



Bioethics and Human Rights: The Genomic Editing Technique Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR-CAS9) and the Contemporary Biotechnological Challenges

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Abstract

This article deals with biotechnological advances, especially in the field of editing and genetic engineering. In contemporary times, the possibility of manipulating the human genetic heritage and creating perfect organisms is no longer a simple theoretical hypothesis, notably from the development of the genomic editing technique Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR-CAS9), a system created from immunological mechanisms of bacteria that allows the modification of the human genome. In this sense, supported by the matrix of global bioethics, it aims to investigate the immediate and mediate implications of human genetic editing in the contemporary world, through an exploratory methodology and literature review, highlighting divergent positions in Brazil and abroad. In the end, it is possible to conclude that the establishment of limits to biotechnological advances is a measure that is imposed, in respect of the determining border between techno science's and human rights, not disregarding, however, the benefits of biotechnology, but considering ethical, legal, humanitarian and social criteria.

Keywords: Bioethics; Human Rights; Genomic Editing; CRISPR-CAS9; Eugenics

Abbreviations: RNA: Ribonucleic Acids; DNA: Deoxyribonucleic Acid; SciELO: Scientific Electronic Library Online; UNESCO: United Nations Educational Scientific and Cultural Organization.

Introduction

The social impacts of new biotechnological technologies raise questions about ethical and moral customs, especially those that encompass themes related to fundamental rights

and guarantees, human dignity, life and death, segregating divergent positions on the subject [1].

An example is the various genetic editing techniques, which impact and divide social thought, stimulating international debates [2]. Among them, the genomic editing technique Clustered Regularly Interspaced Short Palindromic Repeat (CRISPR-CAS9) has been gaining prominence, with exponential development since 2012, through the research of geneticists Jennifer Doudna and Emmanuelle Charpentier

, expanding the horizons of editing the human genome and generating new ethical dilemmas around the production of perfect organisms [3], presenting itself as a “fast, direct and low-cost technique, accessible to the vast majority of laboratories” [4].

The system created from the immunological mechanisms of bacteria, its ability to cleave the DNA molecule by means of an endonuclease (Cas9), controlled by a paired sequence of ribonucleic acids (RNA), in the target regions has been proven. Due to this ability, the system is applied to regions in the DNA of cells of different origins, to promote cleavage in the double-stranded target sequences. In response to sequence interruption, the cellular machinery repairs the cleavage, even with the alteration made, thus accepting the modification of the human genome.

This method of genetic manipulation consists of the insertion, removal or replacement of deoxyribonucleic acid (DNA) in the genome of the organism by means of enzymes that “cut” the bonds of the molecule, the nucleases. The cut occurs in certain regions of the genome, where the breakage of the double strand of DNA occurs, however, the strands can be repaired through homologous or non-homologous union mechanisms, even after loss of nucleotides, which make up the molecule [5].

Given these premises, it appears that the research problem aims to ask to what extent the new biotechnological advances fulfill the promises of human genetic engineering and what are the consequences for human beings, as beings with rights and dignity? In this sense, the present investigation has the scope to raise ethical questions about the social impacts that genetic editing can cause, highlighting the opposing and favorable positions of theorists and experts on the subject in Brazil and abroad.

In fact, based on the matrix of global bioethics, it intends to investigate the immediate and mediate implications of genetic editing in the contemporary world, through an exploratory methodology and a bibliographic review, both physical and online, in which the research was carried out in databases, such as Google Scholar and Scientific Electronic Library Online (SciELO), using determining keywords, for example, gene editing, CRISPR-CAS9, bioethics and human rights.

For last, the research resulted in the finding of divergent positions regarding the application of genetic editing, also pointing out that the inconsistencies outlined regarding the application of the CRISPR-CAS9 technique, lead us to a general understanding, which evidence the establishment of limits to biotechnological advances, with respect to the decisive boundary between technosciences and human rights, not

disregarding, however, the benefits of biotechnology, but considering ethical, legal, humanitarian and social criteria. Conferring them, due to these researches, the 2020 Nobel Prize in Chemistry, Dominguez [6].

