

Genetic editing: a scientific and bioethical assessment of the first case in humans in Peru

Edición genética: una valoración científica y bioética del primer caso en seres humanos en el Perú

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Abstract

The gene-editing technique, CRISPR/Cas9, is a revolutionary tool with a transdisciplinary scope that has the potential to transform various fields of knowledge. This paper addresses the definition of CRISPR/Cas9 and explores, from a biomedical perspective, its advantages and disadvantages at both the laboratory and clinical levels, studying its applicability in basic and translational research, as well as in therapies already approved for humans. In this context, this work discusses several CRISPR experiences reported in our country, emphasizing the first research experience using CRISPR/Cas9 in human cells. In said study, this technique was used for gene-editing treatment and autologous cell therapy for a hereditary form of retinitis pigmentosa (RP), found so far only in patients from a Peruvian community. Furthermore, an ethical analysis of the use and application of gene editing with this tool is provided, based on the personalist principles of bioethics.

Keywords: Gene editing, CRISPR, cell therapy, health, personalist bioethics.

Contribution

The main contribution of this article is to analyze the CRISPR/Cas9 gene-editing technique not only as a biotechnological milestone but also as an ethical challenge that requires a legal and social response in the Latin American context. This work succeeds in bringing into dialogue advances in genetic engineering—specifically, research involving human cells for the treatment of retinitis pigmentosa in Peru—with the pillars of personalist bioethics. At the same time, it seeks to engage with the contemporary debate on the limits of human genome manipulation, proposing a clear distinction between somatic gene therapy and germline modification, always from the perspective of respect for the ontological dignity and integrity of the human person.

1. Introduction

Among the various gene-editing systems developed to date, the CRISPR/Cas mechanism (an acronym for Clustered Regularly Interspaced Short Palindromic Repeats-Cas9) has revolutionized the field of biotechnology and genetic engineering. Colloquially known as “molecular scissors” due to its ability to specifically cut regions of the genome, it is unique in that it is modular. This has made it the tool of choice for genetic and genomic manipulation of various biological systems, ranging from microorganisms to humans (1).

Over the past decade, there have been significant advances in modifying CRISPR/Cas tools to improve their specificity and safety. Innovations have included the development of Cas nuclease variants, as well as improvements in guide RNA design to reduce off-target effects, which is essential for the safer clinical use of this technology (2,3). The refinement of these techniques has enabled applications in a variety of fields, including medicine and biotechnology, facilitating research and treatments for diseases that previously had no cure (4).

2. Problem Statement

Indeed, the technique’s ease of use and versatility have made this tool an excellent alternative for facilitating its application across various industries, not only in countries of the Global North but also in Latin America, including Peru. In this regard, this paper addresses the concept of gene editing using the CRISPR/Cas9 tool from a scientific and biomedical perspective, analyzing its specific characteristics and therapeutic applications. It also discusses the first case of gene editing in human cells for research purposes reported in Peru; furthermore, it includes a bioethical analysis based on personalist principles. Thus, this paper aims to raise awareness of the research on gene editing already being conducted in our field and seeks

to promote legislation that prioritizes the well-being of society and is in line with technological advancements so that they may be used for this purpose.

3. What is the CRISPR/Cas system?

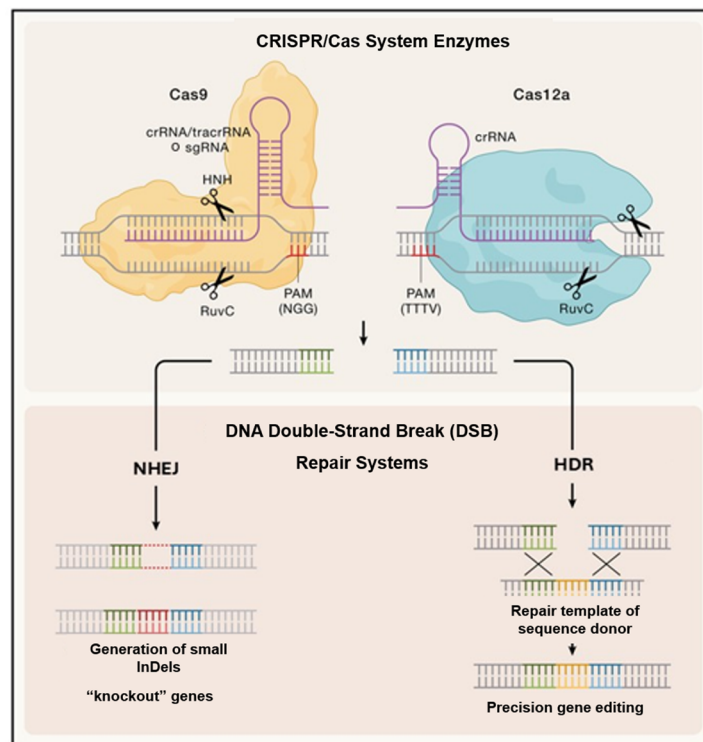
Currently, the CRISPR/Cas system is a fundamental tool for genetic engineering, allowing for the targeted introduction of genetic variants into DNA across a wide range of biological contexts. The CRISPR/Cas system, in its most basic form, consists of the Cas9 nuclease protein and a single guide RNA (sgRNA) that recognizes and targets a specific DNA sequence through RNA-DNA base pairing, as shown in Figure 1. Once at the target sequence, the CRISPR/Cas system requires the presence of a PAM (protospacer-adjacent motif) sequence downstream of the recognition site. The most widely used Cas enzyme (Cas9), derived from *Streptococcus pyogenes*, recognizes a 20-nucleotide DNA sequence immediately followed by a 3-nucleotide PAM sequence “NGG,” where N represents 1 nucleotide of any identity [A/T/C/G], followed by 2 guanine nucleotides (5).

The boom in CRISPR/Cas gene-editing technology began in 1987 (6), when a group of microbiologists was investigating the presence of small, mysterious “arrays” of “clustered regularly interspaced short palindromic repeats” (CRISPR) in the genomes of certain bacteria. In the course of their research, this group of scientists found that the arrays were not “isolated,” but were located in close proximity to protein-coding genes, which they later named Cas (Cas: CRISPR-associated). What drew attention to these CRISPR regions was that some of the genetic sequences comprising them matched almost perfectly with sequences found in viral genomes.

This match suggested that the arrays were a kind of adaptive immune system used by bacteria to prevent viral infection. This suspicion would eventually be confirmed, demonstrating that CRISPR/Cas systems use RNA molecules —transcribed from their own sequence

and homologous to viral DNA— to guide Cas proteins to cut and destroy viral DNA or RNA (7,4), see Figure 1.

Figure 1. The CRISPR/Cas system, its components, and the mechanisms necessary for gene editing.



Source: Compiled by the author.

Genome editing based on the CRISPR system uses nuclease enzymes, such as Cas9 and Cas12a, guided by short RNA strands to recognize and cleave target DNA at specific sites. The Cas9 enzyme, for example, uses a dual guide RNA consisting of a CRISPR RNA (or crRNA) and a CRISPR transactivator RNA (tracrRNA) or a single guide RNA (gRNA), whereas Cas12a requires only a crRNA.

