Ethical Considerations of Genetic Engineering

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Jillian Bracaglia
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Signature ___ Jillian Bracaglia _____ Date __4/26/20__
Jillian Bracaglia

Abstract

The biotechnology field is one that has seen major growth in the past century. One of the latest areas of growth is that of genetic engineering. The base of genetic engineering is direct manipulation of an organism's genes. This has many applications including agriculture, scientific research, health care, and technology. Genetic engineering has had success in the agriculture industry and has been growing in the scientific research and healthcare field. The application of genetic engineering to biomedical challenges has enormous potential for creating solutions to genetic based diseases. With this positive potential comes a lot of negative potential for mistakes, severe consequences, and possible future implications on our society. This broad range of possible effects necessitates a discussion of the ethics of genetic engineering.

Ethical Considerations of Genetic Engineering

Introduction

If engineering is the application of math and science to solve problems, genetic engineering is engineering with the idea that the solution to a problem is within an organism's genes. Genetic engineering has recently seen aggressive bursts in progress and applications. It has the potential to affect many things, ranging from human diseases to agricultural hardships. In this thesis I will dive into the possible applications of, regulations of, and ethical considerations of genetic engineering.

Applications and Regulations

Genetic engineering is defined as the direct manipulation or altering of one or more of an organism's genes (What is genetic engineering?, n.d.) (David M. Bodine, n.d.). An organism is a broad term but defined clearly. An organism is any individual entity that embodies the properties of life ("Organism," 2020). It is broad because it can apply to anything from a single-celled life form to a plant to an animal or human, not including viruses. Every organism is built from genes they inherit from their parent organisms, in other words genes are the basic physical unit of inheritance. Every gene is a building block that is put together with other genes to create all the functions and physical characteristics an organism has. DNA, or deoxyribonucleic acid, is the basic unit of genes. The sequence of DNA determines the information available for building or maintaining an organism; information such as development, functioning, growth, and reproduction.

In humans, genes can vary in size from a few hundred DNA units to more than 2 million units. It is estimated that humans have between 20,000 and 25,000 genes. Humans inherit two copies of each gene, one from each parent. Most genes are the same in all humans, but there is a

small number of genes that are slightly different between people. Alleles are forms of the same gene with small differences in their DNA sequence. It is these small differences that contribute to each person's unique features (U.S. National Library of Medicine, 2020c).

Returning to the idea that problems can be solved using an organism's genes, there are some terms involved with genetic engineering that require definition. GMOs have become popular mainly from innovation in agriculture. GMO stands for genetically modified organism, and it can be defined as a plant, animal, microorganism or other organism whose genetic makeup has been modified in a laboratory using genetic engineering or transgenic technology (What is a GMO? – The Non-GMO Project, 2016). Gene therapy is a proposed type of medical treatment where new DNA is introduced into a patient to treat a genetic disease. The new DNA typically contains a sequence for a functioning gene to correct the effect of a disease-causing error, or mutation, in the patient's own genes (Gene Therapy, 2017). Genome editing is a term that has broader applications and is used to describe making specific changes to the DNA of a cell or an organism by forcing a cell or organism to repair a mutation (U.S. National Library of Medicine, 2020a). The last two definitions that are pertinent are that of somatic cells and germline cells for humans. Somatic cells are cells of the body that are not the reproductive cells. Any effects of altering of the genes within these cells will not be passed down to offspring. Germline cells are reproductive cells, and they are the cells that are responsible for passing genes on to offspring. Any effects from altering genes within these cells will be passed down to offspring and subsequent generations (Curran, 2020).

Genetic engineering has been applied as a solution to many areas where altering an organism's characteristics in a particular way could benefit stakeholders. These areas include scientific research, agriculture, technology, and medical treatments. In scientific research,

organisms like mice undergo genetic engineering for the discovery of the function of specific genes. In agriculture, genetic engineering has been utilized to improve the resilience and nutritional value of crops like potatoes, tomatoes, and rice. The United States is the world's leading producer of genetically modified crops. In 2012, the US accounted for over 40% of the total amount of genetically modified crops. In 2013, 93% of the soybeans, 90% of the cotton, and 90% of the corn grown in the US were genetically engineered for either herbicide tolerance or insect resistance (Acosta, 2014). Genetic engineering as medical treatments has only progressed as far as clinical trials partially due to the state of current regulations on genetic engineering on humans and public opinion, which is still mixed in general on genetic engineering.