Manipulation of Genetic Heritage and the Fourth Generation of Rights

Questions concerning new technologies, aimed at editing and genetic engineering, have already been demonstrated as an object of studies or theoretical hypotheses for some time. Norberto Bobbio raised the theme in his work “The era of rights”, published in 1990, dealing with the forms of protection of the interests of societies, but, in addition to the contemporary concept of society, protection of the interests of humanity.

In this sense, Bobbio teachings alluded to the moment of each historical period experienced by humanity, each with its specific questions and practical implications. It even states that “new needs are born as a result of changing social conditions and when technical development makes it possible to satisfy them” [7].

This understanding synthesizes the thesis of the “generation of rights”, presupposing the idea of coexistence of the fundamental rights of being, insofar as they are postulated, or “dimensions of rights”, which in the view of many theorists refers to the overlapping of human rights, gradually, according to the need for implementation. However, this discussion is only for terminological and theoretical purposes, not being the objective of the present work.

Initially, the existence of 3 phases of fundamental human rights was considered: “the development of human rights went through three phases” [7]. He considered, therefore, that the first generation (Negative rights - freedom) was about the rights concerning freedom, which assumed a non-imposing and absolutist form of the State, that is, freedom was the objective of an idealized society, with respect to the human freedom.

In the second generation of rights (Positive rights - equality), the objective was positive action by the State, aiming at the realization of social rights. In this way, the aim was to protect the interests of the community, which results in the concepts of people, society and nation, giving effectiveness to the State’s action to ensure the population’s right to equality.

In the third-generation rights (Diffuse and collective rights - fraternity and solidarity), he came to the understanding of maintaining an unpolluted environment, concluding that

it is a right of humanity - present and future generations - not to live in a polluted environment, but in a harmonious environment, where the protection of the historical-cultural heritage of humanity and the sustainability of lives prevails.

Therefore, it ends its hypothesis raising the question about the fourth generation, which is related to biotechnology and genetic manipulation, considering:

But there are already new requirements that could only be called fourth-generation rights, referring to the increasingly traumatic effects of biological research, which will allow manipulation of the genetic heritage of each individual. What are the limits of this possible (and increasingly certain in the future) manipulation? One more proof, if that were still necessary, that rights are not born all at once. They are born when they should or can be born [7].

Indeed, it is evident that the fourth generation presupposes the right to democracy, equality and genetic pluralism of humanity, presenting a previous concern regarding the need to implement norms that control the effects of biotechnological research. Oliveira ponders that “through this generation, the legal foundations of technological advances and their constitutional limits are determined” [8]. It is noted, therefore, that the social implications caused by genetic and biotechnological research deserve a critical, conscious and plural view, since these studies can raise several questions and implications, positive or negative.

In Brazil there is express protection related to Human Rights and Biotechnology. The genetic material of human beings is expressly protected by the Brazilian Federal Constitution of 1988, and in the same way, understood as an inherent part of human dignity (article 1^o, III, of the Federal Constitution). For example, the provisions of art. 225, § 1^o, II, of CF/88 [9]; in art. 2, III, IV, VI, VII e VIII, of the Universal Declaration on Bioethics and Human Rights [10], adopted by acclamation on 19 October 2005 by the 33rd session of the UNESCO general conference; as well as in article 10, of the Universal Declaration on the Human Genome and Human Rights [11], approved on November 11, 1997, to which many countries are signatories, including Brazil, establishing ethical limits in relation to the intervention of heritage human genetics.

In fact, the aforementioned legislation and guidelines in force have similar aspects, namely, the protection of the Dignity of the Human Person, which reflects in the protection of the human genetic heritage, as well as the maintenance of the diversity of the genetic material, in order to avoid that, by for example, there is a conflict of interests between the liberality of parents' choice, that is, the voluntary

manipulation of the genetic material of the being, and the maintenance of biodiversity and its consequent conservation, as a common concern in favor of the interests of humanity.

Biotechnological Development: Ethical and Social Impacts

It is understood that scientific and technological development, especially the great and overwhelming advances in molecular biology and biotechnology applied to medicine that have taken place in the last 30 years [12], directly impact people's lives as human beings. That coexist in societies and that have different perceptions about different subjects and facts in the contemporary world.

It is no different with the life sciences, while all scientific discoveries, which advance simultaneously with society, have the specific purpose of generating effects on human life, either by immediate contributions, for example, the cure of diseases, congenital or no, as well as prevention, through a previous diagnosis that points to a pathology and, thus, there is treatment in a timely manner, aiming, in both cases, for well-being, health, and physiological stability of the being.

