Forum: European Union Council

Issue: Addressing the Question and Ethics of Human Genetic Engineering

Student Officer: Tamina Jung

Position: Deputy President

Introduction

Humans have altered the genomes of species for thousands of years simply through selective breeding, or artificial selection as contrasted with natural selection. The common goal is to strengthen useful traits in plants and animals. It wasn't until mankind discovered the code of life, DNA, that we fully understood the process of genetic modification. In the 1970s, the direct manipulation of DNA by humans (besides influencing the breeding and mutations) has started to take place. Methods of manipulation can either be isolating and copying the genetic material of interest using recombinant DNA or by artificially synthesising the DNA. A vector is then created and used to insert the "new" DNA into the host organism. The first recombinant DNA molecule was made by Paul Berg in 1972 by combining DNA from the monkey virus SV40 with the lambda virus. The first genetically modified organism was created when Herbert Boyer and Stanley Cohen inserted a recombinant DNA molecule into a bacterium in 1973. Recently, on November 25, 2018, Chinese geneticist He JianKui is the first to make a genetically modified human baby. Further research such as those could help to potentially decrease, or even eliminate, the incidence of many serious genetic diseases, reducing human suffering worldwide. However, many others consider this doing as unnatural, unethical, even dangerous and that it should not be an option. Who is right?

Definition of Key Terms

Genetic engineering

The artificial manipulation, modification, and recombination of DNA or other nucleic acid molecules in order to modify an organism or population of organism. (Also often called genetic modification or genetic manipulation)

Genetically modified organism (GMO)

Any organism whose genetic material has been altered using genetic engineering techniques. In other words, a GMO is an organism altered in a way that does not occur naturally by mating and/or natural recombination.

Somatic genetic modification

Method, which includes adding, cutting, or changing the genes in body cells of an existing person, typically to alleviate a medical condition. These gene therapy techniques are approaching clinical practice, but only for a few conditions.

Germline genetic modification

Method, which includes changing the genes in eggs, sperm, or stem cells in early embryos. Alterations made in this process would appear in every cell of the person, who developed from the gamete or embryo, and also in all subsequent generations.

CRISPR (clustered regularly interspaced short palindromic repeats)

A family of DNA sequences found within the genomes or prokaryotic organisms such as bacteria and archaea. These sequences are derived from DNA fragments from viruses that have previously infected the prokaryote and are used to detect and destroy DNA from similar viruses during subsequent infections. Hence these sequences play a key role in the antiviral defense system of prokaryotes.

Background Information

General Overview

Genetic engineering opens up new possibilities for mankind. As Stephen Hawking once said: “with genetic engineering, we will be able to increase e the complexity of our DNA, and improve the human race.” For a long time, genetic engineering was extremely expensive, complicated, and took a long time to do.

This has changed with the revolutionary new technology CRISPR. CRISPR is a “DNA archive” inside a bacterium that stores DNA fragments from viruses that have previously infected the bacterium. When the virus infects the bacterium again, a protein called CAS9 compares DNA fragments of the newly intruding virus with the one stored in CRISPR. If a perfect match is found, the protein CAS9 cuts of the DNA fragment, making it useless. The incredible thing about the CRISPR system (includes CAS9) is that it is programmable. Scientists can insert a DNA fragment of their choice into a CRISPR system and put it in a living body, where they will function as stated above. In 2015, scientists use CRISPR to cut the HIV virus put of living cells from patients in the lab, proving that it was possible. Other viruses, viruses that hide inside human DNA like Herpes could be eradicated with this method as well. CRISPR can also be used to genetically edit cells inside the immune system, which can enhance their ability to detect cancer cells. A modified version of the CAS9 protein can even “cure” genetic disease that occur inside a human body due

to natural mutation. With further research on this topic, “incurables” such as Trisomy 21 or colour blindness can be cured.

Despite the benefits genetic engineering bring or could potentially bring, it is ethically charged. There are two types of genetic engineering. The somatic genetic modification is the process of editing genes of an existing person, which means the changes made are limited to the individual and die with them. The germline genetic modification, however, edits genes inside egg cells, sperm cells, or stem cells of an early embryo, meaning the alterations made during this process will be inherited by future generations and could eventually affect the entire gene pool irreversibly. Many opponents of genetic engineering are concerned that any genome editing, even for therapeutic uses, will start us on a slippery slope to using it for non-therapeutic and enhancement purposes. Because it can also be used to create genetically modified humans, often called “designer babies”. Thus, the safety of these procedures is of primary concern. There is a possibility of off-target effects (edits in the wrong place) and mosaicism (some cells carry the edit but others do not). As with many new technologies, there is concern that genome editing will only be accessible to the wealthy and will increase existing disparities in access to health care and other interventions. Some worry that taken to its extreme, germline editing could create classes of individuals defined by the quality of their engineered genome.

Major Countries and Organizations Involved

ESGCT - European society of Gene and Cell Therapy

Promote basic and clinical research in gene therapy and genetic vaccines by facilitating education, the exchange of information and technology, and by serving as a professional adviser to stakeholder communities and regulatory bodies in Europe.

United Kingdom

British authorities have become the first in the world to license a gene-editing technique on human embryos for research. The editing of genomes of human embryos with the use of a technique known as CRISPR-CAS9 by researcher from the Francis Crick Institute in London is permitted. For now, it is illegal for them to implant the genetically modified embryo into a woman. Researchers have to destroy the embryo after studying them for seven days.

