International Journal of Creative and Open Research in Engineering and Management
ISSN: **3108-1754 (Online)**
Volume 02 Issue 04 April-2026 | Impact Factor: 3.5

CRISPR-Based Genome Editing: From Molecular Mechanism to Clinical Applications and Future Prospects

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How to Cite this Article:

Kaur, K., Kaushal, G. & Navneet, (2026). CRISPR-Based Genome Editing: From Molecular Mechanism to Clinical Applications and Future Prospects. International Journal of Creative and Open Research in Engineering and Management, 02(04). https://doi.org/10.55041/ijcope.v2i4.661

https://doi.org/10.55041/ijcope.v2i4.661

Abstract

The paper outlines the radically changing role of CRISPR gene-editing technology in conceptualizing and treating various pathological disorders. CRISPR has advanced over the last ten years since its early days of laboratory research through clinical therapeutics, proving the fact that genetic anomalies could be corrected at the locus of their emergence. The current paper clarifies the current uses of CRISPR in various fields, such as hematologic disorders, eye conditions, cancer treatment, liver diseases, myopathies, and viral infections. Case examples like the sickle cell disease and thalassemia have shown how the process of correcting a defective hemoglobin gene can enhance the production of active erythrocytes in patients. Also the extension of CRISPR complexes into an intravascular environment has allowed individuals who are blind due to genetic factors to see black and white images of some visual cues. The article further compares the recent versions of the CRISPR platform, including Base Editing and Prime Editing, which are designed to provide greater nucleotide specificity and minimize cases of double Addressing breaks. These sophisticated modalities operate on the same principles as editorial corrections, allowing the replacement of individual nucleotides or the replacement of predefined regions of the genome. The results emphasize the rapid development of CRISPR as a powerful therapeutic tool that can be used to alleviate a host of inherited and genetic disorders.

Keywords: CRISPR, Gene Editing, DNA Repair, Cas9, Clinical Trials, Disease Treatment,

1. Introduction

Cells are minute structures that are the building blocks of life of all things living. Within each cell there is a substance referred to as DNA (Deoxyribonucleic Acid). All the information that our body requires to grow, work as well as remain healthy is contained in DNA [1]. It resembles a book of instruction with four little letters known as bases A, T, G and C. These letters are organized to create instructions that regulate all that exists in the body such as the height that we are as well as the colour of our eyes [2]. DNA is undercut into smaller sections called genes. The genes specifically do a task, including the production of a protein that provides the body with good functioning. An example is that there is one gene that will regulate the colour of eyes, another will assist in the formation of blood cells, and another will maintain heart in good health. In case a gene functions properly in a body, it remains healthy [3]. However, occasionally some slight alteration or error occurs in the DNA code or sequence this is known as a mutation. Mutations may occur by nature or due to environmental factors such as radiation or chemicals. Once mutation takes place, it might cause the gene to cease functioning normally and cause diseases like sickle cell anemia, cystic fibrosis or muscular dystrophy. During many years, physicians had an opportunity to cure the symptoms of these disorders, but not the cause. Drugs might alleviate the pain or suppress the symptoms, but they were not able to repair the broken gene within the cell [4]. This prompted scientists to seek new remedies to the issue at the DNA level. It was in the process of that search that one of the greatest discoveries in modern biology was made gene editing. Transformation or correction of a small fragment of DNA within a living cell is called gene editing. It also empowers the scientists to fix the precise mutation that is responsible to cause the disease rather than treating the symptoms [5]. The most popular and effective gene-editing instrument that has been found hitherto is known as CRISPR. CRISPR is an acronym that means Clustered regular interspersed short palindromic repeats. The initial discovery of this system was in bacteria in 1980s, but then scientists did not know what this system did later, researchers discovered that CRISPR is a natural defenses mechanism that is used by bacteria to protect themselves against viruses [6]. As the virus assaults, the bacteria cut and retain the minute fragments of the virus DNA within their DNA with CRISPR sequences. In case of a second attack of the virus, the bacteria rely on this stored data to identify and eliminate it with the assistance of a protein known as Cas (CRISPR -associated). In 2012, the genes of human beings, animals, and plants could be edited with the help of this bacterial system, which was revealed by two researchers, Jennifer Doudna and Emmanuelle Charpentier. They developed an instrument that can cut and alter DNA in a living cell. They were revolutionary in their discovery and established a new era of genetics and biotechnology. They won the Nobel Prize in Chemistry in 2020 in regard to this pioneering piece of work. CRISPR is similar to a mini scissor. It can slice the DNA at a specific location and then it enables the cell to fix itself in an appropriate manner [7]. It employs two components, one of these being a guide RNA (gRNA) that identifies the target DNA sequence, and the other one is a Cas9 enzyme that cuts the DNA. This renders CRISPR easy, rapid and less costly in comparison to the previous gene-editing instruments such as Zinc Finger Nucleases (ZFNs) and TALENs. CRISPR has become the most popular gene editing tool in the entire world due to its simple design and high success rate [8]. Over the past one decade, CRISPR has been applied in the treatment and study of numerous diseases. It was found that the period between 2015 and 2025 witnessed significant achievements by scientists in the application of CRISPR to human gene therapy. It has been applied to effectively cure such blood diseases as sickle cell and beta thalassemia by repairing the defective gene in blood stem cells. It is also undergoing clinical trials of eye conditions like Leber congenital amaurosis where CRISPR is used to fix the faulty gene in the eye directly [9]. Also, researchers consider CRISPR as cancer, muscle, and liver studies. Non-medical applications of CRISPR are also in progress - to create tougher and less prone to diseases crops, to learn more about the role the genes play in growth and wellbeing in animals. This demonstrates that CRISPR is a powerful technology that has numerous applications in science and medicine. although CRISPR is highly promising, it contains certain issues. It occasionally cuts the inappropriate part of the DNA, so-called an off-target effect. Such error may lead to new mutations or undesirable outcomes [10]. The second issue is that of safe delivery of CRISPR to the interior parts of the body it is challenging to make sure that the delivery is limited to the target cells. Ethical concerns regarding the application of CRISPR in human embryos or altering physical aspects have also raised questions in the scientific community. Scientists have developed new and better versions of CRISPR that include base editing and prime editing to minimize safety concerns [11]. They are more precise and can be used in human beings since these techniques are capable of correcting minor errors in DNA without severing two strands of the DNA. These newer versions of CRISPR can assist in treating incurable diseases in the future. Millions of patients with genetic diseases have been given

hope again by CRISPR. It enables physicians and scientists to directly improve the causes of the issue and fix them forever. When used and created with sense of responsibility, CRISPR can assist in the creation of a future where diseases are not treated but actually cured on a genetic level. It still remains one of the best examples of how science and technology can collaborate to enhance human life and health [12].

2. How CRISPR Works

CRISPR might be a little daunting and unclear, but its concept is simple. It is an accurate molecular tool that can pinpoint a specific short sequence of deoxyribonucleic acid in a cell and then cut the sequence or otherwise alter it. These specific modifications have the potential to interfere with disease causing pathogenic mechanisms or correction of harmful genetic variations that cause disease [13]. The genomic DNA can be seen as a bulky collection of instructions to understand how CRISPR works. All segments mark physiological processes that are important, e.g. hematopoiesis, digestion or osteogenesis. The slightest misplaced nucleotide in this informational repertoire may trigger disease. CRISPR is similar to a precise editor, which recognizes the faulty locus in the genomic text and performs a precise correction [14].

