v. 5, n. 20, 2025

International Journal of Health Science

Acceptance date: 12/05/2025

THERAPEUTIC POTENTIAL OF GENE EDITING TO FIGHT CANCER - USING CRISPR-Cas9

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Abstract: Objective: The aim of this study was to review the therapeutic potential of gene editing using CRISPR-Cas9 technology in the treatment of cancer, analyzing its application in the inactivation of oncogenes, reactivation of tumor suppressor genes, modulation of the tumor microenvironment and the development of preclinical models. **Methodology:** An exploratory and qualitative literature review was carried out. The data was obtained from databases such as PubMed (National Library of Medicine), Lilacs (Latin American and Caribbean Literature in Health Sciences), Scielo (Scientific Electronic Library Online), Google Scholar, Regional Council of Biomedicine and Federal Council of Biomedicine. The search included studies in Portuguese, English and Spanish and focused on the central theme "Therapeutic potential of gene editing to fight cancer - use of CRISPR-Cas9". The key terms used for the search included: "advanced genetic technologies", "history of CRISPR-Cas9", "cell and gene therapy", "gene editing", "CRISPR-Cas9", "cancer treatment". **Final considerations:** CRISPR-Cas9 technology has revolutionized biotechnology and has great potential in cancer treatment, allowing precise genomic editing such as silencing oncogenes, reactivating suppressor genes and modifying immune cells. In this context, biomedical professionals play a crucial role in the development of research aimed at creating new technologies, promoting the evolution of biomedicine. Despite promising advances in pre-clinical and clinical studies, there are still challenges such as off-target effects, low repair efficiency, immune responses and limitations in gene delivery. As research progresses, CRISPR-Cas9 could become a pillar of precision medicine in oncology.

Keywords: CRISPR-Cas9, Cell and gene therapy, Gene editing, Cancer, Biomedicine.

INTRODUCTION

Cancer remains one of the leading causes of mortality worldwide and is characterized by the uncontrolled growth of malignant cells, with the potential for tissue invasion and the formation of metastases (INSTITUTO NACIONAL DO CÂNCER, 2022). The elucidation of the molecular mechanisms underlying oncogenesis has been fundamental to the development of target therapies (TAN; TAN, 2022). In this scenario, gene editing has emerged as a promising approach, enabling precise modifications to the genome and corrections of mutations associated with cancer (COELHO et al., 2023). Among the tools available, the CRISPR-Cas9 system stands out, widely recognized for its efficiency, versatility and precision (MISHRA et al., 2023). The therapeutic potential of CRISPR-Cas9 technology represents a significant advance in precision medicine by allowing the specific editing of genetic sequences associated with carcinogenesis. This innovative approach has been widely studied for the development of more effective therapies, from the inactivation of oncogenes to the modulation of immune system cells to improve anti-tumor response (BOUMELHA et al., 2024; THEGE et al., 2022; ZHAO et al., 2021). However, challenges such as editing specificity, off-target effects and ethical and regulatory issues still need to be overcome (SHINWARI; TANVEER; KHALIL, 2017). Thus, understanding the potential, limitations and prospects of CRISPR-Cas9 in the oncology context is essential for its safe and effective clinical application.

The origin of CRISPR technology dates back to the late 1980s, when Japanese researchers identified a genomic locus with repeated sequences interspersed with spacers in the DNA of the bacterium *Escherichia coli*. Later, in the early 2000s, these sequences were observed in other microorganisms, leading to the name CRISPR (Clustered Regularly In-

terspaced Short Palindromic Repeats). The functional understanding of this system culminated, in 2012, in the development of the CRISPR-Cas9 gene editing technique, based on an RNA-guided endonuclease (CARLI; SOUZA; PEREIRA, 2017).

According to Siqueira (2024), CRISPR--Cas9 represents "molecular scissors" capable of cutting and editing specific DNA sequences, initially used by bacteria as a defense mechanism against viral infections. This tool has become essential in modern biotechnology, allowing the targeted editing of the genome of practically any cell type.

Originally identified as a bacterial adaptive immunity mechanism, the CRISPR-Cas9 system has been adapted for gene editing in eukaryotic cells (ÁLVAREZ; JULIÁN; PATARROYO, 2022). The technology uses an RNA (gRNA)-guided endonuclease (Cas9) that recognizes a specific target sequence, inducing double-strand breaks in the DNA. These breaks are repaired by cellular mechanisms such as non-homologous end joining (NHEJ) or homologous recombination (HDR), enabling gene insertions, deletions or substitutions (MENDES et al., 2024). This precision makes CRISPR-Cas9 a powerful tool for functional gene research and the development of gene therapies.

CRISPR-Cas9 applications range from correcting mutations in hereditary diseases and treating neoplasms to modifying immune system cells to fight viral infections such as HIV (MENDES et al., 2024). In oncology, the focus has been on silencing pro-tumor genes and identifying therapeutic targets for the development of innovative drugs (BRESOLIN; WIETHÖLTER; KIRSTEN, 2021).