Recognition of the target DNA depends on complementarity with the crRNA or gRNA sequence, as well as the presence of a motif adjacent to the protospacer (PAM). Cas9 recognizes an “NGG” PAM sequence, while Cas12a requires a “TTTV” PAM sequence. Following recognition of the target sequence, the nucleases catalyze DNA cleavage, generating a double-strand break (DSB) in the DNA. Repair of the DSB via cellular DNA repair pathways leads to the introduction of genetic modifications (edits). End-joining pathways result in short insertions or deletions (InDels), whereas homologous recombination (HDR) uses an exogenous sequence template or donor as a template for repairing the cleaved DNA; this allows for the insertion of precise genetic modifications near the site of the DSB. Image modified from (8).

On the other hand, studies from the early 1990s, using endonucleases (enzymes capable of cutting DNA), demonstrated that a double-strand break (double-strand breaks, DSB) in the genomic DNA of mammalian cells stimulated the repair of the same “broken” sequence through the homologous recombination repair system (homology-directed repair, HDR). This approach established the concept of genome editing using DSB-inducing enzymes. This led to the development of various types of modified nucleases, such as zinc-finger nucleases (Zinc-finger nucleases, ZFN), developed in the early 2000s, and later, transcription activator-like effector nucleases (transcription activator-like effector nucleases, TALEN) in 2010–2011. These two nucleases laid the foundation for genome editing, but their labor-intensive design and manufacturing limited their use to highly specialized laboratories with substantial financial resources.

The discovery and development of CRISPR-associated nucleases —Cas proteins— marked a revolutionary change due to their simplicity of programming (which depends on the sgRNA sequence), specificity, and versatility (10). Consequently, the CRISPR/Cas system has been adapted in numerous ways, enabling the cleavage of DNA and RNA molecules in any type of cell so that they can

be altered by leveraging the cell's own repair systems, all with unprecedented ease. Over the past decade, CRISPR/Cas has democratized access to gene-editing tools, becoming an indispensable tool for advancing fundamental and applied research in animals, plants, and humans (11).

4. Characteristics of CRISPR/Cas

In its most basic form, the CRISPR/Cas system offers a number of advantages over other systems and approaches to gene editing. Paradoxically, some of the areas where CRISPR/Cas has advantages over other gene-editing systems are also areas that present opportunities for improvement to achieve an ideal gene-editing system.

a) Specificity and programmability: The specificity of recognition and cleavage of the target sequence (whether DNA or RNA) depends on base complementarity between the sequence of the crRNA-tracrRNA complex or the sgRNA and the target sequence itself (in addition to the presence of the PAM motif). The recognition sequence is typically 20 nucleotides long on average. Due to this RNA-DNA base complementarity for recognizing the target DNA, the same Cas9 protein can be used to recognize a wide range of DNA sequences simply by swapping out the sgRNA, which contributes to its high programmability.

However, the specificity of the CRISPR/Cas system has been a cause for concern since its introduction into the field of gene editing. Although the CRISPR/Cas system derives its high specificity from the “pairing” of RNA-DNA sequences, it is well known that this complementarity is not always perfect, as the system tolerates some bases not “pairing” correctly. This allows the sgRNA to bind to “non-target” sequences, producing DSBs in sequences other than those originally intended; this is known as “off target” effects.

Despite these Cas9 mismatches, most of them do not result in cuts in “off-target” DNA due to intrinsic checkpoints in the Cas9

binding and excision mechanism (12,13,14,15). Although this may be acceptable for various CRISPR-mediated inactivation applications (including clinical applications), many therapeutic applications require much higher levels of precision and cannot tolerate the introduction of unintended genetic edits.

To reduce the “off-target” effects of CRISPR/Cas nucleases, a combination of rational design and selection has been used to develop high-fidelity Cas variants, such as SpCas9-HF1 (16), evoCas9(17), and HiFiCas9 (18), among others. Increasing the precision of gene editing using CRISPR/Cas also requires a better understanding of DNA repair processes, which is independent of improvements to the system or its components.

b) Availability of target sites/PAMs: The CRISPR/Cas system’s ability to recognize target sites depends not only on the specific sequence of the sgRNA but also on the presence of a PAM motif positioned immediately downstream of the target sequence. Although the “NGG” PAM sequence of SpCas9—the most widely used Cas enzyme— theoretically allows it to find a target sequence every 8 nucleotides on average, SpCas9 cannot be easily used in some genomic regions with a high A/T content (adenines and/or thymines), which prevents the formation of the PAM sequence necessary for its function. To overcome this limitation, natural variants of Cas9 have been identified in other microorganisms, with alternative PAM specificities for genome editing. However, many of these have more restrictive PAM specificities (19,20). To overcome the limitation imposed by the presence of the PAM motif, a series of artificial Cas9 variants with modified or “relaxed” PAM specificities have been developed in recent years. Although these modifications broaden the range of PAM motifs that can be selected, the use of “relaxed” PAMs is associated with a significant decrease in specificity (19), which increases the likelihood of “off targets” and reduces editing efficiency at the target site.

5. Control of Post-Cut Repair Systems with CRISPR/Cas

As mentioned, the primary function of the CRISPR/Cas system during gene editing is to create cuts in the target DNA (or RNA) sequence. The insertion or deletion of genetic information is guided by the various DNA repair systems of the target cell. Of these systems, two have been most widely utilized by CRISPR/Cas users to achieve their gene-editing goals: i) the Non-Homologous End Joining (NHEJ) system and ii) the Homology-Directed Repair (HDR) system.

NHEJ is the default repair system and the one most frequently used by the cell once a DNA break is detected. Its main disadvantage is that this system often produces random insertions or deletions in the target sequence (21,22). The HDR system, on the other hand, is much less frequently used by cells since it requires the presence of a template strand for repairing the DNA break. This template strand, which can be synthesized and supplied to the cell by researchers, allows for the specific insertion or deletion of sequences. It should be noted that the use of HDR is generally limited to dividing cells and often produces mixed results (double editing) due to simultaneous editing resulting from different repair pathways (24,25). However, it is known that the generation of DSBs within a cell's genome using specific nucleases, including Cas, significantly improves the HDR rate in mammalian cells (26).

As a result, many studies aim to boost the HDR repair rate and thereby increase the efficiency of specific sequence introduction (27). To overcome these limitations, it has been shown that the design (28,29) and selection of the repair template strand and its delivery greatly affect HDR efficiency (27,30). In addition, attempts have been made to manipulate the cell cycle (31,25,32,33) to temporarily slow down the S phase or increase the proportion of cells in the G2/M phase, thereby favoring the HDR system. Other methods

focus on promoting the selection of the HDR system over NHEJ in the target cell by suppressing key NHEJ factors (34).

Despite these improvements, the potential genotoxic effects of nonspecific DSBs have driven the development of editing technologies that do not rely on DSBs, thereby eliminating the need for HDR. These approaches include base editing via “prime editing” and CRISPR-based recombinases and transposases (8).

