Title
Human Biology: Literature Review of Genetic Engineering

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Abstract

The purpose of our research study was to determine the social and ethical aspects of genetic engineering. What originally began as a way to decrease an embryo's risk of genetic diseases has now become a way to alter its appearance; this paper aims to challenge the risks of genetic engineering. To dive deeper into our research question, we were able to examine sources on a global level to determine the perspectives of genetic engineering in different parts of the world. As the current field of genetic engineering is under speculation by many providers, evaluating the pros and cons of each scenario can determine the efficacy of genetic engineering. Employing clinical technology and socially ethical framework were two main criterias which were used in determining the parameters in understanding if genetic engineering is a viable treatment option. The research examined explains any known sideaffects, while also bringing to light the unknown side effects that can result from genetic alterations of an embryo. In summation, this paper aims to highlight embryonic effects and how genetic engineering could challenge their integration into society itself.

Introduction

The current state of the field we are researching is still under speculation as to how ethical genetic modification of human embryos are. The prior research conducted in this field discusses the possibilities of genetic engineering which include technologies that involve manipulating embryo's sex and hereditary diseases. The present gaps in the research are how substantially beneficial the technology is, who has access to this advanced technology, and if

these modifying procedures are ethical to conduct in the first place. Our research team's overarching question is: to what extent should genetic engineering be socially ethical in order to be used as a considerable treatment technology?

The parameters we will use to describe a considerable treatment technology are: clinical technology conducting treatment with at least an 80% success rate; and results in a net benefit that exceeds the net cost for the subject. The socially ethical framework that we will use to evaluate our question throughout this paper are based on two notions: (1) no harmful or adverse effects must occur to the human subject during and after treatment is administered, and (2) if trials are successful in treatment, there must be accessibility to this technology no matter patient socioeconomic status.

Originally, genetic engineering began as a method of curing generational diseases. For example, the blood disorder thalassemia runs in the bloodline of families. This disorder affects the body's natural ability to produce a sufficient amount of protein known as hemoglobin. Genetic engineering was used as a method to eliminate the gene from the offspring; however, it has since advanced and shifted from a procedure used to cure medical conditions into a procedure used to alter an offspring's appearance, intelligence, and gender. If this technology can alter a human's genetic sequencing to provide potential for a longer and healthier life, should we as a society allow this same technology to alter an offspring in a way of the parent's choosing?

Currently, China specifically has some of the most advanced and in-depth research on embryonic alterations. They are a powerhouse in terms of their economy, and it is predicted that

many nations will soon follow after them in normalizing genetic engineering due to their economic success. As previously stated, a team in China in April 2015 were the first to use genome editing technologies on human embryos with the goal to correct the gene for thalassaemia using “non-viable” IVF embryos (Munsie p.1). Since this event in 2015, split arguments arose ranging from that it may be better to specifically create embryos for the purpose of research and the betterment of scientific discovery, to objections that it may be unethical by creating embryos whose sole purpose is to be used for research, never becoming viable to grow into a living being (Munsie p.1). However, this scientific race to become the most advanced in genetic engineering has resulted in a disregard for the embryo's safety itself and whether or not the practice itself is ethical.

Methodology

As a group, we used certain inclusion and elimination methods to choose the papers best fitting for our research. First we searched for papers with “genetically modified human embryos” in the title and abstract from multiple search engines such as Google Scholar, Science Direct, and BMJ Journals: Journal of Medical Ethics. Based on this unfiltered search, BMJ produced 350 results, Science Direct produced 61,115 results, and Google scholar produced 391,000 results. This helped narrow down our search to content about specifically modifying human embryos. To sift through the thousands of papers, we searched for papers that included clinical trials about our topic. We used this method because we wanted to choose papers that explained the results and impacts of modifying human embryos. This would help us build a discussion about whether these clinical trials we researched are within the parameters of our ethical framework and

considerable treatment technologies. As explained in the beginning, the parameters we will use to describe our ethical framework and considerable treatment technology are: no harmful or adverse effects must occur to the human subject during and after treatment is administered; if trials are successful in treatment, there must be accessibility to this technology no matter patient socioeconomic status; and as for treatment technology, the treatment should have at least an 80% success rate; and results in a net benefit that exceeds the net cost for the subject. We will use these parameters to evaluate our question throughout this paper. We need to know what the impact(s) are on the embryos when they are older after genetic engineering has taken place in vitro.

