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UPDATE

Gene editing: the risks and benefits of modifying human DNA

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Abstract

The article analyzes discussions on human genetic editing found in scientific articles, institutional statements and delivered at the *International Summit on Gene Editing* held in 2015. This analysis has the objective of to explaining and reflecting on arguments favorable and contrary to DNA modification. Gene editing techniques have benefits such as: the treatment of diseases; creation of model organisms for basic biomedical research; development of transgenic foods, among other applications. However, discussions have been held in order to determine the risks of this technology. The Interlocutors, in these discussions, assume divergent positions, condemning gene editing, praising it or recommending caution in the execution of experiments. The article critically analyzes scientific discourses around the theme, seeking to highlight the argumentative strategies present in the debates.
Keywords: Gene editing. Biotechnology. Bioethics. Containment of biohazards.

Resumo

Edição genética: riscos e benefícios da modificação do DNA humano

O artigo analisa discussões sobre edição genética humana encontradas em artigos científicos, declarações institucionais e proferidas no *International Summit on Gene Editing* realizado em 2015. Objetiva-se explicitar e refletir sobre argumentos favoráveis e contrários à modificação do DNA. A edição genética pode desenvolver novas terapêuticas, organismos-modelo para pesquisa biomédica de base e alimentos transgênicos, entre outras aplicações. Contudo, os debates buscam determinar os riscos dessa tecnologia, e seus interlocutores assumem posicionamentos divergentes, condenando a edição genética, enaltecendo-a ou recomendando cautela na execução de experimentos. O artigo analisa criticamente discursos científicos sobre o tema, buscando evidenciar as estratégias argumentativas presentes nos debates.
Palavras-chave: Edição de genes. Biotecnologia. Bioética. Contenção de riscos biológicos.

Resumen

Edición génica: riesgos y beneficios de la modificación del ADN humano

El artículo analiza debates sobre edición génica humana encontrados en artículos científicos, declaraciones institucionales y proferidas en el *International Summit on Gene Editing* realizado en 2015. Se tiene como objetivo explicitar y reflexionar sobre los argumentos favorables y contrarios a la modificación del ADN. La edición génica puede desarrollar nuevos tratamientos, organismos-modelo para la investigación biomédica de base y alimentos transgénicos, entre otras aplicaciones. No obstante, los debates buscan determinar los riesgos de esta tecnología, y sus interlocutores asumen posiciones divergentes, condenando la edición génica, enalteciéndola o recomendando cautela en la ejecución de experimentos. El artículo analiza críticamente los discursos científicos en torno al tema, buscando evidenciar las estrategias argumentativas presentes en los debates.
Palabras clave: Edición génica. Biotecnología. Bioética. Contención de riesgos biológicos.

Declara não haver conflito de interesse.

In April 2015, Chinese researchers led by Junjiu Huang of the Sun Yat-sen University conducted a study that was innovative, yet controversial. The study consisted of an experiment on gene-editing human embryos to repair mutations in the HBB gene, which is the encoder of the beta-globin protein [1]. Hemoglobin is composed of this protein, and the mutation in its gene is related to the beta thalassemia disease.

Gene editing is a procedure in which specific segments of DNA are deleted, which enables their replacement by new gene sequences [2]. The term "editing" refers to the metaphor of producing a text, in which letters are erased and then rewritten. The DNA of all kinds of living creatures can be edited for different purposes: to treat diseases, to create transgenic foods, to improve human non-pathological characteristics, among others.

More recently, in August 2017, a similar experiment was published by the journal *Nature*. Conducted at the Oregon Health & Science University by scientist Hong Ma and her team, the study aimed to repair MYBPC3 gene mutation in human embryos [3]. This variation is known to cause hypertrophic cardiomyopathy disorder, characterized by the thickening of the cardiac musculature.

However, research like this raises controversy over the acceptability and effects of human DNA manipulation. Debates have been established across the media and in the scientific literature problematizing the scientific, ethical, and social implications of this practice. While some authors condemn gene editing, others praise it recommending caution during future experiments.

Therefore, this article aims to analyze controversies regarding gene-editing human embryos, addressing arguments that are favorable and contrary to the procedure. The *corpus analysis* consists of discursive productions within the scientific community – such as articles, institutional reports, and conferences – published and held between 2015 and 2017. It is a theoretical study, based on the interpretation and analyzes of specialized bibliography.

