Forum: Third General Assembly

Issue: Examining the risks and consequences of human genetic engineering

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Introduction

Technology in the modern world takes shape in many ways, growing at an unprecedented rate. It has already penetrated various fields and will continue to infiltrate almost all aspects of humanity. One such technology is human genetic engineering, which has seen significant advancements in recent years. Over the years, genetic engineering has encompassed many areas of biology, including artificial insemination, in vitro fertilization and most recently, recombinant DNA technology and genome editing. (Augustyn). Genome editing, which can result in malignant genes being removed from humans, particularly has caught the world's attention. The potential for disease prevention, treatment, and the enhancement of physical and mental capabilities, makes the concept very attractive. However, due to the rapidly growing field, it is important, now, more than ever, to examine its risks and consequences, as well as the ethical dilemmas that may arise. There are many risks associated with modifying one's DNA, including genetic mutations and long-term health consequences. In addition, as a result of the expensive procedures, social inequality will be exacerbated. Addressing this issue requires both feasible short term *and* long-term solutions, collaborating with key scientists and member states to ensure human genetic engineering is as safe as possible moving forward. It is imperative that the United Nations tackle this issue given its global relevance and rising prevalence, as well as to establish the ground work for the future.

Definition of Key Terms

Human Genetic Engineering

A process that uses laboratory-based technologies to alter the genetic makeup of an organism, revolving around recombinant DNA technology and genome editing. Over the years, genetic engineering in humans has been applied to the production of cancer therapies.

Mutations

Mutations are issues that can arise both naturally and artificially. This causes changes to the human genome, thus altering the proteins they code for, and therefore the function of that gene. Although there is a small chance that a mutation is advantageous, they are mostly harmful. With human genetic engineering being susceptible to accidents, it's important to develop accurate practices to avoid mutations.

Germline Genome Editing

Germline Genome Editing refers to genetic editing which occurs in the germline cells - sperm, egg and zygote. Mutations in germline cells cause hereditary diseases, but through genomic editing of these cells, it's possible to remove genetic diseases. However, germline genome editing is regarded as ethically permissible due to the risks involved.

Somatic Genome Editing

Somatic Genome Editing refers to genetic editing which occurs in the somatic cells, or body cells. Mutations in these cells cause diseases that last a human's lifetime (but doesn't pass onto offspring). Somatic Genome Editing is much more common than Germline Genome Editing, and has been successful in the past especially with regard to sickle cell anemia and some cancer treatments.

Designer Babies

With the potential of genetically engineering a human embryo, and then implanting that embryo into a womb, the risk of designer babies increases. Essentially, these are babies who have been genetically manipulated to have genetic advancements, such as more favorable traits. This is considered unethical and is opposed by many religious groups.

Background

In the late 1800s, DNA was discovered by Friedrich Meischer who had successfully isolated it from the white blood cell. However, it's actual role and function to the human body was not discovered until much later. In the 1940s, scientists were unsure what contained genetic material - DNA or proteins. Hershey and Chase concocted an experiment to determine the host of genetic material in 1950 - through the use of bacteriophages. From this experiment, DNA was recognized as containing genetic material. The first few genetic engineering experiments revolved around recombinant engineering, which essentially involved inserting DNA from other organisms into each other. At the time, this was not seen as acceptable, especially to those with strong religious beliefs - this believed that it was an insult to God. There were also many concerns about the many unknown risks and consequences. It wasn't until the Asilomar Conference in 1975 were some regulations and safety rules established. In 2003, the Human Genome Project was completed, a breakthrough in the biological world. As these milestones were taking place, the public view of human genetic engineering also shifted, with more and more people recognizing it's benefits.

Human genome editing has the potential to advance our ability to treat and cure disease, but the full impact will only be realized if we deploy it for the benefit of all people, instead of fueling more health inequity between and within countries" are the words of Tedros Adhanom Ghebreyesus, the Director-General of the World Health Organization (WHO). Essentially, human genetic engineering has the potential to change lives, but can also exacerbate social issues.

Impact

In the past few years, human genetic engineering has made enormous strides to tackle diseases. Most recently, in December 2023, a genome editing technique via CRISPR was approved, which provides two methods to treat sickle cell disease. Sickle cell disease impacts millions around the world, and causes issues with the heart, so this advancement has the potential to benefit many. Apart from sickle cell anemia, various other conditions like hemophilia and cancer can be tackled. However, there are a myriad of risks and consequences involved as well - some are listed below.

