THE SOCIETAL IMPLICATIONS OF ADOPTING CRISPR TECHNOLOGY

A Research Paper submitted to the Department of Engineering and Society

In Partial Fulfillment of the Requirements for the Degree

Bachelor of Science in Biomedical Engineering

By

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March 25, 2021

On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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INTRODUCTION

With nearly a quarter of deaths in the United States related to cardiovascular disease and over 26 million adults suffering from type II diabetes, researchers are encouraged to study the complex mechanisms involved in such illness to develop efficient therapies. Understanding the endocrine signaling pathways, and the downstream effects of gene expressions can be a powerful tool in the fight against prominent diseases. My technical research project will seek to improve the efficiency of gene expression analysis using bioinformatics, in an effort to provide researchers with more tools to comprehend the human genome. This project may be of use to those within a lab setting but, there is room for this kind of research to produce results that the general population may benefit from. The knowledge of human gene expressions can be translated into human genome editing with the use of CRISPR/Cas9 technology. Human gene editing has the potential to mitigate, and in some cases remove, the presence of certain diseases and disorders. Though CRISPR has made reasonable progress in labs, significant safety and efficacy trials are needed before the new technology is released for clinical use. It is my belief that gene editing technology will succeed in these trials eventually, however the societal implications of this therapy remain to be discussed before the general public chooses to utilize it. Using the Social Construction of Technology(SCOT) framework, my STS paper seeks to discuss the societal factors involved in the adoption of human genome editing into the clinical space and advocate for its adoption.

THE MEDICAL BENEFITS OF GENE EDITING

Though the U.S has made many medical strides, there are still a considerable amount of diseases and disorders that millions suffer and even die from like diabetes, HIV/AIDS, sickle cell

disease, and congenital heart disease. According to the CDC, there are approximately 100,000 people in the U.S. with sickle cell disease (SCD) (CDC, 2020). Though the percentage of sickle-cell related child mortality has decreased significantly since 1986, 1.5 per 100 African American children with SCD die from the disease. Another debilitating treatable disease afflicting thousands of Americans is HIV/AIDS. Currently there are approximately 1.2 million Americans with the disease. Fortunately, the severity of the disease is subsiding with only 11,300 total HIV/AID related deaths in 2007 ("HIV.org"). This does not remove from the fact that thousands of people continue to live with the debilitating disease and have the potential to spread it despite modern treatment. Some of these ailments are treatable but not necessarily curable, meaning symptoms may persist but only to a lesser degree. Health complications on this level may benefit from alternative new therapies such as the slowly emerging human genome editing technology. CRISPR which stands for 'Clustered Regularly Interspaced Short Palindromic Repeats', is a relatively new genetic engineering technology that allows one to insert or disable certain genes within an organism's DNA. CRISPR creators, Dr. Jennifer Doudna and Emmanuelle Charpentier helped advance the technology from being an immune mechanism in bacteria to a technique that could enhance the precision of human gene editing for the betterment of humankind (Cohen, 2017). Figure 1 below further depicts the basic mechanisms of CRISPR technology on DNA. Gene editing technology of this caliber has the potential to mitigate the emergence of difficult to treat diseases and may very well be a cure to some troublesome conditions.

