

The Ethics of Gene Editing in Humans

Eric Hund

Sacred Heart University

The Ethics of Gene Editing in Humans

2

Eric Hund

Professor Little and Professor Stannard

Honors Capstone

12 March 2020

## The Ethics of Gene Editing

### **Introduction**

Since its discovery, gene editing has always been a controversial idea met with intense opposition. Gene editing is a type of genetic engineering where deoxyribonucleic acid (DNA) is inserted, modified, or deleted within an organism.<sup>1</sup> With the emergence of Clustered Regularly Interspaced Short Palindromic Repeats, more commonly known as CRISPR, these controversial ideas have become a reality. CRISPR is a somewhat new gene editing technology that allows scientists to edit the DNA of existing cells in a cheap and efficient way. One way this technology is being researched is in unborn embryos. Researchers can use CRISPR to edit the DNA when there is only one cell, and since this DNA will be the code for the rest of the cells in the body, the newly modified DNA will be present in every cell in the body. However, there are major ethical concerns with this type of gene editing. Some of these concerns are that the embryo cannot consent to any procedures done to it, the question of whether editing the human genome make us less human, and where the line should be drawn in regards to using gene editing. If ethical, this technology can aid in the prevention and elimination of genetic disease that are present from birth and also in the enhancement of humans. Many researchers also theorize alternate uses of gene editing techniques, in which the DNA of existing cells can be edited to fight off tumors.

While many believe that editing genes in humans is unethical and can lead to biological and ethical problems, this technology needs to be researched and must be used if it can prevent genetic disease without causing harm; this technology may also be helpful in guiding future human evolution once people are more familiar with the CRISPR technology.

### **History of DNA and Gene Editing**

Since the discovery of DNA in 1953 by Watson and Crick, genetics have been thoroughly studied. DNA is a self-replicating material that is present in all living organisms and it is the carrier of genetic information. Our current understanding of genetics is that specific base pairs, Adenine (A) and Thymine (T) pair together, while Guanine (G) and Cytosine (C) pair together. These pairs form the basis for DNA and any change in these base pairs results in a mutation. A sequence of these pairs code for specific genes determine, for example, hair color, eye color, or skin tone. CRISPR consists of two components- a cas9 protein and a guide RNA. The cas9 protein is used to cut the DNA so that the guide RNA recognizes the correct sequence of nucleic acids to be edited.<sup>2</sup> This works similar to the search and replace function in a word document. Just how the document searches for a sequence of letters and replaces it with a different sequence, the guide RNA searches for the defunct sequence, while the cas9 protein cuts open the DNA, or the document, so the RNA can lay down the correct base pair. For example, researchers know that Huntington's disease is caused by an increase of the number of 3 nucleic acids, C, A, and G. CRISPR could in theory locate this gene, cut open the DNA, and delete the incorrect sequences. Doing this would remove the gene that codes for Huntington's disease to be present in the person's phenotype, or physical characteristics.

### **Current Regulations and Studies**

At this current point in time, there are very few official regulations in regard to using CRISPR and other gene editing techniques. This is due to the fact that it can be hard to determine distinct lines and frameworks that encompass all current and future aspects of this new technology. Currently, experiments are not allowed to be done to human embryos due to the unknown risks that could occur. Most of the research is focused on somatic, or body cells of live animals such as mice. It is important to determine specific regulations on what type of research can be done, as there are questions about the long term risks of using germline editing. A group of Chinese researchers recently claimed to perform an experiment on a human zygote by using gene editing to develop resistance to HIV. While many experts question the authenticity of these claims, the consensus of the general public and scientific community was that this experiment should not have been performed.