The tumor microenvironment plays a crucial role in neoplastic progression and resistance to therapies. Gene editing mediated by CRISPR-Cas9 has been used to modify tumor stromal cells or the immune system in order to potentiate the anti-tumor response. Studies have shown that editing the PD-1 gene in T lymphocytes increases their cytotoxic activity against tumor cells, which opens up prospects for new immunotherapeutic approaches (BIGGI; SIMIONI, 2019).

Despite its great therapeutic potential, CRISPR-Cas9 technology faces important challenges. Because it is derived from bacteria, its components can induce an immune response in the host. Studies have already demonstrated pre-existing immunogenicity against the Cas9 protein in healthy humans, both humorally and cellularly. Thus, mitigating the system's immunogenicity is still a significant obstacle in clinical trials (MENGSTIE; WONDIMU, 2021).

In addition to technical issues, gene editing raises important ethical and biosafety dilemmas. Costa et al. (2021) highlight concerns about the misuse of CRISPR-Cas9, including the intentional creation of human strains carrying diseases such as Alzheimer's and Parkinson's, as well as the misappropriation of human genetic material. These issues emphasize the need for strict regulatory guidelines and responsible use of the technology.

Cancer, therefore, is characterized as one of the most complex and lethal diseases that promote uncontrolled cell proliferation, therapeutic resistance and metastatic capacity. Conventional therapies, such as chemotherapy and radiotherapy, often have limited efficacy and significant side effects (MINISTÉRIO DA SAÚDE). This disease therefore requires innovative therapeutic approaches. CRISPR--Cas9, with its capacity for precise genome editing, is emerging as one of the most promising strategies in the fight against the disease. The inactivation of oncogenes, the reactivation of suppressor genes, the modulation of the tumor microenvironment and the generation of preclinical models are just some of the possibilities offered by this revolutionary tool. The aim of this study was to review the

therapeutic potential of gene editing using CRISPR-Cas9 technology in the treatment of cancer, analyzing its application in the inactivation of oncogenes, reactivation of tumor suppressor genes, modulation of the tumor microenvironment and the development of preclinical models.

THEORETICAL BASIS

CRISPR-Cas9 research is evolving rapidly. Advances in editing specificity, the development of more efficient delivery systems and the combination with other therapeutic modalities, such as immunotherapies, could broaden its clinical applications. Ongoing clinical trials will provide crucial data on the safety and efficacy of this approach in cancer treatment. CRISPR-Cas9 represents a revolution in medicine, directly influencing biomedicine by offering a promising approach to cancer treatment through precise genome editing. Although technical and ethical challenges remain, continued advances in research could consolidate this technology as an effective therapeutic tool against various neoplasms.

MECHANISM OF ACTION OF CRISPR-Cas9

CRISPR technology, an acronym for *Clustered Regularly Interspaced Short Palindromic Repeats*, refers to an adaptive defense system mediated by ribonucleic acid (RNA), present in bacteria and archaea, whose primary function is to protect these organisms against exogenous genetic elements, such as bacteriophages and plasmids (CARDOSO; SIQUEIRA, 2023). According to the same authors, this system is based on the incorporation of viral DNA fragments into the bacterial genome, forming a kind of immunological memory located in the CRISPR loci. In this way, the mechanism allows the body to efficiently recognize and neutralize the invading agent in subsequent infections.

Among the CRISPR systems, CRISPR--Cas9 stands out as one of the most studied, consisting of three fundamental stages: adaptation, expression and interference. During the adaptation phase, segments of DNA from invading phages are identified and integrated into the CRISPR locus as new spacers. In the next phase, called expression, the CRISPR region is transcribed into pre-crRNA (CRISPR precursor RNA), regulated by a leader sequence. Finally, in the interference stage, the mature crRNA associates with the Cas9 endonuclease, forming a ribonucleoprotein complex that specifically recognizes and cleaves viral DNA by inducing double-strand breaks (DSBs), neutralizing the genetic threat (WINTER et al., 2021).

After DNA cleavage by the Cas9 endonuclease, cells activate endogenous repair mechanisms, which can follow two main pathways: *Homology Directed Repair* (HDR) and *Non-Homologous End Joining* (NHEJ). In the HDR mechanism, it is possible to insert an exogenous DNA sequence with homology to the target region, enabling precise editing of the genome. In contrast, in the absence of a repair template, the NHEJ pathway prevails, which, although prone to inducing unwanted mutations, can be strategically exploited in therapeutic contexts for the deletion of specific genes, such as oncogenes involved in tumorigenesis (CARDOSO; SIQUEIRA, 2023).

