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Does a Perfect World Need Perfect Genes?

In November of 2018, a Chinese scientist, He Jiankui, claimed that he had successfully modified human embryos using the CRISPR/Cas9 gene editing system to birth a pair of healthy twin girls. By editing a gene that is required for HIV enter to the cell, He claimed that the girls would be immune to HIV, especially significant as the father of the two girls was HIV positive. While his claims have not been published in a peer-reviewed journal nor verified by the scientific community, the attempt at such a major scientific endeavor garnered massive condemnation from the scientists and institutions around the world. Human embryos have been genetically altered using CRISPR before, however, all edited embryos were destroyed and never grown even remotely close enough to birth. The ethics of gene editing have been discussed before, but now the advent of editing the human genome appears to be within reach, necessitating a more in-depth and focused discussion into the ethical permissibility of such alterations.

The first and most obvious argument for editing the human genome is the elimination of genetic disorders and diseases. Studies have shown that, every year, around 6% of all children are born with a severe birth defect or disease[1]. These children with serious birth defects have a much higher infant mortality rate than children without birth defects. With gene editing, conditions such as cystic fibrosis, which affects 1 out of every 3000 infants born a year, and

[1] Christianson, A., C. P. Howson, and B. Modell. 2005. "March of Dimes: Global Report on Birth Defects, the Hidden Toll of Dying and Disabled Children." March of Dimes: Global Report on Birth Defects, the Hidden Toll of Dying and Disabled Children. https://www.cabdirect.org/cabdirect/abstract/20063029121.

hemophilia, which affects 1 in 4,500, could be completely eliminated[2,3]. This technology could prevent the hereditary transmission of these disorders, thus avoiding the need for treatment in generation after generation. Gene editing could also allow for the preservation of heterozygous advantageous to infant survival in specific populations. For example, sickle cell anemia is a hereditary blood disorder resulting from a mutated protein in the red blood cell that causes the structure of the cell to transform into a sickle shape, causing clotting, anemia, or death[4]. While the homozygous genotype for sickle cell can potentially be fatal, the heterozygous genotype has the benefit of providing protection against malaria in infants without producing harmful traits associated with sickle cell anemia. In West Africa, this heterozygous genotype is advantageous in reducing infant mortality from malaria[5]. With efficient genomic manipulation, the carrier genotype can be selected for in the West African region while eliminating the homozygous sickle cell phenotype, giving the most benefit to patients. In regions of the world where malaria is not endemic, the sickle cell allele could be eliminated entirely. The versatility that gene editing provides thus could ensure the most good could be achieved for each patient.

The ability to eliminate a disease directly follows the concept of beneficence, the principle binding healthcare professionals to provide the most good for the patient. If the medical community has the ability to eliminate harm to patients, not pursing this course of action would violate this key theory of medical ethics. This plays into another principle of medical ethics, the

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[2] Reference, Genetics Home. n.d. "Cystic Fibrosis." Genetics Home Reference. Accessed December 26, 2018. https://ghr.nlm.nih.gov/condition/cystic-fibrosis.

[3] Reference, Genetics Home. n.d. "Hemophilia." Genetics Home Reference. Accessed December 26, 2018. https://ghr.nlm.nih.gov/condition/hemophilia.

[4] "Sickle Cell Disease | National Heart, Lung, and Blood Institute (NHLBI)." n.d. Accessed December 27, 2018. https://www.nhlbi.nih.gov/health-topics/sickle-cell-disease.

[5] Aidoo, Michael, Dianne J Terlouw, Margarette S Kolczak, Peter D McElroy, Feiko O ter Kuile, Simon Kariuki, Bernard L Nahlen, Altaf A Lal, and Venkatachalam Udhayakumar. 2002. "Protective Effects of the Sickle Cell Gene against Malaria Morbidity and Mortality." The Lancet 359 (9314): 1311–12. https://doi.org/10.1016/S0140-6736(02)08273-9.

idea of nonmaleficence, which states that a healthcare provider must do no harm to a patient. If the physician knows the child will be born with a genetic disorder, it is conceivably their responsibility as a healthcare professional to prevent this harm if possible and gene editing gives the physician to fulfill this principle.

