CRISPR-Cas9 Technology in Germline Editing: A Scientific Evaluation

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AP Seminar

2025

On November 25, 2018, Jiankui He, an associate professor at the Southern University of Science and Technology, revealed the birth of two babies in China whose CCR5 genes had been edited using CRISPR technology to make them resistant to HIV (Zhou et al., 2020). His experiment sparked global outrage and raised ethical, medical, and legal questions regarding gene editing. CRISPR-Cas9, adapted for gene editing in 2012 by Jennifer Doudna and Emmanuelle Charpentier, transformed the gene editing field due to its precision, efficiency, and affordability (Welter, 2020). This technology allows scientists to modify DNA by adding, removing, or altering genetic sequences, presenting new opportunities to cure genetic disorders, prevent hereditary diseases, and enhance human health. (Zhang et al., 2023). However, its application in human embryos remains highly controversial, raising concerns about unintended edits and the possibility of "designer babies". While gene editing has already been used for both types of gene editing, is currently legal in the United States, germline editing is strictly prohibited because of its risks and lack of extensive research. As scientific breakthroughs continue to surpass current regulations, scientists and policymakers must clarify how CRISPR-Cas9 technology, if fully legalized, should be applied in the future so that clear policies can be established to ensure its safe and responsible use. In light of this complexity, the research question posed is: Should CRISPR technology be legalized for application on human embryos in the United States? CRISPR technology should be legalized for germline editing in the U.S., considering its strong potential to cure genetic diseases and consistent accuracy.

Potential of CRISPR

CRISPR technology has the potential to effectively combat genetic disorders and diseases. Yi-ran Zhang, Li-quan Zhou, and Tai-lang Yin, researchers affiliated with both the Institute of Reproductive Health at Huazhong University of Science and Technology and the Hubei Clinic Research Center at Wuhan University, found that CRISPR/Cas9 can be used to treat diseases such as amyotrophic lateral sclerosis (ALS), sickle cell disease (SCD), and brain tumors (Zhang et al., 2023). For instance, CRISPR can correct the gene mutation that causes misshapen red blood cells, thereby curing the possibility of sickle cell disease. These findings demonstrate the potential of CRISPR technology to be a powerful tool for treating genetic disorders and life-threatening diseases. By successfully targeting a wide range

of medical conditions, CRISPR demonstrates its versatility in what types of disorders it can treat, presenting the potential to prevent, cure, and even eradicate a plethora of genetic disorders that modern scientists are currently desperate to find solutions to. Similarly, Udani Gamage and other fellow researchers affiliated with the University of Colombo, a leading research university in Sri Lanka, concluded that using CRISPR technology is a cheaper, more effective, and less time-consuming method to cure β-thalassemia, a genetic blood disorder that reduces or stops the production of beta-globin, a protein needed for hemoglobin formation. (Gamage et al., 2023). Current treatments, such as lifelong blood transfusions or bone marrow transplants, are costly, time-consuming, and often inaccessible to many patients. However, by directly targeting and correcting the genetic mutation responsible for β-thalassemia, CRISPR can effectively address the disease at its root rather than temporarily managing its symptoms. Although the majority of current research primarily addresses somatic gene editing, which limits gene alterations to individuals, the progress already made by researchers and the newfound reconsideration of ethical guidelines show great potential for research to shift more into germline editing. Correspondingly, K. Vishnupriya, S.O. Ohm Prakash, and M. Kavitha, researchers affiliated with the School of Biosciences and Technology at Vellore Institute of Technology, established that CRISPR-Cas9 technology could potentially treat previously untreatable conditions such as prenatal, congenital, immunodeficiency, and genetic disorders, as well as certain cancers. (Vishnupriya et al., 2019). Traditional treatments for congenital and genetic disorders often focus on managing symptoms rather than correcting the underlying cause, leaving patients with lifelong medical challenges. However, by directly modifying defective genes at the embryonic or cellular level, CRISPR technology could prevent these conditions before they are expressed. Additionally, its application in treating cancer could lead to more targeted and effective treatments to reduce reliance on current invasive procedures like chemotherapy and radiation. Moreover, Khaled Rahman, PhD, a research scientist and software engineer at Meta, and M. Sohel Rahman, a professor at Bangladesh University of Engineering and Technology (BUET), have discovered that CRISPRpred, a system designed to predict the on-target activity of sgRNAs, has outperformed Azimuth, a competing tool developed by

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Microsoft, by 5% (Rahman & Rahman, 2017), which suggests significant progress already being made in the development of CRISPR technology. By continuing to improve predictive tools like CRISPRpred, researchers can increase the safety and efficiency of CRISPR-based therapies, which furthers its potential to treat genetic disorders with greater precision and reliability.

Accuracy and Risks

CRISPR technology has proven to have consistent accuracy with minimal risks, as seen in the latest research on genome editing. According to research led by Qi Zhou from the Reproductive Center of Wuhan University, which was published by Oxford University Press in 2020, CRISPR works by creating double-strand breaks in target DNA, which activate repair mechanisms such as non-homologous end joining (NHEJ) and homologous recombination (HR). In other words, CRISPR can disrupt, insert, and connect specific genes, which is fundamentally how this technology functions. (Zhou et al., 2020). By understanding how CRISPR technology works, scientists can develop ways to enhance its precision and reduce errors. For example, researchers can improve gRNA design, a synthetic RNA sequence used to direct the Cas9 protein to a specific DNA sequence, so that CRISPR only targets the intended genes to minimize unintended mutations. Furthermore, Ines Martin-Martin, alongside other researchers affiliated with the Laboratory of Malaria and Vector Research at the National Institutes of Health, illustrated how the Cas9 protein acts as an RNA-guided enzyme that accurately locates and cuts DNA by using a single guide RNA (sgRNA) to match the target sequence, creating a double-strand break (DSB) in the DNA. (Martin-Martin et al., 2018). This guide RNA ensures that the Cas9 protein cuts only at the intended location, reducing the risk of unwanted genetic changes. Also, by creating a precise double-strand break (DSB), scientists can more accurately edit genes, whether by removing faulty ones or inserting corrected versions. Conversely, further research conducted by Khaled and M. Sohel Rahman indicated that Cas9-based genome editing does have the possibility to cause off-target effects, leading to unintended genetic modifications in other areas of the genome. (Rahman & Rahman, 2017). This raises concerns about the safety and reliability of CRISPR for medical applications, especially in human embryo editing. Despite ongoing efforts to improve its accuracy by improving guide RNA design and developing more accurate prediction models like CRISPRpred, there is always going to be a possibility that CRISPR technology could make faulty edits. However, an article by researchers from the Institutes of Microbiology and Biotechnology of the University of Agriculture Faisalabad, published in the Journal of Biomedical Science, asserts that using a modified version of CRISPR could address the issue of off-target activity in cells by being more precise (Khan et al., 2018) As long as further research is conducted to refine CRISPR's accuracy, its potential for treating genetic disorders remains promising, making it a valuable tool for the future of medicine.

Conclusion

Overall, given its consistent accuracy and strong potential to treat genetic disorders, the controlled use of CRISPR for germline editing in the U.S. should be considered. The ability to fix mutations responsible for conditions like ALS, sickle cell disease, and other cognitive disorders demonstrates CRISPR's great medical potential, especially with current measures being taken to improve precision and reduce unintended effects. As the scientific community continues to develop CRISPR, policymakers and medical professionals must consider the implications of this technology to ensure its responsible implementation. The decisions made today will determine whether CRISPR remains a mere concept that creates societal fear and uncertainty or becomes a lifesaving tool to eradicate genetic diseases.

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