OPINION PIECE

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A Bioethical Analysis of Gene Editing

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ABSTRACT

New developments in gene editing methods include the possibility to alter embryos for disease resistance. This could allow for increased immunity in the future, but at what cost? Gene editing may have unintended consequences. Some alterations may prevent the development of one disease but increase susceptibility to another. Other genes persist in populations for complex evolutionary reasons. Scientists must therefore consider the consequences and bioethics associated with these genetic changes. With examples such as the CCR5 coreceptor and major histocompatibility complex, it becomes clear that this type of genetic enhancement is immoral when evaluating it from biological, evolutionary, social, and economic perspectives. First, having the ability to select for certain desirable genes limits genetic diversity, which creates a barrier for evolution. Selecting for certain genes perpetuates the concept of *ideal genes* resembling dangerous eugenic ideologies. Should these procedures become more prevalent, the issue of accessibility arises. If these expensive procedures are only available to those who can afford them, the opportunity gap between the poor and the rich will widen. An investigation of case studies and ethical implications demonstrates that genomic editing is immoral and impermissible.

Keywords: Bioethics, gene editing, genomics, CCR5, MHC, evolution

In 2018, Chinese scientist He Jiankui shocked the world by stating that he had altered the genome of two embryos to confer resistance to the Human Immunodeficiency Virus (HIV).[1] This sparked debate in the scientific community and brought an ethical debate on the permissibility of gene editing to the forefront.[2] On one hand, alterations could provide immunity to genetic conditions. However, risks far outweigh potential benefits. The genome is complex, and protective alterations for one medical condition may pose a risk for another debilitating disorder. Additionally, many genes persist in the population for evolutionary purposes, and the removal of a malicious gene could have unintended consequences. For these reasons, attempts to edit human embryos are immoral.

One example of the ramifications of gene editing is He's embryonic alterations of the CCR5 coreceptor, which is a protein that allows HIV to enter human cells.[3] The literature shows that those who are homozygous for a 32 base pair deletion in the gene (CCR5-delta32) are resistant to HIV.[3] However, the homozygous mutation that confers HIV resistance increases susceptibility to flaviviruses like Zika and West Nile Virus.[4,5] Studies in mice without wild type CCR5 proved fatal upon infection with West Nile Virus.[6] Furthermore, in a meta-analysis of American cohorts, a higher number of patients with West Nile Virus are homozygous for CCR5-delta32 than those that possess the wild-type alleles.[7] Even more concerning, around 5% of West Nile patients had this homozygous genotype, which is higher than the 1% in a typical population.[6] While the promise of preventing HIV may seem tantalizing, scientists are exposing altered embryos to the possibility of developing other dangerous and potentially fatal diseases.

Many genes that seem detrimental in a population may be advantageous in other ways, which is why gene editing should be prohibited. The major histocompatibility complex (MHC) is a section of the genome that helps regulate the immune system, and human leukocyte antigen (HLA) genes in this area have many genetic variations.[8] This likely fosters pathogen resistance and makes the immune system adaptable. However, the MHC region also has genes that are linked to autoimmune conditions, cancers, and schizophrenia.[9] Since these detrimental genes are in close proximity to the HLA genes, they "hitchhike" with the beneficial HLA genes; they cannot be eliminated with-

out eliminating pathogen resistance.[9]

These examples demonstrate that gene editing should not be permitted . The genetic hitchhiking described above creates evolutionary trade-offs, as editing the genome could remove a detrimental gene at the expense of another. This also raises larger issues about which alterations should be pursued. This may reduce population diversity, which is a barrier to evolution. The effects of genetic selection may mimic populations affected by genetic drift, as certain traits may disappear with changes in the frequency of certain genes perceived as desirable or undesirable.[10] Although more desirable traits may seem to be genetically favourable, cases of genetic hitchhiking and the breaking news about He's experiment suggest the importance of these genetic tradeoffs. This artificial selection of traits may disrupt natural selective pressures. The decrease in genetic diversity may then make populations more susceptible to changes.[10,11] This evolutionary perspective is crucial in the ethical debate surrounding gene editing, and no physician should be given this power.