### **Should We Edit Genes**

While it is clear that this technology has many potential benefits, it is necessary to look at the potential drawback and concerns, especially since this has never been possible in humans until recently. There are two main ethical questions that must be answered, the first is should we edit human genomes at all. The second is if it is decided that editing genes is ethical, how far should we go. One of the most common counterarguments for editing the genes of an embryo to eliminate genetic disease is that the embryo cannot consent to this treatment. While this is true, this is not a valid reason to not go through with the treatment. There are four main principles of ethics, and they are autonomy, beneficence, nonmaleficence and justice. The principle of beneficence states that there is a moral obligation to act for the benefit of others while balancing

the benefits with the potential risks or harms. It can be assumed that a person born with no genetic diseases due to this technology would be thankful that they do not have to suffer because of something they do not have control over. It is also necessary to look at how this would affect the human race as a whole. In this case, one could argue that the potential benefits of preventing a genetic disease for the rest of the human race, would far outweigh the consequence of the embryo not being able to consent to the medical treatment. If a specific disease was prevented in enough people over a long period of time, it can be assumed that this disease would disappear from the human race. While this may not follow the rules of natural selection that we are accustomed to, this technology has the potential to guide the future evolution of the human race. This principle can be seen in modern medicine when someone is unconscious, they cannot consent to any medical procedures that might be done to them. However, using the principle of beneficence, medical professionals would be obligated to treat that person.

While one could argue that autonomy, another ethical principle, does not support the previous claim that medical intervention should be given to those who cannot consent, that would not be true. Autonomy is defined as “a norm that obliges us to respect the decisions (self determination) of adults who have decision making capacity.”<sup>3</sup> In this case, the embryo does not have the means to make a decision, so the parents of the child should be allowed to decide as they have autonomy. It is logical to assume that most parents would choose to rid their unborn baby of the possibility of genetic disease before it is born, as long as the procedure does not have any high risks. In modern medicine, it is generally accepted that parents are the main decision maker of their children’s health until they are 18 years old. Since the parents would be able to decide medical treatment of the child after it is born, it should also be their responsibility when it

## The Ethics of Gene Editing in Humans

6

is still inside the mother's womb. Gene editing would be no different, if the parent determined that using this technology would be in their best interest, then it should be used.

Another common argument against editing genes involves the argument of human dignity. First, it is necessary to define human dignity. While a clear definition for human dignity does not exist, Immanuel Kant, an enlightenment philosopher defines dignity as the inherent worth of the human person, which grounds a duty to treat people not as mere means, but as ends in themselves.<sup>4</sup> In short, this means that dignity is something that all people have that makes them worthy of respect no matter. . Many authors believe that human dignity is strongly linked to the human genome, and that any modification to that genome makes the person less human.<sup>5</sup> While this may seem to make sense on the surface, this does not add up when looking at this issue from a philosophical and biological perspective. As long as the ethical principles of beneficence are being considered and every human being is given the same rights to this treatment, it should be ethical. Everyday, mutations occur when human cells divide. A mutation is defined as a permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people.<sup>6</sup> Mutations are what guided evolution by natural selection throughout history. Without these alterations in the genome humans never would have evolved to where they are today. Evolution by natural selection works over time because nature favors certain traits that are more likely to survive and reproduce than other traits. In turn, this causes these traits to become more frequent over time. Therefore, changes in the germline, directly or indirectly are necessary in order to advance the human species, or any species and have no impact on the dignity of the species.

One topic that must be discussed is the potential biological side effects of short term and long term use of gene editing techniques. At this time gene editing in embryos are only being done on mice, and not on humans. So far, there have not been any obvious concerns or side effects, but it is important to note that humans are much different from mice and some of these side effects may not be visible at first. One scientist, Jennifer Doudna discusses some possible negative side effects that are current being studied. One point of discussion is the possibility of the edited gene being chimeric.<sup>7</sup> Chimeric genes refer to a gene that is formed from the combination of two or more gene sequences. This type of mutation could have devastating effects on an unborn child. An example of a long term problem that could arise is the gene that is being edited could have been selected for by nature for an unknown reason, so the edited gene could be a negative adaptation. While it is important to note that neither of these side effects have been seen in any experiments done so far, these are the current concerns of scientists studying technology. If studies show that these effects are common with gene editing, it will be necessary to reevaluate the risks and benefits to using this technology in its current state.