6. Delivery

As we have seen, the CRISPR/Cas system offers us an unprecedented opportunity to alter a cell’s genetic information in a simple and specific manner; however, for this to occur, the components of the CRISPR/Cas system (namely Cas nucleases and sgRNA) must selectively reach the target cell, enter and traverse its cytoplasm, and finally perform their function in the cell nucleus. To facilitate this transit, various vectors capable of transporting the components of the CRISPR/Cas system to the cell nucleus are being developed. In addition to this journey, the components of the CRISPR/Cas system must overcome an obstacle inherent to the organism being modified, as these components can trigger the immune system.

The targeted and specific delivery of CRISPR/Cas9 system components is a limiting factor for most gene-editing applications in vivo and ex vivo.

For example, in humans with no known exposure to the CRISPR/Cas system, pre-existing anti-Cas9 antibodies and reactive T cells have been identified. This pre-existing immune response to the CRISPR/Cas system has been associated with poor therapeutic outcomes in disease models in dogs and non-human primates (37). Various strategies have been proposed to counteract these problems, ranging from the design of modified Cas9 proteins to eliminate immunogenic epitopes from their structure to the modulation of immune responses, among others (36,38,39).

7. Therapeutic Applications of CRISPR/Cas

CRISPR/Cas gene-editing technology has the potential to treat diseases by permanently correcting genetic variants or altering disease-causing genes with great precision and efficiency. Since the first demonstration of CRISPR/Cas-based gene editing, the field has evolved rapidly. First-generation DSB-dependent genome editors, such as Cas9 and Cas12a, have become more versatile and precise, with a reduction in their potential off-target effects. However, safety concerns persist due to “off-target” effects and the potential genotoxic consequences of DSBs in the target sequence (40,41), including the induction of a p53-mediated DNA damage response and cell cycle arrest (42).

Over the past decade, the CRISPR/Cas system has enabled the development of a multitude of therapeutic approaches for genetic diseases, several of which have progressed from preclinical studies to human clinical trials. This includes *in vivo* and *ex vivo* gene-editing strategies. *In vivo* therapeutic editing approaches involve delivering gene-editing components to affected tissues within the human body (43). In contrast, *ex vivo* approaches involve collecting cells from a patient, editing them in a laboratory, and then transplanting the edited cells back into the same patient (autologous transplantation) or into a different patient (allogeneic transplantation). These approaches are primarily used in cancer immunotherapy (44).

8. Ex vivo Therapeutic Applications

Ex vivo gene editing of the genome of patient-derived cells, followed by their expansion and re-transplantation, is a powerful strategy for treating genetic disorders related to blood cells. This is demonstrated by treatments for hemoglobinopathies such as sickle cell disease (SCD) and transfusion-dependent β -thalassemia (TDT), which are now approved in Europe, the United Kingdom, and the

United States. Instead of correcting specific mutations, CRISPR has been used to reactivate fetal γ -globin (HBG) by modifying the sequence of the BCL11A gene with CRISPR/Cas (45).

Chimeric antigen receptor T-cell (CAR-T) therapies are based on the generation of T cells that recognize and attack cancer markers such as CD19 and BCMA, among others. Transplanting CAR-T cells into an affected patient leads to the destruction of the neoplasms (44). In currently approved autologous CAR-T cell therapies, the gene encoding the CAR is randomly inserted into the genome via transduction with a viral vector. If the CRISPR/Cas system were used, this insertion could be directed to a specific target site. CRISPR-edited allogeneic CAR-T cells could improve functionality, streamline production, and ensure better quality control compared to current therapies (46).

Currently, several clinical trials are investigating CRISPR/Cas-edited CAR-T cell therapies to treat various blood cancers. A notable example is the use of CAR-T cells with multiplexed CRISPR/Cas editing (where multiple target sequences are modified simultaneously) to treat relapsed T-cell leukemia in pediatric patients, a previously incurable condition (47).

A new strategy for genomic therapies combines gene editing using CRISPR ex vivo with iPSC (induced pluripotent stem cell) technologies. This approach has recently been developed with the aim of controlling type 1 diabetes. The plan is to modify the genome of iPSCs, differentiate them into pancreatic endoderm cells, and encapsulate them in biocompatible devices for implantation in patients to enable insulin production in vivo, which would have the potential to control type 1 diabetes physiologically (48).

9. In vivo Therapeutic Applications

As for in vivo therapeutic editing, this requires the direct administration of the components of the CRISPR/Cas system to the affected

patients specifically to the affected organs or tissues, through localized or systemic administration of these components. The CRISPR/Cas system is currently being used in clinical settings to develop (potentially curative) treatments for diseases as diverse as hemoglobinopathies, chronic bacterial infections, inflammatory diseases, cancer, cardiovascular disease, HIV/AIDS, diabetes, and autoimmune disorders, among others (8,11).

Many preclinical studies (in animal models) have demonstrated the validity of this therapeutic approach in a wide variety of genetically caused conditions, including Duchenne muscular dystrophy, Leber congenital amaurosis, transthyretin-related cardiac amyloidosis, and familial hypercholesterolemia (8). In familial hypercholesterolemia, using non-human primates as a preclinical model, serum LDL cholesterol levels have been significantly reduced without affecting germline tissues, laying the groundwork for Phase 1 clinical trials (49).

In late 2023, the first CRISPR-based drug was approved: Casgevy, a curative treatment for sickle cell disease (SCD) and transfusion-dependent beta-thalassemia (TDT). Casgevy was jointly developed by Vertex Pharmaceuticals and CRISPR Therapeutics, and its cost is estimated at \$2 million per patient. But this is not the only curative treatment currently in development; Editas Medicine is also conducting Phase 1/2 trials for SCD and TDT using the CRISPR system with the Cas12a protein (a protein similar to the well-known Cas9). This marks the first clinical use of Cas12. The results obtained from this trial so far demonstrate high efficacy. Meanwhile, Beam Therapeutics has also initiated Phase 1/2 clinical trials for the same diseases, using another variant of the CRISPR/Cas system: base editing.

10. The Present and Future of CRISPR/Cas

First-generation CRISPR technologies, primarily based on endogenous repair or site-specific double-strand breaks (DSBs), have been

complemented by second-generation technologies, such as base editing and primary editing, which allow for direct modification of the target DNA without generating DSBs. These are generally considered safer and offer more predictable editing results. Emerging third-generation CRISPR technologies are being developed to address two major unmet needs in the field: achieving the precise insertion of large (gene-sized) fragments and genetic regulation without genome editing, through epigenome engineering (51).

The continued advancement of these and other technologies is enabled by two approaches: on the one hand, screening the metagenome to discover new molecular systems, and on the other, synthetic biology and AI-assisted molecular engineering (52,53).

Areas requiring further research include the development of more specific and less immunogenic delivery vectors, the reduction of off-target effects, and greater control over editing outcomes, thereby improving both the precision and accuracy of genome editing (52,53,54).

Looking ahead, nucleic acid-guided systems are likely to remain central to genome editing due to their ease of programmability and adaptability, compared to technologies based exclusively on proteins. However, their mode of application could evolve, with potential shifts toward more transient editing approaches to minimize the risk of long-term unintended genetic changes or transient delivery methods to reduce genomic disruption and immune response (54).

The main challenges are expected to lie in delivery methods, especially for organs other than blood and the liver, and for certain types of ex vivo cells. Advances in in vivo delivery methods, such as those seen in the development of mRNA vaccines, will likely significantly catalyze the application of CRISPR technologies. Furthermore, even for tissues and cells that are already editable using available methods, more basic research will be needed to identify safe editing targets (54).