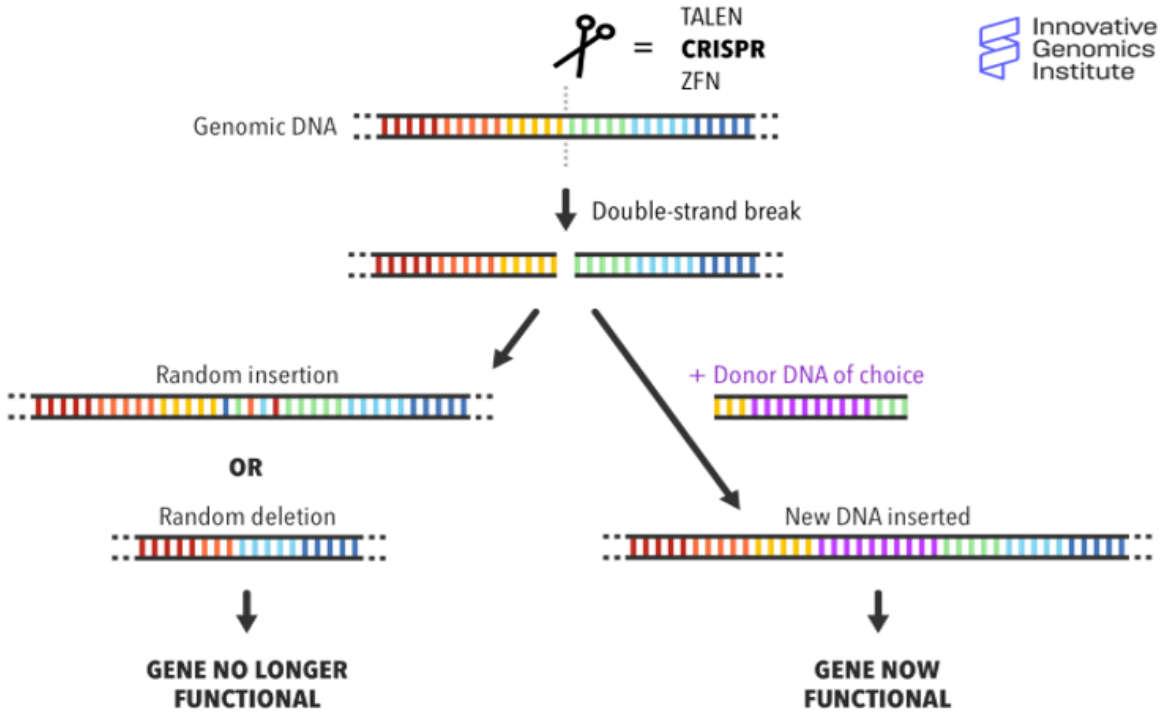

Figure 1: Basic Mechanics of CRISPR: Depicts the two main functions of CRISPR technology on DNA. On the left, random deletion and insertion is used to inhibit gene expressions. On the right, a selected DNA strand is inserted into the original DNA sequence which leads to new functional gene expression (Innovative Genomics Institute)

To further understand its potential, researchers at several universities have already incorporated this technique into practice. One research group sought to incorporate the technology to combat HIV. University of California researcher, Yuet Kan, spearheaded a research study in 2014 which sought to use CRISPR technology to insert HIV-resistant genes within white blood cells. They found that the edited white blood cells were resistant to the virus, but further trials would have to be conducted for efficacy in an *in vivo* study (Aldhous, 2014). There have also been applications in cancer research. Oncologists at the Barts Cancer Institute published a review article detailing the use of CRISPR-Cas9 to expedite the development of oncolytic viruses, which are viruses that target cancer cells, and to evaluate its application in viral biology

research (Yuan et al., 2016). Another research group at MIT used CRISPR technology to cure mice suffering from a liver disorder by correcting the mutated gene (Yin et al 2014). At the time this was one of the first research documents that proved the effectiveness of CRISPR-Cas9 to successfully cure an organism of disease.

THE INVASIVE NATURE OF HUMAN GENOME EDITING

Human genome editing needs to undergo clinical trials and meet certain governmental regulations before it is considered to be commercially available. Currently, the FDA has a 'Guidance Draft for Industry' which details the suggested regulations and non-binding recommendations for intentionally genetically altered animals (FDA 2017). This document is an updated draft version of the official FDA 'Guidance For Industry' regulation on genetically modified animals. What this draft suggests is that the FDA acknowledges the advancement of genetic engineering techniques, and is preparing legislation and regulation for its arrival (FDA 2017).

Besides government approval, human genome editing may face other subtle obstacles in the form of public perception. As previously mentioned, research labs have conducted studies that confirm the benefits of CRISPR technology through disease mitigation and disease removal (Aldhous 2014) (Yin et al, 2014 pp.551-553). These results and others of the like, give credibility and raise confidence of the therapy's future success. Though researchers trust the technology, human genome editing techniques don't really benefit the general public unless they trust in the therapy as well. With any new technology there will always be doubters, skeptics, and conservatives but this is a completely different avenue of scientific innovation. The altering of

human DNA that can then be passed onto future generations has a level of invasiveness and human augmentation that we haven't seen before.

Science author and journalist, Walter Issacson writes about the nuances concerning human genome editing in his Wall Street Journal article, 'What Gene Editing Can Do for Humankind'. Issacson understands the immense benefits CRISPR can provide for humankind but also acknowledges the risks that may arise if genetic modification morphs from a health treatment for many, to genetic enhancements for the wealthy in the form of 'designer babies'. The idea of genetic enhancements to make offspring stronger, taller, or more intelligent complicates the public perception of CRISPR because these genetic augmentations have the potential to perpetuate inequality, especially if they're more accessible to the wealthy.