This ability to induce controlled DNA breaks and direct their repair is one of the most promising properties of CRISPR-Cas9 technology for therapeutic applications, particularly in the field of oncology. The high specificity of the Cas9 enzyme, guided by specific RNAs (gRNAs) for target regions of the genome, contributes to minimizing *off-target* effects, a fundamental aspect for ensuring safety and efficacy in clinical contexts (ALCANTARA et al., 2019).

The applicability of the CRISPR-Cas9 system in cancer treatment is directly related to its ability to promote permanent and highly targeted genetic alterations. Compared to approaches such as *RNA interference* (RNAi), which acts on the post-transcriptional silencing of genes, CRISPR-Cas9 enables modifications directly to the DNA, offering a more lasting, precise and effective alternative (CARDOSO; SIQUEIRA, 2023).

In addition, tumor cells often have specific genomic signatures, which makes it possible to use CRISPR-Cas9 technology to silence oncogenic genes or correct point mutations in tumor suppressor genes. The system's operational simplicity, combined with its high efficiency and specificity, positions CRISPR-Cas9 as a valuable tool in the advancement of personalized medicine, contributing to the development of more effective and individualized cancer therapies (ALCANTARA et al., 2019).

The ability to edit genes associated with tumor development and progression makes CRISPR-Cas9 a promising therapeutic strategy, overcoming some of the limitations inherent in conventional therapies, such as chemotherapy and radiotherapy, which have less selectivity and greater systemic toxicity. Gene editing can, for example, inactivate hyperactive oncogenes or restore the function of tumor suppressor genes, enabling more specific and less aggressive interventions in the patient's body (CARDOSO; SIQUEIRA, 2023).

THERAPEUTIC APPLICATIONS IN CANCER TREATMENT

Cancer is a disease of genomic origin, characterized by alterations in different classes of genes that regulate cell growth, division and survival. Among these genes are the proto-oncogenes, which, under physiological conditions, promote the progression of the cell cycle. However, mutations in these genes can convert them into oncogenes, resulting in constitutive activation and uncontrolled cell proliferation (GRAZIANO; GONZALO, 2017). In contrast, tumor suppressor genes act as negative regulators of cell division, participating in DNA repair processes and inducing apoptosis. The inactivation of these genes compromises genomic integrity, favoring the accumulation of mutations and the formation of neoplasms. Thus, tumorigenesis can occur both through the activation of oncogenes and the loss of function of suppressor genes (BRESOLIN; WIETHÖLTER; KIRSTEN, 2021).

In this context, CRISPR-Cas9 technology is emerging as a promising therapeutic strategy due to its high precision and efficiency in genomic editing. Its use has been widely explored in cancer research, especially due to the multifactorial complexity involved in cancer development. The technique allows for the construction of *in vitro* tumor models, which are fundamental for investigating the genetic determinants of neoplasia and for identifying new therapeutic targets (SIQUEIRA, 2024).

Several studies have used the CRISPR--Cas9 system to silence genes associated with oncogenesis in specific cell lines. After editing and validating the inactivation of target genes, functional assays are conducted to assess changes in cell behavior, such as proliferation, migration, invasion and colony formation (BRESOLIN; WIETHÖLTER; KIRSTEN, 2021). The results of these experiments have shown significant reductions in the proliferative and invasive capacity of tumor cells, an increase in the rate of apoptosis and a decrease in cell viability, reinforcing the potential of CRISPR-Cas9 as a tool for developing targeted and personalized therapies (BRESOLIN; WIETHÖLTER; KIRSTEN, 2021).

One of the most relevant examples of the application of the CRISPR-Cas9 system in oncology is the treatment of cervical cancer, the main etiology of which is associated with persistent infection by the Human Papillo-

International Journal of Health Science ISSN 2764-0159 DOI https://doi.org/10.22533/at.ed.15952025240415

mavirus (HPV). Considering the viral origin of the CRISPR system as a bacterial adaptive defense mechanism, its use makes it possible to target the viral genome integrated into infected cells (SIQUEIRA, 2024). Through the use of a specific guide RNA (sgRNA), the Cas9 enzyme can be directed to the E6 and E7 viral oncogenes, promoting their cleavage and consequent inactivation. Silencing these genes induces tumor cell apoptosis, since the E6 protein is involved in the degradation of p53, while E7 inhibits the action of the pRb protein, both of which have critical functions as tumor suppressors (SIQUEIRA, 2024).

Studies have shown the effectiveness of this approach, demonstrating a significant reduction in the expression of E6 and E7 in infected cells. The results are even more promising when gene therapy is associated with the use of chemotherapy drugs, such as cisplatin (CDDP), enhancing the anti-tumor effects. In addition, the high specificity of the CRISPR--Cas9 system also allows selective targeting of pre-cancerous cells, reinforcing its clinical applicability and safety (SIQUEIRA, 2024).