The range of diseases that could be treated using CRISPR will expand with the development of new delivery vectors and the characterization of disease-causing variants and their corrective strategies.

Advances outside the field of CRISPR are expected to drive these technologies in new directions, enhancing their capabilities. In this context, the rise of AI-based methods will enable the precise modeling of complex genomic editing landscapes, predict on- and off-target outcomes, and design more capable genomic editors, thereby accelerating the implementation of safe therapeutic approaches (52,55).

11. Case Study in Peru: CRISPR/Cas, Gene Therapy, and Retinitis Pigmentosa

According to the literature, the first case of gene editing in human samples in Peru occurred in the context of a research project for the treatment, using autologous cell therapy, of an inherited form of retinitis pigmentosa (RP) detected in the community of Parán, in the highlands of Lima, Peru. The variant responsible for this disease was identified by Peruvian scientists at the Center for Research in Genetics and Molecular Biology (CIGBM) at the University of San Martín de Porres beginning in 2012 and reported in 2018.

The study, titled “Molecular Platform for Corrective Gene Therapy in Retinitis Pigmentosa Using Autologous Transplantation of Genetically Modified Induced Pluripotent Stem Cells (iPSCs) via CRISPR/Cas9 Technology: A Multifamily Case from Parán,” was funded in 2019 by Concytec, the World Bank, and the University of San Martín de Porres. The objective of this project was to establish, for the first time in the country, a molecular platform for using genetically modified induced pluripotent stem cells (iPSCs) for autologous gene therapy in patients with RP.

Retinitis pigmentosa is a genetic disorder that causes progressive vision loss (57). The study, conducted by Villegas-Llerena C et al., focused on correcting the “Parán mutation,” an 11-base-pair deletion in exon 6 of the RPGR gene (NM_001034853.2(RPGR): c.578_588del (p. Ser193fs)), which results in a frameshift at the nucleotide level. Therefore, the project focused on the genomic

modification of this variant in iPSCs derived from patients affected by this multifamily case.

To achieve this, work was conducted to standardize protocols for converting skin fibroblasts into iPSCs. These induced pluripotent stem cells could differentiate into any cell type and to divide indefinitely, making them a renewable and reliable source for autologous replacement therapies in diseases where specific cell types are destroyed, as is the case with RP. In addition, protocols were developed to differentiate iPSCs into retinal cells and organoids (three-dimensional cell cultures).

The project also included the standardization of gene-editing protocols in iPSCs using the CRISPR/Cas9 technique, as this tool enables precise and programmable genome editing (58). The standardized protocols were applied sequentially: iPSCs were derived from skin biopsies of volunteer patients, the genetic variant responsible for RP was corrected, and the corrected iPSCs were differentiated into retinal cells and organoids. The edited iPSC lines were characterized and cryopreserved for future use (manuscript in preparation).

The study by Villegas-Llerena et al. was completed in 2022 and is, to the best of our knowledge, the first project in Peru to have involved CRISPR/Cas9 gene editing of human cells for research purposes in gene and cell therapy. Other projects have included the use of CRISPR technology for the rapid and accurate diagnosis of infectious diseases (59,60) and for precision agriculture, including the reduction of cadmium uptake in cocoa (61). Recently, CRISPR/Cas9 gene editing has been used in Peru to model, in cell lines, variants of uncertain significance (VUS) found in Peruvian patients with hereditary breast cancer (62). In this latest research, the objective was to generate cellular models that facilitate the study of VUS-type genetic variants, which tend to be abundant in under-studied cohorts, such as the Peruvian population.

The use of CRISPR for gene editing is a reality in Peru and other Latin American countries (63); therefore, its presence in various

fields of research is expected to increase. In this regard, it is important to emphasize the significance of this technique and its regulation in our region. As will be discussed in the following section, we consider it important to distinguish between germline gene editing and somatic gene editing. Public policymakers and the public should also be aware that gene editing is not synonymous with genetic enhancement; rather, CRISPR technology can be used in the healthcare sector for disease diagnosis, gene therapy, and a better understanding of the etiology of various diseases, for research and clinical medicine purposes.

Although there is not yet specific national regulation governing the use of gene editing in Peru, the Peruvian research projects cited above have been made possible following their evaluation and approval by ethics committees specializing in human medicine. We believe it is important to raise awareness of these projects and help foster the necessary national dialogue to achieve regulations that support well-designed research projects at the basic, translational, and clinical levels, addressing local health needs.

12. Ethical considerations

Applied ethics in the context of life and the health sciences is known as bioethics, a discipline whose object of study is human behavior regarding interventions on human beings, analyzed in light of moral principles and values; through this, we can assess the goodness or badness of human actions, which is determined using a system of values as a reference. This analysis applies to the following scenarios or circumstances: a) all matters of value that arise for health professionals in their professional practice; b) biomedical and behavioral research, regardless of whether or not it has therapeutic implications; c) social issues related to public health, ranging from global health to birth control; and d) animal and plant life; in this regard, it considers the ethical principles regarding respect for human life,

which belongs to the realm of objectivity and must serve as the ultimate goal of ethical action (64).

With regard to biomedical research, bioethics analyzes genetic procedures or techniques intended to enhance the human person, such as CRISPR/Cas9, a genetic technology that, while promising to improve the quality of human life, simultaneously raises ethical questions regarding its risks and benefits; however, the guiding principle in evaluating such technologies will always be to ensure that all means or tools currently available respect the integrity of the person—understood as a psychosomatic -spiritual, where the use of technology is always at the service of the human being—that is, remembering that technology is a means to an end, which must be carried out in a controlled manner and, at the same time, benefit humanity. Technological development must be analyzed not only from a therapeutic perspective but also in terms of its significance for social coexistence and the humanization of health and life. The ethical use of technoscience should take into account the ontological dignity of the person, a supreme value embodied in the existence of our soma, or body, which allows us to be present and exist in this world as people; and therefore, our corporeality is just as worthy as the other human dimensions: the intellect, freedom, speech, or any specific characteristic invoked to define what it means to be human. In conclusion, if genetic procedures and/or techniques expose the body to disproportionate risk or harm, this would constitute an affront to human dignity; therefore, advocating for prudence in experimentation requires not only a quantitative but also a qualitative assessment (65,66).

Regarding the CRISPR/Cas9 method, trials conducted on human somatic cells have shown that technical challenges still exist in relation to repair mechanisms due to off-target effects, among other factors; however, the reliability of the technique is continually improving, with safer and more optimal versions now available (67,68). For example, in the treatment of oncological or immune-related diseases, non-viral nanotechnological systems have been studied; these

offer significant improvements in the stability, specificity, and efficacy of CRISPR/Cas9 delivery. The integration of nanotechnology with gene editing via CRISPR/Cas9 represents a promising emerging strategy for the personalized treatment of oncological and immunological diseases (69,70). In addition to the technical challenges for clinical implementation, advances in biosafety, robust clinical validation, and solid regulatory frameworks are needed to guide its responsible use. By evaluating all these aspects in CRISPR/Cas9 research, taking both technical and ethical considerations into account, we can move forward with clinical trials in humans; a recent example of this is the FDA's approval of the first drug using this technique for the treatment of sickle cell anemia. Consequently, the use and application of this technique can help us understand, prevent, and cure many specific genetic disorders while simultaneously addressing the ethical and safety issues surrounding genome editing. It is therefore important to evaluate these procedures while respecting human dignity and integrity, ensuring that the use of the technique does not "reduce a person to an object" or "instrumentalize" them (71,72).