Some may argue that there are currently a variety of different methods for selecting against hereditary diseases. In vitro fertilization (IVF) is one common method used to assist in the conception of a child by harvesting mature eggs and fertilizing them with sperm in a lab. The embryo is then implanted in the mother's uterus. IVF is the most common form of assistive reproductive technology employed today. Preimplantation genetic diagnosis (PGD) is another technology often used in tandem with IVF. PGD analyzes the fertilized egg for and genetic disorders or defects. Abortion, or termination of the pregnancy, can also be used if a mutation arises or the fetus is developing improperly, thus preventing the birth of the child. These methods do provide a way to increase the chances of having a healthy child, but they cannot ensure it and in the case of IVF, the success rate of a live birth sits at 40%. IVF and PGD are often costly options, making it hard for multiple rounds of treatment[6]. The ethics of abortion are also questioned by some segments of society. Furthermore, PGD is only truly effective at detecting single gene disorders, such as Huntington's and cystic fibrosis[6]. Diseases that are caused by multiple mutations or multiple genes are much harder to detect and require hundreds of fertilized eggs[6]. PGD cannot detect or determine affecting risk factors in embryos for cancer, diabetes, heart disease, or other comparable ailments. PGD also is not able to differentiate between an unaffected fertilized egg and a carrier egg. This means that if the child ends up being a carrier for

[6] Savulescu, Julian, Jonathan Pugh, Thomas Douglas, and Christopher Gyngell. 2015. "The Moral Imperative to Continue Gene Editing Research on Human Embryos." Protein & Cell 6 (7): 476–79. https://doi.org/10.1007/s13238-015-0184-y.

the disease, the child and their mate will have to utilize the same assistive reproductive technology. On the other hand, with gene editing, the gene can be mutated to the most beneficial genotype, thus eliminating the possibility of passing on the carrier trait. Gene editing will provide the ability to eliminate hereditary diseases. It is the only technology that goes far enough to ensure a healthy offspring.

While the benefits of gene editing seem very clear cut, the drawbacks to this technology run much deeper. As a consequence of gene editing, discrimination will be a very big issue, both in short-term and long-term forms. Short-term discrimination will come from the eradication of certain disabled populations and the advent of Neo-Eugenics. While eliminating certain genetic disorders that provide no possible advantage to the human population such as cystic fibrosis and hemophilia, gene editing provides the ability to correct disorders such as dwarfism and deafness. These are two disabilities with quite long-life spans and large numbers of affected individuals. While they may not fit the definition of a "normal" human, many of these people take pride in their disability and do not see themselves as suffering from their respective disorder. This would reinforce the stereotype that living with a disability correlates with a lower quality of life[7]. Gene editing provides a way to prevent people to live with these disorders. This technology is marketed as a method for correcting mistakes in the human genome, classifying these large groups of people as errors to be corrected. This is would result in the eventual discrimination against these disabled groups through society looking askance at those who have not used gene editing to prevent these disabilities. Furthermore, a decrease in the number of disabled persons would have a negative affect on the amount of rights and resources attributed to these

individuals[7]. Directed embryo modification would see discrimination against disabled populations through the reduction in population sizes and resources.

Long-term discrimination can come from the creation of a super human class. The future of gene editing provides the possibility of increasing a person's intelligence, height, strength, and other such qualities. Altering these traits will allow for there to be quantifiable differences between unedited and edited humans. The edited human will be able to outperform regular humans in almost every task, taking high skill-level professions for themselves, and leaving low level jobs for unedited humans, a similar class hierarchy system similar to that seen in the 1997 film *Gattaca*. Furthermore, the discrimination could potentially be divided among socio-economic lines depending on the affordability of gene editing technology. If gene editing remains a premium technology, much like current assistive reproductive technology, then genes would be irregularly distributed through the population. The more desirable traits would become common among the upper class of society and the less desirable traits would be found more frequently in the lower classes of society[7]. This will only worsen current disparities between these groups, beating back the narrative that the solution to a variety of societal problems lies within gene editing.