2.1 The Discovery of CRISPR System

A long time ago, scientists have noticed an interesting phenomenon among the populations of bacteria. They discovered that bacterial genomes have unique blocks of DNA that resemble short and repeated motifs [15]. These sequences were named CRISPR, which is an abbreviation of Clustered Regularly Interspaced Short Palindromic Repeats. At first, it was not known what functional meaning these elements had Later studies found that bacteria use CRISPR as a defense mechanism, which helps them to protect themselves against viral attacks. Upon bacterium invasion by bacteriophage, the bacterium stores a piece of the viral DNA and inserts this piece into bacterial CRISPR locus [16]. When re-exposed to the same virus, the bacterium perceives the fragment stored and then cuts the viral genome with a specific nuclease, which is usually known as Cas. This specific cleavage deactivates the virus saving bacterial integrity. Researchers inferred that had bacterial CRISPR systems the ability to induce targeted genetic excision, similar plans can be used in eukaryotic organisms, such as humans. This future usage propelled the modern technologies of gene-editing [17].

2.2 The Main Components of CRISPR System

CRISPR works with two main components: the guide RNA (gRNA) and the Cas enzyme. The guide RNA is a small piece of RNA, a molecule very similar to DNA, and its main job is to locate the exact position on the DNA where the editing needs to happen. You can think of the guide RNA as a GPS system or an address label that directs CRISPR to the correct gene. It ensures that the Cas enzyme reaches the right spot without searching the entire genome [18]. The second component is the Cas enzyme, most commonly Cas9, which stands for CRISPR associated protein 9. This enzyme acts like a pair of molecular scissors. Once the guide RNA brings Cas9 to the target gene, Cas9 makes a cut in both strands of the DNA. This cut allows scientists to either remove a faulty section of the gene or insert the correct version [19]. While Cas9 is the most widely used enzyme, there are other types such as Cas12 and Cas13, which have slightly different functions and can be used depending on the type of gene editing required. Together, the guide RNA and Cas enzyme form a highly precise and efficient tool that makes gene editing possible. When the guide RNA and Cas9 are put together, they form the CRISPRCas9 complex. This is the working tool that goes inside the cell, finds the target gene, and cuts it [20]. The guide RNA is more or less a mini-GPS that scans the genome in search of the precise DNA sequence, which is to be edited. When it locates the complementary site, it transports Cas9 enzyme to the site. Cas9 then functions as a pair of scissors made of molecules, and as such, it slices the DNA at the right location. Once this dissection is achieved then the cell attempts to fix the rupture [21]. One may employ this repair procedure in various ways. One can either delete a gene, insert a new fragment of DNA, or destroy the original gene to make it malfunction. In other events, the fixed DNA strand may receive a completely new sequence. The figure goes a long way to present a visual representation of how CRISPR can remove or repair and replace genes depending on the objectives of scientists [22].

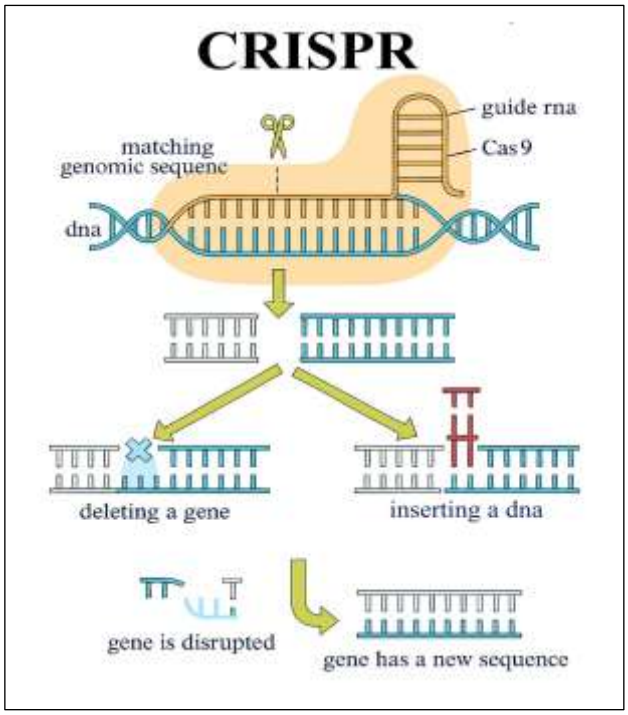

Fig. 1: The Main Components of CRISPR System

Ligand: The figure depicts how CRISPR-Cas9 gene editing works. The gRNA is paired with the corresponding DNA sequence and guides the cas9 enzyme to the genome prominence. Cas9 subsequently cuts the DNA into a double strand [23]. The natural repair system of the cell comes into play after the cut and results in varied effects like deleting a gene, introducing new DNA, disrupting gene functioning or forming a new DNA sequence. This fact illustrates the ability of CRISPR that allows controlled and targeted modification of genes [24].

Captions: The process of CRISPR-Cas9 gene-editing demonstrates how the guide RNA guides the Cas9 enzyme to a particular sequence of DNA, where the DNA is broken and subsequently repaired to remove, insert, disrupt, or rewrite a gene [25].

2.3 The Working Mechanism Fig: 02

Fig 2: The action of the CRISPR-Cas9 gene editing system within a cell

The diagram illustrates the detailed process of the action of the CRISPR-Cas9 gene editing system within a cell. The entire process starts with the identification of the specific gene or DNA sequence that has to be changed [26]. After the target is identified, scientists create a guide RNA (gRNA) which is compatible with that specific area of DNA. As a guiding RNA, this one serves as a locator and assists CRISMP in the right location of a genome. Secondly, the guide RNA binds itself to the Cas9 enzyme, which forms the CRISPR-Cas9 complex. This complex will then be incorporated in the target cell and it will scan for similar sequence of DNA [27]. Cas9 cleaves the two strands of DNA at the point of finding the precise location by the guide RNA. The break occurs close to a short sequence known as the PAM site needed so that CRISPR can take effect [28]. Once the DNA is cut, it is repaired by the natural system of the cell. This mending may occur in two forms. One of them is Non-Homologous End Joining (NHEJ), using which the ends of the broken DNA are directly reconnected. This tends to interfere with the gene or removes a section of the gene. The other technique is the Homology-Directed Repair (HDR), which resorts to the use of a new template of DNA inserted by the scientists. This enables the cell to make an insertion of a fixed or altered gene sequence [29]. CRISPR can be used to delete, repair or replace the target gene by use of these repair pathways. The end product is an edited gene that has worked, and it assists in fixing genetic errors or producing new genetic alterations [30].

2.4 Types of CRISPR Systems

CRISPR technology has a range of different enzymes, each with a different mechanism of operation. CRISPR-Cas9 is the most commonly used system which works by creating two strands breakages at the targeted locations within the genome. This is an ability that allows accurate excision, replacement or repair of DNA segments. Although the application of Cas9 has been very successful in both gene-editing projects, and preclinical studies, its ability to create strong DNA lesions in some cases raises questions about the possibility of off-target editing. CRISPR -Cas12 is another leading system [31]. Even though it is also designed to cleave DNA, its cleavage mechanism differs with that of Cas9. Cas12 cleaves the genome not to form a blunt, but a staggered or sticky-end cut, which in many ways improves the precision of genome editing and reduces the number of unintended genomic impacts [32]. As a result, there is a growing interest in Cas12 to use it in advanced gene-editing development and diagnostic systems. CRISPR -Cas13 is the third major system and unlike Cas9 and Cas12; it specifically targets and cleaves RNA instead of DNA. It is this characteristic that makes Cas13 a highly valuable tool in antiviral research, with many viruses, such as influenza and SARS-CoV-2, containing RNA genomes [33]. Cas13 has the capacity to sabotage the spread of infection and so the viral RNA is degraded before it can act. Each of the systems is specific to specific investigative situations in molecular biology. Cellular homeostasis is usually recovered once a genomic locus has been altered or repaired. Genome editing may stop the disease progression or even result in total remission of the phenotype when a pathogenic phenotype is caused by a harmful allele [34]. A good example is the case of sickle cell disease CRISPR technology has been used to fix β -globin (HBB) coding sequence, hematopoietic progenitors produce erythrocytes with normal haemoglobin. CRISPR systems are used in laboratories worldwide to probe the role of thousands of genes; the technology can be used to determine the interaction between genotypes and phenotypes and show how small changes can cause significant physiological outcomes [35].