However, in addition to the immediate benefits provided by these advances, on several occasions, there is a scientific claim of an evolutionary nature that, in general terms, reflects the idea of dominion over life.

This fact can be verified by observing the manifestations of International Councils, for example, the United Nations Educational Scientific and Cultural Organization (UNESCO), concerning the topic of genetic engineering; reports of abuse against human beings, conditioned to inappropriate experiences, in order to “test their ability”; the absence of regulatory force to lead to ideal and ethical medical and scientific conduct; highly fatal and unknown hazards that could occur from incorrect medical application; as well as interventions in the legal-social scope on issues related to consolidated fundamental rights and guarantees, referring to death, reproduction, health and life [11,13,14].

Therefore, the need to launch a new critical perspective on the practical issues provided by new technologies, in relation to human genetic material, is evident, considering that, as pondered by Bobbio, the absence of regulatory guidelines, regarding the practices of techniques of bioengineering, can raise ethical, moral and social problems, until then, not considered by man.

In fact, new theoretical and practical studies emerged that, according to the need and evolution, were spreading the questions and answers about the effective manifestation of biotechnological practices in society, in view of the need to regulate something unknown, which, automatically,

conferred unlimited powers on its creators and enforcers.

The Impacts of Human Genetic Engineering on Society on the Light of Bioethics and Biolaw

Faced with the need to impose limits, especially legal ones, able to regulate the application of genetic engineering in society, theoretical studies such as bioethics and biolaw emerge as a way of questioning the applicability without limits of technosciences and biotechnologies, thus promoting a broad debate about concepts and practices raised in the field of bioengineering.

In this sense, the practical approach of the studies is related to life and the ways in which some type of injury can occur to it, in a particular or plural way. It is understood, therefore, that when dealing with life, it refers in a broad sense, that is, humanity. In Diniz's conception, "biolaw, a legal study that, taking bioethics and biogenetics as immediate sources, would have life as its main object" [15].

Concerning the Concept of Biolaw, Maluf Provides:

Biolaw is mainly associated with the universe of five subjects: Bioethics, Civil Law, Criminal Law, Environmental Law and Constitutional Law (in the light of article 5, item IX, of the Federal Constitution of 1988, which proclaims the freedom of scientific activity as a one of the fundamental rights, without, however, failing to penalize any dangerous act (malpractice) in the doctor-patient relationship and the scientist's malpractice, taking into account conflicting issues such as abortion, euthanasia, assisted suicide, artificial insemination, organ transplantation, GMOs and therapeutic cloning and scientific) [16].

It is inferred from the brief concepts that studies in the field of Biolaw cover every phenomenon in an objective way and legal practice, with the aim of tracing the decisive frontier between the conscious application of genetic editing in contemporary society, without, however, overcoming the ethical barriers that involving human dignity, the diversity of human genetic material, personality rights, etc.

Therefore, Biolaw studies serve us as a source of appreciation and projection of a critical look at something that presents itself in such a beneficial way in society, but that if carried out in a negligent way and only of a scientific nature, can cause adverse effects to the objectives. Origin, physiological and social well-being. Furthermore, at the Brazilian level, Barboza asserts that: there is no chapter in our Constitution dedicated or pertinent to Bioethics or Biolaw. In fact, all constitutional provisions relating to human life, its preservation and quality are intertwined with Biolaw, which is not restricted to issues related to health, the environment

or technology [17].

Finally, it is possible to assert that the collaborative and interdisciplinary practice of studies related to biotechnological matters for the enactment of new laws, has the purpose of protecting the interests of humanity in the face of the unknown. Thus, the studies of Biolaw are also presented as a way to reach the best results regarding the practical technoscientific applications, in attention to the basic principles of Human Rights.

Genetic Discoveries and the Dangers of Universal and Particular Eugenics

Genetic discoveries arise for humanity and are perceived, originally, as the best way to solve problems considered, until then, as incurable, irremediable and incurable. However, the development of these discoveries and diffuse interests to the original objectives had opposite effects, raising questions that permeated the mere application in favor of social well-being.