THE SOCIETAL IMPLICATION OF GENE EDITING THERAPY

Though human genome editing has a long way before commercial clinical use and full government approval, the immense benefit this therapy has the potential to provide may be undermined or dismissed by the public. Ever since the emergence of CRISPR/Cas9 technology became public knowledge, journalists, scientists, and ethicists have documented their impressions on the subject. Their opinions have the potential to seep into public discourse and effect the way people perceive the therapy. In 2018, Pew Research Study conducted a series of public surveys to gauge perception of human genome editing technology. Of those surveyed, 72% of U.S adults agree that genetic alterations to babies are permissible as long as it is strictly for medical purposes (Funk & Hefferon 2018 p. 1). However, the other surveys in the document suggest that there is a more cautious perception of the CRISPR. For example, highly religious Americans are more reluctant of gene editing if it involves embryonic testing or if it leads to

genetic enhancements. These statistics could be attributed to a variety of reasons that are not necessarily founded in religion, though it does appear that religious individuals are more likely to be wary of certain scientific advancements.

Genetic Determinism and Religious Thought on Gene Editing

One theologian who is against the use of human gene editing, is Ted Peters author of 'Playing God*?:* Genetic Determinism and Human Freedom'. Peters comes across as cautious and wary towards human gene editing technology, but instead of building upon archaic arguments like 'science is evil' and 'gene editing is blasphemous', Peters chooses to acknowledge the fact that genes are not entirely deterministic of an individuals' future. To highlight some of the talking points of theologians had toward CRISPR like science, Peters references Pope John Paul II claiming,

> The problem with genetic engineering and other reproductive technologies is that they place our destiny in our own hands and lead to the temptation to go beyond the limits of a reasonable dominion nature. (Peters, 2003 p. 12)

The use of language like 'destiny', 'temptation', and 'reasonable dominion' all have some semblance to religious terminology surrounding 'sin' and subservience to a higher power. Statements like these also exude an aura of genetic determinism, which essentially boils down to the idea that 'we are our genetic makeup', therefore tampering with our genes is the equivalent of changing our human essence. Refuting genetic determinism is not a difficult task. The assumption that genes are the 'end all be all' of every individuals' life journey is an egregious statement. For example, take a man who is genetically blessed to be over 6'4''. A genetic determinist might say that this person is predestined to join professional sports, while a non-determinist would simply acknowledge the person's height as just another characteristic. Yes, it

is true that genes can and do play a role in defining people's strengths and weaknesses, but that does not necessarily determine their path in life nor does it remove an individual's autonomy. Though religious Americans are likely to be wary of the technology due to the implication of humans 'playing God', others may be trepidatious because of ignorance or an acknowledgement of the potential socio-economic disparities that may exacerbate during the therapy's lifetime.

Socio-economic and socio-political pitfalls

Even if CRISPR technology garners governmental and societal approval, we also need to consider the socio-economic consequences that may arise. The emergence of new medical practices commonly have limited availability and a hefty price tag. There could be concerns that those who are able to afford this therapy may be in a persistent 'high-priority' pool when providing medical care (Funk & Hefferon 2018 p. 1). As mentioned before, the ability of the wealthy to genetically modify their offspring and pass on those genes to the following generation is a concerning thought. Those who are financially prosperous will have more opportunities to deprive those who are not in other areas of life, namely sports and education. Genetic enhancements may lead to wider disparity, but there is the argument that the wealth gap may persist and increase independently of genetic modifications. This is not to claim that genetic enhancements are not a concern. It is a potential consequence that should not deter the public from accepting CRISPR technology as a medical marvel. To comment on the potential drawbacks of gene editing, bioethicist Francoise Baylis wrote a book addressing the capabilities and implications of CRISPR technology (Baylis 2019). One worry she has about genetic modification is that it will reach a degree where those who are not genetically enhanced will undergo some level of scrutiny. She writes, "A specific worry is that 'difference' will be seen as 'disability', and as something to be eliminated, not accommodated" (Baylis, 2019, pp.6-7). This

is a point that, if substantiated, would be a major socio-political detriment as discrimination would rise and less people will be given opportunities to rise socio-econommically.