Gene editing

Technical characteristics

The development of gene editing techniques started in the 1990s, representing, for some authors, a true revolution in the field of biotechnology [4]. The procedure received this named because it actually "deletes" specific segments of DNA and inserts new genes into the site – both germ and somatic cells can be edited [2]. In the case of germ cells (ovules and sperm) and precursor cells, genetic modifications are transmitted to the offspring. Some researchers also include embryos in the initial stage of formation under the same category. In turn, somatic cells refer to all other cells in the body. Modifications in these cells are not hereditary.

The editing process takes place during two main phases: first, DNA recognition and cleavage; and then, the repair phase of the molecule. Currently, there are four techniques, or editing tools, which consist of enzymes modified by human interference, namely: 1) meganucleases; 2) *zinc-finger nucleases*; 3) *transcription activator-like effector nucleases*; and 4) CRISPR-Cas9. Such tools have "recognition" devices that allow them to adhere to specific nucleotide sequences of the target DNA; and "cleavage" devices, which allow the nucleotides of the target DNA to be sectioned [2].

Once the nucleotides are sectioned, the so-called "*double-strand breaks*" [5] are generated, triggering endogenous mechanisms as a natural way of repairing DNA damage. The editing process uses these features to make the genetic modifications desired. There are two main repair processes, namely: *non-homologous end joining (NHEJ)*; and *homology-directed repair (HDR)* [5].

The NHEJ mechanism connects the ends of the cleaved segment of the DNA molecule and is considered useful when inactivating the gene action (*gene knockout*). The knockout of the gene that causes Huntington's disease, or the receptor encoding gene to which the HIV virus connects when invading the body's cells can be mentioned as examples.

The second mechanism (HDR) uses templates to regenerate double-stranded breaks. Scientists can insert external DNA templates into the cells along with editing tools. Such outer templates contain selected genes, which supply the matrix of the new DNA segment to be created at the cleavage site [5].

Applications

The development of editing techniques enables the modification of genomes of all sorts of living creatures. These techniques affect different areas such as disease management, basic biomedical research,

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agriculture and environmental sciences. They could also be used to customize human characteristics for extra-therapeutic enhancement purposes.

Among the benefits of editing designed to treat diseases is the enhancement of gene and cellular therapies. At least nine areas would benefit from the advances in these fields: 1) Infectiology; 2) oncology; 3) hematology; 4) hepatology; 5) neurology; 6) dermatology; 7) ophthalmology; 8) pneumology; and 9) organ transplantation [5].

In addition to clinical applications, gene editing make it possible to create isogenic and animal modified cell lines to be used in basic biomedical research. Isogenic cells have a specific and standardized genetic profile, whereas modified animals (known as "chimeras") have characteristics inherent to the human body. Thus, researchers have at their disposal experimental models of control that facilitate the generalization of empirical knowledge [2].

The gene that encodes the myostatin protein, which limits muscle growth, is among the several genes that can be edited. Once the action of a gene is inhibited, the mass of animals, such as pigs and cattle, can increase significantly, making them more attractive to consumers, which will certainly affect the transgenic food industry [6].

By intervening on the DNA of living beings, gene editing can also have macro-environmental effects. The optimization of the *gene drive* mechanism (genetic induction) [6] is an example of its systemic applications. Through the *gene drive* mechanism, genetically modified organisms are released into nature in order to disseminate a certain genetic variant, prevailing over the species already present in the environment.

Finally, advances in the field of life sciences improve not only the treatment of diseases, but also the enhancement of human capacities, such as cognition, physical performance, and longevity. In theory, editing techniques would enable gene manipulation so that cognitive and physical traits on demand could be passed onto individuals [7].

Controversies on gene editing

Although the practice of gene editing presents potential benefits to society, the experiment conducted by Junjiu Huang and colleagues caused great public commotion. By modifying the DNA of human germ cells, producing hereditary modifications that can be incorporated into the genetic repertoire of our species, the researchers crossed a limit that many believe should not be trespassed.

It is necessary to map out the controversies on human gene editing, describing the arguments favorable and contrary to the procedure for further analysis. The controversies were drawn from three sets of discursive productions, namely: 1) scientific articles; 2) institutional statements; 3) the International Summit on Gene Editing conferences, held in 2015.