In addition to the complexities outlined, there are questions about what might happen when scientists cross the line between gene therapy for the treatment of genetic conditions and enhancement of already healthy genes. When scientists have the ability and access to technology that allows for gene editing, they are solely responsible for deciding what should be changed. From both a philosophical and an evolutionary perspective, this amount of power is dangerous. The issue of eugenics also arises within this debate. The power to alter certain genes perceived as undesirable, partnered with the goal of creating an *ideal population* takes this debate about ethics to a more dangerous level.[12] This concept of *ideal* is completely subjective and strongly fosters discrimination, which may impact specific disabled communities.[12]

Many healthcare systems worldwide operate on a basic needs system, which provides a standard level of healthcare for all members of society. The growing interest in gene editing may jeopardize equitable access. This genetic enhancement will likely be a luxury. Procedures of this nature may only be available to those who can afford it, and it is estimated that certain forms of gene therapy could cost as much as $1 Million USD.[13,14] Socio-economic class already determines who can get medical procedures in many places worldwide, and this may also apply to gene editing in the future.[13] This would further expand the opportunity gap between the rich and the poor, which is problematic.[13]

Any genomic modification has both biological ramifications and ethical considerations, and any theoretical benefits must be weighed against potential risks. Given these consequences, both for the embryo and in terms of greater societal implications, this type of genetic modification cannot be permitted.

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REFERENCES

(1) Cohen J, 2019. Did CRISPR help—or harm—the first-ever gene-edited babies? [Internet]. Science | AAAS. 2019 [cited 2020 Feb 8]. Available from: https://www.sciencemag.org/news/2019/08/did-crispr-help-or-harm-first-ever-gene-edited-babies

(2) Saey, T, 2018. Researcher defends creating CRISPR twins, fails to quell controversy [Internet]. Science News. 2018 [cited 2020 Feb 9]. Available from: https://www.sciencenews.org/article/researcher-defends-creating-crispr-babies-fails-quell-controversy

(3) Ni J, Wang D, Wang S. The CCR5-Delta32 Genetic Polymorphism and HIV-1 Infection Susceptibility: a Meta-analysis. Open Med (Wars). 2018 Oct 16;13:467–74. 4. Klein RS. A Moving Target: The Multiple Roles of CCR5 in Infectious Diseases. J Infect Dis. 2008 Jan 15;197(2):183–6.

(5) Flaviviridae | Viral Hemorrhagic Fevers (VHFs) | CDC [Internet]. 2019 [cited 2020 Feb 11]. Available from: https://www.cdc.gov/vhf/virus-families/flaviviridae.html

(6) Van Epps HL. CCR5 thwarts West Nile virus. J Exp Med. 2006 Jan 23;203(1):4.

(7) Lim JK, Louie CY, Glaser C, Jean C, Johnson B, Johnson H, et al. Genetic deficiency of chemokine receptor CCR5 is a strong risk factor for symptomatic West Nile virus infection: a meta-analysis of 4 cohorts in the US epidemic. J Infect Dis. 2008 Jan 15;197(2):262–5.

(8) Charles A Janeway J, Travers P, Walport M, Shlomchik MJ. The major histocompatibility complex and its functions. Immunobiology: The Immune System in Health and Disease 5th edition [Internet]. 2001 [cited 2020 Feb 12]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK27156/

(9) Lenz TL, Spirin V, Jordan DM, Sunyaev SR. Excess of Deleterious Mutations around HLA Genes Reveals Evolutionary Cost of Balancing Selection. Mol Biol Evol. 2016;33(10):2555–64.

(10) Lacy RC. Importance of Genetic Variation to the Viability of Mammalian Populations. Journal of Mammalogy [Internet]. 1997 May 21 [cited 2020 Feb 13]; 78 (2):320–35. Available from: https://academic.oup.com/jmammal/article/78/2/320/909513

(11) O'Brien SJ, Evermann JF. Interactive influence of infectious disease and genetic diversity in natural populations. ScienceDirect [Internet]. 1988 Oct [cited 2020 Feb 13]; 3(10):254–9. Available from: https://www.sciencedirect.com/science/article/abs/pii/0169534788900584

(12) Krishan K, Kanchan T, Singh B. Human Genome Editing and Ethical Considerations. Science and Engineering Ethics [Internet]. 2015 Aug [cited 2020 Feb 14]; 22 (2):597–9. Available from: https://link.springer.com/article/10.1007/s11948-015-9675-8

(13) High KA, Skinner MW. Cell Phones and Landlines: The Impact of Gene Therapy on the Cost and Availability of Treatment for Hemophilia. Cell [Internet]. 2011Oct1 [cited 2020Feb13];9(10):1749–50. Available from: https://www.cell.com/molecular-therapy-family/molecular-therapy/comments/S1525-0016(16)32762-9

(14) Morrison C. $1-million price tag set for Glybera gene therapy. Nature [Internet]. 2018Mar6 [cited 2020 Feb 14]; 33:217–8. Available from: https://www.nature.com/articles/nbt0315-217