International Journal of Multidisciplinary Research in Biotechnology, Pharmacy, Dental and Medical Sciences (IJMRBPDMS)

Advances in Gene Editing for Treating Inherited Genetic Disorders: A Comprehensive Review

Edupalli Anusha
Department of Computer Science and Engineering
BVSR Engineering College
Chimakurthy, Andhra Pradesh, India- 523226
Email: anusha.1014@gmail.com

ABSTRACT

Technologies that deal in gene editing have transformed the medical sector especially in the area of curing inherited genetic cases. The fact that one can now accurately edit the genome of an individual has created opportunities in treating ailments that are a result of a given gene mutation. CRISPR-Cas9 has become the most promising tool among the other methods of gene editing because it is precise, thus easy to process, and flexible enough to be used across a variety of platforms. This review article answers all the research questions comprehensively, giving an overview of the current research achievements in gene editing approaches to treat hereditary genetic diseases and focuses specifically on CRISPR-Cas9 and its functions. We discuss the hidden science behind gene editing, the progress of clinical trials and the recent accomplishments using gene editing as a treatment of inherited illnesses such as sickle cell anemia, cystic fibrosis and Duchenne muscular dystrophy. There is also the issues of gene editing and ethical concerns like off-target effects, the mode of delivery and to what extent germ-line editing may be regulated that are included in the paper. Also, we talk about the future of gene editing technologies and how they may become a canonical method of treatment of inherited genetic illnesses. As depicted in this review, although there is promise and challenges to clinical applications of gene editing, this review provides an eye opener into the future of gene therapies in diseases of inherited genetic predisposition.
Keywords: gene editing, CRISPR-Cas9, inherited genetic disorders, gene therapy, clinical trials.

Keywords: **gene editing, CRISPR-Cas9, inherited genetic disorders, gene therapy, clinical trials.**

DOI: AWAITING

1. Introduction

This review teases out how different gene-editing tools, such as CRISPR-Cas9, base editing, and prime editing, work, assessing their efficacy, specificity and safety profiles in preclinical and clinical research. Moreover, it evaluates the present-day difficulties regarding the implementation of such therapeutics agents into the target cells and tissues efficiently, an essential move toward unlocking their therapeutic potential (Cavazza et al., 2025). It also takes a closer look at ethical issues of gene-editing technologies and the problems they may cause including germline editing, off-target effects, and fair access to the advanced therapies. Lastly, this paper will present the prospects of gene editing research, such as the next-generation tools that will be more accurate and have a wider scope of application and methods of addressing the existing obstacles of delivery and ethics to expand the clinical use of those tools. Hereditary genetical disorders have been a burden on millions of individuals across the world; they mainly involve mutation of the one or more than one-gene factor resulting in debilitating or life-threatening diseases. Conventional

methods of treating these disorders have emphasized more on controls of the symptoms than in curing the disorder due to the genes. More recent developments in gene editing technologies, however, have come up with a revolutionary way to treat these disorders on the genetic level itself as opposed to the treatment on the symptomatic level, addressing not the outcome, but the cause (Cao et al., 2025). As one of the methods among the many devised, CRISPR-Cas9 comes out as the most "potent and successful one in use, owing to its accuracy and specific gene editing capabilities" (Richardson et al., 2023). In this paper, the progress of using gene editing as a therapeutic tool in inherited genetic diseases will be discussed in respect not only of technical details of delivering such innovative treatments but also in clinical development of the new therapies. In particular, it involves addressing CRISPR-Cas9/Cas12/Cas13 nucleases, DNA base editors, prime editors, and DNA RNA base editors, which are also big steps forward in precision biology (base base editing, base editing editing, metal editing) in genetic manipulation (Tao et al., 2023).