3. Applications of CRISPR in Disease Treatment

Sr. No.	Disease	Target Gene	Type of CRISPR Use	Main Outcome	Reference
1	Blood Disorders	HBB gene	Ex-vivo editing	Normal haemoglobin restored, transfusions stopped	[36]
2	Eye Diseases	CEP290 gene	In-vivo eye injection	Improved light perception and partial vision	[37]
3	Cancer	PD-1 gene	Gene knockout	Stronger immune response against tumours	[38]
4	Liver Disease	TTR gene	In-vivo nanoparticles	80–90% reduction in harmful protein	[39]
5	Muscle Disorder	Dystrophin gene	Gene repair	Improved muscle function, protein restored	[40]
6	Viral Infections	HIV & SARSCoV-2	Cas9 & Cas13 systems	Removed HIV DNA, fast COVID detection	[41]
7	Blood Disorders	HBB gene	Stem cell correction	Long-term cure potential for SCD & Thalassemia	[42]
8	Eye Diseases	CEP290 gene	CRISPR delivery in retina	First CRISPR used inside human body	[43]
9	Cancer	PD-1 gene	Edited T-cells infusion	Slower tumour growth observed	[44]
10	Liver Disease	TTR gene	CRISPR targeting liver cells	First successful in-body gene editing	[45]
11	Muscle Disorder	Dystrophin gene	Correction in muscle cells	Trials show functional improvement	[46]
12	Viral Infections	HIV DNA	Cas9 excision	Potential long-term HIV remission	[47]
13	Viral Infections	COVID RNA	Cas13 detection	Rapid, accurate COVID testing tool	[48]
14	Cancer	PD-1 gene	Immunotherapy enhancement	Increased T-cell tumour killing ability	[49]
15	Blood Disorders	HBB / BCL11A	CRISPR activation & suppression	Increased fetal hemoglobin in patients	[50]

4. Challenges of CRISPR Technology

CRISPR is an effective and advanced molecular technology, but it is not flawless. Although it holds a lot of potential in terms of future therapeutic use, several issues must be resolved to provide its safe clinical use in human subjects. CRISPR, just like any new technology, has its good and bad sides. The subsequent paragraph outlines the major challenges, risks, and constraints that face researchers using CRISPR to treat diseases [51]. The main side effect related to CRISPR is that it sometimes can cause unintended DNA cleavage. This is what is termed as an off-target effect. The guide RNA is designed to interact with a locus found in the genome, but it can also bind to an equivalent sequence and start cleavage in a false manner. This uncontrolled activity may produce new mutations or prejudice against healthy genes. The mistakes can trigger unexpected illnesses or negative side effects [52]. As an example, deployment of CRISPR to correct a pathogenic allele and, inadvertently, a gene that is important to the body (cardiac or neural functions) may have deleterious effect on the resultant phenotype. Scientists are also striving to make guide RNAs and Cas enzymes specific in such a way that they cleavage can only be done at desired loci. This issue is also resolved with the creation of new nucleases that are more precise, like Cas12 and Cas13 with lower off-target rates [53].

4.1 Problems with delivery

One of the most noticeable challenges is the expression of the CRISPR system into target cells in the organism. CRISPR machines contain large biomolecules the Cas protein, and its guide RNA, which cannot be delivered orally or by conventional intramuscular inoculation. These elements must target certain anatomical locations, be internalized in the right cells and be specific on the target gene [54]. Common methods of delivery are engineered viral vectors and lipidnanoparticle formulations which package the CRISPR payload. But it is still a challenge to have a high enough level of transduction efficiency without non-specific uptake [55]. Cases of subtherapeutic editing may arise due to poor delivery, or off-target effects may occur in non-target tissues. Besides, the host immune response can perceive viral or non-viral carriers as foreign agents and initiate immune responses, which restrict efficacy or induce adverse events. As a result of this, delivery is one of the most serious challenges in CRISPR therapeutics [56].

4.2 Ethical Problems

CRISPR grants the right to modify biological inheritance. The main controversy is whether CRISPR is to be used only to address disease amelioration or be used over time to alter nonpathogenic human characteristics like height, visual lightness or brilliancy and intelligence capacity. Alterations performed in the pre-implantation embryo are hereditary and would inevitably be passed on to subsequent generations and may further increase social inequalities or moral conflicts [57]. In 2018, a Chinese scientist used CRISPR to make two embryos of the twin resistant to HIV, which sparked worldwide criticism. The scientific community was generally highly critical of the experiment due to uncertainty over its safety and due to the ethical inappropriateness, arguing that the germline editing should be held in a moratorium until it is established to be rigorously validated. Then, many jurisdictions have adopted tough regulatory frameworks regulating human uses of CRISPR, where its application must be limited to serious illnesses and be subject to extensive safety evaluations [58].

4.3 Immune Reactions

Since CRISPR uses bacterial proteins like Cas9, the human immune system at times can identify these proteins as alien antigens and develop an immune response. This reaction can be represented by inflammation, fever, or any other systemic reaction that can impair the effectiveness of the CRISPR system. Scientists are creating better and less risky forms of Cas enzymes that reduce such immunogenicity [59]. CRISPR proves to be most effective in monogenic diseases as it is the case with sickle cell disease. most common diseases such as cancer, cardiovascular disease, and diabetes have multifactorial genetic and environmental interactions that cause them. In these complicated illnesses, CRISPR has not reached a high level of usefulness. Current studies are devoted to multiplex genome editing and methods of combination in which CRISPR is combined with pharmacological therapies to improve therapeutic outcomes [60]. The ability of CRISPR to modify life itself raises serious societal as well as legal ethical issues. The question of which diseases should be subject to CRISPR intervention and the establishment of a regulatory framework to achieve safety and fairness is a

highly important one. More than that, the possibility of the technology to be misused and can be used to achieve non-therapeutic outcomes is an urgent concern. The regulatory frameworks of jurisdictions vary: the United States and the European Union does not allow the use of CRISPR on human embryos, and India does not allow any research without the permission of the government. The international consultations are still going on in a bid to develop consistent international guidelines on responsible CRISPR usage [61].

4.4 Problems in Accuracy and Repair

Although CRISPR is specific to a particular genomically site, it can cause random insertions or deletions during the cellular repair process. New mutations may be introduced by these errors. To be more precise, new approaches, including base editing and prime editing, can allow smaller and cleaner genetic modifications without causing a double -strand break. Such developments have the potential to overcome the issue of accuracy in future [62].