The other area where the ethical evaluation of the CRISPR/Cas9 technique is debated is its therapeutic application in germline cells, which —unlike what is expected in somatic cells— would have an impact on both the individual and their offspring. Therefore, it is necessary to establish appropriate regulations to ensure the responsible use of CRISPR. There is concern that this technique could be used to "genetically enhance" the individual, promoting the selection of the "fittest" for human survival, a path toward eugenics proposed by sociobiology and transhumanism as philosophical currents that interpret human values in biological terms, disregarding the fact that the individual's uniqueness and plurality are also the foundation of their ontological dignity. Furthermore, there is controversy surrounding the application of CRISPR/Cas9 to human embryos, highlighting the ethical complexity of conducting research on entities that cannot give their consent (72).

Regarding regulatory issues, the International Commission on the Clinical Use of Human Germline Genome Editing (ICCUHGGE) states that, currently, in preclinical research on embryos, only the possibility of performing edits on zygotes is being analyzed; on the one hand, by introducing the enzymes into the oocyte at the same time as the sperm, and on the other, by introducing the enzymes into the pronuclei or cytoplasm of the fertilized oocyte. Although advances have been made in the CRISPR system for editing, sufficiently safe repair mechanisms have not yet been implemented, as this depends on technical considerations such as “cellular characteristics, including the stage of the cell cycle, the components of the DNA damage response present, other factors influencing DNA repair, and, potentially, genetic background,” as well as ethical considerations, such as the balance of potential risks and benefits in each particular situation. Thus, the ICCUGHHE notes that one of the most significant risks of the current use of CRISPR is off-target modifications that could cause another disease (73).

Internationally, there are regulations based on ethical principles that prohibit germline gene editing, such as those of the NIH (U.S.) and the WHO. In line with these regulations, Article 13 of the Oviedo Convention states that genome editing is permitted only for the purposes of disease prevention, diagnosis, and therapy, but genetic editing in germline cells is prohibited because it cannot be controlled and the consequences for future generations are unpredictable. Therefore, it is important to maintain the ban on applying this technique to the human germline and to ensure that research on somatic cells is not conducted at the expense of embryonic life. In this regard, we can cite the case of the Chinese researcher, He Jiankui, who applied CRISPR/Cas9 to human embryos without taking the necessary safety precautions associated with this technique, nor having assessed the risks and benefits for the research subjects, and for violating legal and ethical standards, which resulted in his failure to obtain approval from an institutional ethics committee and lack of endorsement from his country’s health institute. This has

major repercussions for society and the scientific community, since—given the lack of transparency, oversight, and regulation of the process—it will be very difficult to know the future outcomes for the twins (74).

In conclusion, when CRISPR/Cas9 is applied to somatic cells, the modification would not affect offspring; it would, however, raise ethical dilemmas related to the well-being of the participating individual and the potential risks to their future health. In the case of germline cells, the effects of genetic modification could impact future generations, which would require a much more thorough ethical analysis in accordance with personalist ethical principles. Likewise, the use of embryos as a “means” for genetic modification raises an ethical debate regarding the rights of the embryo, since, from a biological standpoint, they are human beings, and from the personalist perspective of bioethics, every embryo is a person and a subject of rights. In this regard, the question arises regarding the limitations on the use of this technique: Should it be permitted only to prevent serious diseases, or also to “enhance” physical or cognitive characteristics that are not necessarily pathological? The purpose of this discussion is that, while genetic modification to treat or prevent diseases represents a significant advance in medicine, human enhancement through the modification of non-pathological characteristics may result in social and psychological risks. Finally, the argument regarding accessibility and equity holds that, although gene therapies have the potential to improve quality of life and eliminate genetic diseases, the costs associated with these technologies are high, raising serious concerns about inequality in access. Although CRISPR/Cas9 represents a significant advance in medicine, it brings with it complex ethical dilemmas that must be considered; and while the technique has the potential to revolutionize the treatment of genetic diseases, its use must be carefully regulated and evaluated from an ethical perspective to prevent abuses, inequalities, and possible unintended consequences for human society.

Conclusions

As discussed in this paper, CRISPR is a gene-editing tool that has revolutionized the field of science due to its precision, versatility, and simplicity compared to previous techniques. Its importance lies in its ability to modify DNA in a specific and efficient manner, opening doors to the treatment of genetic diseases, advances in biotechnology, and basic research.

CRISPR/Cas technology allows DNA to be “cut” at specific sites in the genome using a guide RNA (gRNA) that directs the Cas enzyme to the sequence of interest. Once the DNA is cut, the cells repair the damage, a process that can be harnessed to insert, delete, or correct genetic sequences at will. This is extremely useful for studying genetic diseases, as it allows for the creation of *in vitro* and *in vivo* models more quickly and at a lower cost. It also has potential applications *in vivo* and *ex vivo* gene therapies to correct mutations that cause diseases such as cystic fibrosis, sickle cell anemia, or certain types of cancer. In fact, the first CRISPR-based therapy for sickle cell anemia was approved by the FDA in late 2023, and several clinical trials are currently underway.

From a scientific perspective, CRISPR has democratized gene editing, enabling laboratories around the world to generate and study genetic modifications according to local needs. This is also the case in Latin America, specifically in Peru, where various research projects are already underway in both the agricultural and healthcare sectors. The studies range from disease diagnosis and modeling of genetic variants of uncertain clinical significance to research in cell therapy. Some examples have been cited throughout this paper.

From a bioethical perspective, it is important to recognize that this tool is not infallible, as its application can lead to off target changes capable of producing undesirable effects in the human genome. In response to this challenge, intensive work is underway on various approaches to make CRISPR a safer technique. On the other hand, its use in germline cells is considered unacceptable, as genetic

modification would occur without the informed consent of the person being modified. Furthermore, this change would affect that individual's offspring and, more broadly, the human gene pool. Another risk is its use in enhancing certain traits that may have eugenic implications. In this context, a moratorium on the use of CRISPR in germ cells is already in place, and Doudna—one of the discoverers of CRISPR—has been among the voices leading this call (76).

As for its use in somatic cells, its application is considered acceptable when conducted in the context of disease research and for therapeutic purposes. Its use takes on greater significance when applied to research in low- and middle-income countries, as it facilitates the study of issues relevant to their local realities. To regulate its use, it is necessary to support research ethics committees so that they can evaluate specialized projects from both technical and bioethical perspectives. Likewise, it is recommended that the country's governing body for science—in Peru's case, Concytec—maintain a registry of projects related to genetic modification in both the health sector and other economic sectors.

In summary, CRISPR represents a crucial tool for advancing medicine, biology, and biotechnology, with enormous potential to solve global and local problems in various fields. In this regard, we believe it is important to highlight projects related to this topic carried out in Peru and to provide a scientific and bioethical perspective on the issue that can serve as inspiration for public policymakers and decision-makers who legislate and regulate its use in the country.