In summary, the authors analyzed agree that gene editing of human somatic cells is beneficial when it is intended for the treatment of pathologies; and that basic and clinical research must be conducted to improve editing techniques. However, they have different opinions on editing human germ cells and editing (somatic and germ) for enhancement purposes.

Controversies among scientific papers

According to Cressey and Cyranoski [8], the journals *Nature* and *Science* refused to publish Huang's experiment, considering it to be unacceptable from an ethical point of view. Despite the refusal, both journals expressed their views on articles that counterbalanced aspects favorable to and contrary to human embryo editing.

In the article entitled "*Don't edit the human germline*" published by *Nature*, Edward Lanphier and colleagues stated that gene somatic cell editing is a promising therapeutic tool, but that the risks of germ cell editing would make the latter *dangerously and ethically unacceptable* [9]. According to them, the risks include random mutations occurring in the modified genome, deleterious consequences for future generations, extrapolation of the procedure for non-therapeutic purposes, and negative impact on social perception about somatic cell editing. In view of this scenario, the authors recommend the establishment of a *voluntary moratorium* with the objective of *discouraging human germ modifications* [10].

Days after the publication of this text, *Science* published the article "*A prudent path forward for genomic engineering and germline gene modification*", signed by David Baltimore, the 1975 Nobel Prize winner of Medicine; Paul Berg, pioneer of recombinant DNA technology; Jennifer Doudna, one of the creators of the CRISPR-Cas9 technique,

among others [11]. In contrast to the opinions of Lanphier and colleagues, the group acknowledges the great therapeutic potential in germ cell editing as well as the benefits of gene editing for baseline research and biosphere reconfiguration.

However, because of the current state of the techniques, Baltimore and colleagues [11] recommend the suspension of procedures involving the birth of modified embryos. Consequently, the group encourages and supports experiments that assess the effectiveness and manage the risks of human embryo editing. In their words, *higher risks can be tolerated when the reward for success is high, but such risks also demand confidence in the resulting effectiveness* [12].

In addition to strongly supporting the techniques, Julian Savulescu and colleagues [13] argue that embryo editing experiments are not only necessary, but also represent a "moral imperative". According to the authors, *to refrain from engaging in life-saving research is to be morally responsible for predictable and preventable deaths* [14]. They declare that unknown consequences for future generations would not justify a moratorium. New technologies always produce imponderable effects. However, the prohibition is not at all justified: instead of prohibitions, regulations would be more appropriate measures to ensure the correct use of interventions deemed beneficial to health and useful for the improvement of non-pathological human characteristics (such as longevity) [13].

Controversies among institutional statements

The topic has also been discussed in statements and reports produced by research institutions. In April of 2015, Francis S. Collins [15], director of the National Institutes of Health (NIH), spoke up about gene editing technology and its relationship to federal research funding. In his words, *the NIH will not fund any use of gene editing technology in human embryos* [15].

For him, although these technologies have undergone important advances, *there are arguments against the engagement in this activity.* These include serious and immeasurable safety issues, ethical issues involving germline modifications that affect future generations without their consent, and the current lack of medical applications that justify the use of CRISPR-Cas9 in embryos [15].

Similarly, the International Bioethics Committee of the United Nations Educational, Scientific and Cultural Organization (Unesco) [16] stated in a report that *gene therapy could be a watershed in the history of medicine and the editing of genomes is, without a doubt, one of the most promising undertakings of science, and for all mankind* [17]. However, he warned that the *germ gene editing raises serious concerns* when mentioning the research conducted by Huang's team [17].

For Unesco, *the human genome underlies the fundamental unity of all members of the human family*, shaping *the heritage of humanity* [18]. Consequently, interventions *must be permitted only for preventive, diagnostic, and therapeutic purposes, without the modification of the offspring* [18]. It is up to society to establish a *moratorium on human germline engineering* [19].

On the other hand, the International Society for Stem Cell Research supports *laboratory research involving modification of the nuclear genome of gametes, zygotes, and/or the preimplantation of human embryos carried out according to strict Emro guidelines* [embryo research oversight] [20]. For the institution, research of this nature aims to produce knowledge, being necessary to clarify the safety of potential strategies designed to prevent genetic disorders. However, until the scientific and ethical basis is properly substantiated, *ISSCR declares that any attempt to modify the nuclear genome of human embryos for enhancement purposes is premature and must be strictly prohibited at this time* [20]. It is understood that "reproductive purposes" mean the practice that leads to the actual birth of a child.