One possible solution to this problem is to make gene editing affordable and available to everyone. Another solution is to restrict what traits and genes may be altered with gene editing. As noted above, certain diseases and ailments are easily classified, such as Huntington's and hemophilia, but many do not consider how certain disadvantages have affected other people. A man who stands 5'2" could argue that his short stature has affected his life through severe

[7] Zaret, Anna. n.d. "Editing Embryos: Considering Restrictions on Genetically Engineering Humans." HASTINGS LAW JOURNAL 67: 37.

bullying and psychological trauma in his youth. An obese woman might say that her genetic disposition towards heart disease and obesity affects her life by restricting her life span. The list of diseases and disorders that warrant gene editing will need to be compiled by a group of physicians, lawmakers, and sociologists to effectively evaluate how gene editing should be restricted. This, however, cannot guarantee that gene editing will exclusively be used for the restricted list of disorders. PGD began as a method for detecting diseases, but it has increasingly become a tool for sex selection and other cosmetic preferences of the parents[7]. Cosmetic medical procedures, such as liposuction, Botox, and rhinoplasty, are already quite popular in America, so it is reasonable to assume that while it may not be popular immediately, genetic augmentation will be used as a tool for cosmetic selection of children. Gene technology has been improperly used before, as in the case of gene therapy, which was originally developed to help children suffering from muscular dystrophy. Scientists are attempting to use gene therapy to strengthen the affected children's muscles, however, this same technology can be used by athletes to augment their strength[8]. The inability to ensure that this technology will be responsibly used presents another hurdle for the ethical permissibility of gene editing.

Gene editing and CRISPR is currently not safe for use in humans. While the discussions on its limitations and restrictions have begun now, there is a considerable amount of time before gene editing becomes a safe and commercial practice. Two of the most prestigious scientific journals, *Nature* and *Cell*, have released many different editorial columns calling for restraint or the all-out termination of such research, refusing to publish any papers. Many technologically advanced countries, including the U.K, EU, South Korea, and Australia have out right banned

[8] Frankel, Mark S. 2003. "Inheritable Genetic Modification and a Brave New World: Did Huxley Have It Wrong?" Hastings Center Report 33 (2): 31–36. https://doi.org/10.2307/3528152.

any form of gene manipulation in human embryos[9]. However, research still in continues like the U.S., China, and Russia, where gene editing is either permitted under harsh restrictions or proceeds under ambiguous guidelines[9]. The frequency of such research is very sparse and does not allow the embryo to develop. This rare research has shown though that consistent safe gene editing is very far off. In 2015, a group of Chinese scientists modified tripronuclear zygotes using CRISPR/Cas9 to correct a blood disorder in the embryo[10]. While the scientists were successful in correcting the gene, there were a significant number of unexpected mutations that resulted in the embryo obtaining multiple other blood disorders before being destroyed[10]. This experiment demonstrated that scientist currently have a very remedial understanding of how altering one gene affects other genes in the cell. The scientists used tripronuclear zygotes, which means that 2 sperm cells fertilized one egg, to try and avoid the ethical issues of a normal zygote because tripronuclear zygotes can never develop into a fetus. Nevertheless, This experiment was also highly criticized by the scientific community. The experiment concluded that the CRISPR/Cas9 system is far from being able to be used in a clinical setting, much less commercialized. This is why the birth of twin girls edited using CRISPR/Cas9 in November 2018 garnered massive condemnation. Performing such and experiment at this time in the development of the technology is dangerous and reckless. More research in gene editing is necessary, but it also must be conducted in the right setting and environment.