Conflict of Interest

The authors of the article declare that they have no conflict of interest in its preparation. SRPM and CNVLL have participated as researchers in the first case of CRISPR/Cas and its potential use in gene therapy in Peru, cited in this work.

References

1. Wang JY, Doudna JA. CRISPR technology: A decade of genome editing is only the beginning. *Science*. 2023; 379(6629):eadd8643. <https://doi.org/10.1126/science.add8643>
2. Liu Q, He D, Xie L. Prediction of off-target specificity and cell-specific fitness of CRISPR-Cas system using attention boosted deep learning and network-based gene feature. *PLoS Comput Biol*. 2019; 15(10):e1007480. <https://doi.org/10.1371/journal.pcbi.1007480>
3. Wu Q, Cui L, Liu Y, Li R, Dai M, Xia Z. CRISPR-Cas systems target endogenous genes to impact bacterial physiology and alter mammalian immune responses. *Mol Biomed*. 2022; 3(1):22. <https://doi.org/10.1186/s43556-022-00085-w>
4. Barrangou R, Fremaux C, Deveau H, Richards M, Boyaval P, Moineau S. CRISPR provides acquired resistance against viruses in prokaryotes. *Science*. 2007; 315(5819):1709-12. <https://doi.org/10.1126/science.1138140>
5. Jinek M, Chylinski K, Fonfara I, Hauer M, Doudna JA, Charpentier E. A programmable dual-RNA-guided DNA endonuclease in adaptive bacterial immunity. *Science*. 2012; 337(6096):816-21. <https://doi.org/10.1126/science.1226796>
6. Ishino Y, Shinagawa H, Makino K, Amemura M, Nakata A. Nucleotide sequence of the *iap* gene, responsible for alkaline phosphatase isozyme conversion in *Escherichia coli*, and identification of the gene product. *J Bacteriol*. 1987; 169(12):5429-33. <https://doi.org/10.1128/jb.169.12.5429-5433.1987>
7. Brouns SJJ, Jore MM, Lundgren M, Westra ER, Slijkhuis RJH, Snijders APL. Small CRISPR RNAs guide antiviral defense in prokaryotes. *Science*. 2008; 321(5891):960-4. <https://doi.org/10.1126/science.1159689>
8. Pacesa M, Pelea O, Jinek M. Past, present, and future of CRISPR genome editing technologies. *Cell*. 2024; 187(5):1076-100. <https://doi.org/10.1016/j.cell.2024.01.042>
9. Jasin M. Genetic manipulation of genomes with rare-cutting endonucleases. *Trends Genet*. 1996; 12(6):224-8. [https://doi.org/10.1016/0168-9525\(96\)10019-6](https://doi.org/10.1016/0168-9525(96)10019-6)
10. Doudna JA, Charpentier E. Genome editing. The new frontier of genome engineering with CRISPR-Cas9. *Science*. 2014; 346(6213):1258096. <https://doi.org/10.1126/science.1258096>
11. Wang JY, Doudna JA. CRISPR technology: A decade of genome editing is only the beginning. *Science*. 2023; 379(6629):eadd8643. <https://doi.org/10.1126/science.add8643>
12. Bravo JPK, Liu MS, Hibshman GN, Dangerfield TL, Jung K, McCool RS. Structural basis for mismatch surveillance by CRISPR-Cas9. *Nature*. 2022; 603(7900):343-7. <https://doi.org/10.1038/s41586-022-04655-8>
13. Lin S, Staahl BT, Alla RK, Doudna JA. Enhanced homology-directed human genome engineering by controlled timing of CRISPR/Cas9 delivery. *eLife*. 2014; 3:e04766. <https://doi.org/10.7554/eLife.04766>

14. Boyle EA, Becker WR, Bai HB, Chen JS, Doudna JA, Greenleaf WJ. Quantification of Cas9 binding and cleavage across diverse guide sequences maps landscapes of target engagement. *Sci Adv*. 2021; 7(8):eabe5432. <https://doi.org/10.1126/sciadv.abe5496>
15. Pacesa M, Loeff L, Querques I, Muckenfuss LM, Sawicka M, Jinek M. R-loop formation and conformational activation mechanisms of Cas9. *Nature*. 2022; 609(7925):191-6. <https://doi.org/10.1038/s41586-023-06779-x>
16. Kleinstiver BP, Pattanayak V, Prew MS, Tsai SQ, Nguyen NT, Zheng Z, et al. High-fidelity CRISPR-Cas9 nucleases with no detectable genome-wide off-target effects. *Nature*. 2016; 529(7587):490-5. <https://doi.org/10.1038/nature16526>
17. Casini A, Olivieri M, Petris G, Montagna C, Reginato G, Maule G. A highly specific SpCas9 variant is identified by in vivo screening in yeast. *Nat Biotechnol*. 2018; 36(3):265-71. <https://doi.org/10.1038/nbt.4066>
18. Vakulskas CA, Dever DP, Rettig GR, Turk R, Jacobi AM, Collingwood MA. A high-fidelity Cas9 mutant delivered as a ribonucleoprotein complex enables efficient gene editing in human hematopoietic stem and progenitor cells. *Nat Med*. 2018; 24(8):1216-24. <https://doi.org/10.1038/s41591-018-0137-0>
19. Collias D, Beisel CL. CRISPR technologies and the search for the PAM-free nuclease. *Nat Commun*. 2021; 12(1):555. <https://doi.org/10.1038/s41467-020-20633-y>
20. Gleditsch D, Pausch P, Müller-Esparza H, Özcan A, Guo X, Bange G. PAM identification by CRISPR-Cas effector complexes: Diversified mechanisms and structures. *RNA Biol*. 2019; 16(4):504-17. <https://doi.org/10.1080/15476286.2018.1504546>
21. Ceccaldi R, Sarangi P, D'Andrea AD. The Fanconi anaemia pathway: New players and new functions. *Nat Rev Mol Cell Biol*. 2016; 17(6):337-49. <https://doi.org/10.1038/nrm.2016.48>
22. Lieber MR. The mechanism of human nonhomologous DNA end joining. *J Biol Chem*. 2008; 283(1):1-5. <https://doi.org/10.1074/jbc.R700039200>
23. Liao H, Wu J, VanDusen NJ, Li Y, Zheng Y. CRISPR-Cas9-mediated homology-directed repair for precise gene editing. *Mol Ther Nucleic Acids*. 2024; 35(4):102344. <https://doi.org/10.1016/j.omtn.2024.102344>
24. Moynahan ME, Jasin M. Mitotic homologous recombination maintains genomic stability and suppresses tumorigenesis. *Nat Rev Mol Cell Biol*. 2010; 11(3):196-207. <https://doi.org/10.1038/nrm2851>
25. Heyer WD, Ehmsen KT, Liu J. Regulation of homologous recombination in eukaryotes. *Annu Rev Genet*. 2010; 44:113-39. <https://doi.org/10.1146/annurev-genet-051710-150955>
26. Rouet P, Smih F, Jasin M. Expression of a site-specific endonuclease stimulates homologous recombination in mammalian cells. *Proc Natl Acad Sci U S A*. 1994; 91(13):6064-8. <https://doi.org/10.1073/pnas.91.13.6064>
27. Yang H, Ren S, Yu S, Pan H, Li T, Ge S. Methods favoring homology-directed repair choice in response to CRISPR/Cas9 induced-double strand breaks. *Int J Mol Sci*. 2020; 21(18):6861. <https://doi.org/10.3390/ijms21186461>