2. Origin of the Research

In this paper, the molecular workings of CRISPR-Cas9 will be discussed, its various applications in treating monogenic and polygenic inherited diseases, and critically analyzed is the ethical implications surrounding CRISPR-Cas9 and where it is headed in clinical translations. This involves reviewing some of the clinical trials currently going on using CRISPR to treat such diseases as beta-thalassemia and sickle cell disease with some promising early findings being recorded (Bickmore & Van Steensel, 2013). Although these preliminary therapies are promising, roadblocks still exist in the full potential of an editing mechanism and ensuring minimal off-target editing activity to guarantee safety and efficiency (Bickmore & Van Steensel, 2013). Moreover, legal systems are quickly developing to respond to the unprecedented needs of the gene-editing technology, where the ethical aspects, especially the implications of altering germline, should indeed be considered (Anliker et al., 2022) (Davis & Yeddula, 2024). Thorough awareness of these concerns, as well as a profound examination of the fringes of the ethical landscape are essential factors in transferring the disruptive potential of CRISPR-Cas9 to the practical realm of secure, beneficial clinical applications of such technology in inherited genetic disorders. In the past, gene therapy that entails transferring genetic material in the cells to complete a defective gene or produce a useful protein in the cells had a major challenge such as prolonged expression and immunogenicity. With the emergence of a form of technology called gene editing, specifically CRISPR-Cas9, much of those initial problems are being sidestepped by simply rewriting the genetic mutations existing within the patient, their very DNA, thus providing a more fitting and enduring method of therapy (Bickmore & Van Steensel, 2013).

3. Justification

These developments are thoroughly reviewed in this paper, and their clinical implication on the treatment of inherited genetic diseases. In particular, the nature of the CRISPR-Cas9 method with its transformative power is reviewed, with current and potential future applications in rectifying the disease-producing mutations being discussed (Bickmore & Van Steensel, 2013). Applications of bacterial immune systems allowed developing a revolutionary gene-editing tool with the peculiarity to target and manipulate DNA sequences with unprecedented opportunities of therapeutic intervention (Martinez-Lage et al., 2017). The versatility of CRISPR-Cas9 in tackling various genetic pathologies is covered by the fact that the outcome of its targeted changes is determined by the size and nature of the modifications that may be made, including single-nucleotide variants, insertions, and deletions (Richardson et al., 2023). The enzyme known as CRISPR-associated protein 9 works as a molecular pair of scissors, and it is guided to its location by means of a small RNA molecule to a particular DNA site, where the CRISPR-associated protein 9 enzyme generates a break in the two DNA strands (Bickmore & Van Steensel, 2013). This is because it is a perfectly cleaved process through which either the interruption of genes or any other new genetic material could be introduced via natural cellular repairing processes correcting a pathogenic mutation (Tavakoli et al., 2021). The current drive in CRISPR technology has seen it move swiftly between the grounds of fundamental research to being a clinical stage therapy modality with substantial evidence of potential to treat otherwise untreatable genetic disorders (Anliker et al., 2022).

4. Study Goals Objectives Study Goals

The aims of the study are

1. To discuss the developments of gene editing technologies and in particular CRISPR-Cas9, as a potential treatment of inherited genetic diseases.
2. To determine the nature of the present clinical uses of gene editing in sickle cell anemia, cystic fibrosis, and Duchenne muscular dystrophy.
3. To discuss the problem of gene editing and its off-target effects, delivery routes, and ethical considerations.

4. The discussion of future possibilities of gene editing in the treatment of inherited genetic diseases.

5. Literature Review

The given review explores the conceptual principles and technical usage of gene editing with a focus on CRISPR-Cas9 system, which has transformed the field of molecular biology and genetic engineering (Bickmore & Van Steensel, 2013). In contrast to the previous approaches to genetic engineering that tended to insert foreign DNA, the CRISPR-Cas9 can be applied to make targeted changes in the current genome (Khan, 2024). Through this technology, and other modern methods, like TALENs and ZFNs, it is now possible to make precise changes to DNA, thus presenting greater food control over genetic material than ever before (Richardson et al., 2023). In particular, gene editing enables the insertion, deletion, or exchange of genetic material, which provides the prospects of therapeutic approaches to a tremendous number of inherited and acquired pathologies (Jambula, 2023). The discussion that follows will set out in more detail the specific ways in which each of these nucleases have been used to cause genomic changes, and present their relative advantages and shortcomings as methods that achieve precisely controlled genetic modifications. The introduction of CRISPR-Cas9, especially, in particular, has greatly increased the speed with which genetic research and therapies develop because of its low complexity, effectiveness, and adaptability, making it the most common type of gene editing (Tao et al., 2023). The swiftness of its adoption and the success of this system in generating specific genetic perturbations has resulted in paradigm shifts in the development of animal models, genetic screens, and the multiplex editing of genes (Wang & Doudna, 2023).