In addition to silencing viral oncogenes, the CRISPR-Cas9 system can be used to reactivate tumor suppressor genes, such as the Phosphatase and Tensin Homolog (PTEN). This gene plays a crucial role in the negative regulation of signaling pathways associated with cell survival, cell cycle progression and tumor migration. Loss or reduced expression of PTEN is implicated in several types of cancer, including melanoma and triple-negative breast cancer (TNBC) (MOSES et al., 2019). Gene reactivation strategies using the CRISPR/dCas9 system - a catalytically inactive variant of Cas9 coupled to transcriptional activators - have been shown to be effective in inducing PTEN expression, promoting the inhibition of oncogenic pathways and configuring an innovative and promising therapeutic approach.

Another relevant aspect of the application of CRISPR-Cas9 technology in cancer treatment refers to the genetic modification of immune cells, especially T lymphocytes. This approach can be carried out by deleting the PDCD1 gene, responsible for encoding the PD-1 protein, or by introducing chimeric antigen receptors (CAR-T) into these cells (LOPES, 2021). In the first case, the deletion of PD-1 prevents the inhibition of the immune response by tumor cells, which normally use the interaction between PD-1 and its ligand, PD-L1, to suppress the activity of T lymphocytes. CAR-T cell engineering, on the other hand, allows lymphocytes to recognize and eliminate tumor cells in a highly specific way, significantly increasing the effectiveness of the anti-tumor immune response (LOPES, 2021).

The immunosuppressive conditions that characterize the tumour microenvironment continue to be a challenge for the effectiveness of immunotherapy. However, the CRISPR-Cas9 system has also been used to edit genes that regulate this environment. A notable example is the ablation of the KDM3A gene, which resulted in greater sensitivity of refractory tumors to immunotherapy. This effect was attributed to modulation of EGFR receptor expression, mediated by signaling pathways involving the factors KLF5 and SMAD4, as well as increased inflammatory activity of tumor-infiltrating T cells (CARDOSO; SIQUEIRA, 2023).

Furthermore, when combined with other therapeutic strategies, such as chemotherapy or immunotherapy, CRISPR-Cas9-mediated genomic editing demonstrates a synergistic effect, enhancing treatment efficacy and reducing systemic side effects. This ability to act in a multifocal and personalized way on genetic and immunological targets positions the technology as a strategic and promising ally in the fight against cancer (SIQUEIRA, 2024).

PRE-CLINICAL MODELS AND ONGOING CLINICAL TRIALS

Following promising results obtained in pre-clinical studies, CRISPR/Cas9 technology was quickly incorporated into the scope of clinical applications, especially in the field of oncology. Since 2016, several clinical trials have been conducted with an emphasis on cancer immunotherapy, with the PD-1/PD-L1 pathway being one of the most relevant therapeutic targets. According to Xu et al. (2021), at least eighteen clinical trials have been initiated since the clinical introduction of CRISPR/Cas9, eight of which focus specifically on the modulation of PD-1 (programmed cell death protein 1).

PD-1 is a protein expressed in T and B lymphocytes and myeloid cells, whose interaction with its ligand, PD-L1 - often present in tumor cells - plays a crucial role in inhibiting the anti-tumor immune response, favoring immune evasion by neoplastic cells (XU et al., 2021). To this end, this mechanism has been widely explored as a therapeutic target, especially in the context of modern immunotherapy.

The initial milestone in the clinical use of the technology occurred in 2016, when Chinese researchers carried out the first phase I human clinical trial (NCT02793856). In this study, autologous T lymphocytes from patients with Non-Small Cell Lung Cancer (NSCLC) were edited by CRISPR/Cas9 with the aim of inactivating the PDCD1 gene, which encodes the PD-1 protein, in order to enhance the immune response against the tumor (BIGGI; SIMIONI, 2019; XU et al., 2021).

In the context of Non-Small Cell Lung Cancer (NSCLC), PD-1 deactivation has shown encouraging clinical results. In studies with T lymphocytes obtained from patients and healthy donors, gene editing resulted in a loss of PD-1 expression, without compromising the proliferative capacity of T cells. In addition, an increase in the production of inflammatory cytokines was observed, indicating a more robust immune response (BIGGI; SIMIONI, 2019).

Later advances made it possible to apply the technology to CAR-T cells (chimeric antigen receptors), combining lentivirus vectors with the CRISPR/Cas9 system to generate T-CAR cells deficient in PD-1. This strategy resulted in a more than 50% reduction in PD-1 expression, without impairing cell activation. In murine models, in vivo trials have shown complete tumor elimination, provided that the administered dose of CAR-T cells was adequate (BIGGI; SIMIONI, 2019).

In view of these advances, CRISPR/Cas9 technology is now being explored in other types of cancer. Xu et al. (2021) report clinical trials in liver cancer (NCT04417764), prostate (NCT03525652), esophagus (NCT0308171) and Epstein-Barr virus-associated neoplasms (NCT03044743), all with the aim of deactivating PD-1 in autologous T lymphocytes.