UNESCO

Independent experts of the organization’s International Bioethics Committee (IBC) published a report “*Updating its Reflection on the Human Genome and Human Rights.*” In it, the experts argue that “gene therapy could be a watershed in the history of medicine and genome editing is unquestionably one of the most promising undertakings of science for the sake of all humankind.” The have called for a

temporary ban on genetic "editing" of the human germline, calling for a wide public debate on genetic modification of human DNA.

Source: Araki and Ishii, Reproductive Biology and Endocrinology, 2014

Timeline of Events

Date	Description of event
1973	First GMO created
1997	Universal Declaration on the Human Genome and Human Rights issued by UNESCO
2007	First evidence that CRISPR was an adaptive immune system was published
25/11/2018	Chinese geneticist He JianKui is the first to make a genetically modified human baby using the CRISPR technique

1-3/12/2018	First international summit on human gene editing

UN Involvement

The **Universal Declaration on the Human Genome and Human Rights** is a document that was issued by the United Nations Educational, Scientific and Cultural Organization (UNESCO) at its 29th session in 1997. It was unanimously passed by the seventy-seven national delegations in attendance. Link: (might be good to briefly look through)

http://portal.unesco.org/en/ev.php-URL_ID=13177&URL_DO=DO_TOPIC&URL_SECTION=201.html

Relevant UN Treaties and Events

- Universal Declaration on the Human Genome and Human Rights (1997)
- Report of the International Bioethics Committee (IBC) on Updating its Reflection on the Human Genome and Human Rights (2015)

Previous Attempts to solve the Issue / possible solutions

An international summit on human gene editing took place December 1-3, 2015, in Washington, D.C. Co-hosted with the Chinese Academy of Sciences and the U.K.'s Royal Society, the summit convened experts from around the world to discuss the scientific, ethical, and governance issues associated with human gene-editing research.

After three days of thoughtful discussion of these issues, the members of the Organizing Committee for the International Summit on Human Gene Editing have reached the following conclusions:

1. Basic and Preclinical Research

Intensive basic and preclinical research is clearly needed and should proceed, subject to appropriate legal and ethical rules and oversight, on

(i) technologies for editing genetic sequences in human cells,

(ii) the potential benefits and risks of proposed clinical uses, and

(iii) understanding the biology of human embryos and germline cells. If, in the process of research, early human embryos or germline cells undergo gene editing, the modified cells should not be used to establish a pregnancy.

2. Clinical Use*: Somatic

Many promising and valuable clinical applications of gene editing are directed at altering genetic sequences only in somatic cells – that is, cells whose genomes are not transmitted to the next generation. Examples that have been proposed include editing genes for sickle-cell anemia in blood cells or for improving the ability of immune cells to target cancer. There is a need to understand the risks, such as inaccurate editing, and the potential benefits of each proposed genetic modification. Because proposed clinical uses are intended to affect only the individual who receives them, they can be appropriately and rigorously evaluated within existing and evolving regulatory frameworks for gene therapy, and regulators can weigh risks and potential benefits in approving clinical trials and therapies.

3. Clinical Use: Germline

Gene editing might also be used, in principle, to make genetic alterations in gametes or embryos, which will be carried by all of the cells of a resulting child and will be passed on to subsequent generations as part of the human gene pool. Examples that have been proposed range from avoidance of severe inherited diseases to 'enhancement' of human capabilities. Such modifications of human genomes might include the introduction of naturally occurring variants or totally novel genetic changes thought to be beneficial.

Germline editing poses many important issues, including:

(i) the risks of inaccurate editing (such as off-target mutations) and incomplete editing of the cells of early-stage embryos (mosaicism);

(ii) the difficulty of predicting harmful effects that genetic changes may have under the wide range of circumstances experienced by the human population, including interactions with other genetic variants and with the environment;

(iii) the obligation to consider implications for both the individual and the future generations who will carry the genetic alterations;

(iv) the fact that, once introduced into the human population, genetic alterations would be difficult to remove and would not remain within any single community or country;

(v) the possibility that permanent genetic 'enhancements' to subsets of the population could exacerbate social inequities or be used coercively; and

(vi) the moral and ethical considerations in purposefully altering human evolution using this technology.

It would be irresponsible to proceed with any clinical use of germline editing unless and until

(i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of risks, potential benefits, and alternatives, and

(ii) there is broad societal consensus about the appropriateness of the proposed application. Moreover, any clinical use should proceed only under appropriate regulatory oversight. At present, these criteria have not been met for any proposed clinical use: the safety issues have not yet been adequately explored; the cases of most compelling benefit are limited; and many nations have legislative or regulatory bans on germline modification. However, as scientific knowledge advances and societal views evolve, the clinical use of germline editing should be revisited on a regular basis.

4. Need for an Ongoing Forum

While each nation ultimately has the authority to regulate activities under its jurisdiction, the human genome is shared among all nations. The international community should strive to establish norms concerning acceptable uses of human germline editing and to harmonize regulations, in order to discourage unacceptable activities while advancing human health and welfare.

We therefore call upon the national academies that co-hosted the summit – the U.S. National Academy of Sciences and U.S. National Academy of Medicine; the Royal Society; and the Chinese Academy of Sciences – to take the lead in creating an ongoing international forum to discuss potential clinical uses of gene editing; help inform decisions by national policymakers and others; formulate recommendations and guidelines; and promote coordination among nations.

The forum should be inclusive among nations and engage a wide range of perspectives and expertise – including from biomedical scientists, social scientists, ethicists, health care providers, patients and their families, people with disabilities, policymakers, regulators, research funders, faith leaders, public interest advocates, industry representatives, and members of the general public.

* “Clinical use” includes both clinical research and therapy.

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