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The Application Progress and Prospects of Gene Editing Technology in the Field of Biopharmaceuticals

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Abstract: This study systematically reviews the application progress of gene editing technology in the field of biopharmaceuticals, analyzes the technology development trend and industrialization prospects. Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated protein 9 (CRISPR-CAS9) technology has made breakthrough progress in the field of biopharmaceuticals with its precise positioning of guide Ribonucleic Acid (RNA) and efficient cleavage ability of CAS9 protein. In cell engineering, the efficiency of recombinant protein production has been significantly improved through metabolic pathway optimization, anti-apoptosis mechanism enhancement and precise regulation of glycosylation. In the field of cell therapy, gene editing technology has achieved optimization of Chimeric Antigen Receptor T-Cell (CAR-T cell) therapy, and the universal Universal Chimeric Antigen Receptor T-cell 19 (UCART19) have a complete remission rate of 82% for relapsed/refractory B-cell leukemia. In drug development, the construction of precise disease models has increased the efficiency of lead compound screening by 5-10 times. CRISPR therapy has restored hemoglobin levels to 80% of the normal range in the treatment of β-thalassemia. Gene editing technology is driving biopharmaceuticals into a new era of precision medicine, but it still needs to be continuously improved in terms of off-target effect control, delivery system optimization and safety assessment.

Keywords: Gene Editing, CRISPR-CAS9, Biopharmaceuticals, Cell Engineering, Molecular Biology

1. Introduction

Gene editing technology, as the core driving force of the modern biotechnology revolution, is reshaping the innovation landscape of the biopharmaceutical industry. As the global biopharmaceutical market size has rapidly grown from 204.8 billion the United States (US) dollars in 2015 to 379.5 billion US dollars in 2023, the industry's demand for high-precision and high-efficiency technological tools is becoming increasingly urgent. The increasing demand for personalized medical care and the growing number of chronic diseases such as diabetes and cancer have brought a historic opportunity for the application of gene editing technology. Traditional biopharmaceutical technologies are confronted with problems such as insufficient targeting and high production costs. The development of gene editing technology has undergone three generations of technological innovations: Zinc finger nuclease (ZFN) achieved Deoxyribonucleic Acid (DNA) specific cutting through artificially designed zinc finger proteins, pioneering targeted editing. Transcription activator-like effector nuclease (TALEN) significantly enhances the flexibility of recognition sites by utilizing a modular protein structure; The CRISPR-CAS9 system, with its precise positioning of guide Ribonucleic Acid (RNA) and efficient cleavage of CAS9 protein, has completely overturned the technical paradigm of genome editing. Among them, CRISPR technology, with its characteristics of simple design, low cost and high editing efficiency, has promoted the development in fields such as glycosylation engineering of Chinese Hamster Ovary (CHO) cells and optimization of CAR-T cell therapy, shortening the preparation cycle of CAR-T cells by 40% and increasing the expression level of therapeutic proteins by 30% to 50%.

In the field of biopharmaceuticals, gene editing technology is accelerating its transformation from basic research to industrialization. Its core value is reflected in three dimensions: At the cell engineering level, by precisely regulating the metabolic pathways and glycosylase systems

of CHO cells, the industry problem of quality fluctuations between batches of recombinant protein drugs has been solved; In terms of innovative treatment methods, the development of universal CAR-T cells based on CRISPR technology has significantly improved accessibility for patients and reduced treatment costs by 60%. In the reconstruction of the drug research and development system, the accuracy rate of disease models generated by base editing technology is as high as 95%, which greatly accelerates the process of target validation and lead compound screening. At present, 12 gene therapy drugs have been approved for marketing worldwide, including CRISPR therapy. This therapy has completely transformed the treatment of β -thalassemia, achieving permanent cure with just one treatment and ushering in a new era of precision medicine in biopharmaceuticals. However, issues such as reducing off-target effects, improving the effectiveness of in vivo distribution, and large-scale production remain obstacles to technological change. The new-generation base editing system (tBE) reduces the off-target rate to below 0.01% through the "keyless" mechanism, providing a safer technical platform for drug transformation.