The versatility of the CRISPR/Cas9 system, with the possibility of making multiple edits simultaneously, combined with its technical ease, gives it a central role in so-called precision medicine. The technology enables the identification of genomic vulnerabilities specific to each tumor, making it possible to develop personalized therapeutic strategies (LI et al., 2020).

The results accumulated to date demonstrate the potential of CRISPR/Cas9 in modulating the anti-tumor immune response, especially through PD-1 editing. However, as Li et al. (2020) warn, technical and clinical challenges remain, including the risks of off-target effects, immune responses against the Cas9 system and the need to optimize gene delivery vectors. As these obstacles are overcome, CRISPR/Cas9 is likely to become a transformative tool in cancer treatment, offering more effective, safer and individualized approaches.

CHALLENGES, LIMITATIONS AND FUTURE PROSPECTS OF CRISPR-Cas9 TECHNOLOGY IN ONCOLOGY

Since its discovery, CRISPR/Cas9 technology has revolutionized genetic engineering by offering a robust, precise and versatile platform for genomic editing in various organisms. In the field of oncology, its impact has been particularly significant, contributing significantly to both the elucidation of the molecular mechanisms of cancer and the development of personalized therapeutic strategies (CARDOSO; SIQUEIRA, 2023). Thanks to its specificity in modifying target sequences, the CRISPR/Cas9 platform is emerging as a promising alternative for tackling different types of cancer (YANG et al., 2021).

However, the therapeutic application of CRISPR/Cas9 still faces considerable technical challenges. One of the main problems is the occurrence of *off-target* effects, in which the Cas9 endonuclease promotes unintentional cleavages in genomic regions similar to the target sequence. These events compromise the safety of clinical interventions, especially in complex eukaryotic organisms such as humans (YANG et al., 2021). The specificity of Cas9 is mediated by the guide RNA (gRNA) and the presence of the adjacent proto-spacer motif (PAM), and imperfect pairings can lead to non-specific genomic editing. Although bioinformatics tools such as CCTop and Cas-OFFinder help predict possible side effects, there are still limitations in detecting epigenetic modifications and complex genomic structures (YANG et al., 2021).

To get around these limitations, various strategies have been developed, including the use of high-fidelity Cas9 variants (such as eSpCas9, HF-Cas9, HypaCas9 and Sniper-Cas9), nickases and conditional activation systems. The use of next-generation sequencing (NGS) has been fundamental in identifying unwanted mutations and validating the genomic safety of experiments (YANG et al., 2021).

For this technology, another relevant technical challenge is the low efficiency of homologous recombination (HDR), especially at certain loci. Strategies such as the use of ssDNA donor molecules and chemical modulators have been used to optimize the process, although adverse effects such as cell apoptosis induced by activation of the p53 pathway have been observed, notably in pluripotent stem cells (YANG et al., 2021). In this context, innovative approaches have emerged, such as base editors and prime editors, capable of promoting punctual modifications without inducing double-strand breaks in the DNA, reducing the risks of genomic instability (YANG et al., 2021).

In addition, immune responses against bacterial components, such as the SpCas9 and SaCas9 proteins, represent a barrier to clinical use. These proteins can be recognized as antigens by the human immune system, triggering inflammatory or cytotoxic responses (NIDHI et al., 2021). According to the same authors, structural modifications to the REC1 domain of Cas9 are being investigated in order to prevent immune recognition. In addition, activation of the TP53 gene in response to DNA breaks can result in programmed cell death, requiring a careful balance between therapeutic efficacy and possible adverse effects

In order to overcome these limitations, other proteins from the CRISPR-Cas family have been explored. Cas12, especially the Cas12a (Cpf1) variant, has advantages such as the generation of cohesive ends and the absence of the HNH domain, which makes it an interesting alternative for genome editing (BHARATHKUMAR et al., 2022). Variants such as BhCas12b and CeCas12a have shown high activity in human cells, with gains in specificity and efficiency (BHARATHKUMAR et al., 2022).

Another emerging approach involves the use of Cas13, a ribonuclease capable of editing and modulating RNA with high specificity,

without directly interfering with DNA. This enzyme recognizes the target RNA through a crRNA and, by activating its HEPN domains, promotes specific cleavage. Its reversible action, combined with the independence of the PAM sequence, makes this technology attractive for temporary therapies and molecular diagnostics (BHARATHKUMAR et al., 2022).

Efficient delivery of the components of the CRISPR system remains one of the main challenges for its clinical application. Several platforms have been used, such as plasmids, viral vectors and ribonucleoprotein complexes ((NIDHI et al., 2021)RNPs), each with advantages and limitations . In this context, nanotechnology has stood out as a promising strategy, allowing the encapsulation, protection and controlled release of CRISPR/Cas9 components by means of specific nanoparticles (ÁLVAREZ et al., 2022; XU et al., 2021).