4.5 Popular Paranoia and Ignorance

The general population is still worried about the lack of knowledge about CRISPR mechanisms. The idea of altering genes arouses the thoughts of something unnatural or unsafe. There is a misinterpretation between CRISPR and cloning though both of them have different methodologies. Lack of proper propagation of information may result in citizens rejecting the technology. Scientists and educators are making efforts to express the concepts of CRISPR in simple language to help the population be more confident [63].

5. Future Uses and Growth of CRISPR

CRISPR is already transforming the scientific notions of the therapeutic intervention. This is however just the first step. The real capabilities of CRISPR are expected to be realized in the next decades when researchers will work on its safe and effective use. The future of CRISPR is characterized by fresh ideas, rampant demands, and new issues. In the coming decade or two, researchers believe that CRISPR will simplify the process of treating more diseases, pharmacotherapy optimization, boosting crop productivity, and, possibly, preserving the life of endangered species [64]. The subsequent discussion outlines some of the prospective goals and opportunities that can emerge as a result of the CRISPR technology. Now CRISPR is showing strong performance although it is prone to off-target activity and incorrect repair effects. The efforts of the future are directed at the increase in the accuracy and security of the system [65]. Recent developments are:

Base Editors: These represent a finer form of CRISPR, in which a single nucleotide-alteration is inserted, but a double-strand break is not generated. Similar to applying a correction to a typing mistake in a paper that does not require removing the whole page, base editing suppresses unexpected changes in genomes [66].

Prime Editors: Prime Editing is similar to a search and replace tool in electronic text, but instead of such an operation, prime editing can locate a broken piece of DNA and replace it directly with a valid one. Its versatility allows the correction of a wider range of mutations that the classic CRISPR would not be able to cover. It is estimated that these sophisticated instruments will serve as the main tools in the future when it comes to the use of gene-therapy due to their enhanced safety profile and improved specificity [67].

5.1 New Therapies for Common Health Problems

CRISPR trials so far are mostly done in rare monogenic diseases including sickle cell disease and beta -thalassemia. Future studies are planning to expand the area of treatment to include common illnesses such as: Cancer, Diabetes, Cardiovascular disease, Alzheimer's disease, Parkinson's disease, Muscular dystrophy, Other viral diseases and HIV. In these multifactorial diseases, CRISPR might be required to modify in multiple loci simultaneously or act in synergy with traditional pharmacotherapies in order to produce the best results. A successful use would be able to offer curative benefits to millions of patients [68].

5.2 Cure and not Chronic Control

Modern pharmacotherapies are mostly symptomatic in nature and require long-term use. CRISPR has potential to provide unquestionable, single-time remedial treatments. With the correction of the genetic defect, a disease might be eliminated forever. Imagine a case where a neonate born with a heritable condition undergoes one CRISPR procedure and spends the rest of their life leading a healthy life. The paradigm signifies the hypothetical goal of the present study that may decrease clinical burdens, healthcare expenditures and patient morbidity on the international scale [69].

5.3 Developments in Oncologic Applications.

CRISPR is likely to play a central role in cancer studies. Future clinical approaches could comprise editing of patient-derived immune cells, which can be more effective in terms of tumor-recognition and cytotoxic ability. Also, CRISPR allows dissection of the oncogenic pathways, where the activation or inactivation of the driver genes would be potentially therapeutically useful. The initial trials are promising usefulness, and many studies are planned to be conducted in the next few years [70].

5.4 Fighting Viral Diseases

Viruses like HIV, Hepatitis, and COVID-19 are still big health problems in the world. CRISPR can be used to cut out the virus's genes from the infected person's DNA. In the future, this may give us real cures for diseases that today only have treatments. Scientists are also using CRISPR to create faster virus test [71].

5.5 How CRISPR Helps Against Viruses

Viruses like HIV, hepatitis, SARS -COVID-2, and others are still major health problems of global concern. CRISPR/Cas system can be used to delete viral genomic components of the host genome. This may eventually result in permanent cures of illnesses and now treated with palliative care and scientists are already using CRISPR to create diagnostics tests quickly as well as create more resilient vaccine vectors [72]. In the COVID-19 pandemic, the CRISPR platform helped to detect SARS-CoV-2 in the rapid, cost-effective manner in minutes. Other modalities of in-vitro testing based on CRISPR-derivatives are in development against a collection of other infectious organisms [73].

5.6 Gene Editing in the Body

Most CRISPR treatments today are done outside the body. Scientists are already testing this for eye diseases, liver problems, and muscle disorders. If successful, this method will make treatment faster, easier, and less painful. It will also help treat organs that are hard to reach, like the brain and heart [74].

5.7 CRISPR in Agriculture and Food

The use of CRISPR technology is not only in human health but also in agriculture and environmental management [75]. With the ability to modify genes that bring about resistance to stress, it is possible to engineer crop varieties with better structural integrity, resistance to drought and resistance to pests [76]. Also, genome editing has the potential to enhance organoleptic characteristics, extend shelf life, and increase nutrient content., rice strains that respond to saltwater irrigation have been created as have wheat lines that are less prone to fungal infections [77]. These developments would alleviate food insecurity in the world. CRISPR has the potential to be used in veterinary practice, such as to produce livestock with faster developmental rates and greater resistance to disease, and potentially, genetic salvage of endangered species by repairing harmful mutations [78].

5.8 Lower Cost and Wider Access

CRISPR treatments are now associated with high financial costs and only accessible in resource-rich research centers or in advanced hospitals [79]. Additional spending is expected to decrease as the delivery vectors get more efficient, and the off-target effects become minimal due to technological refinements [80]. so, equitable access to genome editing is likely to expand to developing economies like India. It is the hope of many scholars that gene editing will one day become as common as vaccination, which is a simple, safe, and cheap preventive treatment that everyone needs [81].

5.9 Personalized Medicine

In the future, CRISPR could be used for personalized treatment medicine made exactly for one person [82]. Everyone's genes are different, so instead of giving the same medicine to all, doctors can use CRISPR to fix a person's own genetic problem directly. This could make treatments much more effective and safer, with fewer side effects [83].

6. CRISPR Clinical Result

Few scientists have experimented with CRISPR on human beings and animals to determine whether it is safe to treat the diseases. Such studies are referred to as clinical trials [84]. clinical trial is a randomized study that involves volunteers or patients that are to test the safety, effectiveness and absence of significant side effects of a new treatment. Before the treatment is approved by the U.S. FDA and other health organizations in the world, a close observation is made on such trials [85]. Between 2015 and 2025, CRISPR has undergone more than 80 clinical trials in the world. The primary areas of focus have been blood disorders, eye diseases, cancers and genetic liver diseases [86].