We also decided to choose papers that were published before the last 10 years (between 2012-2023) and papers that explained a standard of ethics. This method is to ensure we write about updated content and information, which will also help us discuss new and current evidence on the topic. This method was substantial to our research because we also needed a standard of ethics to use as a measurement to show whether the practice of genetically modifying human embryos was socially ethical to continue researching and conducting trials in this field.

Results

In one clinical trial, a study regarding genetic engineering's effectiveness on red blood cells, specifically testing it on sickle cell anemia was using CRISPR technology. The complications of sickle cell anemia consist of chronic pain, strokes, organ damage, anemia, or in severe cases, death. The trial experiment intends to increase levels of fetal hemoglobin. The

difference between this form of hemoglobin is that it is made within infants and children in which adult bodies cannot make it because humans switch from two different hemoglobin types before and after birth. This trial is to help prove that genetic engineering technology would allow us to stimulate the production of fetal hemoglobin.

This is an ethical approach, however, the trial hopes to test its effectiveness. The purpose of this trial is to use fetal hemoglobin, also called delta hemoglobin, because it is not affected by the mutation that causes sickle cell anemia. Instead, the trial hopes to show an increase in the participants' fetal hemoglobin so that when the patient grows and is affected by sickle cell anemia, they will still have cells that are immune through the process of genetic engineering facilitated through CRISPR.

The procedure of the trial will be to harvest the participant's red blood cells so the treatment may take place outside of the patient's body. The scientists will essentially be altering their blood and then placing it back in them by using chemotherapy to get rid of the mutation in the blood, then replace the infected cells with the fetal-edited ones. The edited blood will be placed back into their body through IV to enter the bloodstream and circulate. The trial will be testing the patient's acceptance of the genome-edited blood cells and if successful, scientists believe genetic engineering may advance past embryonic development stages and can instead be implemented into the recovery of adults.

In another trial, He Jiankui and his team in Shenzhen, China conducted a clinical trial to eliminate the CCR5 gene from embryos using CRISPR technology. This gene enables HIV infection, and the purpose for this trial was to eliminate it genetically so future generations won't

be born with HIV. He used couples to participate in the trial where the father was infected with HIV and the mother would be implanted with the fertilized modified embryo (Raposo 1).

The entire results of the trial are unknown because Chinese regulation does not provide a legal basis for the trial they conducted (Raposo p.1). As of 2003, under the "Ethical Guiding Principles for Research on Embryonic Stem Cell" issued by China's Ministry of Science and Technology, there is a ban on research to be performed on human in vitro embryos after the 14th day of existence, and its subsequent implantation into a human uterus. Since there is a violation under Chinese regulation, the publication of their entire works for this trial is not complete.

However, in November 2018, the media gained insight on some of the trial's results and found that the trial was successful in eliminating the CCR5 gene in twin girls, named Lulu and Nana for anonymity purposes and are still being studied and monitored since their birth (Park p.1). Upon the review of He's data, some scientists found evidence of mosaicism in the twin girls, which is evidence of patchwork gene editing where two or more genetically different sets of cells are found, which can affect the benefits of their resistance to HIV (Park p.3). Furthermore, despite the research of this potentially beneficial and groundbreaking trial to use genetic modification as a prevention method of HIV, the scientific community also knows that the CCR5 gene is related to major brain functions. Ethically, this trial may have some objections if He Jiankui and his team may have managed to modify the intelligence of two human beings, with the potential of better memory and higher IQ.

Discussion

After reviewing the literature and data of the clinical trials of various papers, we have

made some comparisons between these studies. Firstly, these studies show that there is an advancement within genetic engineering in humans. This technology that has been developed is able to alter the very cells of a human outside of its body and place it back into it. This technology is also able to alter and delete human genes so genetic diseases won't be passed down to further generations. Even though this technology has great potential for eradicating diseases in lineages, there are unknown consequences that could arise that can only be told with time.

We have concluded that, specifically, scientists no longer want to limit the use of this technology to fetuses, but instead implement the methods into adult life. From the perspective of fetuses, they will be altered before their knowledge and consent, and will also not be aware of the ramifications of their treatment. From the perspective of adults, they will be given the choice and access to alter themselves to their liking. For the sake of research and medical advancement, scientists will insist on upgrading their trials to human adults to see how far this technology can take human civilization.