In terms of current regulations on genetic engineering, policy and regulation is more developed for certain genetic engineering products than others as well as differing between US, other countries, and international governing groups.

In the US, there is no federal regulation that bans protocols or places restrictions on experiments that manipulate human DNA. However, there is federal control in the form of allocation of federal funds, approval of clinical trials, and approval to market a product. The Dickey-Wicker Amendment was passed in 1995 and it forbids the National Institutes of Health from funding research involved in the manipulation of human embryos; this protects against germline gene editing. Any human clinical trials that involve gene editing must be approved by the FDA. Any treatment that involves gene editing must acquire FDA approval before it can be marketed in the US as a cure, treatment, or prevention against a disease. The official position of the FDA is that federal money can be used to research somatic cell gene therapy, but it cannot be used to research germline cell gene therapy (Curran, 2020).

While there is also no federal legislation that is specific to GMOs in the US, there is much more precedent for ensuring the GMO products of genetic engineering are safe and follow a standard of quality. The US approach to regulating GMOs is focused on the nature of the product instead of the process in which it was produced. This approach was determined in the Coordinated Framework for Regulation of Biotechnology, published in 1986. Based on the type of product, GMO products fall under different regulatory bodies. Plant GMOs are regulated by the US Department of Agriculture's Animal and Plant Health Inspection Service under the Plant Protection Act. GMOs in food, drugs, and biological products are regulated by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act. GMO pesticides and microorganisms are regulated by the Environmental Protection Agency pursuant to the Federal Insecticide, Fungicide and Rodenticide Act and the Toxic Substances Control Act (Acosta, 2014).

The European Union has strict and comprehensive regulations on GMOs, however their definition of a GMO is "an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination". (https://www.loc.gov/law/help/restrictions-on-gmos/eu.php) In general the EU's stance on genetic engineering, human or otherwise, is opposed. Human germline cell gene editing is prohibited in the EU (Baylis & Ikemoto, 2017).

China issued new regulations relatively recently stating that clinical gene editing research required national approval. This was in response to an experiment done in November, 2018 by a Chinese scientist named He Jiankui who used gene editing technology on twin baby girls to potentially make them immune to AIDS. This experiment caused outrage because he did not properly study the possible side effects. It is a widely accepted research model to test an

experiment on cells, then small mammals like rats, then large mammals like pigs, then humans. He never conducted the experiments on any animals, and this was seen as having very little regard for the welfare of the human babies he experimented on. The model of conducting experiments on various levels of life forms is widely accepted because of its potential to provide an idea of all of the possible effects of the experiment, negative and positive. Without that information gathered before He conducted it on human babies, He has no way to know if he did make his subjects immune to HIV or if he caused major damage that could become evident as the children grow and develop (Normile, 2019) (Curran, 2020).

Russia does not have comprehensive regulations set for genetic engineering on humans yet but it does have an approval and registration system for products of modern biotechnology (Roudik, 2015). By contrast to China, there is a Russian biologist, Denis Rebrikov, who wants to perform gene editing on human eggs to remove a mutation that impairs hearing. He will not begin these experiments until the Russian Ministry of Health gives him approval to do so (Cyranoski, 2019). The Russian Ministry of Health is unlikely to give him approval as experiments involving gene editing on human embryos and germ cells have been deemed premature. Russia has recently stated “We agree with the director-general of the World Health Organization (WHO) that comprehensive research is needed into the technical and ethical consequences of using the technology. We support the WHO advisory committee’s recommendations to develop global standards for the governance and oversight of human-genome editing, and to create a public registry of clinical research on the effects of applying it to human somatic and germ cells.” They go further to state “Russian science recognizes the basic ethical principles that underpin the decisions of the United Nations, the United Nations Educational, Scientific and Cultural Organization, the WHO and other international

organizations, as well as the provisions of the Council of Europe's Convention on Human Rights and Biomedicine. These principles will define the system of ethical expertise and inform how Russia regulates the field (Grebenshchikova, 2019).