As for embryo research, the document provided the following guidelines: 1) experiments must be evaluated by qualified committees, composed of scientists, ethicists, and community members; 2) it is necessary to obtain informed, explicit and up-to-date consent from donors of biomaterials used in the research; 3) long-term risks must be monitored; 4) researchers must publish the results of their studies in order to enable independent observers to analyze the evidence, whether or not supporting the conclusions [21].

In February 2017, the National Academy of Science and the National Academy of Medicine [22] issued the report "*Human genome editing: science, ethics, and governance*". The document represents the summary of the topics discussed during the

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International Summit on Gene Editing. The group supported editing experiments on somatic cells, provided they are performed for treatment purposes only and subject to the same legal instruments that regulate gene therapy [22].

They also accept experiments in human germ cells if: availability of preclinical data on risks and benefits of the procedure for the health of the patient; restricted use of techniques to prevent serious illness; absence of reasonable treatment alternatives; rigorous monitoring of the effects of the techniques during trials, in the long term and on future generations; elaboration of mechanisms to prevent non-therapeutic uses of techniques, such as uses for enhancement and transparency, not to mention respect towards patient privacy [22].

Controversies raised during the International Summit on Gene Editing

In December 2015, the Chinese Academy of Sciences, the American National Academy of Medicine, the National Academy of Sciences, and the British Royal Society organized the *International Summit on Gene Editing* held in Washington, DC, to deepen the discussions on scientific articles and institutional statements. The forum brought together speakers and participants from more than 20 countries representing natural and human sciences, as well as regular folks and potential beneficiaries of the technique, such as patients and people with special needs.

Over the course of three days, the perspectives presented reached a common ground, but also brought up many divergences. These points can be grouped into three thematic axes, namely: 1) technical aspects and applications of human gene editing; 2) its ethical, legal, and social implications; and 3) mechanisms for its regulation and governance.

Lecturers have acknowledged that gene editing techniques contribute to basic biomedical research, as well as to the creation of new therapies [23]. The modification of the DNA of somatic and germ cells would treat diseases such as sickle cell anemia, hepatitis, immunodeficiencies, infertility, cancers, cystic fibrosis, Huntington's disease, among others. However, Eric Lander, a member of the organizing committee, was cautious and pointed out that genes have multiple functions, so modifying one that caused a certain pathology could have adverse consequences. For example, the knockout of the CCR5 gene reduces the chances of HIV infection but makes the individual more susceptible to the WestNile virus [23].

In turn, the ethical, social, and legal implications of gene editing were questioned by keynote speakers such as John Harris of the University of Manchester, Hille Haker of Loyola University in Chicago, and Ruha Benjamin of Princeton University. Harris focused on the fact that there would be nothing intrinsically wrong about modifying the genome of the species, either in somatic cells or in embryos. On the contrary, *the world, scientists, patients, and our descendants need gene editing to be pursued as a goal* [24]. For him, considerations on DNA modification must focus on the safety and efficacy of the technique, instead of objections based, for example, on the sanctity and inviolability of the human genome, on the effects on future generations, and on the impossibility of obtaining informed consent for embryo research [24].

Opponents of the gene editing ignore the fact that not only assisted reproduction, but all forms of reproduction generate new risky and unpredictable heritable combinations, Harris said ironically. The so-called natural reproduction is a "genetic lottery" and children are born every day, victims of congenital disorders [24], because evolution is susceptible to errors and our DNA is constantly changing. So, for Harris, *we will need, at some point, to reach beyond our fragile planet and our fragile nature* [25].

According to the researcher, somatic and germ gene editing techniques will make it possible to treat diseases and improve the adaptive capacities of our species. However, the procedure must be safe and effective before being applied. He also emphasizes that no technology or medication is completely risk-free [23].

In contrast to this perspective, Hille Haker also proposed a two-year moratorium that could prohibit baseline research using the technique until its clinical application was definitively and internationally banned by the United Nations (ONU) and regional regulatory bodies. According to the German theologian, society aims to *promote a better life for all and to ensure that everyone lives with dignity and freedom* [25]. Gene germ editing would not only fail to ensure these conditions, but the uncertainty of its risks could bring more harm than good. In addition, Haker stated that the technique disrespects the moral status of embryos by treating them as a product and morally neutral [23].

