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CRISPR: Redefining the Future of Human Health

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ABSTRACT

CRISPR, or Clustered Regularly Interspaced Palindromic Repeats, are segments of DNA that are naturally found in many bacteria and form the basis of the immune system protecting organisms from foreign elements and viruses (Makarova, 67). These CRISPR sequences contain palindromic sequences with "spacer" sequences from viral infections, which allow the bacteria to "remember" the foreign invading DNA (Morange, 221). The CRISPR-associated (Cas) proteins help the CRISPR sequences recognize and cut complementary sequences, thus neutralizing the danger efficiently from the viral genome.

Discovered in the late 1980s (Morange, 221), CRISPR systems have been extensively researched, allowing scientists to classify CRISPR-Cas into various types based on their functional molecules and genetic composition. Currently, we understand that there are two main classes: Class 1, which includes multi-protein effector complexes, and Class 2, where there is a single, multi-effector protein, as seen with Cas9 (Makarova, 68). Due to advancements in current research, the number of classes discovered has gone from five types and sixteen subtypes to six types and thirty-three subtypes.

Throughout time, technology has evolved in biotechnology by utilizing shorter guide RNAs to direct the Cas9 enzyme to the specific DNA sequence where the cut is intended to occur. As opposed to previous genome editing tools such as ZFNs (Zinc Finger Nucleases), which utilize opposite DNA strands to "cut," or TALENs (Transcription Activator-Like Effector Nucleases), which use DNA-binding domains to cut DNA at the target site, CRISPR-Cas 9 sends the RNA molecules, guiding the Cas9 enzyme to a specific DNA sequence (Severi & Akbari, 2). CRISPR-Cas9 is derived from a bacterial adaptive immune system, allowing for a more precise cut at the targeted DNA site. Due to this innovative breakthrough in the field of biotechnology, CRISPR has since broadened its scope in various fields, including agriculture, therapeutic research, and diagnostics, as it is substantially more affordable and efficient compared to previous methods, such as TALENs and ZFNs.

METHODS: LITERATURE REVIEW APPROACH

The paper utilizes a narrative literature review format to synthesize information regarding CRISPR-based technologies and their various applications in inherited genetic disorders. Prime source selection was a high priority for the paper which is why the sources were chosen from peer-reviewed research articles, clinical trial reports, and authoritative reviews. Databases such as Google Scholar and ScienceDirect were used to identify sources between the time frames from 2013 to 2025 in order to prioritize current and

relevant clinical studies and publications. Finally, a societal viewpoint was also taken under consideration as ethical analyses and policy discussions were also identified in order to put scientific advances in a border societal standpoint.

CRISPR'S HISTORY AND SCIENTIFIC DEVELOPMENT

Since the first CRISPR sequence was discovered in 1987 as a repeated DNA sequence, it has proven itself to be a potent resource for gene editing through its vital role in microbial adaptive immunity. Continued research has proved that these sequences were able to "remember" past viral infections (Morange, 221-222). In short, the mechanism utilizes Cas proteins to recognize and then "cleave" the viral DNA based on this memory (Morange, 223).

Later in the 1990s, Mojica and others discovered fragments of viral DNA implanted with the genomes of archaea and bacteria (Gostimskaya 778). Such components came together to function as a prokaryotic immune system recognizing and destroying invading genetic material, with proteins like Cas9 acting as "genetic scissors" (Gostimskaya 779). As the researchers progressed, they found out the elements needed for CRISPR function, mainly the Cas nuclease, CRISPR RNAs (crRNA), and trans-activating RNAs (tracrRNA), which would be later combined into a single guide RNA (sgRNA) to make for efficient laboratory use (Gostimskaya 780). These two components collaborate to identify matching genetic sequences and cleave them with high accuracy. In 2012, researchers Jennifer Doudna and Emmanuelle Charpentier modified this system by combining both the crRNAs and tracRNAs into a single guide RNA (sgRNA) in order for the CRISPR Cas9 program to easily identify target genetic sequences, turning a bacterial defense system into a revolutionary genetic editing tool.

WHY CRISPR IS NECESSARY

CRISPR has been a revolutionary tool in treating diseases once thought to be untreatable offering scientists a way to execute medical procedures more efficiently and safely than alternative methods. Inherited genetic diseases like sickle cell disease, cystic fibrosis, and Huntington's disease are still prevalent in today's world and are caused by mutations in a person's gene sequence, causing abnormal protein function or buildup, leading to life-threatening symptoms. Unlike traditional methods, where treatments just scratch the surface of the disease without identifying the underlying cause of the issue, CRISPR allows scientists to correct or replace the gene responsible for the faulty protein synthesis, better enabling them to deal with the disease. Such potential isn't just valuable for treating genetic disorders but has huge potential in the field of therapeutic practices by permanently treating the root cause of the disease so that carriers of various inherited disorders do not pass it down to future generations.