28. Paquet D, Kwart D, Chen A, Sproul A, Jacob S, Teo S. Efficient introduction of specific homozygous and heterozygous mutations using CRISPR/Cas9. *Nature*. 2016; 533(7601):125-9. <https://doi.org/10.1038/nature17664>
29. Richardson CD, Ray GJ, DeWitt MA, Curie GL, Corn JE. Enhancing homology-directed genome editing by catalytically active and inactive CRISPR-Cas9 using asymmetric donor DNA. *Nat Biotechnol*. 2016; 34(3):339-44. <https://doi.org/10.1038/nbt.3481>
30. Yeh CD, Richardson CD, Corn JE. Advances in genome editing through control of DNA repair pathways. *Nat Cell Biol*. 2019; 21(12):1468-78. <https://doi.org/10.1038/s41556-019-0425-z>
31. Yang D, Scavuzzo MA, Chmielowiec J, Sharp R, Bajic A, Borowiak M. Enrichment of G2/M cell cycle phase in human pluripotent stem cells enhances HDR-mediated gene repair with customizable endonucleases. *Sci Rep*. 2016; 6:21264. <https://doi.org/10.1038/srep21264>
32. Wienert B, Nguyen DN, Guenther A, Feng SJ, Locke MN, Wyman SK. Timed inhibition of CDC7 increases CRISPR-Cas9 mediated templated repair. *Nat Commun*. 2020; 11(1):2109. <https://doi.org/10.1038/s41467-020-15845-1>
33. Lin Y, Cradick TJ, Brown MT, Deshmukh H, Ranjan P, Sarode N. CRISPR/Cas9 systems have off-target activity with insertions or deletions between target DNA and guide RNA sequences. *Nucleic Acids Res*. 2014; 42(11):7473-85. <https://doi.org/10.1093/nar/gku402>
34. Riesenberger S, Kanis P, Macak D, Wollny D, Düsterhöft D, Kowalewski J. Efficient high-precision homology-directed repair-dependent genome editing by HD-Robust. *Nat Methods*. 2023; 20(9):1388-99. <https://doi.org/10.1038/s41592-023-01949-1>
35. Charlesworth CT, Deshpande PS, Dever DP, Camarena J, Lemgart VT, Cromer MK. Identification of preexisting adaptive immunity to Cas9 proteins in humans. *Nat Med*. 2019; 25(2):249-54. <https://doi.org/10.1038/s41591-018-0326-x>
36. Wagner DL, Amini L, Wendering DJ, Burkhardt LM, Akyüz L, Reinke P. High prevalence of *Streptococcus pyogenes* Cas9-reactive T cells within the adult human population. *Nat Med*. 2019; 25(2):242-8. <https://doi.org/10.1038/s41591-018-0204-6>
37. Hakim CH, Kumar SRP, Pérez-López DO, Wasala NB, Zhang D, Yue Y. Cas9-specific immune responses compromise local and systemic AAV CRISPR therapy in multiple dystrophic canine models. *Nat Commun*. 2021; 12(1):6769. <https://doi.org/10.1038/s41467-021-26830-7>
38. Ferdosi SR, Ewaisha R, Moghadam F, Krishna S, Park JG, Ebrahimkhani MR. Multifunctional CRISPR-Cas9 with engineered immunosilenced human T cell epitopes. *Nat Commun*. 2019; 10(1):1842. <https://doi.org/10.1038/s41467-019-09693-x>
39. Doudna JA. The promise and challenge of therapeutic genome editing. *Nature*. 2020; 578(7794):229-36. <https://doi.org/10.1038/s41586-020-1978-5>
40. Wu X, Scott DA, Kriz AJ, Chiu AC, Hsu PD, Dadon DB. Genome-wide binding of the CRISPR endonuclease Cas9 in mammalian cells. *Nat Biotechnol*. 2014; 32(7):670-6. <https://doi.org/10.1038/nbt.2889>

41. Kosicki M, Tomberg K, Bradley A. Repair of double-strand breaks induced by CRISPR–Cas9 leads to large deletions and complex rearrangements. *Nat Biotechnol.* 2018; 36(8):765-71. <https://doi.org/10.1038/nbt.4192>
42. Haapaniemi E, Botla S, Persson J, Schmierer B, Taipale J. CRISPR–Cas9 genome editing induces a p53-mediated DNA damage response. *Nat Med.* 2018; 24(7):927-30. <https://doi.org/10.1038/s41591-018-0049-z>
43. Modell AE, Lim D, Nguyen TM, Sreekanth V, Choudhary A. CRISPR-based therapeutics: Current challenges and future applications. *Trends Pharmacol Sci.* 2022; 43(2):151-61. <https://doi.org/10.1016/j.tips.2021.10.012>
44. Cappell KM, Kochenderfer JN. Long-term outcomes following CAR T cell therapy: What we know so far. *Nat Rev Clin Oncol.* 2023; 20(6):359-71. <https://doi.org/10.1038/s41571-023-00754-1>
45. Frangoul H, Altshuler D, Cappellini MD, Chen YS, Domm J, Eustace BK. CRISPR–Cas9 gene editing for sickle cell disease and β -thalassemia. *N Engl J Med.* 2021; 384(3):252-60. <https://doi.org/10.1056/NEJMoa2031054>
46. Song P, Zhang Q, Xu Z, Shi Y, Jing R, Luo D. CRISPR/Cas-based CAR-T cells: production and application. *Biomark Res.* 2024; 12(1):54. <https://doi.org/10.1186/s40364-024-00602-z>
47. Chiesa R, Georgiadis C, Syed F, Zhan H, Etuk A, Gkazi SA. Base-edited CAR7 T cells for relapsed T-cell acute lymphoblastic leukemia. *N Engl J Med.* 2023; 389(10):899-910. <https://doi.org/10.1056/NEJMoa2300709>
48. Shapiro AMJ, Thompson D, Donner TW, Bellin MD, Hsueh W, Pettus J. Insulin expression and C-peptide in type 1 diabetes subjects implanted with stem cell-derived pancreatic endoderm cells in an encapsulation device. *Cell Rep Med.* 2021; 2(12):100466. <https://doi.org/10.1016/j.xcrm.2021.100466>
49. Lee RG, Mazzola AM, Braun MC, Platt C, Vafai SB, Kathiresan S. Efficacy and safety of an investigational single-course CRISPR base-editing therapy targeting PCSK9 in nonhuman primate and mouse models. *Circulation.* 2023; 147(3):242-53. <https://doi.org/10.1161/CIRCULATIONAHA.122.062132>
50. Walters M, Frangoul H, McKinney C, Pineiro L, Mapara M, Dalal J. Reni-Cel, an investigational AsCas12a gene-edited cell medicine, led to sustained hemoglobin normalization and increased fetal hemoglobin in patients with severe sickle cell disease treated in the RUBY trial. *Transplant Cell Ther.* 2025; 31(2):S21-2. <https://doi.org/10.1016/j.jtct.2025.01.039>
51. Patsali P, Kleanthous M, Lederer CW. Disruptive technology: CRISPR/Cas-based tools and approaches. *Mol Diagn Ther.* 2019; 23(2):187-200. <https://doi.org/10.1007/s40291-019-00391-4>
52. Jeong SH, Lee HJ, Lee SJ. Recent advances in CRISPR-Cas technologies for synthetic biology. *J Microbiol.* 2023; 61(1):13-36. <https://doi.org/10.1007/s12275-022-00005-5>
53. Choubisa V. CRISPR-Cas9 off-target predictions using CNN and double CNN: Comparative analysis. *Int J Sci Res Arch.* 2024; 12(1):1074-80. <https://doi.org/10.30574/ijrsra.2024.12.1.0927>