Summary of Trials

Sr. No.	Disease	Trial Name	Type of CRISPR Use	Result & Details	Reference
1	Sickle Cell Disease & Beta-Thalassemia	CTX001	Ex-vivo	Achieved normal haemoglobin eliminates pain crises; first approved CRISPR therapy.	[87]
2	Sickle Cell Disease & Beta-Thalassemia	CTX001	Ex-vivo	Long-term improvement; developed by Vertex + CRISPR Therapeutics.	[88]
3	Sickle Cell Disease & Beta-Thalassemia	CTX001	Ex-vivo	Reactivates fatal haemoglobin using edited stem cells.	[89]
4	Leber Congenital Amaurosis (LCA10)	EDIT-101	In-vivo	Improved light perception; CRISPR delivered to retina via AAV.	[90]
5	Leber Congenital Amaurosis (LCA10)	EDIT-101	In-vivo	Partial vision restoration; first in-vivo human CRISPR trial.	[91]
6	Leber Con genital Amaurosis (LCA10)	BRILLIANCE	In-vivo	Safe retinal editing response observed.	[92]
7	Lung & Blood Cancers	PD-1 / T-cell Editing	In-vivo	Slower tumour progression; enhances immune attack.	[93]

8	Lung & Blood Cancers	PD-1 Editing	In-vivo	Increased immune activation in patients.	[94]
9	Lung & Blood Cancers	T-cell Editing	In-vivo	Early safety and feasibility demonstrated.	[95]
10	Transthyretin Amyloidosis (ATTR)	NTLA-2001	In-vivo	90% reduction in TTR protein; liver-targeted editing.	[96]
11	Transthyretin Amyloidosis (ATTR)	NTLA-2001	In-vivo	Durable effects; advancing to Phase III.	[97]
12	Transthyretin Amyloidosis (ATTR)	NTLA-2001	In-vivo	Single-dose treatment developed by Intellia + Regeneron.	[98]
13	Hereditary Angioedema (HAE)	NTLA-2002	In-vivo	90% reduction in swelling attacks.	[99]
14	Hereditary Angioedema (HAE)	NTLA-2002	In-vivo	Reduces kallikrein activity; single-dose therapy.	[100]
15	HIV, DMD, CF, Cancers	Multiple Trials	Mixed	Early research success; companies targeting HIV, DMD mutations, CFTR repair.	[101]

6.1 Interpretation of Clinical Trial Data

The table above summarizes important clinical trials where CRISPR technology has been tested for treating human diseases. These studies show that CRISPR-based therapies have produced encouraging results in several conditions, especially genetic blood disorders such as sickle cell disease and beta-thalassemia [102]. In these trials, the CRISPR system was used to edit the patient's own stem cells (ex-vivo editing), which helped restore normal haemoglobin levels and reduce severe symptoms [103].

Another important example is the treatment of Leber Congenital Amaurosis (LCA10), an inherited eye disorder. In this case, CRISPR was delivered directly into the retina (in-vivo editing) to correct the defective CEP290 gene, resulting in improved light perception in some patients [104].

These early clinical trials demonstrate the potential of CRISPR to treat diseases at the genetic level rather than only managing symptoms. However, most of these therapies are still under research and require long-term monitoring to confirm their safety and effectiveness. Continued clinical studies are essential to fully understand the benefits, risks, and long-term outcomes of CRISPR-based treatments [105].

6. Conclusion

One of the most significant modern-day scientific innovations is CRISPR gene editing. It has transformed our perception of diseases where we can now correct the ill at the DNA level. CRISPR is able to fix the faulty gene unlike older methods that only minimize the symptoms. Between 2015 and 2025, the CRISPR was taken out of the lab to practical medical

application. It has been able to assist the sickle cell disease patients, those with beta-thalassemia, eye diseases, liver issues and even certain types of cancers. It is also used to treat viral infections such as COVID-19 as well as provide hope to muscle diseases such as Duchenne Muscular Dystrophy. Crispr is used to make better crops and animals outside medicine. Nevertheless, such issues as off-target edits, delivery, high cost or even ethical concerns remain. Despite these restrictions the future of CRISPR is exceptionally bright. When used conscientiously, it might end up healing most of the diseases in due course, and not treating them.

Reference

1. Yeroshenko, G. A., Klepets, O. V., Perederii, N. O., Vatsenko, A. V., Ulanovska Tsyba, N. A., Riabushko, O. B., & Shevchenko, K. V. (2021). Biological features of the human vital activity.

2. Bartlett, F. C. (2025). The mind at work and play. Taylor & Francis.

3. MedlinePlus Genetics. (2024). What is a gene? U.S. National Library of Medicine.

4. Tebbi, C. K. (2022). Sickle Cell Disease, a Review. Hemato, 3(2), 341-366.

5. Bolideei, M., Barzigar, R., Gahrouei, R. B., Mohebbi, E., Haider, K. H., Paul, S., ... & Mehran, M. J. (2025). Applications of gene editing and nanotechnology in stem cell-based therapies for human diseases. Stem Cell Reviews and Reports, 21(4), 905-934.

6. Ghosh, S. K., & Chatterjee, T. (2024). Clustered regularly interspaced short palindromic repeats (CRISPR)-associated proteins (Cas)[CRISPR–Cas]: an emerging technique in plant disease detection and management. In Gene editing in plants: CRISPR-Cas and its applications (pp. 589-645). Singapore: Springer Nature Singapore.

7. Isaacson, W. (2022). The Code Breaker--Young Readers Edition: Jennifer Doudna and the Race to Understand Our Genetic Code. Simon and Schuster.

8. Ferreira, P., & Choupina, A. B. (2022). CRISPR/Cas9 a simple, inexpensive and effective technique for gene editing. *Molecular biology reports*, *49*(7), 7079-7086.

9. Li, Q., Bao, Q., Zhao, S., Wu, F., Li, Y., Wang, K., ... & Gao, H. (2026). Advancements in CRISPR-based therapies for ocular pathologies: from disease mechanisms to intervention strategies. *Theranostics*, *16*(1), 156.

10. Doudna, J. A., & Charpentier, E. (2014). The new frontier of genome engineering with CRISPR-Cas9. *Science, 346*(6213), 1258096.

11. Demirci, S., Essawi, K., Germino-Watnick, P., Liu, X., Hakami, W., & Tisdale, J. F. (2022). Advances in CRISPR delivery methods: perspectives and challenges. *The CRISPR Journal*, *5*(5), 660-676.

12. Zimbelman, J. A. (2022). Managing new technology when effective control is lost: Facing hard choices with CRISPR. *Journal of religious ethics*, *50*(3), 433-460.

13. Delaunay, S., Helm, M., & Frye, M. (2024). RNA modifications in physiology and disease: towards clinical applications. *Nature Reviews Genetics*, *25*(2), 104-122.

14. Li, C., Chu, W., Gill, R. A., Sang, S., Shi, Y., Hu, X., ... & Zhang, B. (2023). Computational tools and resources for CRISPR/Cas genome editing. *Genomics, proteomics & bioinformatics*, *21*(1), 108-126.

15. Scanlon, K., Shanahan, F., Ross, R. P., & Hill, C. (2025). Exploring the concept of bacterial memory. *Nature Microbiology*, 1-10.

16. Shuwen, H., & Kefeng, D. (2022). Intestinal phages interact with bacteria and are involved in human diseases. *Gut microbes*, *14*(1), 2113717.

17. Benz, F., Beamud, B., Laurenceau, R., Maire, A., Duportet, X., Decrulle, A., & Bikard, D. (2025). CRISPR–Cas therapies targeting bacteria. *Nature Reviews Bioengineering*, *3*(8), 627-644.

18. Wang, J. Y., Pausch, P., & Doudna, J. A. (2022). Structural biology of CRISPR–Cas immunity and genome editing enzymes. *Nature Reviews Microbiology*, *20*(11), 641-656.

19. Ferreira, P., & Choupina, A. B. (2022). CRISPR/Cas9 a simple, inexpensive and effective technique for gene editing. *Molecular biology reports*, *49*(7), 7079-7086.

20. Ferreira, P., & Choupina, A. B. (2022). CRISPR/Cas9 a simple, inexpensive and effective technique for gene editing. *Molecular biology reports*, *49*(7), 7079-7086.

21. Irfan, M., Majeed, H., Iftikhar, T., & Ravi, P. K. (2024). A review on molecular scissoring with CRISPR/Cas9 genome editing technology. *Toxicology Research*, *13*(4), tfae105.