6. Materials/ methods

This research will be based on the qualitative methodology, where it will be necessary to conduct the review and evaluation of peer-reviewed literature, clinical trial reports, and the most recent developments in gene editing to treat inherited genetic disorders. The search of databases (PubMed, Google Scholar, and ScienceDirect) will be performed based on such terms as "gene editing," "CRISPR-Cas9," "clinical trials," and inherited genetic disorders. The chosen articles will also be reviewed to gain a clear picture of what the process of gene editing in clinical practice currently is regarding whether and to what extent it has been successful and what difficulties it encounters.

7. Findings and Discussion

In this section, the most important results of the analyzed literature will be summarized

- Clinical CCRISPR-Cas 9: Clinical trials and research have confirmed the promise of CRISPR-Cas9 in disease curing genetic disorders such as sickle cell anemia whereby patients after having received gene-editing therapies demonstrated an improvement in their condition in a remarkable way.
- Precision and off-target effects: CRISPR-Cas9 is highly efficient but one of the problems is that of off-target mutations. It also talks about attempts to gain more specificity using newer formulations of CRISPR, like CRISPR/Cas12.
- Delivery problems: There is also the problem of efficient delivery of CRISPR components into target cells. There is an effort to combat this problem through new avenues of attack, including nanoparticles and viral vectors.
- Ethical and regulatory issues: CRISPR in humans, especially on germline editing, have ethical issues on unintended results. In this section, the author will talk on the current controversies on how to regulate the subject of gene editing on human beings.

8. The study was limited in the following ways

Such intrinsic volatility is only magnified with the speed of technological innovation that, in turn, introduces new applications and considerations prior to the existing frameworks being able to settle down (Dow, 2015). Examples include the active development of CRISPR-Cas9, whose undesirable off-target effects have to be reassessed repeatedly and where safe high-fidelity variants continue to be formed, a process that has outpaced the formulation of robust regulatory advice (Bickmore & Van Steensel, 2013). Moreover, the risks of unintended outcomes and inadvertent inclusion of germline modification or creating biological weapons make the necessity of effective international regulatory frameworks more apparent, as it is the only way to reduce risks of such a powerful technology (AyanoLou et al., 2020; Davis and Yeddula, 2024). This involves the necessity of drawing clear ethical lines regarding its use in human germline editing, the need to design international regulations so that they can harmoniously work to regulate its clinical translation (Anliker et al., 2022; Brokowski & Adli, 2018). Even beyond such direct clinical and regulatory issues, societal repercussions of increased availability of these advanced therapies to wider, more diverse populations, such as the threat mitigating health disparities, pose even greater ethical dilemma that

needs to be engaged and policies developed actively (Brokowski & Adli, 2018). Such complexities demand both a multidisciplinary collaboration and an interdisciplinary assessment with the focus on the incorporation of scientific innovations and scientific breakthroughs along with including ethical consideration and sound formulation of policies so as to have a responsible innovation. This is particularly important since promises of CRISPR-based therapies to change the treatment of a wide range of diseases depend on the ability to pass through these thorny ethical and regulatory thickets with sophistication (Brokowski & Adli, 2018)

9. Future Scope

The present paper critically examines the present-day state of gene editing technology and its future direction especially in the context of its possible use in reducing inherited genetic diseases. It enters the essential aspect of superior specificity of CRISPR-based systems to reduce any off-target effects and discovery of superior delivery systems that are key components to the efficacy of therapy (Bickmore & Van Steensel, 2013).

The paper evaluates clinical trials growth to include more genetic disorders and the inherent multifaceted considerations in terms of regulation and morality in the germline editing. This review explores the edge of genetic engineering and genome editing studies, their edge-cutting implementations, and benefits of the historical era of modern medicine (Khan, 2024).

The conversation identifies the active progress in streamlining genome modification as framed by the further enhancement of ex vivo gene editing pre-eminence and the necessity of localized in vivo CRISPR/Cas9 system introduction into particular organs and cell types (Wei et al., 2020).

It also applies the concept of the synthetic biology and functional genomics to further promote the genome-editing technology, particularly in the context of the diagnosis and treatment of diseases caused by single-base-pair changes rather than merely insertion or deletion (Chen et al., 2019).

10. Conclusion

The ability to treat genetic conditions (in the case of inherited diseases), especially using CRISPR-Cas9, is potentially revolutionary as these gene disorders could be treated with precise targets. This has also made great advancements, but it is still faced with challenges pertain to off-target effect, how it can be delivered, and cultural issues. With research and clinical trials advancing, gene editing is set to be the foundation to the personalized medicine that holds the promise to cure genetic disease, which until recently was considered incurable.