In "The Case Against perfection: ethics in the age of genetic engineering", Michael Sandel states that these findings presented themselves, at the same time, as a promise and a dilemma, in a way that, "[...] capable of treating and preventing a range of debilitating diseases. The dilemma is that our newly discovered genetic knowledge may also allow for the manipulation of our own nature" [18].

In all his work, Sandel uses questions to encourage debate, asking the reader with questions of an ethical and moral nature, but also points out some answers about what is considered a dilemma, such as stating that "the moral dilemma arises when people use such therapies not to cure a disease, but to go beyond health, to improve their physical or cognitive abilities, to rise above the general norm [18].

Based on this understanding, the author deals with Eugenics, approaching its different concepts and, also, discussing its creation and its temporal cut, which gave rise to the understanding of "old eugenics", also considered as universal eugenics and the "new eugenics", when referring to the contemporary idea of designer parents, which also addresses as private eugenics or liberal eugenics.

The concept of eugenics is based on the ambition to improve the human race. Created from the term "well-born", originated by Francis Galton, in 1883, inspired by the revolutionary studies of his cousin, Charles Darwin, leading him to develop statistical studies, based on heredity. Considering that it would be possible to reproduce an overly talented race of humans, through careful marriages over

several consecutive generations [18].

Consequently, the idea of eugenics spread throughout the United States at the beginning of the 20th century, however, with the objective of coercively sterilizing all people considered to be unqualified, namely, field workers, prisoners, occupants of hospitals and asylums, among others. This intention aimed at not reproducing individuals considered deficient or outside the parameters considered ideal [19].

Thus, positive eugenics was defined as any action that implied the reproduction of healthy humans or the improvement of physical or mental aspects, and negative eugenics was defined as any action that limited the reproduction of people with genetic diseases, considered as poor reproduction [18]. The movement had repercussions, constituting adepts who welcomed the ideals and even demanded from the State laws that regulate the compulsory sterilization of people with undesirable genes, an opportunity in which more than 60 thousand people were coercively sterilized in 1907, in the state of Indiana, United States [19].

In Germany, the eugenic idea manifested itself from nationalist and racial supremacy. In the spotlight, Hitler, a Nazi admirer who faithfully followed eugenics plans of identification, segregation, forced sterilization, euthanasia and mass extermination of those considered impure in the face of established and idealized racial parameters [10]. Indeed, after the whole scenario of mass murders and genocide that took place in the Second World War, the American eugenics movements had a strong retreat. However, some states in the country still practiced eugenic practices around 1970, while only in 2002 and 2003 governors of some states proceeded with formal public apologies to victims of coercive sterilizations promoted by the state [19].

Therefore, it is possible to identify that, according to its origin, eugenics directs the focus on a group of individuals considered superior who, thus, keep their characteristics saved in heredity. While those considered inferior are interrupted from continuing their genetic peculiarities [20-22].

Continuing his study, Sandel reproduces the questioning about eugenic practices in contemporary times and their consequences in a particular scope, according to the liberality of parents, for example, proceeding with the following questions: "Is eugenics objectionable only when coercive? Or is there something wrong with even non-coercive ways of controlling the genetic load of the next generation?" [19].

In this way, it encourages questioning by bringing positions of theorists of paramount importance to social-

philosophical issues, for example, philosophers Ronald Dworkin, Robert Nozick and John Rawls, emphasizing that both present arguments in favor of the exercise of liberal eugenics, as long as it is based on respecting the rights of the personality of the future human being; in the non-coercive and excluding character of the State, as occurred by the eugenicist movements at the beginning of the 20th century. XX; and a supposed genetic improvement, naturalized from the genetic combinations carried out over time.

However, the author asserts that "it is not a social reform movement, but a way for privileged parents to have the kind of children they want and arm them for success in a competitive society" [19]. In a demonstration of controversy on the subject, it also highlights the opinion of the German political philosopher Jurgen Habermas, who demonstrates arguments against the practice of eugenics, even though it is of a liberal nature by the parents, arguing that the exercise of this practice would imply a violation of the principles of autonomy and equality, resulting in the domination of parents over their children, especially and genetically designed.

Although it does not harm the child or reduce its autonomy, eugenics perpetrated by the parents is objectionable because it expresses and establishes a certain attitude towards the world - an attitude of domination, which does not value the gift character of human powers and achievements and disregards that part of the world. Freedom that consists of a persistent negotiation with what is given to us [19].