Another consequence of gene editing that must be considered is how this will change our long-term evolution. While some would argue that evolution due to natural selection has slowed down for humans, that does not mean that we have to stop evolution due to unnatural selection. Human evolution is already at a strange point, due to the fact that we are no longer in the food chain for the most part. Because of this fact, human evolution has fundamentally changed to be more culturally based than biologically based. This is due to the fact that it is more beneficial in regard to fitness for humans to be more evolved socially and culturally, rather than physically. It can be argued that this is the way that evolution should naturally progress, but if we are able to

remove millions of people's suffering due to disease, we are obligated to do that. While some would argue that nature is better at evolution than we would be able to change unnaturally, this statement is not universally accepted. This is because the mutation for the correct gene would need to be randomly mutated and then be selected for through natural selection. If we sped up the process of creating these mutations, our unnatural selection would coexist with natural selection, so that nature would still be helping us evolve naturally.

### **Where Should We Draw the Line**

An interesting point of discussion is if gene editing is allowed, where should the ethical line be drawn. One interesting framework to look at this through is the enhancement versus prevention lens. While at first glance this may seem like a perfect and simple solution, it is much more complicated when you analyze the situation further. Currently, governments and research communities have agreed to focus all of their efforts on prevention of disease using this technology. It has been decided that at this time, this is the only ethical way to research and use this technology. In its current infantile stages, this is a good way to look at research of gene editing technology. The focus should be on preventing diseases in both embryos and somatic cells. However, this line quickly gets blurred when you take a closer look at the research. A recent study has reported successfully using gene editing technology to increase the production of Klotho protein human cells.<sup>8</sup> This is done by upregulating the gene that produces Klotho protein.<sup>9</sup> The goal of this research was to reduce the risk of age-related degenerative conditions such as Alzheimer's disease. This works by reversing the loss in neurological function in older adults. However, upregulation of this gene has been shown to have unintended side effect such as enhanced cognition and increased life span by up to 30%.<sup>9,10</sup> While some people would argue



that this falls outside the scope of ethical research due to the enhancement effects of the gene, it should be considered that all of these potential side effects are positive. If the cost of reducing the risk of these horrible genetic diseases is increased cognition and increased life span, it should certainly fall in the scope of acceptable research topics. One possible solution for this dilemma could be to only give this treatment to a small number of somatic body cells in adults who are starting to develop these conditions. It might have a smaller effect on these degenerative diseases, but it could also help to eliminate the ethical concerns of enhancement.

Another example of a potential grey area would be if there was a more efficient muscle building gene, would that fall under enhancement or prevention. At first, it may clearly seem like this is enhancement because it would be a cosmetic change and may enhance athletic ability. However, there are many conditions, especially in the elderly populations, that are linked to low muscle mass. Modern research has shown that variables such as gait speed, grip strength, and some components of muscular fitness are linked closely with mortality, morbidity, and quality of life.<sup>11,12,13</sup> Modern medicine is also not against doing surgeries for simple cosmetic enhancements. I am not suggesting that gene editing should be used simply for cosmetic enhancements, just that it should not be ruled out before considering the consequences. Because of this, it is necessary to use a different lens to look at when discussing what types of gene editing. At this current stage, it is necessary to look at each gene on a case by case basis through the lens of beneficence. If the benefits outweigh the potential risks, it should be researched thoroughly. Since gene editing is a fairly new concept, it is necessary for research and application to be monitored closely. Instead of trying to establish all-encompassing guidelines and regulations, the best way to do it would be to look at each case individually. There is no way

## The Ethics of Gene Editing in Humans

10

to know how this technology will evolve so trying to establish guidelines now will make it harder to have correct guidelines in the future. This is similar to Artificial Intelligence (AI) technology, as it is also a somewhat new field where the technology has rapidly increased. For example, many countries are focusing their efforts on researching AI, rather than trying to implement it as soon as possible.

While there are many ethical concerns regarding these topics, one of the more prevalent is who would be able to access to these preventions or enhancements. While CRISPR technology is much cheaper than any previous technology, it is obviously not affordable to everyone who may want to use. To combat this, the government and medical insurance companies should cover the more drastic genetic diseases even if they include enhancement side effects. Using the ethical principle of justice, which is defined as something that obliges us to equitably distribute benefits, risks, costs, and resources, all people should at the minimum have equal access to disease prevention techniques.<sup>3</sup> One counterargument to this could be that it is unrealistic to expect insurance companies or governments to cover these costs, however, it is important to note that \$236 billion was spent in the United States in 2013 just treating circulatory disorders.<sup>14</sup> While the initial cost of reducing genetic disease may be higher than treatment costs, it will quickly pay for itself in monetary value and societal value. It will be beneficial because people who are healthy are more valuable to an economy. Using the principle of beneficence, the government should have a moral obligation act in the benefit of others, and this includes keeping the general population as healthy as possible.