During her presentation, Ruha Benjamin addressed the possibility that the gene editing could stir up discriminatory behavior in our societies while promoting injustices and inequalities. As an example, the researcher discussed the so-called *ableism*: a set of beliefs or practices that devalue and discriminate against people with physical, intellectual, or psychiatric disabilities, considering that the absence of deficiencies is the normality model.

In the words of Benjamin, *the concern here is that people with disabilities would be less valued socially, as genetic technologies become more common* [26]. Gene editing therapies would reinforce current social norms, leading to the disempowerment of the blind, the deaf, wheelchair-bound individuals, among others. As the researcher pointed out, scientific development is permeated by values and interests, leading to relations of exclusion. Thus, she emphasized the need to include these people in the decision-making process of technology creation, enforcing the community motto: *Nothing about us, without us* [26].

The authors' speeches articulate with the third field of discussions, related to the governance of human gene editing, since the globalized nature of biotechnology makes its control challenging. As pointed out by Alta Charo of the University of Wisconsin, policies diverge among countries whose laws and guidelines may be permissive or more restrictive [23]. According to Ephrat Levy-Lahad of the Hebrew University of Jerusalem, the Israeli government is likely to *welcome the clinical use of genetically modified embryos* [27]. The country supports prenatal interventions and offers services to the population such as preimplantation genetic diagnosis.

Germany's position towards the Embryo Protection Law *prohibits artificial modifications in the genetic information of the human germline and the use of human germ cells with artificially altered genetic information for fertilization* [28], which Bärbel Friedrich of the German National Academy of Sciences also highlights. Legal differences among countries can stimulate the practice of medical tourism, when people travel to certain places in order to use health services that are not available in their countries of residence.

Analysis of controversies

In order to discuss the controversies on gene editing, this article starts from the premise that language is a social practice This means understanding speech as a collective action, capable of influencing the world by making the realm of realities possible. Linguistic productions expose how social institutions organize themselves, the relationships that individuals establish among themselves, the production of knowledge, and the cultural values of a certain historical conjuncture.

The first aspect analyzed refers to the centrality related to the concept of risk, how contemporaneity deals with technoscientific development. The notion operates as a privileged intelligibility key for events that affect human existence in its multiple dimensions.

Authors like Mary Jane Spink [29] is dedicated to the observation of this phenomenon. "Risk" means the possibility of damaging or losing something valued. The norm on which this notion is based upon today results from historical events and epistemic transformations, such as the secularization of society, the strengthening of rationalism, the emergence of statistics as a science, the diffusion of a securitarian mentality, the development of game theory and probability studies, among other factors [29].

Controversies raised among scientific articles, institutional statements, and the international forum show that, for the authors, judgment on gene editing must be based on the balance between possible harm and benefit. However, on the one hand, the authors assume that risk analysis is the most appropriate way of considering the issue, yet they disagree on how they assess, manage, and communicate risks. Their disagreement consists of antagonistic positions, which can be called "precautionary" and "pro-rationalists".

Cautionism characterizes the argument of Unesco [16], Lanphier and colleagues [30], Francis Collins [15], Eric Lander [23], Hille Haker [23], and Ruha Benjamin [23,31]. It is inspired by the *precautionary principle*, which has become a recurring figure for the debate on the impact – still hard to measure and potentially catastrophic – of new technologies on the environment and the population.

The principle determines that preventive actions are taken based on technologies whose effects on human life and the environment are not fully known yet. Lack of data, causal links that are poorly elucidated, or lack of scientific consensus on harmful effects should not hinder the control of products and activities. This reverses the burden of

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proof, and the proponents of a new practice must prove how safe their actions are [32].

Pro-rationalism, on the other hand, is based on the *proactionary principle*, elaborated by the philosopher Max More, [33], for whom precautionary actions fail to equate the risks and benefits of new technologies in a rational, objective, and well-informed manner. For the philosopher, if the precautionary principle was to be applied literally, *it would have prevented the development of artifacts known to human life today, such as airplanes, aspirins, computed tomography, all kinds of medications, all forms of energy, knives, and penicillin (which is toxic to some animals)* [34].

As technology is crucial for the survival and adaptation of the human species, the precautionary principle leads to the paradox of exposing us to danger by preventing us from taking the necessary risks. More [33] warns that lack of action is in itself a risk to be avoided. On the other hand, the proactionary principle would consist of decision-making strategies, supported by scientifically validated methods of risk analysis that ensure values such as creativity, freedom, and technological advancement [33].