Off Target Results

Off-target results occur as a consequence of mutations. There are three types of mutations - substitutions, insertions and deletions. Substitutions are the type of mutation that would work best for genomic editing - they simply replace a base in the base sequence, and therefore only impact one amino acid. However, insertions and deletions (inserting or deleting a base) can impact the entire base sequence and thus might unintentionally affect other genes. This could impact the proteins coded for and thus alter their function and structure, causing unforeseen health issues (Rubeis).

Cancer Risk

Major off-target results can result in cancer risk. This is because this interrupts the cell cycle, which in turn leads to tumor formation. (Genetic Engineering - Risks, Benefits and Perceptions). Not only is this harmful for the patient, it raises major ethical concerns.

Equity and Access

Given the high costs associated with human genetic engineering, not all individuals would be able to afford such care, even if they should require it. This would exacerbate social issues and inequality. Further, it's important to consider therapy vs. enhancement. Priority should be given to individuals who *require* genetic engineering to tackle any diseases, rather than individuals attempting to change or enhance traits without there being an urgent issue.

Enhancement and Perfection

Some individuals might utilize human genetic engineering to enhance already existing traits to make themselves more "perfect". One example of this is with designer babies. However, this raises serious concerns, especially from religious groups who believe that it shouldn't be possible to change individuals from their "natural" selves. In the long-term, this could lead to a genetic underclass - a group that is genetically disadvantaged.

Major Parties Involved

World Health Organization

The World Health Organization acknowledges the need to examine this up and coming technology and in 2018, established the Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing (shortened to The Committee). The purpose of this committee was to consider various ethical and social challenges. This paved the way to publish *A framework for Governance* in 2021. This framework advocates for collaboration with research institutions, creating judicial rulings, and expanding research.

United States of America

The United States of America has a highly regulated and strict genetic engineering program. Genetic therapy is permitted with stem cells but with many restrictions in place, while gene therapy in germline cells is completely restricted. In order to carry out any gene therapy, the process must be approved by the Office for Human Research Protections and Food and Drug Administration (FDA). In 2017, human embryos were genetically altered via CRISPR for the first time by Professor Shoukhrat Mitalipov with the Oregon Health and Science University. Although this was successful, it raised controversy.

Japan

Japan is much more open to genetic engineering and gene therapy in comparison to the USA. Germline gene editing is permitted for research, as established in 2018. However, germline gene editing for reproductive purposes is *strictly* prohibited. Just like with the USA, researchers must be approved by the Ministry of Education, Culture, Sports, Science and Technology as well as an ethics panel. Apart from CRISPR, a program called NICER has been developed which supposedly contains lesser mutations - this is one of the main risks of human genetic engineering (NICER).

European Union

The European Union has completely restricted gene editing in germline/embryonic cells, with some research allowed. Essentially, genetic editing done to produce designer babies or genetically enhancing the embryo in any way is prohibited. With stem cells for therapy, many studies have been undertaken, with research yielding potential solutions to liver disease, blood disorders, and melanoma (Genetic Literacy Project). Treatment for beta thalassemia, a blood disorder that results in anemia, was of particular importance. The solution was a drug - *zynteglo* - which essentially reintroduces healthy copies of the gene. This is a much safer option compared to a blood transfusion.

China

Since 2003, China has been establishing frameworks and regulations associated with genetic engineering and genetic modifications. The National Medical Products Administration published a *Guidance for Human Gene Therapy Research and its Products* which essentially called for a strict process in which every stage had to be approved by involved associations. (CFDA) China was the first country to genetically edit a human embryo (2015),

triggering a domino effect as many countries began trials thereafter. Using CRISPR, a gene associated with a blood disorder was modified, however, the embryos were not implanted into wombs and many of them were unsuccessful. Since then, many new studies and trials have been adopted.

Timeline of Events

Human Genetic Engineering is a relatively new process and did not gain traction until after 2000. Therefore, there have been rapid advancements made in the past 10-15 years, but a great amount of work still needs to be done to establish global frameworks and set laws and regulations into place.