The research into gene editing needs to continue, but with the right rules and regulations under the supervision of the proper authority. The November 2018 experiment by He Jiankui

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[9] Insider, Skye Gould, Kevin Loria, Business. n.d. "This Map Shows Where Researchers Might Design the First Genetically Engineered Baby." Business Insider. Accessed December 28, 2018. https://www.businessinsider.com/what-countries-allow-researchers-to-edit-human-embryos-2015-10.

[10] Liang, Puping, Yanwen Xu, Xiya Zhang, Chenhui Ding, Rui Huang, Zhen Zhang, Jie Lv, et al. 2015. "CRISPR/Cas9-Mediated Gene Editing in Human Tripronuclear Zygotes." Protein & Cell 6 (5): 363–72. https://doi.org/10.1007/s13238-015-0153-5.

displayed how this research is currently occurring without the proper oversight. This has stirred fears of repeating the infamous Tuskegee experiment. In 1932, the Tuskegee institute began a study of examining the effects of untreated syphilis in African American men[11]. The researchers, however, did not obtain informed consent from the participants, nor did they notify the participants that they were receiving a placebo treatment[11]. The men were under the perception that they were receiving treatment for syphilis and even when penicillin was proven to be effective against syphilis, none of the participants were offered the treatment[11]. This is a prime example of researchers taking advantage of a disenfranchised population for benefit of medical research. For the ethical research of human gene editing, proper safeguards and regulations must be put in place to ensure the proper treatment of research subjects.

Editing the human genome will become a reality. There are many benefits to this technology that simply cannot be ignored. The principle of beneficence underscores the need for physicians to try to acquire the ability to erase hereditary diseases and prevent terminal illnesses in infants. Even beyond eliminating certain diseases such as Huntington's and Tay-Sachs, gene editing is able to provide certain populations with advantageous genotypes to increase infant survival rates, as with sickle cell. Current assisted reproductive technologies are costly and do not go far enough to ensure a healthy child. Furthermore, the embryo is limited by the genotypes of the parent and cannot change risk factors. Gene editing has the ability to greatly increase the chances of survival for a variety of different at-risk children across the world.

In conclusion, gene editing is a double-edged sword. It has the ability to bring a new level of care to patients all across the world. Hereditary diseases could no longer be an issue.

[11] "Tuskegee Study - Timeline - CDC - NCHHSTP." 2018. October 3, 2018. https://www.cdc.gov/tuskegee/timeline.htm.

However, there are a number of significant drawbacks to this technology, moreover, there are currently no restrictions on what genes and traits are not allowed to be edited. The elimination of certain diseases and disorders comes with the elimination of certain populations as well. Disabled populations will face harsh discrimination and as their populations continue to decrease in size, the amount of resources available to them will proportionally decrease. The potential for the creation of a super-human class further highlights the potential for mass discrimination. Socio-economic inequalities can also be worsened depending on the cost of gene editing, as a premium technology can cause a disproportionate distribution of genes among society. The technology behind gene editing is also far from perfect. Safety of the patient is a major concern. Many countries out right avoid any embryo manipulation and the countries that do participate, the number of researchers and grants attributed to this research is very low. Recent studies have shown that our current understanding of how genes affect the development of a fetus is very poor and even altering one gene can have unintended consequences, such as uncontrolled mutations. If this research continues, it needs to progress under the most ethical conditions possible. Such high-risk research often cannot find many willing volunteers, especially since so many factors are unknown.

The experiment conducted by He Jiankui in November 2018 was reckless and has the potential to set the entire field of gene editing back by decades if it fails. Gene editing is a necessary technology for the medical field and has the potential to be one of the most revolutionary medical techniques ever created. However, that is not to say there are not serious considerations that must be taken into account before this research progresses. Only through lengthy discussion and debate between scientists, lawmakers, philosophers, physicians, religious leaders, and other experts can gene editing be effectively implemented into society. While gene-

editing has the potential to advance human evolution to new heights, it also can worsen problems already present in our society.