This review aims to systematically sort out the development trajectory of the gene editing technology system and deeply analyze its innovative applications in key links of biopharmaceuticals. This article will focus on three major application scenarios: CHO cell engineering modification, cell therapy optimization, and gene drug development. By integrating the latest clinical data, it will explore the industrialization path of the technology and discuss innovative methods such as drug delivery system innovation and AI-assisted design, providing decision-making guidance for the industry and helping it understand technological development trends and formulate development plans.

2. Overview of Gene Editing Technology

2.1 Main Types of Gene Editing Technologies

Gene editing technology has undergone multiple generations of technological innovation measures during its development process. It covers different types such as ZFN, TALEN, large-scale nuclease (MegaTAL), and the CRISPR-CAS9 system. As for ZFN, it recognizes specific DNA sequences by relying on the artificially designed zinc finger protein structure, and it fuses with FokI nuclease to form a dimer, thereby achieving DNA cutting operations. However, ZFN has the problems of being overly complex in design and relatively high in cost [1]. Looking at TALEN again, it uses that modular TAL effector protein to recognize single-base sequences and also relies on FokI to complete the cleavage action. In terms of flexibility, TALEN is superior to ZFN, but the entire process of its construction still appears rather cumbersome [2]. MegaTAL, on the other hand, combines a wide range of nucleases with TALEN technology. By leveraging the high specificity of homing nucleases and the programmable nature of TAL effector proteins, it achieves the goal of precise editing. However, its application scope is relatively limited on the whole. In addition, there are chemical editing techniques like the artificial restricted DNA cutter (ARCUT), which use chemical reagents to achieve targeted cutting. However, the process is very complex and the efficiency is relatively low.

2.2 Principles and Characteristics of CRISPR-CAS9 Technology

The CRISPR-CAS9 system recognizes the target DNA sequence by means of the complex formed by guide RNA (that is, gRNA) and CAS9 protein, and generates double-strand breaks (DSB) under the guidance of the adjacent motif of the original spacer sequence. Subsequently, the purpose of gene editing is achieved through non-homologous end connection or homology-directed repair (HDR) methods. Its most prominent advantage lies in the fact that it is relatively simple and convenient to design, requires a relatively low cost, and can also carry out related operations on multiple gene loci simultaneously. Take practical examples. In the glycosylation engineering of CHO cells, CRISPR-CAS9 has increased the expression level of therapeutic proteins by 30% to 50%, and in the field of CAR-T cell therapy, it has also significantly shortened the preparation cycle [3]. Compared with ZFN and TALEN, the off-target effects of CRISPR have been reduced by means of high-fidelity CAS9 variants and the dual sgRNA strategy. In addition, some technologies derived from CRISPR, such as base editing and lead editing, have further achieved the effect of

single-base modification without DSB, which also endows clinical applications with higher safety[4].

3. Application of Gene Editing in Cell Line Engineering

In the continuous development of gene editing technology, precise molecular tools have been brought to cell line engineering, effectively enhancing the efficiency of recombinant protein production and significantly improving product quality. Mammalian cell lines like CHO cells have become mainstream expression systems in the field of biopharmaceuticals due to their outstanding post-translational modification capabilities of proteins. In recent years, by using related technologies such as ZFN, TALEN, and CRISPR/CAS9 to carry out targeted modification operations on cell lines, breakthroughs have been made in multiple aspects including metabolic regulation, anti-apoptotic enhancement, and glycosylation optimization.