Cationic nanocarriers, which are positively charged nanoscale drug delivery systems such as liposomes and polymers, interact with the components of the CRISPR system by electrostatic attraction, increasing stability and promoting efficient transfection (XU et al., 2021). Studies show that hyper-ramified polymers and copolymers such as PBAE (Poly(beta-amino esters)) and PAMAM (poly(amidoamine)) improve intracellular delivery and minimize adverse effects. Inorganic nanoparticles, such as black phosphorus sheets (BPs), have also shown efficacy in localized delivery of RNP complexes, with significant gene deletions in tumor models (XU et al., 2021). Additional innovations include the use of DNA nanoclews and boronic acid-functionalized copolymers, which have demonstrated high performance in protecting and targeting CRISPR complexes (WANG et al., 2022; XU et al., 2021).

Despite these advances, the application of genome editing in humans continues to be surrounded by ethical and legal issues. Concerns involving long-term risks, germline modification and the possible use of the technology for human genetic enhancement have been widely debated (NIDHI et al., 2021). According to Costa et al. (2021), it is essential to develop strict regulations and encourage public debate based on respect for human dignity and bioethical responsibility.

In addition, biosafety risks, such as the possibility of using gene editing in biological conflicts, cannot be overlooked. The ease of access and low operating cost of the CRISPR system increase the risk of its application by unskilled individuals or those with malicious intentions (NIDHI et al., 2021). It is therefore essential that the advancement of technology goes hand in hand with governance policies, control mechanisms and a scientific culture based on ethics and social responsibility.

THERAPEUTIC POTENTIAL OF GENE EDITING TO FIGHT CANCER AND IMPLICATIONS FOR BIOMEDICAL PRACTICE

Biomedicine plays a fundamental role in both the research and clinical application of these therapies. Biomedical scientists are key professionals in the development of new genetic therapies, as their training encompasses an in-depth understanding of molecular biology, genetics and laboratory technologies. The biomedical technician's technical-scientific training allows them to work in molecular biology, pharmacogenomics, translational neuroscience and cell therapy laboratories, which are essential areas for the advancement of gene therapy (CONSELHO FEDERAL DE BIOMEDICINA-CFBM, 2022).

CFBM Resolution 341/2021 establishes that biomedical professionals can assume technical responsibility for industrial processes and services involving the application of biotechnology. The duties include carrying out biotechnological processes using living organisms and/or cellular components (such

as enzymes, cells, fungi and bacteria) and developing biotechnological products and equipment. The resolution also recognizes the role of biomedical professionals in activities involving genetics, consolidating their role in applications involving genetic manipulation and, potentially, gene editing (CONSELHO FEDERAL DE BIOMEDICINA-CFBM, 2021). In addition, CFBM Regulation 001/2022 recognizes the specialty of Genetic Counseling as a biomedical qualification, with the possibility of working in clinical and laboratory contexts involving genetic diagnosis and analysis. The regulation establishes that the biomedical practitioner, duly qualified, can work on different fronts of clinical genetics, including preconception, prenatal, postnatal and oncogenetic contexts (CONSELHO FEDERAL DE BIOMEDICINA-CFBM, 2022).

The biomedical doctor is a key professional in the development of new gene therapies, since their training encompasses an in-depth understanding of molecular biology, genetics and laboratory technologies. Biomedical applications are involved in the design and improvement of new gene editing strategies, such as CRISPR-Cas9, in order to optimize accuracy and reduce the risks of adverse effects (BHATTACHARJEE et al., 2022). In addition, they contribute to the development of new CRISPR delivery platforms, such as systems based on nanoparticles or viral vectors, which are essential for ensuring the efficacy of the technique in human cells. Constant innovation in this field is crucial, as new approaches can result in safer therapies, such as precision medicine (AZEEZ et al., 2024).

Evaluating the efficacy of these therapies is another fundamental aspect of the biomedical doctor's work, which includes monitoring patients' response to treatment, detecting possible adverse effects and carrying out clinical trials to confirm the viability of therapies on a large scale. This contribution is essential if CRISPR-based therapies are to be implemented effectively and safely in the clinical environment. Continuous monitoring is vital to detect early any complications associated with the use of CRISPR-Cas9, such as the insertion of off-target mutations or tumor resistance. In this way, the biomedical specialist, working in collaboration with other healthcare professionals, can adjust treatments in a personalized way and ensure that the patient receives the best therapy available.