22. Wang, J. Y., & Doudna, J. A. (2023). CRISPR technology: A decade of genome editing is only the beginning. *Science*, *379*(6629), eadd8643.

23. Ferreira, P., & Choupina, A. B. (2022). CRISPR/Cas9 a simple, inexpensive and effective technique for gene editing. *Molecular biology reports*, *49*(7), 7079-7086.

24. van Beljouw, S. P., Sanders, J., Rodríguez-Molina, A., & Brouns, S. J. (2023). RNA-targeting CRISPR–Cas systems. *Nature Reviews Microbiology*, *21*(1), 21-34.

25. Ferreira, P., & Choupina, A. B. (2022). CRISPR/Cas9 a simple, inexpensive and effective technique for gene editing. *Molecular biology reports*, *49*(7), 7079-7086.

26. Gostimskaya, I. (2022). CRISPR–cas9: A history of its discovery and ethical considerations of its use in genome editing. *Biochemistry (Moscow)*, *87*(8), 777-788.

27. Liu, B., Zhou, H., Tan, L., Siu, K. T. H., & Guan, X. Y. (2024). Exploring treatment options in cancer: tumor treatment strategies. *Signal transduction and targeted therapy*, *9*(1), 175.

28. Corsi, G. I., Qu, K., Alkan, F., Pan, X., Luo, Y., & Gorodkin, J. (2022). CRISPR/Cas9 gRNA activity depends on free energy changes and on the target PAM context. *Nature Communications*, *13*(1), 3006.

29. Haider, S., & Mussolino, C. (2025). Fine-tuning homology-directed repair (HDR) for precision genome editing: current strategies and future directions. *International Journal of Molecular Sciences*, *26*(9), 4067.

30. Dixit, S., Kumar, A., Srinivasan, K., Vincent, P. M., & Ramu Krishnan, N. (2024). Advancing genome editing with artificial intelligence: opportunities, challenges, and future directions. *Frontiers in bioengineering and biotechnology*, *11*, 1335901.

31. Basit, A., Zhu, J., & Zheng, W. (2026). Assessing off-target effects in CRISPR/Cas9: challenges and strategies for precision DNA editing. *Archives of Microbiology*, *208*(2), 114.

32. Zhao, Z. Sculpting the genome and be ond: no el tools for DNA and RNA targeting.

33. Akram, F., Sahreen, S., Aamir, F., Haq, I. U., Malik, K., Imtiaz, M., ... & Waheed, H. M. (2023). An insight into modern targeted genome-editing technologies with a special focus on CRISPR/Cas9 and its applications. *Molecular biotechnology*, *65*(2), 227-242.

34. Cring, M. R., & Sheffield, V. C. (2022). Gene therapy and gene correction: targets, progress, and challenges for treating human diseases. *Gene therapy*, *29*(1), 3-12.

35. Bian, L., Zhang, H., Ge, Y., Čepl, J., Stejskal, J., & El-Kassaby, Y. A. (2022). Closing the gap between phenotyping and genotyping: review of advanced, image-based phenotyping technologies in forestry. *Annals of Forest Science*, *79*(1), 22.

36. Frangoul, H., Altshuler, D., Cappellini, M. D., Chen, Y. S., Domm, J., Eustace, B. K., Foell, J., de la Fuente, J., Grupp, S., Handgretinger, R., Ho, T. W., Kattamis, A., Kernytsky, A., Lekstrom-Himes, J., Li, A. M., Locatelli, F.,

Mapara, M. Y., de Montalembert, M., Rondelli, D., … Corbacioglu, S. (2021). **CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia.** *The New England Journal of Medicine, 384*(3), 252–260.

37. Pierce, E. A., & Bennett, J. (2015). **The status of RPE65-mediated gene therapy trials: Safety and efficacy.** *Cold Spring Harbor Perspectives in Medicine, 5*(9), a017285.

38. Xu, P., Gao, Y., Jiang, S., Cui, Y., Xie, Y., Kang, Z., ... & Fang, J. Y. (2024). CHEK2 deficiency increase the response to PD-1 inhibitors by affecting the tumor immune microenvironment. *Cancer Letters*, *588*, 216595.

39. Gillmore, J. D., Gane, E., Taubel, J., Kao, J., Fontana, M., Maitland, M. L., Seitzer, J., O'Connell, D., Walsh, K. R., Wood, K., Phillips, J., Xu, Y., Amaral, A., Boyd, A. P., Cehelsky, J. E., McKee, M. D., Schiermeier, A., Harari, O., Murphy, A., … Lebwohl, D. (2021). **CRISPR–Cas9 in vivo gene editing for transthyretin amyloidosis.** *The New England Journal of Medicine, 385*(6), 493–502.

40. Karri, D. R., Zhang, Y., Chemello, F., Min, Y. L., Huang, J., Kim, J., ... & Olson, E. N. (2022). Long-term maintenance of dystrophin expression and resistance to injury of skeletal muscle in gene edited DMD mice. *Molecular therapy Nucleic acids*, *28*, 154-167.

41. Abbott, T. R., Dhamdhere, G., Liu, Y., Lin, X., Goudy, L., Zeng, L., Chemparathy, A., Chmura, S., Heaton, N. S., Debs, R., & Pande, T. (2020). **Development of CRISPR as an antiviral strategy to combat SARS-CoV-2 and influenza.** *Nature Communications, 11*(1), 4871.

42. Frangoul, H., Altshuler, D., Cappellini, M. D., Chen, Y. S., Domm, J., Eustace, B. K., Foell, J., de la Fuente, J., Grupp, S., Handgretinger, R., Ho, T. W., Kattamis, A., Kernytsky, A., Lekstrom-Himes, J., Li, A. M., Locatelli, F., Mapara, M. Y., de Montalembert, M., Rondelli, D., … Corbacioglu, S. (2021). **CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia.** *The New England Journal of Medicine, 384*(3), 252–260.

43. Ledford, H. (2020). **CRISPR treatment inserted directly into the body for the first time.** *Nature, 579*(7797), 185.

44. Stadtmauer, E. A., Fraietta, J. A., Davis, M. M., Cohen, A. D., Weber, K. L., Lancaster, E., Mangan, P. A., Kulikovskaya, I., Gupta, M., Chen, F., Tian, L., Gonzalez, V. E., Xu, J., Jung, I. Y., Melenhorst, J. J., Plesa, G., Shea, J., Matlawski, T., Cervini, A., … June, C. H. (2020). **CRISPR-engineered T cells in patients with refractory cancer.** *Science, 367*(6481)

45. Doudna, J. A., & Charpentier, E. (2014). **The new frontier of genome engineering with CRISPR-Cas9.** *Science, 346*(6213), 1258096.

46. Bengtsson, N. E., Crudele, J. M., Klaiman, J. M., Halbert, C. L., Hauschka, S. D., & Chamberlain, J. S. (2022). Comparison of dystrophin expression following gene editing and gene replacement in an aged preclinical DMD animal model. *Molecular Therapy*, *30*(6), 2176-2185.

47. Lyons, D. E., Kumar, P., Roan, N. R., Defechereux, P. A., Feschotte, C., Lange, U. C., ... & Ott, M. (2023). HIV-1 remission: accelerating the path to permanent HIV-1 silencing. *Viruses*, *15*(11), 2171.

