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Ethical Considerations in Human Gene Editing

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ABSTRACT

The rapid advancements in human gene editing, particularly with CRISPR technology, have sparked significant ethical debates. This paper explores the ethical implications of human gene editing, from historical context to current regulatory landscapes. It delves into the concerns surrounding therapeutic versus enhancement purposes, the potential for unforeseen genetic consequences, and the balance between individual autonomy and societal impacts. The discussion includes an overview of various ethical frameworks, international guidelines, and the need for a comprehensive regulatory approach to address the ethical, social, and legal challenges posed by this transformative technology.

Keywords: Human gene editing, CRISPR technology, Bioethics, Genetic modification, Germline editing.

INTRODUCTION

The excitement leading up to the revelation of the first cell-edited human embryos was palpable. Researchers and bioethicists around the world seemed irresistibly drawn to comment. Many were excited for the prospect of removing inherited gene mutations from an embryo in order to prevent future suffering and disease of an individual's descendants. Some forecasted a new era of access, focused on bringing the technology to more people around the globe, more concerned about the implications. Others worried that we were opening a Pandora's box that we might not be able to control. The academic and lay literatures in China expressed both exhilaration and worry. And while the regulatory environment was more supportive of human embryo editing in China than in the US or Europe, for example, the work was not widely celebrated in China. Indeed, most Chinese observers questioned the ethics of the work [1].

DEFINITION AND TECHNIQUES

Notably, human genetic manipulation is much more technically involved and much less developed as a technology than most popular discussions would have it. The present generation of techniques involves several steps: one or more cells are taken from the body of the person who is to be subjected to genetic manipulation; a segment of DNA big enough to include the gene to be manipulated is isolated from the cell and spliced onto another piece of DNA, forming what is called a chimeric DNA molecule; one end of the chimeric DNA is then made somewhat sticky so that it will tend to stick to a corresponding site in the chromosome; finally, the spliced chromosome is allowed to recombine into the cell so that the altered gene replaces the original [4, 5]. Some of these techniques, especially the cloning of the genomes of laboratory animals, are well-established. All of them, taken together with other recent research findings, are now in use in medical research involving humans. Most of them, as we will see in the next two chapters, are assumed by their practitioners to be ready for use in humans in treatment, and some of them for use in reproduction. It is thus possible, in this survey of the topic, we will sometimes, for the reader's convenience, refer to the use of the present generation of genetic manipulation techniques for treatment and use a similar phrase for the parallel use of a somewhat more advanced generation in reproduction. When, in the next two chapters, we discuss explicitly the use of manipulative techniques for these purposes, however, we will seek to confine our discussion to those which are cognitively possible with presently understood abilities to rearrange human DNA according to scientific criteria that are recognized today by well-informed medical researchers [6].

HISTORICAL CONTEXT

The topic of modifying human genomes has been the subject of contemplation for centuries. Examples of individuals or groups that were defined as different or deviant in some way have historically attracted efforts to 'correct' or modify the underlying biological cause. This has taken many forms with the clear objective of attempting to somehow fix the cause of this condition directly. Spilling of blood and the ingestion of blood products has been particularly scrutinized as having biological consequences that are associated with these activities. The storing, transfusing or altering blood in the course of these activities has individual as well as societal and religious implications. The use of ethically obtained and utilized sources of heme protein could facilitate successful use of gene editing techniques [7]. In the past, blood obtained from individuals belonging to the cohort defined as 'carriers' for a transmissible virus was not utilized. Today this approach is not only ethically and scientifically unacceptable, but also practically impossible since a test protective against any originating 'viral threat' is not necessary. It is in the interests of use and of society to do everything possible to prevent newly discovered 'viral threats' from arising. Achieving this objective could facilitate safe use of chimeric proteins used in gene therapy to restore a heme deficiency or to cure the existing disease associated with this genetic disease. During this time, the risk associated with attempting to use gene therapy has undergone a rebirth. However, the potential to develop gene therapy holds the promise exclusively for some individuals with heme-related diseases [8].

MILESTONES IN GENE EDITING

Humans have manipulated genomes for thousands of years, but the advent of gene editing technologies now facilitates this with unprecedented precision and efficacy. In the following sections, we present a brief historic timeline of gene editing technology breakthroughs, and a terse description of each [9, 10].

MILESTONES IN GENE EDITING

Gene editing, or genome editing, refers to modifying a gene of a host organism, either by insertion, deletion and/or replacement. This produces permanent changes. Humans have manipulated genomes for thousands of years, through selective breeding and genetic crossing of various organisms, starting with the domestication of animals and the domestication of plants. The actual understanding of how genetic information is organized and transmitted started with Gregor Mendel, the monk scientist, with his experiments on pea plants at the end of the 19th century. The following landmark demonstrates how humans have developed tools and knowledge to manipulate the genetic material of living organisms [11].