When some modern medical technologies were first being discovered they were considered unethical. For example, Human Growth Hormone (HGH) given to children who are

much shorter than the average for their age was originally seen as an enhancement procedure, but it becoming more accepted. Just like other cosmetic procedures, such as plastic surgery, that are becoming much more mainstream, they are generally becoming much more accepted by the general public and medical communities. Therefore, it is logical to assume that the better gene editing technology becomes and the more familiar society becomes with it, the more accepted it will become in general. Humans tend to be afraid of things they do not understand. The more benefits and positive side effects that are seen from gene editing technology, the more likely these ethical concerns will not matter as much to the general public. This fear relies mainly around the idea of customizing every aspect of a child, like creating a character in a video game. It is not logical to assume that gene editing technology will ever progress to this level, let alone in the near future. It is believed that most, if not all enhancement genes will have tradeoffs. For example if there was a gene that built muscle more efficiently, it would require more energy in the form of Calories. These tradeoffs will become more drastic the more enhanced the gene is.

Another ethical question revolves around the idea of diversity. Many people believe in a slippery slope that if we edit one gene, a slippery slope will emerge until we find the most efficient genome and everyone is the same. While this is a valid concern, it is a fallacy to believe that this is the direction gene editing will go. It is much more likely that a middle ground will emerge where certain, detrimental genes will be eliminated from the genome. While some would argue that eliminating any genes artificially would compromise our human dignity, human dignity is not linked directly with the human genome. The human genome is different in each person due to the mutations that occur throughout a person's life.

Equally important, is it necessary to consider the ethics of choice in this scenario. If there are people who are extremely averse to using gene editing technology due to their religion, personal morals, etc. would they be at a disadvantage in society? While they may be at a slight disadvantage due to the fact they could have a higher chance of contracting genetic diseases, they will still be able to function just as effectively as those people are able to function today. For example, while most of modern society feels like they need to use a smart phone to keep up, there are still people who are very successful while using a phone that does not connect to the internet or not using a cell phone at all. There really is not a choice that can be made, it is an illusion of choice. While this is a true argument, a better comparison would be to think about it in terms of vaccinations. Many vaccinations are required, but they are not required because of your personal health, but for the health of society. If everyone is vaccinated for a specific disease, then community immunity will be developed and the disease will be eradicated from society. This is a similar case for genetic disease and gene editing, in which gene editing will act as a vaccine on a larger scale and a biologic immunity will develop where the human genome is resistant to genetic disease.

### **Conclusion**

In conclusion, there are many different ethical and biological aspects to consider in regard to gene editing technology. CRISPR, the most well-known of these technologies, is advancing quickly and use in humans is becoming a reality. Furthermore, it is necessary that ethical guidelines be developed swiftly. While many people are afraid to use gene editing for many reasons, this is mainly due to fear of the unknown. As more research is conducted and available for the general public, the public opinion will shift into a more favorable one. Because

of these facts, it is necessary that scientific communities allow this research to continue in ethical ways. One of the most common arguments against using this technology to eliminate genetic diseases is that the embryo cannot consent to this treatment. However, the parents have autonomy over the child and can decide the appropriate medical treatment for the unborn child. Using the principle of beneficence, the benefits of potential risks of further research far outweigh the current ethical concerns. One framework that has been developed to discuss the ethics and morality of gene editing is the enhancement vs. prevention framework. While only allowing prevention of disease seems like a great solution, it will not hold up in the long-term studies where most genes have more than one effect. This technology has incredible potential to eliminate the suffering of millions of people around the world and must be researched more thoroughly and used in patients where the benefits outweigh the risks. The ability to control and enhance our own evolution is an incredible power that humans have never been able to do before, so we should be extremely cautious and consider the long term ethical and biological implications before doing anything, but the benefits far outweigh the potential risks at this point in time.