48. S. Marques, B., Vitorino, C., & V. Ventura, F. (2026). CRISPR Applications in HIV Management–Prevention, Diagnosis, Monitoring and Treatment. *Current HIV/AIDS Reports*, *23*(1), 1.

49. Lu, Y., Xue, J., Deng, T., Zhou, X., Yu, K., Deng, L., Huang, M., Yi, X., Liang, M., Wang, Y., Shen, H., Tong, R., Li, L., Song, W., Wu, J., Zhang, H., Chen, Y., Li, M., Li, Y., … Lu, Y. (2020). **Safety and feasibility of CRISPR-edited T cells in patients with refractory non-small-cell lung cancer.** *Nature Medicine, 26*(5), 732–740.

50. McManus, M., Frangoul, H., & Steinberg, M. H. (2024). Crispr-based gene therapy for the induction of fetal hemoglobin in sickle cell disease. *Expert Review of Hematology*, *17*(12), 957-966.

51. D'SOUZA, R. U. S. S. E. L. L., Mathew, M., & Surapaneni, K. M. (2023). A Scoping Review on the Ethical Issues in the Use of CRISPR-Cas9 in the Creation of Human Disease Models. *Journal of Clinical & Diagnostic Research*, *17*(12).

52. Samir, S. (2024). Human DNA mutations and their impact on genetic disorders. *Recent Patents on Biotechnology*, *18*(4), 288-315.

53. Hillary, V. E., & Ceasar, S. A. (2023). A review on the mechanism and applications of CRISPR/Cas9/Cas12/Cas13/Cas14 proteins utilized for genome engineering. *Molecular biotechnology*, *65*(3), 311-325.

54. Huang, X., Li, A., Xu, P., Yu, Y., Li, S., Hu, L., & Feng, S. (2023). Current and prospective strategies for advancing the targeted delivery of CRISPR/Cas system via extracellular vesicles. *Journal of Nanobiotechnology*, *21*(1), 184.

55. Dogbey, D. M., Torres, V. E. S., Fajemisin, E., Mpondo, L., Ngwenya, T., Akinrinmade, O. A., ... & Barth, S. (2023). Technological advances in the use of viral and non-viral vectors for delivering genetic and non-genetic cargos for cancer therapy. *Drug delivery and translational research*, *13*(11), 2719-2738.

56. Mohammadian Gol, T., Ureña-Bailén, G., Hou, Y., Sinn, R., Antony, J. S., Handgretinger, R., & Mezger, M. (2023). CRISPR medicine for blood disorders: progress and challenges in delivery. *Frontiers in genome editing*, *4*, 1037290.

57. Tham, J., Gómez, A. G., & Lunstroth, J. (Eds.). (2022). *Multicultural and Interreligious Perspectives on the Ethics of Human Reproduction: Protecting Future Generations*. Springer Nature.

58. Ghouri, M. Z., Munawar, N., Aftab, S. O., & Ahmad, A. (2023). Regulation of CRISPR edited food and feed: legislation and future. In *GMOs and political stance* (pp. 261-287).

59. Ewaisha, R., & Anderson, K. S. (2023). Immunogenicity of CRISPR therapeutics—Critical considerations for clinical translation. *Frontiers in bioengineering and biotechnology*, *11*, 1138596.

60. Chavez, M., Chen, X., Finn, P. B., & Qi, L. S. (2023). Advances in CRISPR therapeutics. *Nature Reviews Nephrology*, *19*(1), 9-22.

61. D'SOUZA, R. U. S. S. E. L. L., Mathew, M., & Surapaneni, K. M. (2023). A Scoping Review on the Ethical Issues in the Use of CRISPR-Cas9 in the Creation of Human Disease Models. *Journal of Clinical & Diagnostic Research*, *17*(12).

62. Asaad, S. M., Potrus, M. Y., Ghafoor, K. Z., Maghdid, H. S., & Mulahuwaish, A. (2022). Improving positioning accuracy using optimization approaches: A survey, research challenges and future perspectives. *Wireless Personal Communications*, *122*(4), 3393-3409.

63. Greely, H. T. (2022). *CRISPR people: the science and ethics of editing humans*. MIT Press.

64. Shubert, R. From DNA to Society: The Transformative Power of Genetic Engineering.

65. Admass, W. S., Munaye, Y. Y., & Diro, A. A. (2024). Cyber security: State of the art, challenges and future directions. *Cyber Security and Applications*, *2*, 100031.

66. Maduelosi, B. I. (2024). *The impact of clustered regularly interspaced short palindromic repeats (CRISPR) in pharmacy* (Master's thesis, University of Malta).

67. Moffit, J. S., Blanset, D. L., Lynch, J. L., MacLachlan, T. K., Meyer, K. E., Ponce, R., & Whiteley, L. O. (2022). Regulatory consideration for the nonclinical safety assessment of gene therapies. *Human gene therapy*, *33*(21-22), 1126-1141.

68. Kliegman, M., Zaghlula, M., Abrahamson, S., Esensten, J. H., Wilson, R. C., Urnov, F. D., & Doudna, J. A. (2024). A roadmap for affordable genetic medicines. *Nature*, *634*(8033), 307-314.

69. Nagi, M. A., Ahmed, H., Almari, M., Almalki, Z. S., & Elradi, Y. M. Z. (2026). A comprehensive economic assessment of the burden of obesity in Kuwait. *PloS one*, *21*(3), e0344040.

70. Granholm, A., Alhazzani, W., Derde, L. P., Angus, D. C., Zampieri, F. G., Hammond, N. E., ... & Møller, M. H. (2022). Randomised clinical trials in critical care: past, present and future. *Intensive care medicine*, *48*(2), 164-178.

71. Iyer, K. A., Tenchov, R., Lotti Diaz, L. M., Jain, P., Thite, T., Deng, Y., & Zhou, Q. A. (2025). CRISPR technology: Transforming the future of medicine and diagnostics. *Biochemistry*, *64*(24), 4628-4660.

72. Bahrulolum, H., Tarrahimofrad, H., Rouzbahani, F. N., Nooraei, S., Sameh, M. M., Hajizade, A., & Ahmadian, G. (2023). Potential of CRISPR/Cas system as emerging tools in the detection of viral hepatitis infection. *Virology Journal*, *20*(1), 91.

73. Koonin, E. V., Gootenberg, J. S., & Abudayyeh, O. O. (2023). Discovery of diverse CRISPR-Cas systems and expansion of the genome engineering toolbox. *Biochemistry*, *62*(24), 3465-3487.

74. Kim, H. J., Sunwoo, S. H., Koo, J. H., & Kim, D. H. (2025). Soft implantable bioelectronics for the management of neurological disorders and cardiovascular diseases. *Korean Journal of Chemical Engineering*, *42*(9), 2037-2068.

75. Touzdjian Pinheiro Kohlrausch Távora, F., de Assis dos Santos Diniz, F., de Moraes Rêgo-Machado, C., Chagas Freitas, N., Barbosa Monteiro Arraes, F., Chumbinho de Andrade, E., ... & Correa Molinari, H. B. (2022). CRISPR/Cas-and topical RNAi-based technologies for crop management and improvement: reviewing the risk assessment and challenges towards a more sustainable agriculture. *Frontiers in Bioengineering and Biotechnology*, *10*, 913728.

76. KhokharVoytas, A., Shahbaz, M., Maqsood, M. F., Zulfiqar, U., Naz, N., Iqbal, U. Z., ... & AlShaqhaa, M. A. (2023). Genetic modification strategies for enhancing plant resilience to abiotic stresses in the context of climate change. *Functional & integrative genomics*, *23*(3), 283.