CRISPR-CAS'S FUNCTION AND MECHANISM

There are two main components to how the CRISPR system functions: the guide RNA (gRNA) and the Cas enzyme. These two form the ribonucleoprotein complex, which allows for a faster and more efficient way to make the "cut" in the gene sequence. The gRNA directs the Cas enzyme the the target site where a protospacer adjacent motif (PAM) is present, which helps the Cas enzyme recognize where the cut should take place, enabling genome editing (CRISPR Basics Handbook 7). From the point of the cut, there is a double-strand break in the DNA sequence, which is repaired by either non-homologous end joining (NHEJ) or homology-directed repair (HDR).

- Non-homologous end joining (NHEJ) is a less accurate mechanism and binds the broken strands of the DNA without checking for accuracy. Thus, it is much more useful when trying to knock out a gene or when insertions or deletions of a gene segment are taking place.
- Homology-directed repair (HDR) is much more accurate as it utilizes a DNA template (from the cell's original genome or experimental strand) and repairs the broken strands more precisely. Such a method allows for insertions or the replacement of specific gene sequences, which can serve a major role in therapeutic genetic practices.

LIMITATIONS AND GAPS IN CURRENT CRISPR RESEARCH

Although CRISPR Cas9 does promise precise genetic modification, there is a severe problem, limiting its full clinical potential: practical delivery into human cells. Safe tissue-specific delivery remains a major challenge especially in vivo applications where the immune response is triggered and that chance of off-target effects skyrocket. Although viral vectors such as AAVs offer high efficiency, reliability is still a big problem coupled with the concern of immunogenicity making such technology not scalable nor consistent. To continue, long-term safety data remains limited. Throughout many trials we have found that many are recent and involve a small sample size of patients. The potential off-target effects and durability of these CRISPR edits have to be monitored in a long term setting in order to successfully measure the risks associated with vivo therapies. The crux of gene editing not only falls on the capabilities of Cas9 to carry out the splicing of the gene, but it is also heavily dependent on how efficiently the system can be introduced into the gene sequence without causing harm to the cell. Liu et al. state that the greatest challenge in CRISPR-based therapy is ensuring there is "safe and efficient delivery of the CRISPR Cas9 genome-editing system to target cells" (Liu et al. 2). Another limitation is how quickly CRISPR technologies seem to be evolving. Just in recent years we have had numerous technologies including base editing, prime editing, RNA-targeting systems, and many more platforms continuously developing. Thus, many of the recent studies may need revision as new data keeps emerging. Finally the issue of cost effectiveness and global access to such technologies remains one of the biggest issues regarding CRISPR-Cas as there are quite a few significant barriers for global implementation especially in areas where genetic disorders like sickle cell disease are most prevalent.

APPLICATIONS OF NEWER CRISPR TECHNOLOGIES

Once a very common method, Direct Plasmid transfection is being replaced by more sustainable strategies like ribonucleoprotein (RNP) delivery, which drastically limit any unwanted effects and account for a smoother delivery practice (Severi & Akbari 5). Recently, viral vectors have emerged that modify viruses to deliver the genetic materials into the cell. For instance, adeno-associated viruses (AAVs) offer high efficiency but also have drawbacks, including immunogenicity (the virus provoking an immune response, leading to inflammation) and limitations in packaging size. Alternatively, non-viral methods are also on the rise, with some being lipid nanoparticles, hydrogel scaffolds, and exosome-based delivery, especially with in vivo applications – using CRISPR in living organisms instead of isolated tissue (Severi & Akbari 6). To continue, clinical trials conducted on CRISPR's application in genetic disorders are revealing promising results in inherited genetic disorders, namely, sickle cell disease, beta-thalassemia, various cancers, and vision loss (Sherkow and Zettler 11). With each piece of clinical trial and research, we are evermore closer to achieving more efficient methods of therapeutic CRISPR applications.

Jointly, these up-and-coming technologies serve as more refined and safer alternatives, pushing genome editing to the next level.