Internationally, as of 2019, there were no cohesive, legally binding or universally recognized set of rules for gene editing (Curran, 2020). There are two major international protocols that address GMOs. The Cartagena Protocol of 2000 and the Nagoya-Kuala Lumpur Supplementary Protocol of 2010 are both attached to the Convention on Biological Diversity of 1993, and they apply only to transboundary actions. They do not apply to use or transport of GMOs within countries (Johnson, 2014). The Declaration of Helsinki, formed in 1964, is the document that comes closest to an international set of guidelines for human experimentation in medicine but it is a non-legally binding document and doesn't specifically address gene editing. The WHO has announced plans to establish a public registry for both somatic and germline clinical trials as well as established an independent expert panel to advise on the oversight and governance of human germline editing. There is also a separate international commission on the clinical use of human germline genome editing. This commission was established by the US National Academy of Science, the US National Academy of Medicine, and Britain's Royal Society, to recommend standards and criteria for germline genome editing. The commission's report will feed into the WHO process. The WHO has made an interim recommendation that "it would be irresponsible at this time for anyone to proceed with clinical applications of human germline genome editing" ("Human germline editing needs one message," 2019).

There is an international group, the Human Genome Organization (HUGO), that is attempting to become a "U.N. for the human genome". Their purpose is to aid the coordination and collaboration of researchers whose work focuses on human genome research and to

encourage public debate and provide information on the scientific, ethical, social, legal, and commercial implications of human genome projects (McKusick, 2019).

Ethical Considerations

There are many possible ways to break down a discussion of the ethics of genetic engineering. Genetic engineering can be applied in so many ways to so many different areas. While the application of genetic engineering to agriculture is important and is still widely debated, it has a more extensive base of understanding its effects gathered and a longer period of existence than genetic engineering on humans.

Genetic engineering on humans is a much more novel practice with the potential for many extreme results as well as ripple effects. This is why I will focus on genetic engineering specifically on humans.

The ethical question of genetic engineering on the human germline is easy to answer, at least for now, based on our current level of knowledge. It is unethical because there is no opportunity for future generations to choose whether they want the change and there is not enough information known to confidently cover all of the possible side effects. It is unethical to perform a change on an unborn human's DNA that might cause other changes to previously perfectly functioning genes without warning the unborn human of this possibility. This is my personal conclusion I have arrived at, but the US government shares this conclusion (U.S. National Library of Medicine, 2020b).

The ethical question of genetic engineering on the somatic germline is more difficult, and it requires a more in depth look at all of the factors of continuing on with researching and marketing this practice. This will be narrowed to the US. First, the stakeholders involved need to be acknowledged. Stakeholders range from the parents of the offspring with a genetic disease,

the actual patient with a genetic disease, doctors, insurance companies, biological companies creating these gene therapies, biological companies producing alternative treatments, investors, researchers, all the way out to the broad scope of all of us. This brings in the next factor to consider, the cost. Because of our current health care system, the price of gene therapy through genetic engineering affects us all.

Gene therapy, through genetic engineering, has the potential to eliminate many medical conditions. It is most accurately described as a cure while most of our medical treatments today are simply treatments. They focus on treating symptoms, mitigating the effects of the disease, instead of eliminating the disease from the patient. Because a gene therapy should ideally introduce the proper genetic code that is lacking, this effect should eliminate symptoms and disease and last for a patient's lifetime.

If gene therapies are priced high this would most likely result in private insurance companies or government issued insurance covering the cost. This would mean the general population would be involved in paying through federal taxes or higher premium rates and deductibles in insurance policies. There is not a lot of precedent for pricing of cures, and any company is free to price their gene therapy however they want. Moving any drug or gene therapy through the FDA approval process is extremely difficult and expensive. In addition, many gene therapies target rare diseases, which means there is a smaller market to regain research and design costs.

Drugs are often priced based on what a company thinks it can sell it for on the market. This results in a supply and demand economical model. This supply and demand model for medical treatments and cures causes its own ethical dilemma. Supply and demand works fine for the car industry, because consumers have the choice between a luxury car and a basic car. Supply

and demand in health care results in a parent having the choice between health care and financial burden when their child is born with a life-threatening genetic disease. However, companies creating gene therapies need incentive to take on the risk of the research and design process and the FDA approval process.

