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VIEWPOINTS

Should CRISPR be used as a medical intervention tool for biological disorders?

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INTRODUCTION

When Chinese scientist He Jiankui was sentenced to three years in jail for using CRISPR-Cas9 to modify the HIV resistance of a pair of prenatal twin girls, he inadvertently reignited the controversy surrounding gene-editing technologies.[1] Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated protein 9 (Cas9) is a gene-editing tool that allows researchers to manipulate the body's natural repair system by splicing out targeted DNA strands and replacing them with new, customized strands. From medical application to biological manipulation, CRISPR's potential only increases as research develops. However, to date, clinical use of CRISPR-Cas9 is frowned upon internationally, and public opinion remains largely divided.[2] Many European nations agreed in the 1997 Oviedo Convention to completely prohibit clinical germline modifications, while the United States has implemented complicated legal processes that severely limit embryonic research.[2] Whether the usage of gene editing tools will be made accessible for the public once available is an ongoing international debate.

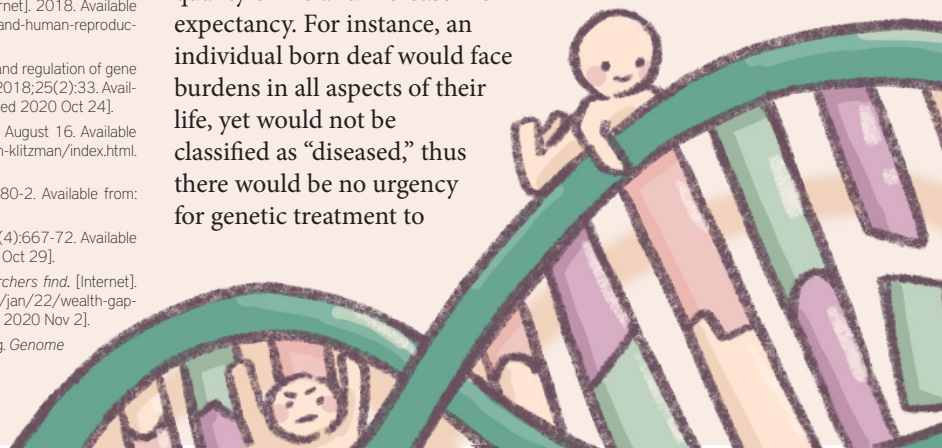
This Viewpoints piece will provide two perspectives on the consequences of public access to future clinical gene editing technologies such as CRISPR-Cas9.

IN FAVOUR OF PUBLIC ACCESS TO GENE EDITING TECHNOLOGIES

CRISPR-Cas9 carries the ability to eradicate life-threatening diseases on a genomic scale. Studies using CRISPR-Cas9 to knock out genes associated with schizophrenia have already clarified scientists' understanding of disease-relevant mutations, with further research aiming to completely eliminate certain disorders.[3] In fact, gene editing tools are currently undergoing trials for the treatment of non-lethal genetic diseases such as autism spectrum disorder.[3] The opposition may argue that while the natural process of evolution does not directly remove genetic disorders from the genome, there is no risk of adverse generational byproducts of genetic alterations —thus relying on risk-bearing artificial practices to achieve similar results is unnecessary.[4] However, though byproducts are a reasonable concern, this argument fails to acknowledge the more precise control that genome editing tools have compared to natural evolutionary changes. CRISPR-Cas9 could create a faster, more efficient method of eliminating genetic predisposition to specific diseases.

For example, the technology could act as a guaranteed method of assisted reproduction for couples who wish to protect their offspring from inherited genetic diseases. Scientists are currently researching practical applications of gene-editing tools on infertility cases as well.[5] Furthermore, CRISPR-Cas9 offers a reliable antiviral strategy for afflicted children suffering from fatal diseases. Historically, such technologies had been used to splice out certain genes and cure children of influenza, a disease with a previous 99% mortality rate for those under the age of five.[6] Overall, gene-editing technology offers protection and treatment for less fortunate individuals, providing a much-deserved chance to overcome such genomic factors outside of their control.