Table 1. Comparison of Major CRISPR Delivery Methods and Applications

Delivery Method	**Mechanism**	**Advantages**	**Limitations**	**Applications**
Hydrogel Scaffolds	A controlled local release	Localized, Biodegradable	Early stage research	Cancer therapy and wound healing
Viral Vectors (AAV)	Virus-mediated gene delivery	Stable, High efficiency	Immunogenicity, limited size	Retinal disorders, SCD
Lipid nanoparticles (LNPs)	Lipid enclosed CRISPR cargo	Non-viral and repeat dosing possible	Inconsistent tissue targeting	Cystic Fibrosis (lung-editing)
RNP Delivery	Cas9 protein + gRNA complex	Lower off-target effects	Short activity window	Ex-vivo, HSPC editing (oncology)
Organoid-Based Editing	Ex-vivo model, patient derived	Precise and personalized	Translation	Cystic fibrosis correction

HYDROGEL SCAFFOLDS FOR GENE EDITING

Aside from the traditional CRISPR Cas9, innovations such as base and prime editing allow for more precise cuts without the consequence of a double-strand break. Unintended mutations and off-target effects are also minimized during this process (Severi & Akbari 5). In the field of therapeutic practices in wound healing and cancer treatment, hydrogel scaffolds have been used to better control the release of CRISPR components (Severi & Akbari 6).

In terms of tissue engineering and regenerative medicine, hydrogel scaffolds provide a stable and relatively localized delivery method for CRISPR-Cas systems. Hydrogel scaffolds release Cas9 proteins moderately so that there is an extended period of activity at the target site with minimal unwanted effects (Severi & Akbari 7). These scaffolds are three-dimensional, water-rich networks, thus dramatically reducing the risk of inflammation and the chance of immune response being triggered, due to the biodegradability of the scaffolds. Recent studies have shown that within living organisms (in vivo), successful injections of hydrogel scaffolds, revealing CRISPR-mediated genome editing, favor their use for therapeutic advancements in inherited genetic disorders. Although the testing for this newer technology is still ongoing, it still supports the research question's emphasis on safe and reliable techniques for CRISPR applications in genetic disorders.

ETHICAL IMPLICATIONS

Although there have been many developments in CRISPR's clinical history, it still has many ethical implications, and its success is deeply tied to the innovation of highly efficient and safe methods that incorporate tissue-specific delivery systems.

In 2018, such technology was being utilized in China to genetically modify human embryos and babies, sparking global outrage (Gostimskaya 777). Since then, CRISPR systems have progressed from bacterial defense to clinical editing tools, highlighting their success in medicine and the need for ethical guidelines to be put in place when experimenting with such inventions.

The continued evolution of CRISPR-Cas 9 has raised many ethical concerns regarding genome editing, especially in the context of hereditary changes in embryos and reproductive cells. As germline editing progresses, there is the risk of passing the unwanted changes done to the genome over to future generations. Since then, major organizations like the World Health Organization have called for regulatory frameworks to be in place to monitor such activity. As time goes on, advancements in CRISPR technology will come with their ethical implications, and must be met with careful regulations and public communication to avert misuse.

CRISPR'S ABILITIES BEYOND GENE EDITING

Even though CRISPR Cas9 has revolutionized the field of gene editing by focusing on DNA sequences, newer models such as the CRISPR Cas13a have shifted their target to RNA, drastically expanding genetic intervention. First discovered in 2015, C2c2, also known as Cas13a, utilizes two HEPN domains (used in RNA cleaving) to cut the RNA instead of DNA, making it functionally different from Cas9 (Addgene 5). Cas13a is different from that of Cas9 as it doesn't require both the cRNA and tracrRNA to bind to and cut the DNA, and only needs the cRNA to bind to the target RNA. Once Cas13a is activated, not only can it cleave the target RNA, but it can also cut off other RNAs in the sequence, revealing its potential for bacterial defense and its future use for diagnostic tools (Addgene 5). Such technology has developed robust platforms like SHERLOCK, an RNA detection program that can locate and specify viruses/diseases like cancer mutations and Zika. Furthermore, a deactivated form of Cas13a can simply bind to the target RNA sequence instead of cleaving it off, so that researchers can study and even regulate protein activity in live tissue and study its processing. The emerging technology of utilizing RNA instead of just DNA for genetic intervention opens up avenues for greater therapeutic ability of CRISPR, as RNA editing systems similar to Cas13a can offer a modulatory control of gene expression.

