CRISPR-CAS9 and Gene Editing: An Ethical Consideration

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The CRISPR-Cas9 system and other gene editing technologies have been a revolutionary breakthrough in bioengineering that enables forms of personalized treatments never dreamed of. However, due to the permanent and heritable changes that germline gene editing can create, CRIPSR technologies have also sparked numerous debates and discussions about the ethics of utilizing these technologies. This paper goes in-depth with different ethical perspectives and considerations of CRISPR and similar technologies.

Keywords: *ethics, CRISPR-CAS9, gene editing, gene therapy*

Introduction

The clustered, regularly interspaced, short palindromic repeats (CRISPR) along with the CRISPR-associated protein 9 (Cas9) system has been a revolutionary bioengineering technology opening up new horizons for personalized treatments. Originating as a "bacterial defense mechanism against phage infection and plasmid transfer in nature" (Jiang and Doudna, 2017), it has been given a new purpose: an RNA-guided methodology to "precisely manipulate virtually any genomic sequence," (Jiang and Doudna, 2017). Its applications are endless, ranging from correcting disease-causing mutations to inactivating specific genes for increased yields in crops to the "elucidation of gene function involved in disease development and progressions," (Jiang and Doudna, 2017). Since these technologies allow researchers and scientists to explore and edit numerous genes at once, they are able to treat and cure genetic disorders (as well as forms of cancer and other diseases) such as cystic fibrosis, Duchenne muscular dystrophy, and sickle cell anemia. Although the technology itself proves to have great promise, it has not achieved its fullest potential due to the possibilities of "unwanted off-target mutations" (Jiang and Doudna, 2017). Future developments in this field will be able to reduce and avoid these mutations to strengthen the usages of CRISPR-Cas9 technologies.

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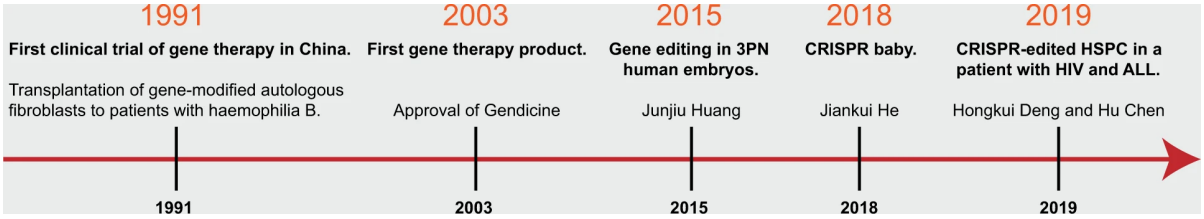

Figure 1. A timeline of gene therapy milestones in China (Wang et al., 2020)

The Problem

The problem is not the technology itself but the ethical perspectives of its use. There are numerous areas where CRISPR can be utilized. These areas have been split into three main categories for easier classification. The first category is to use CRISPR as a method to understand the development of human cells and embryos as well as create treatments to different human diseases. The second category is defined for "gene editing in somatic cells, either *ex vivo* or *in vivo*, to treat or prevent disease," (Rossant, 2018). The third and last category is for germline gene editing, which is defined as "gene editing in gametes or embryos with the aim of correcting disease-causing mutations in the next generation," (Rossant, 2018). Table 1 provides a comparison between somatic modifications and germline modifications. Table 2 summarizes the recommendations of the National Academy of Sciences on human genome editing. It's important to note that the general stance taken here is that germline gene editing should be a "worst-case" scenario and should not be utilized unless all other alternatives have been exhausted.

Somatic Modifications	**Germline Modifications**
Somatic therapies target genes in specific types of cells in an individual: lung cells, skin cells, blood cells, retina etc.	Germline modification is applied to embryos, sperm, or eggs, and alters the genes in all the resultant person's cells
Non-inheritable and only affects the treated individual	Passed onto future generations
First somatic trials occurred approximately two and a half decades ago	Human germline editing of early embryos for research purposes began in 2015
These mutations only show their effects in the cells where they occur.	In most cases, germline mutations are 'silent' in the parent organism in which they originally occurred, except in cases when they affect the gamete production.

Table 1: Somatic vs Germline modifications (NYU, 2020)

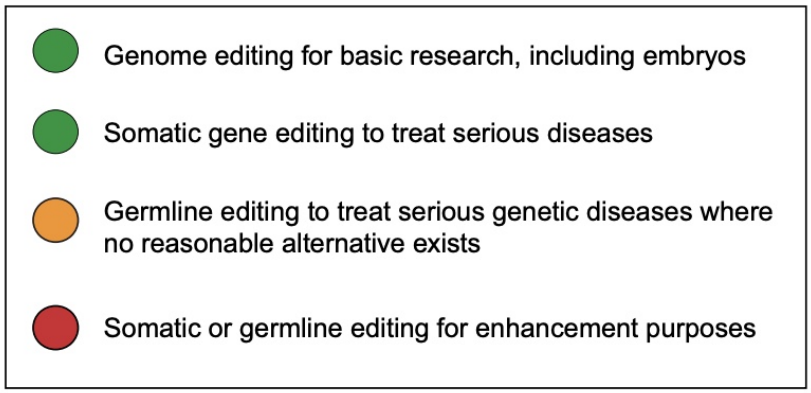

Table 2: Recommendations by the National Academy of Sciences on Human Genome Editing (Rossant, 2018)

Germline gene editing is permanent and a heavily debated topic among development biologists and researchers. Its usage alters an individual's basic instruction manual for their bodies, and as such, can be a problem if used in the "wrong" ways. Many questions persist: 1] What is the line between "right" and "wrong" forms of germline gene editing? 2] Who is able to dictate what traits are normal and which ones constitute a disorder? 3] Who will have access to these forms of gene therapy?(will it be exclusive to the wealthy?), 4] Should germline gene editing be encouraged for the general public?, 5] What researchers/scientists/doctors have access to this technology? (will there be a certification required to deploy these technologies?), 6] Should changing basic features of the body (brain size, height, athletic capabilities, etc) be altered? These are just a few of the questions that have been explored in the past, but there are infinite scenarios that may be even more difficult to answer.