ETHICAL FRAMEWORKS IN BIOETHICS

A diversity of questions has been raised about the ethics of editing the genomes of human beings and other organisms. What are the ethical questions and how can they be addressed? When considering how to regulate gene editing, what is the most ethical way to proceed? Systems of ethics provide guidelines for current and emerging human activities, and conventional bioethics principles notably include the principles of autonomy, beneficence, non-maleficence, and justice. These principles may be used to consider the ethics of human gene editing, but these are not the only bioethics principles that could be applied. There are some ethical frameworks in bioethics, each with its own distinctive goals [12]. Some scholars work within these multiple frameworks either separately or within one general framework. Autonomy refers to the right and capacity for those affected by a decision to make their own decisions based on choices for their own lives. In a framework that emphasizes the principles of non-maleficence and beneficence, the central concern is promoting good outcomes and avoiding or minimizing harm. The principle of justice raises issues related to the fair distribution of the costs and benefits of experimental research, as well as to the question of who gets to have the right to make decisions about future genome editing developments. There are concerns about an imbalance between the positive utilities to one individual or family and negative impacts on some global population, which can give way to psychosocial and emotional pressures not adequately considered. This imbalance could also affect the capacity of society to endorse the trans-generational modification, thus empowering society to pressure families to modify their inheritable traits to meet certain societal drafts, putting at risk the principles of individual and parental choice [13].

PRINCIPLISM APPROACH

This theory, developed by Beauchamp and Childress, is based on four principles: autonomy, nonmaleficence, beneficence, and justice. Autonomy is considered by these authors as an essential principle. It requires respect for the decisions of the person who opts for treatment. The person must act with the capacity to choose, putting into play the competences that define him as a subject; the decision

corresponds to the person who desires the end, making an autonomous election. Nonmaleficence refers to the duty not to harm the patient, to avoid causing damage or at least to demand that the professional does not cause any harm to the patient, especially since the main purpose of performing any act is to prevent any harm. Risks and benefits must have been evaluated before the act and its omission. The principle is established by the Hippocratic precept "Do no harm." Non-maleficence can be exercised in such a way that the professional cannot be involved, witnessing acts of torture or war. The health professional must not abandon the vigilance over those indirect causes that generate damages in the individual; diseases and other damages coming from society are called "structural violence," or total violence, because they have the same effect beneficence. Its purpose is for the patient to avoid the greatest possible number of damages to exercise respect for being capable of determining their balance between damages and benefits. Since he will always respect the trust placed in him and will act in a positive way, suggesting different options for the patient who exercises competence that guarantees welfare and which benefits outweigh the risks. The acceptance of beneficence can be extended to make contributions to the practice of social assistance, which is why the health professional can embrace the commitment. Harming refers to the Hippocratic tradition "Help where needed." The procedure to be performed is known as malfeasance, actions, practices that only favor those who commit them, avoiding responsibilities toward who it is referred to. These distortions in practice generate benefits and difficulties for other professionals, to have the vocation of helping others or to be exonerated with nullities. These professionals, stripped of the principles from the profession when transferring them into the social context, contribute to being a product of an incomplete contract. The principle refers to truthfulness in natural communication. The truth was seen by the ancient Greeks as a guarantor of social relations. They needed face-to-face dialogue to guarantee the truth of communication. They required that the subject to which the truth referred needed to be certain that the elements would be kept in order by its interlocutor, that it would keep watches, to watch over and assure to become the watchman to the truth [14, 15].

CURRENT DEBATES IN HUMAN GENE EDITING

By the early 2000s, society became embroiled in debates about a widening range of genetic technologies that allow for laboratory methods of biomedically relevant gene modification (or gene editing). Four general classes of gene editing technologies have been described by genetics research expert and scholar of public policy on heritable genome editing, John Harris (2004): (1) technologies that allow the insertion of heterologous genes into the genome and are used for the introduction of genes or the sustained expression of proteins not usually present in an individual's genome; (2) technologies that allow the targeted insertion into the genome of a gene that mediates therapeutic effects; (3) technologies that allow the targeted insertion into the genome of a gene that mediates enhancement effects; and (4) technologies that allow the targeted alteration of the existing genes at specific locations within the genome without the controlled introduction of genes from the outside. The third and fourth classes allow avoidance of the creation of a genetically distinct child [16]. Scientific interest in human heritable gene editing resurged after the demonstration of the ease and efficiency of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) and CRISPR-associated (Cas) systems as a genome editing tool in 2012. These and other lab methods are types of gene editing technology that allow potential germline modification. Molecular biologists quickly advanced advances from helping modify non-germline cells, or somatic cells, to general conclusions about possibly making human babies safer, better, or otherwise more to expected parental desires. Technologies have the potential to rescue some single gene mutations and monogenic conditions, but many cultures believe that usage of these technologies are morally unacceptable. Additionally, considerable research and genome manipulation experimentation would be necessitated for safe and efficacious treatments. Yet some individuals are interested in in vitro or in vivo human gene editing despite such observed non-consenting human subjects research risks, especially when the objective is to create a family [17].