ACCEPTING CRISPR WITH STRINGENT REGULATION

CRISPR technology continues to prove its worth through animal lab trials. If this technique develops to be safe for humans, then we can expect to receive a myriad of benefits from this therapy in the future. The adoption of human genome editing requires cooperation from several entities: labs, hospitals/clinics, government agencies, and the public. Safety and efficacy can be accounted for through regulation, however the ethical and societal implications ought to be considered when making the shift towards commercial access. It may be found that a considerable amount of people are not ready for this kind of scientific advancement but that should not halt the process of approval. Rather the hesitation of the public should be used as a sign to evaluate the permissions and capabilities of CRISPR technology.

To visualize the relationship between the many entities involved with adopting CRISPR technology, a simple SCOT model will be used. Figure 2 below shows how labs, hospitals, government agencies, and the public are intertwined with the clinical reception and use of human genome editing. To start, government regulators are heavily considered in the inclusion of CRISPR because they serve as the gatekeepers for the incorporation of technology into the general public. An example of a national regulator would be the U.S. department of Health & Human Services (HHS), which presides over the Food and Drug Administration (FDA), an institution that is responsible for regulating the majority of medical devices and products. Without national and state approval genetic modification technology will never be clinically accessible. Though regulators set the rules, they also benefit from genetic engineering techniques

because their constituents will have access to more therapeutic options for certain incurable diseases. With the rules established, it is up to the manufacturers to meet these standards for safe use. The manufacturers, or labs in this sense, are the most vital element because there is little room for error when it comes to genetic modification of human life. The 'quality' of the product must be infallible and meet all the requirements established by the regulators. Once the product is declared safe and effective the gene editing therapy is ready for distribution to the public. Hospitals and clinics that would offer genetic modification services serve as the distributors.

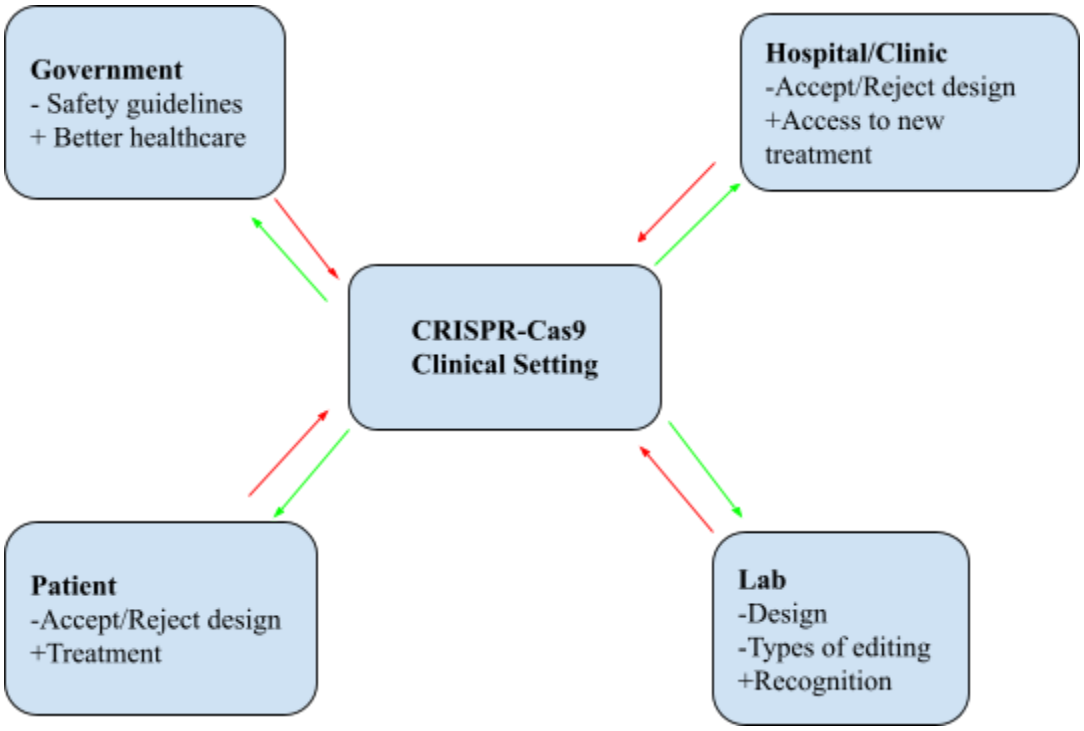

Figure 2: Social Construction of Genetic Engineering. Acknowledges the regulators, consumers, gene labs and clinics that all have stake in the incorporation of human genome editing technology (Edu Jr., 2020).