54. Uddin F, Rudin CM, Sen T. CRISPR gene therapy: Applications, limitations, and implications for the future. *Front Oncol.* 2020; 10:1387. <https://doi.org/10.3389/fonc.2020.01387>
55. Cui Z, Lin L, Zong Y, Chen Y, Wang S. Precision gene editing using deep learning: A case study of the CRISPR-Cas9 editor. *Appl Comput Eng.* 2024; 64(1):134-41. <https://doi.org/10.54254/2755-2721/64/20241357>
56. CONCYTEC/FONDECYT. Resumen de los 190 Proyectos de Investigación Aplicada y Desarrollo Tecnológico. Lima: CONCYTEC; 2019.
57. Kamde SP, Anjankar A. Retinitis pigmentosa: Pathogenesis, diagnostic findings, and treatment. *Cureus.* 2023; 15(10):e47961. <https://doi.org/10.7759/cureus.48006>
58. Ledford H, Callaway E. Pioneers of revolutionary CRISPR gene editing win chemistry Nobel. *Nature.* 2020; 586(7829):346-7. <https://doi.org/10.1038/d41586-020-02765-9>
59. CONCYTEC. Científicos peruanos desarrollan tecnología para diagnóstico rápido y preciso de enfermedades infecciosas [Internet]. Lima: CONCYTEC; 2020 [cited 2026 feb 18].
60. Dueñas E, Nakamoto JA, Cabrera-Sosa L, Huaihua P, Cruz M, Arévalo J. Novel CRISPR-based detection of Leishmania species. *Front Microbiol.* 2022; 13:1044431. <https://doi.org/10.3389/fmicb.2022.958693>
61. Proyecto de Fortalecimiento del SINACTI/ProCiencia. Disminución de la absorción del cadmio en el cacao peruano mediante la edición genética de sus transportadores empleando la tecnología CRISPR-Cas9 (Registro: N.º 026 propuesta_60208) [Internet]. Lima: ProCiencia; 2019 [cited 2026 feb 18]. Available at: <https://proyecto-fortalecimiento-del-sinacti-prociencia.gob.pe/investigacion/disminucion-de-la-absorcion-del-cadmio-en-el-cacao-peruano-mediante-la-edicion-genetica-de-sus-transportadores-empleando-la-tecnologia-crispr-cas9/>
62. Paredes-Moscosso SR, Villegas-Llerena C, Quispe-Bravo BE, Buleje J, Guevara-Fujita ML, Fujita R. Abstract 6338: CRISPR/Cas9 in vitro modelling of a VUS mutation found in Peruvian patients diagnosed with hereditary breast cancer. *Cancer Res.* 2025; 85(8 Suppl 1):6338. <https://doi.org/10.1158/1538-7445.AM2025-6338>
63. Fráncio L, Freitas MV de, Matte U. CRISPR/Cas patents and health-related publications in South America. *An Acad Bras Cienc.* 2023; 95(2):e20220475. <https://doi.org/10.1590/0001-3765202320220629>
64. Ñique C, Cervera M, Díaz R, Domínguez C. Principios bioéticos en el contexto de la pandemia de COVID-19. *Rev Med Hered.* 2020; 31(4):255-65. <https://www.redalyc.org/articulo.oa?id=338065627009>
65. Santa María D Angelo R, Quiceno JD, Torres A, Perochena AC. [The CRISPR/Cas9 techniques applied to human genetic enhancement: a biotechnological, anthropological-philosophical and legal dialogue]. *Cuad Bioet.* 2020; 31(103):343-55.
66. Infante-López DV, Céspedes-Galvis MF, Wilches-Flórez ÁM. CRISPR-Cas9: el debate bioético más allá de la línea germinal. *Pers Bioet.* 2022; 25(2):e2526. <https://doi.org/10.5294/pebi.2021.25.2.9>

67. Gómez-Tatay L, Aznar J. [CRISPR-CAS9. The greatest advancement in genetic edition techniques requires an ethical reflection]. *Cuad Bioet.* 2019;30(99):171-85.
68. Das S, Bano S, Kapse P, Kundu GC. CRISPR based therapeutics: A new paradigm in cancer precision medicine. *Mol Cancer.* 2022; 21(1):85. <https://doi.org/10.1186/s12943-022-01552-6>
69. Ayanoğlu FB, Elçin AE, Elçin YM. Bioethical issues in genome editing by CRISPR-Cas9 technology. *Turk J Biol.* 2020; 44(2):110-20. <https://doi.org/10.3906/biy-1912-52>
70. Xu X, Liu C, Wang Y, Koivisto O, Zhou J, Shu Y. Nanotechnology-based delivery of CRISPR/Cas9 for cancer treatment. *Adv Drug Deliv Rev.* 2021; 176:113891. <https://doi.org/10.1016/j.addr.2021.113891>
71. Adashi EY, Gruppuso PA, Cohen IG. CRISPR therapy of sickle cell disease: The dawning of the gene editing era. *Am J Med.* 2024; 137(5):390-2. <https://doi.org/10.1016/j.amjmed.2023.12.018>
72. Donoso RF, Gómez N, Rodríguez A. Edición genómica con CRISPR-Cas9 y su aplicación en trastornos genéticos. *Rev Cubana Invest Bioméd.* 2024; 42(Supl esp):e3230. Available at: <https://revibiomedica.sld.cu/index.php/ibi/article/view/3354>
73. Ferreyra KA. Consideraciones éticas sobre CRISPR/Cas9: Uso terapéutico en embriones y futura gobernabilidad. *Rev Bioét Der.* 2022; (55):121-38. <https://dx.doi.org/10.1344/rbd2021.54.36115>
74. Palacios ML. CRISPR/Cas9: Edición genética vs. bioética. *Apuntes Bioét.* 2019; 2(1):5-18. <https://revistas.usat.edu.pe/index.php/apuntes/article/view/238/865?download=pdf>
75. Lorenzo D, Esquerda M, Palau F, Cambra FJ. Ethics and genomic editing using the CRISPR-Cas9 technique: Challenges and conflicts. *Nanoethics.* 2022; 16(3):313-21. <https://doi.org/10.1007/s11569-022-00425-y>
76. Doudna J. CRISPR's unwanted anniversary. *Science.* 2019; 366(6467):777. <https://doi.org/10.1126/science.aba1751>