CONCLUSION

CRISPR-Cas9 technology represents one of the most remarkable innovations in contemporary biotechnology, with significant prominence in the field of oncology. Its ability to carry out precise and long-lasting genomic editing offers new therapeutic possibilities, including the silencing of oncogenes, the reactivation of tumor suppressor genes and the modification of immunocompetent cells to intensify the anti-tumor response. Pre-clinical studies and clinical trials have demonstrated its potential as an effective platform for personalized therapies in the treatment of cancer. However, the clinical application of CRISPR-Cas9 faces substantial challenges, such as off-target effects, the limited efficiency of homologous recombination (HDR), adverse immune responses and the difficulties associated with gene delivery methods. Recent advances, such as the development of Cas9 variants with greater specificity and the introduction of new nucleases, such as Cas12 and Cas13, have expanded the possibilities of application with greater precision and safety. Thus, despite the technical barriers and bioethical implications involved, the continuous progress in genome editing strategies points to a promising future. The incorporation of CRISPR-Cas9 technology into precision medicine has the potential to revolutionize cancer treatment, promoting more effective, in-

dividualized interventions with less toxicity, significantly transforming the landscape of modern oncology. In this context, biomedical professionals play a crucial role in implementing and improving CRISPR-Cas9-based therapies. Their training and expertise in molecular biology, genetics and biotechnology is fundamental to the development of new therapeutic approaches and accurate molecular diagnostics. In addition, biomedical professionals contribute directly to monitoring the effects of treatment, assessing its effectiveness and safety over time. Their role in genetic counseling and educating patients about the benefits and risks of gene editing is also essential, ensuring informed and ethical decisions. The continuous evolution of CRISPR-Cas9 technology, combined with the work of biomedical professionals, can profoundly transform oncology, promoting more effective, individualized treatments with less toxicity, bringing about a revolution in the care of cancer patients.

ACKNOWLEDGMENTS

The authors would like to thank the University Center of Integrated Faculties of Ourinhos - Unifio, Ourinhos, SP, Brazil.

REFERENCES

ALCANTARA, R. L. DE et al. A TECNOLOGIA DE CRISPR-CAS9 NA TERAPIA GÊNICA DO CÂNCER DE PULMÃO. **REVISTA BRASILEIRA MILITAR DE CIÊNCIAS**, v. 5, n. 13, 11 dez. 2019.

AVELINO ÁLVAREZ, J. P.; JULIÁN, D.; PATARROYO, R. **Revisión Edición genética mediante la técnica CRISPR-cas 9, uso de nanopartículas en Terapia génica**. [s.l: s.n.]. Disponível em: <http://hdl.handle.net/11349/38684>. Acesso em: 14 fev. 2025.

AZEEZ, S. S. et al. Advances in CRISPR-Cas technology and its applications: revolutionising precision medicine. **Frontiers in Genome Editing**, v. 6, p. 1509924, 2024.

BHARATHKUMAR, N. et al. CRISPR/Cas-Based Modifications for Therapeutic Applications: A Review. **Molecular Biotechnology** Humana Press Inc., , 1 abr. 2022.

BHATTACHARJEE, G. et al. Current approaches in CRISPR-Cas9 mediated gene editing for biomedical and therapeutic applications. **Journal of Controlled Release**, v. 343, p. 703–723, 1 mar. 2022.

BIGGI, A. F. B.; SIMIONI, P. U. Inhibition of PD-1 protein by the CRISPR-Cas9 method as antitumor therapy of non-small cell lung cancers. **Revista da Faculdade de Ciências Médicas de Sorocaba**, v. 21, n. 1, p. 2–7, 6 jun. 2019.

BOUMELHA, J. et al. CRISPR-Cas9 Screening Identifies KRAS-Induced COX2 as a Driver of Immunotherapy Resistance in Lung Cancer. **Cancer Research**, v. 84, n. 14, p. 2231–2246, 15 jul. 2024.

BRESOLIN, E.; WIETHÖLTER, P.; KIRSTEN, K. S. CRISPR: Edição genômica aplicada à Oncologia / CRISPR: Genomic editing applied to Oncology. **Brazilian Journal of Development**, v. 7, n. 9, p. 90908–90927, 20 set. 2021.

CARDOSO, W. C.; SIQUEIRA, A. S. POTENCIAL TERAPÊUTICO CONTRA O CÂNCER UTILIZANDO A TECNOLOGIA DE EDIÇÃO DE GENES CRISPR-CAS9: UMA REVISÃO DA LITERATURA. **Centro de Pesquisas Avançadas em Qualidade de Vida**, v. 14, n. v14n2, p. 1, 2023.

CARLI, G. J. DE; SOUZA, T. A. J. DE; PEREIRA, T. C. A revolucionária técnica de edição genética "CRISPR". **Sociedade Brasileira de Genética**, v. 12, 2017.

COELHO, M. A. et al. Base editing screens map mutations affecting interferon-γ signaling in cancer. **Cancer Cell**, v. 41, n. 2, p. 288- 303.e6, 13 fev. 2023.

COSTA, M. M.; DE CAMPOS BRITO, T. M.; DE CASTRO, F. A. V. Discussões éticas para a tecnologia CRISPR-Cas9. **Episteme Transversalis**, v. 12, n. 2, 2021.