## References

1. Bailey, Stefanie R., and Marcela V. Maus. "Gene Editing for Immune Cell Therapies." *Nature Biotechnology* 37, no. 12 (December 2019): 1425–34.  
<https://doi.org/10.1038/s41587-019-0137-8>
2. King, N. M. P. (2019, June). HUMAN GENE-EDITING RESEARCH: IS THE FUTURE HERE YET? *North Carolina Law Review*, 97(5), 1051-. Gale Academic OneFile.
3. Jahn, W. T. (2011). The 4 basic ethical principles that apply to forensic activities are respect for autonomy, beneficence, nonmaleficence, and justice. *Journal of Chiropractic Medicine*, 10(3), 225–226. <https://doi.org/10.1016/j.jcm.2011.08.004>
4. Bayefsky, R. (2013). Dignity, Honour, and Human Rights: Kant's Perspective. *Political Theory*. <https://doi.org/10.1177/0090591713499762>
5. de Miguel Beriain, I. (2018). Human dignity and gene editing: Using human dignity as an argument against modifying the human genome and germline is a logical fallacy. *EMBO Reports*, 19(10). <https://doi.org/10.15252/embr.201846789>
6. Reference, G. H. (n.d.). *What is a gene mutation and how do mutations occur?* Genetics Home Reference. Retrieved March 11, 2020, from <https://ghr.nlm.nih.gov/primer/mutationsanddisorders/genemutation>
7. Bosley, K. S., Botchan, M., Bredenoord, A. L., Carroll, D., Charo, R. A., Charpentier, E., Cohen, R., Corn, J., Doudna, J., Feng, G., Greely, H. T., Isasi, R., Ji, W., Kim, J.-S., Knoppers, B., Lanphier, E., Li, J., Lovell-Badge, R., Martin, G. S., ... Zhou, Q. (2015).

- CRISPR germline engineering—The community speaks. *Nature Biotechnology*, 33(5), 478–486. <https://doi.org/10.1038/nbt.3227>
8. Chen, C.-D., Zeldich, E., Li, Y., Yuste, A., & Abraham, C. R. (2018). Activation of the Anti-Aging and Cognition-Enhancing Gene *Klotho* by CRISPR-dCas9 Transcriptional Effector Complex. *Journal of Molecular Neuroscience: MN*, 64(2), 175–184. <https://doi.org/10.1007/s12031-017-1011-0>
  9. *Suppression of Aging in Mice by the Hormone Klotho*. (n.d.). Retrieved March 11, 2020, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2536606/>
  10. *Life extension factor klotho enhances cognition*. - PubMed—NCBI. (n.d.). Retrieved March 11, 2020, from <https://www.ncbi.nlm.nih.gov/pubmed/24813892>
  11. Afilalo, J., Eisenberg, M. J., Morin, J.-F., Bergman, H., Monette, J., Noiseux, N., Perrault, L. P., Alexander, K. P., Langlois, Y., Dendukuri, N., Chamoun, P., Kasparian, G., Robichaud, S., Gharacholou, S. M., & Boivin, J.-F. (2010). Gait speed as an incremental predictor of mortality and major morbidity in elderly patients undergoing cardiac surgery. *Journal of the American College of Cardiology*, 56(20), 1668–1676. <https://doi.org/10.1016/j.jacc.2010.06.039>
  12. *Grip strength and mortality: A biomarker of ageing?* - PubMed—NCBI. (n.d.). Retrieved March 11, 2020, from <https://www.ncbi.nlm.nih.gov/pubmed/25982159>
  13. Katzmarzyk, P. T., & Craig, C. L. (2002). Musculoskeletal fitness and risk of mortality. *Medicine and Science in Sports and Exercise*, 34(5), 740–744. <https://doi.org/10.1097/00005768-200205000-00002>

14. *How much does the U.S. spend to treat different diseases? - Peterson-Kaiser Health*

*System Tracker*. (n.d.). Retrieved March 11, 2020, from

<https://www.healthsystemtracker.org/chart-collection/much-u-s-spend-treat-different-diseases/#item-start>