This gene-editing technology also has the potential to improve quality of life and increase life expectancy. For instance, an individual born deaf would face burdens in all aspects of their life, yet would not be classified as "diseased," thus there would be no urgency for genetic treatment to



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prevent death. Still, gene editing treatment for such a patient would be greatly desired by both the individual and their family. Given current successes in developing cures for deafness in murine models, tools such as CRISPR-Cas9 could potentially deactivate similar mutations in human cases as well, while improving societal health quality overall.[7] However, when diving into the field of psychology, one must question whether neurodevelopmental and psychological disorders, such as autism and anxiety, should be genetically altered to protect quality of life. Who is to say that myopia or hyperopia should not be eradicated as well? Currently, clinical practitioners are still in need of a statement concerning ethical boundaries, regulation, and treatment qualification.

While society will always fear uncertainty, by allowing public use, researchers believe that gene editing therapies will have the potential to help millions of people worldwide.[8] From disease elimination to quality of life enhancements, CRISPR-Cas9 offers much-needed improvements to public health and society as a whole.

AGAINST PUBLIC ACCESS TO GENE EDITING TECHNOLOGIES

Despite the benefits previously outlined, there are ethical and practical concerns associated with the public use of CRISPR-Cas9. One such concern involves the potential for CRISPR-Cas9 to become a tool which promotes eugenics, a theory of progressive genomic augmentation, as natural adaptations are already the "apotheosis of engineering excellence," states Dr. Lisa Feldman Barrett, Professor of Psychology at Northeastern University.[9] Many believe that the public use of gene editing would only cause ignorance of the regulatory limitations initially imposed on the practice, and this would lead the public down a slippery slope of gene manipulation.[10] Fear is enrooted in the belief that gene editing technologies will go beyond their initial goal of curing medical disorders, and rather transition into cosmetic, superficial, or dangerous methodologies. The normalization of "designer babies," embryos whose physical flaws are removed prenatally, is a major concern that could lead to social stigmas against non-CRISPR-Cas9 babies.[11]

A major hurdle in healthcare is the disparities in its access resulting from socioeconomic inequalities, whereby wealthier nations have greater access to higher-quality medications and treatments, including CRISPR-Cas9.[12] Although gene editing has enormous potential to become a preventative treatment which improves the health of society at large, it comes with a notable flaw. Being a new, expensive technology, CRISPR-Cas9 will likely only be available at highly specialized facilities at a price similar to modern gene-editing therapies, such as Novartis' $475,000 USD tisagenlecleucel treatment for leukemia.[13] One must take note of the the worst-case situation: those with greater financial resources will be able to upregulate certain genes and increase their overall health quality, inducing physiological benefits that are inaccessible to the majority of society. As the wealth gap grows over the years, a future of biological superiority awaits.[14] Former microbiologist, David King, is one of many that share this concern, with the belief that "once you start creating a society in which rich people's children get biological advantages [...] human equality goes out the window."[7]

Furthermore, some researchers express extensive concern about the generational consequences that may result from this technology. Dana Carroll, a researcher at the Department of Biochemistry at the University of Utah's School of Medicine, worries about the "intrinsic uncertainty about downstream effects" from CRISPR-Cas9.[15] Negative effects, such as unintentional increases in certain genetic diseases from unrelated genomic modification, could harm humanity's future generations.As future generations are not present for this decision, despite bearing the brunt of risk and reward, ethical concerns act as a major hurdle in the practical acceptance of gene-editing tools. Scientists and society cannot predict all of the future consequences of gene-editing and thus, the potential for error exists.[15]

As this innovative technology develops, further modifications may improve the effectiveness of gene editing. What remains in question are the limits, regulations, and ethical considerations that must be set in order to discern whether gene manipulation should be authorized for public use —a notion that many scientists argue is far too complicated to implement at the present time.[15] While CRISPR-Cas9 remains a groundbreaking discovery in healthcare and medicine, society must first address the ethical and practical implications it bears before taking any leaps in public accessibility.