THE USE OF CRISPR CAS13A IN MAMMALIAN SYSTEMS

Beyond the function of Cas13a in bacterial systems, a newer variant named Leptotrichia wadei (LwaCas13a) has revealed promising results in research with safe and effective function in mammalian cells, furthering CRISPR's use in clinical applications. Researchers from Zhang's lab designed LwaCas13a and utilized GFP fusion to stabilize the system in mammalian cells (Addgene 84). Additionally, they found it could cleave RNA using around 20 to 28 nucleotides and it doesn't produce any harmful off-target effects, making it far more reliable than other systems, namely, shRNA, which are prone to cellular damage from said off-target effects (Addgene 84-85). Further research confirms LwaCas13a could be beneficial for liveRNA imaging as well as multiplexed gene knockdown, which all have huge upsides for treating genetic disorders that would be driven by dysregulation in a particular gene sequence. Moreover, Cas13a works with SHERLOCK, an RNA diagnostic/detection system enabling real-time detection of mutated cancer cells and various tumor detections (Addgene 84). Finally, all of these findings come together to support Cas13a's function in clinical therapy, as CRISPR is evolving from its DNA-dependent editing stages to a system that is much more multifaceted and reliable for use via RNA regulation.

INHERITED GENETIC DISEASES

CRISPR-CAS9 GENE THERAPY FOR SICKLE CELL DISEASE

Sickle Cell Disease is one of the most dangerous inherited genetic disorders to combat in the history of medicine, affecting millions globally. Its effects lead to painful symptoms such as organ failure, shortened

life expectancy, and abnormal red blood cell function, leading to poor oxygen and nutrient delivery throughout the body. Sickle Cell Disease (SCD) is caused by a specific mutation in the HBB gene, which is composed of a subunit in adult hemoglobin. This mutation creates hemoglobin S (HbS), a defective version that produces out-of-order sickle-shaped red blood cells. Currently, one of the latest technologies in clinical applications is Exagamlogene autotemcel (exa-cel), which Vertex Pharmaceuticals and CRISPR Therapeutics developed. Exa-cel employs CRISPR-Cas9 to disturb the BCL11A enhancer in hematopoietic stem and progenitor cells (HSPCs), which causes the reactivation of fetal hemoglobin (HbF) and covers for the faulty adult hemoglobin and eases the symptoms of the disease (Frangoul et al. 384). Sickle Cell disease causes the production of hemoglobin S (HbS) as well, which polymerizes under low oxygen conditions. This, in turn, disrupts the red blood cells and leads to "systemic organ damage, hemolysis, and vaso-occlusion" (Park & Bao, 2021).

APPROACHES AND CLINICAL EVIDENCE TO COMBAT SCD

There are currently two ways: CRISPR-based therapies and moving towards gene-editing strategies, rectifying the disease-provoking mutation in HBB and inducing fetal hemoglobin (HbF) to either replace or dilute the dysfunctional adult hemoglobin. Naturally, HbF is protective against Sickle Cell Disease and is typically silenced after birth. HbF has two chains, namely, gamma and alpha chains, and later on in life, it changes from fetal hemoglobin to adult hemoglobin, changing the chains to beta and alpha chains by the gene BCL11A. Recently, many CRISPR methods offer reactivating HbF to act as alternative treatments like hydroxyurea or hematopoietic stem cell transplants.

One method suggests disrupting the BCL11A erythroid-specific enhancer using CRISPR Cas9 in corresponding hematopoietic stem and progenitor cells (HSPCs). During the phase 3 trial in CLIMB SCD-121, researchers found exagamglogene autotemcel (exa-cel) revealed exceptional success. To continue, patients who received HSPCs along with busulfan conditioning demonstrated that" 97% were free from vaso-occlusive crises for over a year," and "100% avoided related hospitalizations" (Frangoul et al., 2024). This non-viral therapy treatment exhibits real-world, clinical potential, offering a wide variety of sustained benefits.

Another strategy, as declared by Sharma et al. in a 2023 study, makes use of CRISPR to disrupt the promoters of the HBG1 and HBG2 genes, which control the gamma-globin expression. While utilizing a tiling guide RNA screen (guide RNAs target overlapping regions of gene sequences for increased disruption of gene function), researchers found gRNA-68, which has been shown to increase HbF levels without setting any unwanted off-target effects. To add on, three patients receiving the therapy maintained fetal hemoglobin levels of "19.0-26.8%," with the HbF-positive cells making up nearly "70-88% of red blood cells," dramatically decreasing symptoms of SCD (Sharma et al., 2023).