Another controversial aspect to be analyzed refers to the effects of the precautionary position within the Brazilian context. In Brazil, *construction, cultivation, production, handling, transportation, transfer, import, export, storage, research, commercialization, consumption, release into the environment, and disposal of genetically modified organisms* [35] are regulated by the Biosafety Law. Sanctioned in March 2005, it seeks to establish *safety standards and mechanisms designed to monitor activities involving genetically modified organisms* [35]. It is consistent with the position of precautionary authors by explicitly prohibiting, as described in clause III of article 6, *genetic engineering in human germ cell, human zygote, and human embryo* [35].

However, before being sanctioned, the law had already received criticism from authors such as Dráuzio Varella [36], who rejected the prohibition on human therapeutic cloning (which requires the creation and destruction of embryos). According to him, the religious bench of the Brazilian National Congress was responsible for this *authoritarian and irrational deliberation* [36]. In his view, the conviction would be motivated by the belief that scientists want to *play God* [37], and that the elimination of embryos is unjustifiable because they are people in the *early stages of development* [37].

It may be hypothesized that the prohibition of genetic engineering in human embryos imposed by the Biosafety Law, including for research purposes only, stems in part from the same forces that led the Congress to ban therapeutic cloning. The idea of embryos having special protection status as well as the uncertainties underlying biotechnology lead society to deal with controversial issues very carefully.

The third aspect to be analyzed is to reflect critically on the genetic essentialism discussed by Unesco in its report. The institution's argument is based on the human rights paradigm and their general principles, which are described in the UN Universal Declaration of Human Rights [38], released in 1948. The declaration states that all individuals are born *free and equal* [39], being members of the same *human family* [40], which ensures inherent and inalienable dignity [38].

Human rights comprise the discursive ground of reports on genetic technologies formulated by Unesco since 1997. Nevertheless, as seen beyond what is found in the UN declaration, the International Bioethics Committee equates the unity of humanity with the DNA of the species [16]. The equivalence is an argumentative strategy that ends up weakening what the institution would like to protect.

The UN concept of humanity does not rely on the biological dimension of the species. It is a transcendental, deontological concept that conceives us as part of the same collectivity, despite cultural and organic differences. This seeks to safeguard human dignity by detaching it from contingent elements, such as the DNA. We all deserve the same respect and care regardless of our physiological characteristics.

However, the Unesco argument ends up contradicting itself by accepting the same genetic essentialism the UN tried to break away from. By treating the genome as the basis of human collectivity – and therefore the basis of our dignity – the institution strives to preserve it. Thus, Unesco legitimizes its refusal towards germ editing, since it produces heritable genetic modifications.

Despite the efforts justified by the institution, essentialism produces its opposite: it undermines the idea of dignity, since any author provided with basic biological knowledge will easily challenge the argument on the genomic unity. The simple process of cell division, which preserves the integrity of our biological tissues, causes permanent mutations

in our DNA, overlooked by correction enzymes that monitor the division process [41]. Differences in genetic sequences are observed not only among individuals, but also among different tissues of the same individual. Therefore, the idea of an identity unit based on DNA cannot be substantiated.

Counterarguments of this kind are presented by authors like John Harris [24], who uses rhetorical tactics such as irony in an attempt to refute Unesco's reasoning. In a sarcastic tone, he recalls that natural reproduction consists of a *genetic lottery*, which produces results that may be unpredictable and deleterious at times. Hence, the author aims, through the discursive effects of derision, to make the editing of germ cells a less fearful practice for the public.

Finally, the fourth controversial aspect involves the proponents of gene editing who use rhetorical strategies to appeal to human sentiment (pathos), such as guilt. This behavior is expressed by Savulescu and colleagues when they state that refusal to accept embryo editing implies moral accountability for *predictable and preventable deaths* [14]. Thus, they can justify their position, according to which gene editing would be a *moral imperative* [13].

Authors like Harris [24], as well as Savulescu and colleagues [13], also encourage the use of editing to treat diseases. Once this technology proves to be safe and effective, it would be legitimate to apply it in germ or somatic cells to enhance non-pathological human characteristics such as cognition, physical endurance, and longevity.

