advancements in delivery systems such as viral vectors and non-viral nanoparticles, allowing for the targeted treatment of hitherto inaccessible areas. Because patient-specific genetic profiles will direct customized therapy approaches, especially for extremely rare illnesses with distinctive mutations, personalized medicine will play a critical role. Furthermore, the combination of bioinformatics and artificial intelligence will improve editing results and speed up the discovery of new genetic targets. In order to ensure responsible use and expedite clinical translation, ethical frameworks and regulatory channels are also anticipated to emerge. Gene editing is shifting medicine from Symptom management to Disease correction to Potential cure. Gene editing will probably become more accessible and

scalable with continuing interdisciplinary research and international cooperation, despite obstacles including immune responses, off-target effects, and high costs. In the end, gene editing has the potential to dramatically improve patient outcomes and quality of life by transforming the management of rare diseases into a proactive, precision-driven field.

IX. CONCLUSION

Gene editing represents a revolutionary advancement in rare disease management, offering precise, targeted, and potentially curative therapies. With technologies such as CRISPR-Cas systems, base editing, and RNA editing, the field is rapidly transitioning toward personalized and precision medicine. While challenges related to safety, ethics, cost, and accessibility remain, ongoing innovations and collaborative efforts are likely to overcome these barriers. Ultimately, gene editing holds the promise of transforming rare diseases from incurable conditions into manageable—or even curable—disorders. The future of gene editing in rare disease management is poised to redefine modern medicine. With advancements in precision, delivery, and personalization, gene editing holds the potential to provide permanent cures and transform healthcare systems globally. However, addressing ethical concerns, ensuring equitable access, and maintaining rigorous safety standards will be critical to fully realizing its benefits.

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