GRAZIANO, S.; GONZALO, S. Mechanisms of oncogene-induced genomic instability. **Biophysical Chemistry**, v. 225, p. 49–57, 1 jun. 2017.

INSTITUTO NACIONAL DO CÂNCER. **Estatísticas de câncer**. Disponível em: <https://www.gov.br/inca/pt-br/assuntos/cancer/numeros>. Acesso em: 21 abr. 2025.

LI, H. et al. Applications of genome editing technology in the targeted therapy of human diseases: mechanisms, advances and prospects. **Signal Transduction and Targeted Therapy 2020 5:1**, v. 5, n. 1, p. 1–23, 3 jan. 2020.

LOPES, J. V. B. V. Análise da utilização da técnica de CRISPCAS9 para o tratamento do cancer de pulmão. 2021.

MENDES, L. M. C. et al. Edição de genes CRISPR-Cas9 e suas aplicações terapêuticas: Uma revisão de literatura. **Research, Society and Development**, v. 13, n. 8, p. e11513846681, 29 ago. 2024.

MENGSTIE, M. A.; WONDIMU, B. Z. Mechanism and applications of crispr/ cas-9-mediated genome editing. **Biologics: Targets and Therapy** Dove Medical Press Ltd, , 2021.

MINISTÉRIO DA SAÚDE. **Câncer: Tratamento**. Disponível em: <https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/c/cancer/tratamento#:~:text=O%20m%C3%A9dico%20vai%20escolher%20o,%C3%9Anico%20de%20Sa%C3%BAde%20(SUS)>. Acesso em: 21 abr. 2025.

MISHRA, G. et al. CRISPR-Cas9: A Potent Gene-editing Tool for the Treatment of Cancer. **Current Molecular Medicine**, v. 24, n. 2, p. 191–204, 15 fev. 2023.

MOSES, C. et al. Activating PTEN Tumor Suppressor Expression with the CRISPR/dCas9 System. **Molecular Therapy Nucleic Acids**, v. 14, p. 287–300, 1 mar. 2019.

NIDHI, S. et al. Novel crispr–cas systems: An updated review of the current achievements, applications, and future research perspectives. **International Journal of Molecular Sciences** MDPI AG, , 1 abr. 2021.

SERVIÇO PÚBLICO FEDERAL CONSELHO FEDERAL DE BIOMEDICINA-CFBM. 2021.

SERVIÇO PÚBLICO FEDERAL CONSELHO FEDERAL DE BIOMEDICINA-CFBM. 2022.

SHINWARI, Z. K.; TANVEER, F.; KHALIL, A. T. Ethical Issues Regarding CRISPR Mediated Genome Editing. **Current Issues in Molecular Biology 2018, Vol. 26, Pages 103-110**, v. 26, n. 1, p. 103–110, 7 set. 2017.

SIQUEIRA, M. C. M.; **A UTILIZAÇÃO DA TECNOLOGIA CRISPR NO TRATAMENTO DO CÂNCER DE COLO DE ÚTERO EM ESTUDOS IN VIVO: UMA REVISÃO SISTEMÁTICA**. 2024. 32p. Trabalho de Conclusão de Curso (Medicina) - Escola Bahiana de Medicina e Saúde Pública, Salvador (BA).

TAN, A. C.; TAN, D. S. W. Targeted Therapies for Lung Cancer Patients with Oncogenic Driver Molecular Alterations. **Journal of Clinical Oncology**, v. 40, n. 6, p. 611–625, 20 fev. 2022.

THEGE, F. I. et al. A Programmable in Vivo CRISPR Activation Model Elucidates the Oncogenic and Immunosuppressive Functions of MYC in Lung Adenocarcinoma. **Cancer Research**, v. 82, n. 15, p. 2761–2776, 1 ago. 2022.

WANG, S. W. et al**.** Current applications and future perspective of CRISPR/Cas9 gene editing in cancer. **Molecular Cancer** BioMed Central Ltd, , 1 dez. 2022.

WINTER, B. C.. A.; VILAÇA, M. M. Edição genética humana por meio da técnica CRISPR-Cas9: apontamentos e reflexões a partir da bioética e do biodireito. **Revista Direitos Fundamentais e Alteridade**, v. 5, n. 2, p. 83-98, 2021.

XU, X. et al. Nanotechnology-based delivery of CRISPR/Cas9 for cancer treatment. **Advanced Drug Delivery Reviews**, v. 176, p. 113891, 1 set. 2021.

YANG, Y. et al. CRISPR/Cas: Advances, Limitations, and Applications for Precision Cancer Research. **Frontiers in Medicine** Frontiers Media S.A., , 3 mar. 2021.

ZHAO, Z. et al. Review of applications of CRISPR-Cas9 gene-editing technology in cancer research. **Biological Procedures Online 2021 23:1**, v. 23, n. 1, p. 1–13, 15 jul. 2021.