One way to determine a fair price for effective gene therapy is to determine the cost of not treating a condition and price it under that number. Luxturna is one of the first true gene therapy products approved in the US and it treats an inherited form of blindness. It is regarded as a cure for the genetically caused blindness, meaning blind people can regain functional vision and therefore lead independent lives. Luxturna costs $850,000 to treat both eyes. For patients with this specific genetic disease, there is no alternative treatment. The CEO of the company selling Luxturna stated “When you actually put together the cost of educating a blind child, the cost of loss of productivity for someone who has to care for a blind child, or productivity losses in terms of themselves. That’s what it amounts to…”. The CEO argued that an untreated blind child would require more than 1 million in expenses throughout the course of their life, and in comparison, Luxturna only costs $850,000 and will restore functional vision (Curran, 2019). Some companies are using this product as a guide for setting their own pricing strategy. This approach of pricing a gene therapy under the cost of not treating it most closely follows a Utilitarian Ethical Approach in that it is doing the most good and least harm for all those involved.

Another way to determine price is to set it at a competitive price to a pre-existing treatment for the same disease. The drug company Novartis bought AveXis, a company that created Zolgensma, a gene therapy that is a cure for spinal muscular atrophy (SMA), for $8.7 billion. Novartis priced this therapy at $2.1 million, a one-time cost. The standard of care and a

preexisting treatment for SMA is Spinraza, owned by Biogen and priced at $750,000 for the first year of treatment, and $375,000 for subsequent years. Novartis can argue their gene therapy is a bargain compared to a lifetime or as little as 5 years of Spinraza treatment (Curran, 2019). There is also the added benefit of the emotional unburdening of being cured instead of yearly hospital stays and merely treating symptoms. From a Common Good Ethical Approach, this is not the most ethical approach because the major benefits go to the company that sells the gene therapy. The gene therapy company can price their cure higher than necessary to strictly make a profit as long as its priced under the current competitor. The patient still faces a large financial burden, and the drug companies lose consumers.

A third way to determine price is to use a cost-effective approach for pricing. In this approach the gene therapy price is compared to the medical benefit. The idea is that the cost of gene therapy should only be as high as the quality of the delivered health benefit. If a gene therapy delivers meager health benefits the price should be low. The QALY (quality adjusted life year) value is a quantitative measurement of the health benefit of a drug or treatment. Based on the assumption that health is a function of length of life and quality of life, a gene therapy can be assigned a QALY value (Curran, 2019). If 1 year of life lived in perfect health is equal to 1 QALY, and Treatment Gene Therapy delivers 8 years of life lived in perfect health while Treatment Drug delivers 13 years of life but not perfect health with frequent hospital stays because of a non-curing imperfect treatment, then Treatment Gene Therapy has a higher QALY value. A higher QALY value should result in higher pricing and should be preferentially funded by insurance. This approach I believe best respects the rights of all who have a stake and follows a Rights Ethical Approach. The companies are rewarded based on how good their product is, the

insurance companies can provide the lowest risk option, and the patients receive the best care possible.

Two important factors to also consider for the ethics of genetic engineering on humans is the safety of doing so and the defining lines between what is elective and what is critical. Both factors require further time and progress made in research. Currently, gene therapies are focusing on critical life-threatening genetic diseases. While gene therapy could be used for more elective areas like changes to appearance, metabolism, and personality I believe the cautious approach the scientific world is taking to genetic engineering on humans will safeguard against these types of gene therapies being available any time soon. While not completely unethical in basic practice, there is a concern that more elective gene therapies would be more accessible to those with more wealth and potentially contribute further to wealth gaps. The general safety of any genetic engineering on humans is still a concern as well, and it is a concern that can only be slowly taken care of through careful data collection, improved methods of tracking any and all changes, and studies done over very long stretches of times to assure we know the full effects.

Conclusion

My purpose was to consider the ethical implications of genetic engineering. Through my exploration I discovered there was a wide range of applications of genetic engineering, and the ethics of these applications are widely debated for various reasons. As a whole, I believe genetic engineering on humans as a means of medical treatment, or curing, can be ethical and benefit many people. There is a lot of unknown still in the scientific world about genetic engineering, and it can be a very effective and ethically handled innovation as long as it is treated very cautiously. Research into how editing our own genes will affect us needs to continue to be

extensively pursued and the scientific community needs to continue the path set with transparency and collaboration.

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