The discussion on germline modification is by no means a new discussion. Since the creation of transgenic mice through the injection of exogenous DNA into mouse zygotes in 1981 (Silver, 2008), there have been theoretical and philosophical discussions about the ethics of germline modification. However, at that point in time, theory and philosophy was all that the discussions were. Technology had not reached the point where creating targeted modification of genomes was very accurate; it was in its early stages of developing as a technology. The bioengineering breakthrough of CRISPR-Cas9 has revolutionized these discussions since they are no longer just theoretical and philosophical, but practical as well. "Direct injection of the Cas9 components into mouse zygotes can produce mutations by non-homologous end-joining at close to 100% efficiency, and more precise alterations, such as point mutations and insertions, can be produced at increasingly higher rates, with various new tricks" (Rossant, 2018). Most recently, there was the scandal that involved the birth of twins through CRISPR embryo implantation (Regalado,

2019a; Cyranoski, 2019) to supposedly make them resistant to the HIV virus. It's supposed because there is yet to be definitive evidence that the experiment was successful. Articles point towards the conclusion that this experiment actually altered the twins' brains (Regalado, 2019b). Chinese biophysicist He Jiankui blatantly "flouted established norms for safety and human protections," (Cyranoski, 2019), creating an international moratorium on the usage of gene editing technologies and related experiments.

Stances and Factors

There are a few main stances that biologists have taken around gene editing and CRISPR. The first stance, and the most common, is that because gene editing technologies provide the ability for researchers and doctors to strip away diseases in embryos and protect future generations, it is justified and ethical to utilize. But, they draw the line here; utilizing CRISPR to enhance an individual's features is unethical and should be rejected. There needs to be ways for the science community to regulate itself to prevent a situation such as the CRISPR twins from China. Director of the Center for Bioethics at Harvard Medical School, Robert Truog, said the following: "To me, the conversation around Dr. He is ... about the oversight of science. The concern is that with technologies that are relatively easy to use, like CRISPR, how does the scientific community regulate itself?" (Bergman, 2019). George Q. Daley, a dean of the Harvard Medical School, also mentioned similar remarks around Dr. He's unethical actions and largely concurs with Truog: "You can't control rogue scientists in any field. But with strongly defined guidelines for responsible professional conduct in place, such ethical violations like those of Dr. He should remain a backwater, because most practitioners will adhere to generally accepted norms. Scientists have a responsibility to come together to articulate professional standards and live by them," (Bergman, 2019). This stance, that germline gene editing is acceptable in areas where there are no other options or to increase the quality of life of an individual (not related to wealth or status), is something that is currently being reflected in forums and discussions about this topic.

The other standpoint is that CRISPR technologies should be available to the general public and should be utilized for anything. Particularly biohackers have been a big part of this trend and have certainly pushed this forward. They claim that science is run by corporations and universities, and in order to abandon those hierarchies, you must rely on the public's curiosity and personal interest in these technologies. Though this viewpoint holds some merit, this form of rebellion could be catastrophic for evolution and future generations. When technology is handed to individuals who are unaware of the immense power it holds, there is always a chance for a calamity. This method has also been used as a guise to experiment on humans unethically, as previously reported in China (Shaw, 2020). Numerous factors come into play when determining the different stances. The questions outlined above highlight just a few of the factors that come into play. There are also socioeconomic and racial questions when deciding how this technology should be utilized. Due to this problem being a question of biological

processes, there are many biological questions about CRISPR technologies as well.

My View

Gene editing and CRISPR technologies have the capability of transforming lives forever by removing and altering genes in our genome. I agree with most development biologists in the field that the technology should only be utilized to prevent individuals from experiencing pain through the form of disorders or diseases. If CRISPR reaches a level in the future where it can safely be deployed to cure diseases and disorders with a high accuracy, then I believe it should be utilized on the populations that need them the most. In a simple sentence, CRISPR should be used for the *good.* In this scenario, I define *good* to be associated with the direct act of improving one's life for the sole purpose or reason of making their quality of life better. This does not include cosmetic changes or enhancements, but rather adopts situations which are the difference between life or death, as well as *medical* conditions that can be cured through CRISPR. With a utilitarian calculus, it can be determined that utilizing CRISPR gene editing technologies for the *good* is beneficial and is something that should be encouraged in the future.

Contrary to some (Grumett, 2004), I do not believe that interjecting with God's natural gene selection is bad, but it must be done underneath the proper circumstances as listed above. I do not agree with the usage of CRISPR to edit the entire human genome with *cosmetic* objectives (such as changing the height, hair color, eye color, etc., of an individual). I believe that the concept of creating a superhuman (either for fashion or for warfare) is unethical and reinforces a binary for what is "normal" and what is "accepted," similar to the ways plastic surgery functions now. Since this binary can potentially harmful for many individuals, I do not believe that it is ethical to for these changes.

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