Sandel ends his thoughts alluding to the questions raised, in order to instigate individual perception towards the liberal and voluntary perspective of eugenics, aiming, in this case, at the manifestation of talent provided by genetic combinations.

Gene Editing: Disagreements about its Application

Bioethics is driven to transformation through advances in science. Discussions between jurists, scientists and moralists collaborate with the constitutionalization of issues related to the matter. And with that, several criteria, such as respect for the human being, profit and responsibility of the researcher, trigger measures of immediate laws, on the human body and its dignity [23].

Ethical and moralistic discussions in the scientific environment involving gene editing, including the CRISPR-CAS9 technique, are recurrent and constant. The positions are segregated in broad aspects about the limitations and applications of the technique in different contexts and human conditions.

Questions have been raised by some authors about the limits of gene editing and human rights, given the consequences of the technique. Addressing the permeability of dominance of man's nature over man, they came to the conclusion that the focus is not on the use or not of the technique, but how and to what extent it should be used [7].

This result can be evidenced in beneficial studies carried out with the technique in cardiovascular diseases, since most of the factors that contribute to the onset of these diseases come from genetic, environmental and behavioral factors [24]. Other examples can be found in improvements in cases of infectology, oncology and hematology, among others.

In contrast, recent studies with mice have shown failures in the selectivity of the target regions of the DNA that is, even causing the elimination of the region of the molecule responsible for triggering a certain disease, adverse effects still unknown may arise, due to mutations in unwanted regions of the sequence. Of DNA nucleotides, which may compromise the functioning of tissues, organs and, consequently, the body's systems [25].

In the book "The Case Against perfection", Sandel defends the current questioning of the impact of genetic improvement techniques on dominant and competitive parents, based on the premise of guiding their children towards the best possible development and well-being. Furthermore, it establishes relationships between these genetic alterations with possible new eugenics, or private/liberal eugenics [19].

However, when referring to the use of techniques requested by parents at the pre-implantation level, the focus, according to experts, is the expectation of the healthy birth of their offspring. And those approaching eugenics, in this context, is going too far as a justification for not using gene [26] 23.

In summary, researches admit the benefits of the technique, as a possible solution for the cure of genetic diseases in the embryonic stage and consider that the misuse can serve as an instrument for new eugenics, but conclude that dialogue would be the best alternative to the ethical control of the technique, instead of new legal and limiting restrictions.

Conclusion

Genetic editing has an evolutionary character, presenting itself as a technique of immediate effectiveness for the prevention and cure of congenital or not diseases. However, there is a risk of improper and risky applications, thus violating the "sacredness of life" and Human Rights. Studies carried out with human germ cells have already been authorized

in some countries, where alterations in the manifestations of the individual's genetic inheritance were carried out. For many scientists, this research has dangerously crossed the ethical line that controls biotechnological growth in the face of man's genetic manipulation.

Due to this, the need to weigh the benefits and adverse effects becomes even more relevant to favor or disadvantage the application of gene editing, not only taking into account biological effects, but considering a broad approach, including the ethical-social impact. That the decision can entail, respecting the individuality of the being and its dignity, therefore, requiring a specific analysis for its feasibility, in view of the clinical case.

The discovery of the technique stimulates theories and deductions about future impacts in a distant way, but advances in health technologies are fast, to the point of losing control of updates in the world. In the not-too-distant future, gene editing, provided by CRISPR-CAS9, for example, will make it possible to transform the human genome in a more efficient and qualified way, allowing both the extinction of hereditary diseases and the synthesis of babies designed by parents in their most diverse bodily or mental manifests [5].

Regarding CRISPR-CAS9, as well as gene editing in general, it provides positive and innovative probabilities when inserted in the context of combating genetic diseases and modifying the genomic content of human and other organisms. The technology is considered fast, direct and low cost, accessible to most laboratories. However, there are risks hitherto unknown, and the beneficial aspects related to this powerful technology demand accurate studies and debates about its social impacts, in order to enable a thorough analysis in scientific, ethical and social areas about this technique [26-30].

Finally, the issue developed studies and legal provisions in order to establish parameters and limits for the viability of gene editing techniques and, thus, present positions on how far the "life sciences" can advance, without any aggression to the human dignity.

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