Overall, the clinical goal is achieved either by silencing repressors like BCL11A or by stimulating the gamma globin directly. More significantly, the approach is conducted outside of the body, and cells are injected back in (ex vivo editing) of autologous HSPCs, and is paired with myeloablative conditioning,

where high radiation or chemotherapy is used to destroy part of the patient's existing bone marrow to fit in the new stem cells that will be replaced.

While such CRISPR methods are certainly efficient and continue to push for advancements in the biotechnology sector, cost and affordability remain one of the biggest concerns in global equitable distribution. Long-term implants, off-target effects, and accessible treatments are all obstacles that need to be tackled before wide-scale CRISPR utilization is possible. Finally, SCD is not only a problem that can be treated with CRISPR, revolutionizing the field of genetic medicine, but it highlights the immense potential of CRISPR to treat inherited genetic disorders and real-time clinical therapy to combat many such diseases that couldn't be treated as easily before.

CRISPR TREATMENT IN CYSTIC FIBROSIS

Cystic fibrosis (CF) is a life-threatening inherited genetic disorder caused by mutations in the cystic fibrosis transmembrane conductance regulator gene (CFTR), which controls a protein that regulates the movement of salt and water across cell membranes. Above 2000 variants can be created from these mutations, which limit CFTR function, leading to chronic respiratory infections, multi-organ failure, and thick mucus buildup (Jakobsen, 2020). Current therapeutic countermeasures, such as Trikafta, are only useful for certain types of mutations, leaving many, especially those with nonsense mutations (introduction of a premature STOP codon, ending the genetic sequence), with no long-term tangible method to fight the infection (Palmgren, 2024).

CRISPR-based therapies are continually showing improvement in their respective field as time progresses. One such study indicates that when lung-selective lipid nanoparticles (SORT LNPs) were utilized to deliver CRISPR-Cas9 and adenine base editors directly to the lung cells of the CF mouse model, the R553X nonsense mutation was fixed with over 50% efficiency. This enabled the CFTR function to return to normal levels and maintained such activity for more than 660 days, revealing unanticipated success in long-term gene repair in lung cells (Palmgren, 2024). This approach is conducted as a non-viral delivery mechanism, allowing for minimal immune response and off-target effects, representing a much safer possibility compared to previous viral methods.

Additionally, ex vivo CRISPR strategies have also shown considerable progress concerning vivo methods. Researchers in the Netherlands used patient-derived intestinal organoids ("mini-guts") to emulate CF and apply base-editing tools to correct the premature STOP codons in the CFTR gene. To continue, results have shown restored protein function without drastic amounts of off-target effects, which were verified throughout the entire genome (Jakobsen, 2020). Through editing the organoids outside of the body, scientists were better able to pre-screen for the right gene correction and limit any immune response the body might have produced during this time. Although clinical guidelines regarding transplants are still a work in progress, such studies push for stronger and more durable cures for CF.

All in all, recent advances in CRISPR technologies inform us regarding the immense potential for CRISPR not only as a one-time cure for CF, but also as a template for treating other inherited genetic disorders through precise genetic editing. The various delivery strategies, mutation-specific base editing, and organoid models all serve for greater personalized invention, taking into consideration individual patients' genetic make-up and clinical use, and more precise gene-editing in the future as CRISPR keeps advancing to higher stages.

CRISPR CAS9 GENE THERAPY FOR CYSTIC FIBROSIS

Since CF is an autosomal recessive disorder, scientists are currently trying to use CRISPR to correct faulty DNA sequences to stop the spread to future generations. In preclinical studies, researchers have established that CRISPR-mediated (HDR) homology-directed repair was effective in correcting the delta F508 mutations in patient-derived epithelial cells, restoring protein and ion channel function back to normal (Schwank et al., 2013; Maul et al., 2019). Moreover, CRISPR base editing variants have been found to edit just a single nucleotide without causing any double-strand breaks in the genetic structure, efficiently minimizing any off-target effects caused by CRISPR-Cas9 (Komor et al., 2016).

The main way gene therapy takes place in CF treatment is through delivery systems that reach the epithelial cells in the airway. As previously discussed, although viral vectors like adeno-associated viruses (AAVs) and lipid nanoparticles have been showing improved success in delivering CRISPR-Cas9 to target tissues (Maule et al., 2019), repeated dosing and triggered immune response have limited the success of such methods. Advances in newer technologies utilizing patient-derived organoids and lipid nanoparticles are currently under testing and research for personalized treatment options, aiming to target drug-resistant CFTR variants. This further expands the therapeutic toolkit for gene therapy and better allows for CRISPR to correct the disease permanently.