Date	Description of event
April 14, 2003	On this day, the Human Genome Project was completed, which was a complete sequence of the human genome. This provided fundamental information about humans, and jump started the process of creating medicine aimed to particular genes, as well as human genetic engineering in general (National Human Genome Research Institute).
December 12, 2012	On this date, a patent was submitted to approve CRISPR. CRISPR has been a revolutionary tool in human genetic engineering, providing highly specific yet rapid modifications of the human genome. It is also applicable to a wide range of organisms (although this agenda focuses only on humans).
April 22, 2015	The first to do it, Chinese scientists genetically engineer and edit the genomes of non-viable (cannot result in a live birth) human embryos. This was also the first proper application of CRISPR. Since many of the embryos were unsuccessful, this raised ethical concerns, with many agreeing that technology was still not ready to fight disease.
July 12, 2021	With the rise of human genetic engineering, the World Health Organization (WHO) released an advisory framework developed by an advisory committee including scientists, ethicists and religious leaders. One of the primary risks and consequences of human genetic engineering is the potential for social inequality. This advisory focuses on ensuring that human genetic engineering is accessible to all, particularly to developing countries. They also emphasize the need to establish processes that thoroughly check the genetic editing to ensure no unintentional mutations occur (World Health Organization).

December 2023	Sickle cell disease is one of the most prominent diseases in the world, impacting nearly 8 million people. Therefore, it was one of the first targets when gene therapy and genetic engineering gained traction. In December 2023, the FDA approved two different therapies which are successful in fixing the disease - one involves substitution of the gene and the other includes adding a new gene. However, this is still not widely available to people. (National Heart, Lung and Blood Institute).

Previous Attempts to Resolve the Issue

Due to the risks involved with genetic engineering, many countries have already placed restrictions or even bans on the process of genetic engineering. Germline editing in particular is deemed too risky to even attempt in some countries. Through this, risks and consequences of genetic engineering are avoided all together. Even if a country allows for human genetic engineering, many of them have strict regulations set in place to minimize harm towards the patient. Projects related to human genetic engineering must undergo rigorous approval processes from respective organizations such as the FDA, and also receive approval from an ethics committee. This way, countries can ensure that research is being carried out in a proper manner. In general, throughout the gene editing process, work is overseen by a committee to ensure mutations are minimal. Further, FDA or other relevant organizations (such as the National Medical Products Administration in China) have oversight in labs and conduct safety checks to ensure the labs run smoothly and effectively under proper guidelines (Mayo Clinic).

Treatments undergo various tests before they are approved for use in the general public. A major part of this is clinical trials, which are conducted on individuals to determine whether the treatment is actually safe for the general public. There are also strict restrictions on *who* can use the gene therapy. For example, individuals under 18, with conditions related to blood, women are generally restricted, etc. Currently, treatments in trials can be used to address serious conditions like cancer, spinal muscular atrophy, hemophilia and sickle cell disease. However, many are not approved for the general public due to the costs involved.

In the past, the United Nations has passed resolutions or frameworks on the broader applications of human genetic engineering, such as about the human genome in 1997, and human cloning in 2005. As aforementioned, in 2021 the WHO issued an advisory which revolved around identifying specific tools for gene editing and facilitating research.

Possible Solutions

- To address this agenda, delegates should consider already existing solutions, their effectiveness, and also incorporate new solutions. New solutions should be short-term and long-term, addressing the core reasons for the issue.
- Further, delegates should recognize the potential benefits of human genetic engineering and keep this in mind when coming up with solutions. This issue is rich and multi-faceted, with various country stances and perspectives to keep in mind.

- Short term solutions include deploying a task team to monitor practices, and ensure adherence to any safety standards. Ethics and regulation teams should be enhanced, with 3rd party individuals to ensure no bias is involved in the practice - this can be done in collaboration with the World Health Organization (WHO).
- Regarding short-tern solutions, global guidelines should be established imminently regarding human gene editing, such as the restrictions placed on editing, the environment of the lab, and other related matters.
- There should be a clear criteria regarding whether research is approved or not. This can also be created in compliance with the WHO.
- Further, before treatments are open to the general public, it should undergo many clinical trials and checks so that unintended risks and consequences do not occur. Further, it should be strictly monitored who has access to such treatments, so it is being used for medical treatment and not genetic enhancement, in order to prevent disparity.
- On the topic of disparity, it is also important that different countries, as well as social classes within countries have the same access to human genetic engineering. This can be done by way of government subsidies, funding programs and perhaps even placing price caps.
- However, it is also important to recognize the potential that human genetic engineering holds. As this is still a fairly new technological advancement, it's important to continue research to expand understanding and fully harness its benefits.
- Even though many studies already exist regarding genetic engineering, delegates can create UN committees which aim to further exploration in the area.
- In addition to furthering knowledge on genetic engineering, it is imperative that each country reports on their advancements to foster open and clear communication. Yet, this should still be balanced with maintaining privacy.
- All in all, this topic presents the need for multi-faceted and innovative solutions.

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