THERAPEUTIC VS. ENHANCEMENTS

One of the fundamental ethical issues surrounding human genetic engineering is its ability to be used for non-medical purposes. One of the characteristics of human genetic engineering is the ability to distinguish between gene therapy - which amends a genetic defect - and enhancement, which goes beyond what would be required to treat a genetic condition. However, many scientists agree that there is no clear boundary between when a genetic modification is deemed therapeutic and when it is deemed enhancement. In fact, it is no longer possible to clearly define "genetic modification" separate from "enhancement". The future progress of new genetic understanding and tools requires a wider and more

comprehensive regulatory scheme. Pre-emptive testing is required for safety and efficacy for germline genetic modification only when a prospective application is gain-of-function enhancement in normal healthy humans. This is necessary to maintain public trust in applications for serious disease, and to enable the National Institutes of Health (NIH), World Health Organization (WHO), or Congress and international organizations to avoid the pressure to intervene or regulate currently planned long-term safety surveillance studies [18]. For the current state of deliberation on human germline genetic modification, this is proposed by shifting the focus to prevention in the current phase of scientific knowledge. The kind of regulatory scheme suggested here will manipulate and enhance elements in human DNA at their basic evolutionary nature. Public trust, political legitimacy, and therefore the ability to protect disease-gene editing and other precautionary measures will even out the prospect of human disease-free prosperity from the healthy. Important to appreciate this domain is that the NIH will not be scientifically delayed before research can be started. The help of the learned scientific community can bring about change in the issues of debate and in the attitudes of the broader public, collective police, and any official regulatory body. It is essential to restrict benefits to public health, promote scientific inquiry, and avoid greater pain by continuing to appreciate the ethical considerations that apply to the use of germline gene editing and enhancement [19].

REGULATORY LANDSCAPE

The rapid progress in gene editing technology and its application in humans calls for appropriate regulatory responses. A number of national and international bodies have already considered human germline genome editing and called for a temporary ban or prohibition of the use of gene editing technologies to alter the human germline. There is recognition that CRISPR, like any new medical technology, needs careful use to minimize safety, ethical, and regulatory risks. With technological improvements and growing commercial interest and activity in CRISPR, there is a need for an international framework of rules and conditions for CRISPR. International agreement is needed on creating global norms and standards for conducting research on and overseeing clinical applications of gene editing technologies [20]. A wide range of regulatory and policy issues need to be addressed with the advent of CRISPR. Current regulatory and policy frameworks at national, European, and global are not fully prepared to meet the emerging social, environmental, ethical, and legal implications of these technologies, in particular around human applications. It is important that countries that have laws pre-dating CRISPR or European laws for which companies currently working on CRISPR are not established comply with them. Any regulatory framework should facilitate innovative products for use in the clinic as well as in other sectors. It is important to have regulation and harmonization that properly manages any potential risks in use of gene editing in humans [21].

INTERNATIONAL GUIDELINES

Human genome editing, particularly germline editing, is now widely considered to be a fundamental moral concern in global bioethics. In this chapter, I will consider some key international guidelines on human gene editing. International guidelines typically allow for some limited forms of gene editing research and clinical application, but they also commonly agree that such research and clinical applications are not currently justified given technical and social limitations [22]. These international guidelines, which usually draw upon international conventions and United Nations reports, usually are not implemented as "hard" law. The United States is more permissive than the international consensus, and its National Academy of Sciences guidelines allow for germline modifications in certain cases. The guidelines in the United Kingdom will likely relax its previous ban on human germline editing research and clinic applications [23]. With the controversial and now seemingly done existence of two living humans having undergone CRISPR-ed germline editing, the demands for ethical governance became louder. Legal inquiry, as it frequently does with emerging technologies, commonly looks to legal devices such as guidelines, statutes, regulations, and judicial rulings to help broker ethnoracial, medical, and legal disputes concerning the permissibilities and isobarisms of human gene editing [24]. While such methods have much to contribute in shaping and guiding thought, practice, and doctrine, they frequently start off at the wrong place with respect to substance. International guidelines, in sharp contrast to conventional legal devices, usually articulate or channel ethics far more often than they are used to regulate or impose restrictions. Hard Law (enforceable, rule-based, governmental laws and regulations) and soft law (nonbinding but persuasive guidelines, principles, and standards) serve complementary but different purposes [25]. Soft law is grounded in the idea that general and vague moral judgments can be codified and deployed to help order human interaction. Such codes have become crucial regulators of global

activities and common standards of behavior. They have been devised in a wide assortment of contexts [26].

CONCLUSION

Human gene editing, while holding immense potential for treating genetic disorders, raises profound ethical questions that require careful consideration. The distinction between therapeutic and enhancement purposes is blurred, necessitating robust ethical guidelines and regulatory frameworks. The international community must collaborate to establish standards that protect individual rights and public welfare while fostering scientific progress. Ethical frameworks such as principlism provide a foundation for evaluating these technologies, emphasizing the principles of autonomy, beneficence, non-maleficence, and justice. As we move forward, it is crucial to balance the benefits of gene editing with the potential risks and moral dilemmas it presents.

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