CONCLUSION

All in all, CRISPR-Cas9 shows remarkable capability and progress in fighting against inherited genetic disorders such as sickle cell disease. By targeting specific point mutations in the gene sequence at the source, the root cause of the disease is solved rather than just treating the symptoms. As opposed to current treatments like lifelong medication or bone marrow transplants, CRISPR offers a more accurate, efficient, and a more permanent solution. While there still are problems regarding safety, ethical use, and cost effectiveness, the progress that has been made so far has proven CRISPR to be a potent tool in the future in the field of biomedicine. Future research should focus on optimizing non-viral, tissue specific delivery systems to ensure progress in scalability and improved safety. Long term clinical monitoring would also be beneficial so that off-target effects are minimized in a controlled setting and improvised durability. Another direction CRISPR based technologies could take is integrating next generation editing tools such as base, prime, and RNA-targeting editors to expand the range of treatable mutations. Overall these future directions would be very helpful for the development of CRISPR Cas and addressing the

issues involving cost reduction and global implementation would be greatly helpful to ensure an equitable deployment of CRISPR therapies. In conclusion, CRISPR-Cas9 is a transformative tool and could very well shape the future of medicine and bring us much closer to completely treating not only sickle cell disease and cystic fibrosis, but many genetic conditions.

REFERENCES

1. Park, So Hyun, and Gang Bao. "CRISPR/Cas9 gene editing for curing sickle cell disease." Google Scholar, Feb. 2021, www.sciencedirect.com/science/article/abs/pii/S1473050221000100. Accessed 29 July 2025.
2. Sharma, Akshay et al. "CRISPR-Cas9 Editing of the HBG1 and HBG2 Promoters to Treat Sickle Cell Disease." The New England journal of medicine vol. 389,9 (2023): 820-832. doi:10.1056/NEJMoa2215643
3. Frangoul, Haydar et al. "Exagamglogene Autotemcel for Severe Sickle Cell Disease." The New England journal of medicine vol. 390,18 (2024): 1649-1662. doi:10.1056/NEJMoa2309676
4. Kozovska a, et al. "CRISPR: History and Perspectives to the Future." Biomedicine & Pharmacotherapy, Elsevier Masson, 16 July 2021, www.sciencedirect.com/science/article/pii/S0753332221006995?via%3Dihub.
5. Gostimskaya, Irina. "CRISPR–cas9: A history of its discovery and ethical considerations of its use in genome editing." *Biochemistry (Moscow)*, vol. 87, no. 8, Aug. 2022, pp. 777–788, https://doi.org/10.1134/s0006297922080090.
6. FAIRsharing Team. *Addgene*. FAIRsharing, 2015.
7. Severi, Ali Alizadeh, and Bahman Akbari. "crispr‐cas9 delivery strategies and applications: Review and update." *Genesis*, vol. 62, no. 3, 10 May 2024, https://doi.org/10.1002/dvg.23598.
8. Morange, Michel. "What history tells US XXXVII. CRISPR-CAS: The discovery of an immune system in prokaryotes." *Journal of Biosciences*, vol. 40, no. 2, 3 May 2015, pp. 221–223, https://doi.org/10.1007/s12038-015-9532-6.
9. Makarova, Kira S., et al. "Evolutionary classification of crispr‐cas systems." *Crispr*, 30 Aug. 2022, pp. 13–38, https://doi.org/10.1002/9781683673798.ch2.
10. "News: Overview: Diseases That Gene Editors Potentially Could Cure." *CRISPR Medicine*, crisprmedicinenews.com/news/overview-diseases-that-gene-editors-potentially-could-cure/. Accessed 12 Aug. 2025.
11. "Interview: Researchers Use CRISPR and Mini-Organs to Cure Cystic Fibrosis." *CRISPR Medicine*, crisprmedicinenews.com/news/researchers-use-crispr-and-mini-organs-to-cure-cystic-fibrosis/. Accessed 12 Aug. 2025.
12. "News: In Vivo Gene Editing of Lung Stem Cells Achieves Long-Term Correction for Cystic Fibrosis." *CRISPR Medicine*, crisprmedicinenews.com/news/in-vivo-gene-editing-of-lung-stem-cells-achieves-long-term-correction-for-cystic-fibrosis/. Accessed 12 Aug. 2025.

13. "News: An Innovative Approach to Treating Cystic Fibrosis Using Base Editors." *CRISPR Medicine*, crisprmedicinenews.com/news/an-innovative-approach-to-treating-cystic-fibrosis-using-base-editors/. Accessed 12 Aug. 2025.