Without the acceptance of these entities there will be little contact between the manufacturers and the consumer. Physicians in clinics and hospitals must be confident in the

gene editing techniques before offering it to their patients. Most importantly, the consumer is responsible for the development of clinically available genetic modifications because the technology does not become adopted without their trust.

THE FUTURE FOR CRISPR

Even though public perception and trust is necessary for human gene editing to be an effective treatment, the government is the entity that is most responsible if major issues emerge after approval. Legislation is the only real factor that can keep human gene editing practices in check. The general public lacks the knowledge to fully understand the mechanisms of CRISPR and other alternative human gene editing technologies. Therefore the burden of responsibility falls to the entity that protects them. It is understood that there are potential socio-economic and socio-political pitfalls that come from the commercial release of CRISPR, like the wealthy having early access and passing on their selected genes, as well as the potential for those who are not gene enhanced to be viewed as second class. Problems like this should be taken seriously by all entities involved with CRISPR technology: government, gene labs, hospitals, and the public. Allowing social tensions to rise actively harms the adoption of CRISPR and has the potential to deter others from utilizing it. Refusal to accept a powerful, life-changing therapy like CRISPR could perpetuate the suffering of thousands of people with currently incurable hereditary diseases. That is why, despite the potential risk, we must seek to adopt human gene editing technology in the clinical setting. There is no doubt that issues may arise with the accessibility of this technology but it is our societal responsibility to be cognizant of them and propose solutions that are ethical and beneficial to all.

WORKS CITED

Aldhous, Peter. (2014, June). Gene editing tool can write HIV out of the picture. *New Scientist*.https://www.newscientist.com/article/dn25698-gene-editing-tool-can-write-hiv-out-of-the-picture/.

Center for Disease Control and Prevention.(n.d.). *Sickle Cell Disease.* https://www.cdc.gov/ncbddd/sicklecell/data.html

Cohen J. (2017, February 15). *How the battle lines over CRISPR were drawn*. Science. https://www.sciencemag.org/news/2017/02/how-battle-lines-over-crispr-were-drawn

Edu, Jr. E: *Social Construction of Genetic Engineering*. [Figure 2] *Prospectus* (Unpublished undergraduate thesis). School of Engineering and Applied Science, University of Virginia. Charlottesville, VA.

Food and Drug Administration. (2017, January). *Guidance for industry regulation of intentionally altered genomic DNA in animals draft guidance*. U.S Food and Drug Administration p. 2-3 https://www.fda.gov/media/135115/download

Francoise Baylis. (2019). *Altered inheritance: CRISPR and the ethics of human genome editing*. (pp. 1-8). Cambridge, MA: Harvard University Press.

Funk, C. & Hefferon, M. (2018, July). Public views of gene editing for babies depend on how it would be used." *Pew Research Center* https://www.pewresearch.org/science/2018/07/26/public-views-of-gene-editing-for-babies-depend-on-how-it-would-be-used/

Issacson, W. (2021, February 19). What human gene editing can do for humankind. *Wall Street Journal,* **https://www.wsj.com/articles/what-gene-editing-can-do-for-humankind-11613750317**

Peters, T. (2003). *Playing god?: Genetic determinism and human freedom.* Routledge

U.S. Statistics.(n.d.). HIV.org. Retrieved March 23, 2020, from https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics

Yin, Hao, Wen Xue, Sidi Chen, Roman L. Bogorad, Eric Benedetti, Markus Grompe, Victor Koteliansky, Phillip A. Sharp, Tyler Jacks, and Daniel G. Anderson. (2014, June) Genome Editing with Cas9 in Adult Mice Corrects a Disease Mutation and Phenotype. *Nature Biotechnology* 32, no. 6 : 551–53. https://doi.org/10.1038/nbt.2884.

Yuan, Ming, Eika Webb, Nicholas Robert Lemoine, and Yaohe Wang. (2016 March). CRISPR-Cas9 as a Powerful Tool for Efficient Creation of Oncolytic Viruses. *Viruses, 8*(3), 72. https://doi.org/10.3390/v8030072.