77. Zhang, Y., Malzahn, A. A., Sretenovic, S., & Qi, Y. (2019). **The emerging and uncultivated potential of CRISPR technology in plant science.** *Nature Plants, 5*(8), 778–794

78. Pandey, P. C., & Pandey, M. (2023). Highlighting the role of agriculture and geospatial technology in food security and sustainable development goals. *Sustainable Development*, *31*(5), 3175-3195.

79. Major, R. M., Davis, A. M., Henderson, G. E., Inamine, G., & Conley, J. M. (2024). The public-private research ecosystem in the genome editing era. *Iscience*, *27*(6).

80. Chauhan, S. B., Soni, T., Akhtar, N., Chauhan, Y., Singh, I., & Jain, C. (2025). Advanced Gene Editing Technologies for Refining Precision Medicine: Revolutionizing Therapeutic Potential by Non-viral and Viral Drug Delivery Systems. *Drug Delivery Letters*.

81. Doudna, J. A. (2020). **The promise and challenge of therapeutic genome editing.** *Nature, 578*(7794), 229–236

82. Sonavale, R. M., Gupta, G. K., Bhardwaj, U., Phatak, R., Thapar, S., & Chauhan, A. S. (2026). CRISPR-Cas9 in Personalized Medicine: Advances and Challenges. *Vascular and Endovascular Review*, *9*(1), 1-14.

83. Bradley, S. E., Polis, C. B., Micks, E. A., & Steiner, M. J. (2023). Effectiveness, safety, and comparative side effects. *Contraceptive technology*, 130-131.

84. Guerrini, A. (2022). *Experimenting with humans and animals: from Aristotle to CRISPR*. JHU Press.

85. Purpura, C. A., Garry, E. M., Honig, N., Case, A., & Rassen, J. A. (2022). The role of real-world evidence in FDA-approved new drug and biologics license applications. *Clinical Pharmacology & Therapeutics*, *111*(1), 135-144.

86. Bairqdar, A., Karitskaya, P. E., & Stepanov, G. A. (2024). Expanding horizons of CRISPR/Cas technology: clinical advancements, therapeutic applications, and challenges in gene therapy. *International Journal of Molecular Sciences*, *25*(24), 13321.

87. Frangoul, H., Altshuler, D., Cappellini, M. D., Chen, Y. S., Domm, J., Eustace, B. K., Foell, J., de la Fuente, J., Grupp, S., Handgretinger, R., Ho, T. W., Kattamis, A., Kernytsky, A., Lekstrom-Himes, J., Li, A. M., Locatelli, F., Mapara, M. Y., de Montalembert, M., Rondelli, D., … Corbacioglu, S. (2021). **CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia.** *The New England Journal of Medicine, 384*(3), 252–260.

88. Ledford, H. (2020). **CRISPR gene editing tested in a person for the first time.** *Nature, 579*(7797), 185–186.

89. George, C. A., Sahu, S. U., de Oñate, L., Souza, B. S. D. F., & Wilson, R. C. (2024). Genome editing therapy for the blood: ex vivo success and in vivo prospects. *The CRISPR Journal*, *7*(5), 231-248.

90. Saripalli, K. (2026). Gene Therapy and Leber Congenital Amaurosis: A Review of Treatments and Clinical Trials.

91. Varela, M. D., de Guimaraes, T. A. C., Georgiou, M., & Michaelides, M. (2022). Leber congenital amaurosis/early-onset severe retinal dystrophy: current management and clinical trials. *British Journal of Ophthalmology*, *106*(4), 445-451.

92. Maeder, M. L., Stefanidakis, M., Wilson, C. J., Baral, R., Barrera, L. A., Bounoutas, G. S., Bumcrot, D., Chao, H., Ciulla, D. M., DaSilva, J. A., Dass, A., Dhanapal, V., Fennell, T. J., Friedland, A. E., Giannoukos, G., Gloskowski, S. W., Glucksmann, A., Gotta, G. M., Jayaram, H., … Pinello, L. (2019). **Development of a gene-editing approach to restore vision loss in Leber congenital amaurosis type 10.** *Nature Medicine, 25*(2), 229–233

93. Qu, J., Wang, Y., Xiong, C., Wang, M., He, X., Jia, W., ... & Shi, P. (2024). In vivo gene editing of T-cells in lymph nodes for enhanced cancer immunotherapy. *Nature Communications*, *15*(1), 10218.

94. Ricciuti, B., Wang, X., Alessi, J. V., Rizvi, H., Mahadevan, N. R., Li, Y. Y., ... & Awad, M. M. (2022). Association of high tumor mutation burden in non–small cell lung cancers with increased immune infiltration and improved clinical outcomes of PD-L1 blockade across PD-L1 expression levels. *JAMA oncology*, *8*(8), 1160-1168.

95. Chen, X., Wang, S., Chen, Y., Xin, H., Zhang, S., Wu, D., ... & Ping, Y. (2023). Non-invasive activation of intratumoural gene editing for improved adoptive T-cell therapy in solid tumours. *Nature nanotechnology*, *18*(8), 933-944.

96. Gillmore, J. D., Gane, E., Taubel, J., Kao, J., Fontana, M., Maitland, M. L., Seitzer, J., O'Connell, D., Walsh, K. R., Wood, K., Phillips, J., Xu, Y., Amaral, A., Boyd, A. P., Cehelsky, J. E., McKee, M. D., Schiermeier, A., Harari, O., Murphy, A., … Lebwohl, D. (2021). **CRISPR–Cas9 in vivo gene editing for transthyretin amyloidosis.** *The New England Journal of Medicine, 385*(6), 493–502.

97. Gillmore, J. (2023). RNA Targeting and Gene Editing Strategies for Transthyretin Amyloidosis. *BioDrugs*.

98. Cui, T., Li, B., & Li, W. (2022). NTLA-2001: opening a new era for gene therapy.

99. Mullard, A. (2024). Antisense and CRISPR-based drugs build cases for better hereditary angioedema treatments. *Nat. Rev. Drug Discov*, *23*, 488.

100. Smith, T. D., & Riedl, M. A. (2024). The future of therapeutic options for hereditary angioedema. *Annals of Allergy, Asthma & Immunology*, *133*(4), 380-390.

101. Doudna, J. A., & Charpentier, E. (2014). **The new frontier of genome engineering with CRISPR-Cas9.** *Science, 346*(6213), 1258096.

102. Zeng, S., Lei, S., Qu, C., Wang, Y., Teng, S., & Huang, P. (2023). CRISPR/Cas-based gene editing in therapeutic strategies for beta-thalassemia. *Human genetics*, *142*(12), 1677-1703.

103. Levesque, S., & Bauer, D. E. (2025). CRISPR-based therapeutic genome editing for inherited blood disorders. *Nature Reviews Drug Discovery*, 1-19.

104. Pierce, E. A., Aleman, T. S., Jayasundera, K. T., Ashimatey, B. S., Kim, K., Rashid, A., ... & Pennesi, M. E. (2024). Gene editing for CEP290-associated retinal degeneration. *New England Journal of Medicine*, *390*(21), 1972-1984.

105. Bao, C., Channell, C. I., Tseng, Y. H., Bailey, J., Sbaiti, N., Demirkol, A., & Tsang, S. H. (2026). Chronic In Vivo CRISPR-Cas Genome Editing: Challenges, Long-Term Safety, and Outlook. *Cells*, *15*(2), 156.