11. References

1. Cao, M., Han, R., Chen, S., Zhao, D., Shi, M., Zou, J., Li, L., & Jiang, H.-K. (2025). Gene Editing: An Effective Tool for the Future Treatment of Kidney Disease. Journal of Inflammation Research, 4001. Dove Medical Press. https://doi.org/10.2147/jir.s506760
2. Cavazza, A., Molina-Estévez, F. J., Reyes, Á. P., Ronco, V., Naseem, A., Malenšek, Š., Pečan, P., Santini, A., Heredia, P., Aguilar-González, A., Boulaiz, H., Ni, Q., Cortijo-Gutierréz, M., Pavlovic, K., Herrera, I., Cerda, B. de la, García-Tenorio, E. M., Richard, E., Granados-Principal, S., … Benabdellah, K. (2025). Advanced Delivery Systems for Gene Editing: A Comprehensive Review from the GenE-HumDi COST Action Working group. Molecular Therapy — Nucleic Acids, 36(1), 102457. Cell Press. https://doi.org/10.1016/j.omtn.2025.102457
3. Richardson, C., Kelsh, R. N., & Richardson, R. J. (2023). New advances in CRISPR/Cas-mediated precise gene-editing techniques. Disease Models & Mechanisms, 16(2). The Company of Biologists. https://doi.org/10.1242/dmm.049874
4. Tao, J., Bauer, D. E., & Chiarle, R. (2023). Assessing and advancing the safety of CRISPR-Cas tools: from DNA to RNA editing. Nature Communications, 14(1). Nature Portfolio. https://doi.org/10.1038/s41467-023-35886-6
5. Anliker, B., Childs, L., Rau, J., Renner, M., Schüle, S., Schuessler-Lenz, M., & Sebe, A. (2022). Regulatory Considerations for Clinical Trial Applications with CRISPR-Based Medicinal Products. The CRISPR Journal, 5(3), 364. Mary Ann Liebert, Inc. https://doi.org/10.1089/crispr.2021.0148
6. Bickmore, W., & Van Steensel, B. (2013). Chromosomes have a complex organization across spatial scales within the cell nucleus.
7. Davis, D. J., & Yeddula, S. G. R. (2024). CRISPR Advancements for Human Health. PubMed, 121(2), 170. https://pubmed.ncbi.nlm.nih.gov/38694604
8. Martínez-Lage, M., Torres, R., & Rodríguez, S. (2017). CRISPR/Cas9 Technology: Applications and Human Disease Modeling. Progress in Molecular Biology and Translational Science, 23.

https://doi.org/10.1016/bs.pmbts.2017.09.002
9. Tavakoli, K., Pour-Aboughadareh, A., Kianersi, F., Poczai, P., Etminan, A., & Shooshtari, L. (2021). Applications of CRISPR-Cas9 as an Advanced Genome Editing System in Life Sciences. BioTech, 10(3), 14. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/biotech10030014
10. Jambula, M. (2023). Evolution of Genetic Engineering in Medicine: Recombinant DNA and CRISPR Gene Editing Technologies. https://doi.org/10.58445/rars.824
11. Khan, N. (2024). Unlocking Innovation in Crop Resilience and Productivity: Breakthroughs in Biotechnology and Sustainable Farming. Deleted Journal, 1(4), 28. https://doi.org/10.53964/id.2024028
12. Wang, J. Y., & Doudna, J. A. (2023). CRISPR technology: A decade of genome editing is only the beginning. Science, 379(6629). American Association for the Advancement of Science. https://doi.org/10.1126/science.add8643
13. Ayanoğlu, F. B., Elçin, A. E., & Elçin, Y. M. (2020). Bioethical issues in genome editing by CRISPR-Cas9 technology. TURKISH JOURNAL OF BIOLOGY, 44(2), 110. https://doi.org/10.3906/biy-1912-52
14. Brokowski, C., & Adli, M. (2018). CRISPR Ethics: Moral Considerations for Applications of a Powerful Tool. Journal of Molecular Biology, 431(1), 88. Elsevier BV. https://doi.org/10.1016/j.jmb.2018.05.044
15. Dow, L. E. (2015). Modeling Disease In Vivo With CRISPR/Cas9. Trends in Molecular Medicine, 21(10), 609. Elsevier BV. https://doi.org/10.1016/j.molmed.2015.07.006