These clinical trials and FDA approval challenges the ethical aspect of testing embryos. The questions that are asked repeatedly are how ethical is testing on embryos and who gets to decide the ethical standards and parameters scientists and society must abide by. The FDA will be faced with the challenge of addressing Type I and Type II errors for a technology that is still relatively new and experimental. Type I errors occur when the clinical technology is approved to be used but causes more adverse effects than beneficial to participants on a large scale. Type II errors occur when the technology is not approved to be used but proves to show actual benefits

to patients that need it. This error could potentially result in deaths or worsened conditions due to the technology not being available to those patients in need. There is still a long way to go on who can establish which ethical standards of practices for this engineering technology to prevent an overwhelming number of Type I and II errors.

Genetic engineering has noticeable technological pros and cons that must be taken into account. A pro is that this technology allows for early detection of life threatening diseases and early detection of the sex of an unborn fetus. These studies showed different genetic engineering focuses, specifically which genes are expressed on and off. On the other hand, these studies also show that making inheritable genetic or cellular modifications of embryos intended for full-term development constitutes uncontrolled human experimentation and that the attendant uncertainties are side-stepped or obscured by most observers. Furthermore, the studies depicted that standardizing embryo dosage could lead to having one embryo better than the other. In conclusion, this technology is still experimental and must be handled with substantial analysis of weighing the net cost and benefits of this treatment technology. Since this technology is still experimental, it will take time to truly understand the side effects and results of genetically modifying humans.

Bibliography

Braverman, I. (2017). *Gene editing, law, and the environment: Life beyond the human* (1st ed.). Routledge.https://www.taylorfrancis.com/chapters/edit/10.4324/9781315168418-8/sex-lies-genetic-engineering-stuart-newman

Deane-Drummond, C.(1995). Genetic engineering for the environment: Ethical implications of the biotechnology revolution. Heythrop Journal, 36(3), 307-327. Available at: http://hdl.handle.net/10034/14636

Goff, L. (2019, February 20). *Gene-Editing Human Embryos: What, How, Why?* Research Blog. https://researchblog.duke.edu/2018/12/14/gene-editing-human-embryos-what-how-why/

Journal of Medical Ethics. (2005, February 1). *The ethics of using genetic engineering for sex selection*. https://jme.bmj.com/content/31/2/116

Maloney, Robert P. (1980) "Some Notes on Genetic Engineering,"The Linacre Quarterly: Vol.47: No. 3 , Article 11. Available at:http://epublications.marquette.edu/lnq/vol47/iss3/11

Munsie, M., & Gyngell, C. (2018, October 1). *Ethical Issues in Genetic Modification and Why Application Matters*. Science Direct. https://www.sciencedirect.com/science/article/pii/S0959437X18300212?casa_token=BnPU06oz_GAAAAAA:o8ZDrQ7J8T4vuVl2VnVf2qGxocfQcMJbSDr_HqSvVgUmeBF9ccfn0ySqH5bgSmEsqiv4S0yC_8E

National Academies of Sciences; Engineering; and Medicine, National Academy of Medicine, National Academy of Sciences, & Committee on Human Gene Editing: Scientific;

Medical; and Ethical Considerations. (2017). *Human genome editing: Science, ethics, and governance*. National Academies Press.

Park, A. (2018, November 29). *How China's Gene-Edited Twins' Lives Could Be Forever Changed by Controversial CRISPR Work*. Time. https://time.com/5466967/crispr-twins-lives/

Raposo, V. L. (2019, August 1). *The First Chinese Edited Babies: A Leap of Faith in Science*. PubMed Central (PMC). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6724388/

Southgate, M. Therese (1972) "Genetic Engineering: Reprise,"The Linacre Quarterly: Vol.39: No. 3 , Article 5. Available at:http://epublications.marquette.edu/lnq/vol39/iss3/5

Turocy, J., Adashi, E. Y., & Egli, D. (2021, March 18). *Heritable Human Genome Editing: Research Progress, Ethical Considerations, and Hurdles to Clinical Practice*. Science Direct. https://www.sciencedirect.com/science/article/pii/S0092867421002257

Veit, W. (2019, January 1). *Should Parents Genetically Engineer Their Children?* CORE. https://core.ac.uk/works/8869070