Human enhancement has become a popular theme during bioethical debates. At least two considerations must be considered when considering this issue. First, it is necessary to distinguish between enhancement and eugenics. Perpetrated by authoritarian states throughout the twentieth century, the latter consisted of a set of fascist measures conceived to purify the human species through the extermination and segregation of vulnerable population groups. On the contrary, the enhancement, according to its proponents, refers to the ability to overcome the constraint mechanisms imposed by nature. For Harris, considering the Darwinian perspective, the DNA results from random mutations motivated by environmental pressures, and therefore, it does not consist of a purpose in itself [24]. Therefore, its modification should not be refused *a priori*.

Nevertheless, it is necessary to look carefully into the supposedly beneficent intention of such enhancement. It is necessary to inquire if a new form of eugenics – called "liberal eugenics" by Haberma [42] – would emerge. Inequality of access to goods and services available through technology can increase the discrimination and stigmatization of certain population groups, as Ruha Benjamin [31] pointed out. Prejudice and discrimination deeply rooted in our culture would be reproduced on a new and amplified scale resulting from the race for unlimited biological perfection.

In addition to the experiments led by Junjiu Huang and Hong Ma, the British Human Fertilisation and Embryology Authority (HFEA) approved, in February 2016, the gene editing of human embryos [43]. However, its approval was restricted to the scope of biomedical research, preventing edited embryos from being implanted, leading to the birth of children.

The first research approved by HFEA was submitted by biologist Kathy Niakan of the Francis Crick Institute in London. Through gene germ editing, Niakan focused on the study of embryonic development to formulate fertility treatments [43]. The procedure was also approved in Sweden, where Fredrik Lanner and colleagues have been conducting studies applying the CRISPR-Cas9 technique to human embryos since 2016 [44]. Researchers seek to understand the mechanisms involved in gene overexpression and silencing.

In April 2016, a new article on human germline editing was published in the *Journal of Assisted Reproduction and Genetics* by Xiangjin Kang and colleagues [45], of the Guangzhou Medical University in China. In order to confer the resistance against HIV infection, tripronuclear zygotes were edited, silencing the gene that encodes the CCR5 protein. In other countries, the practice remains prohibited [46].

Contrary to what pro-rationalist authors suggest, there is no social neutrality in scientific research. Encouraging studies on germline gene editing and developing safer and more effective techniques make its clinical use more feasible and irrefutable. If society believes that embryo editing is unacceptable, it will be difficult to curb the practice, as editing techniques may spread through unregulated or illegal markets. Medical tourism that includes stem cell treatments exemplifies some of the risks caused by this phenomenon.

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As the Nuffield Council on Bioethics states, *scientific discovery and technological innovation are important, but not inevitable*. The most determining factor in shaping technological development is the human agency [47]. It involves decisions on the direction of the research, investments, regulations, institutional *designs*, among other measures. Thus, the human forms that will emerge in the future will result not from inexorable processes but from choices made today.

Final considerations

This work sought to explain and reflect on the controversies related to human gene editing. The reactions of the intellectual *establishment* towards the understanding, management, and communication of the risks and benefits of DNA modification were discussed. The debates evaluated took place on different platforms – scientific articles, institutional statements, and conferences – and the analysis revealed four main aspects.

Initially, the centrality of the notion of risk was identified as a way to understand and regulate the current scientific development. In this sense, two types of trends related to risk analysis stand out from the debates: on the one hand, positions contrary to the human germline editing, denominated precautionary; and, on the other, tolerant supportive positions, called pro-rationalist. The second aspect highlighted by the analysis showed the approximation of precautionary arguments with the Brazilian legislation on genetically modified organisms.

Thirdly, the analysis showed how Unesco's refusal to edit human germ cells implies genetic essentialism by considering DNA as the basis of the deontological concept of humanity. It was discussed how this way of reasoning ends up undermining the institution's defense of human rights. Finally, the fourth aspect pointed to the rhetoric of appealing to the public *pathos*, substantiated by authors like Savulescu and colleagues [13], who seek to evoke specific affections such as the strategy of persuasion.

It is hoped that the examination of this article draws attention to the technical, ethical, and social implications of human DNA modification. It is necessary to problematize the paths taken by science, so that technology is placed at the service of principles such as freedom and justice. Therefore, active engagement in such debates is paramount to steer the course of science in an inclusive and participatory way.

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