3.1 Optimization of Metabolic Pathways and Control of Toxic By-products

During the culture process of CHO cells, it is often the CASe that excessive consumption of glucose and glutamine leads to the production of a series of metabolic by-products such as lactic acid and ammonia. The appearance of these by-products can inhibit cell growth and also reduce protein production. If the CRISPR/CAS9 technology is used to knock out the lactate dehydrogenase A (also known as LDH-A) gene, the accumulation of lactic acid can be reduced by approximately 40% to 60%, and the logarithmic growth phase of cells can also be prolonged. In addition, overexpression operation of glutamine synthase (GS) is carried out. This not only enables the culture to be carried out in a medium without glutamine, but also reduces the ammonia concentration to less than 2 mM. As a result, the microenvironment in which the cells are located can be significantly improved. Recent related studies have introduced yeast pyruvate carboxylase, coupling the tricarboxylic acid cycle and the glycolytic pathway. Under such circumstances, the yield of recombinant antibodies has increased by as much as 1.8 times. Such precise regulatory measures for metabolic engineering have laid a relatively solid foundation for the subsequent development of high-density culture processes.

3.2 Enhancement of Anti-apoptotic Mechanism and Extension of Culture Period

Cell apoptosis has become the key factor restricting the further development of industrial production. By using the TALEN technique to promote the overexpression of the anti-apoptotic proteins, the survival rate of the cells can be maintained above 90% in the later stage of culture, and the titer of the antibody can also increase by as much as six times. The CRISPR mediated BCL2-associated X protein and BCL2 homologous antagonist-killer protein double-gene knockout strain demonstrated even stronger stress resistance. Even under nutrition-restricted conditions, it could still maintain a highly active state for up to 72 hours. In recent related studies, it has also been found that the way of delivering miR-21 through exosomes can inhibit the CASpase-3 pathway, thereby extending the cell culture cycle to a duration of up to 18 days. This undoubtedly opens up a brand-new idea for conducting apoptosis regulation work without gene editing.

3.3 Precise Regulation of Glycosylation and Optimization of Drug Functions

The glycosylation modification of proteins has a direct impact on the efficacy and half-life of therapeutic antibodies. By using the ZFN technology to knockout the α-1, 6-fucosyltransferase, that is, the Fucosyltransferase 8 (FUT8) gene, fucosylated antibodies can be obtained. The Antibody-Dependent Cell-mediated Cytotoxicity (ADCC) activity of this antibody is a full 50 times higher than that of the wild type, and this technology has been applied in the production process of drugs such as ofalfamumab. In terms of sialylation, if the Cytidine monophosphate (CMP) sialic acid transporter is overexpressed, the sialic acid content at the end of IgG can reach 25%, thereby significantly enhancing the anti-inflammatory activity. Furthermore, there are related studies that have utilized CRISPR-activated (CRISPRa), namely activated CRISPR, to up-regulate the expression of β-1, 4-galactosyl transferase.

3.4 Construction of Disease Models and Innovation in Cell Therapy

Gene editing technology has provided precise tools for the study of disease mechanisms. A

study in 2020 demonstrated that by leveraging the CRISPR/CAS9 technology, a model of TP53 mutations was successfully constructed within CHO cells, effectively simulating the characteristics of chemotherapy resistance in tumor cells, thereby establishing a standardized platform for drug screening [5]. In the field of cell therapy, TALEN was used to knockout the T cell receptor alpha constant (TRAC) and CD52 molecule (CD52) genes of CAR-T cells, and then universal UCART19 cells were prepared. Judging from the situation presented in clinical trials, its complete remission rate for relapsed/refractory B-cell leukemia can reach as high as 82%. Also, the operation of knockout of the Programmed Cell Death Protein 1 (PD-1) biallele mediated by CRISPR has suddenly increased the activity of T cells in anti-tumor aspects by three times, and the related therapy has also entered the Phase II clinical stage.

3.5 Directed Evolution of Industrially Produced Cell Lines

The new generation of gene editing technology is promoting the development of cell lines in the direction of directed evolution. With the help of the CRISPR/CAS12a multi-gene editing system, researchers carried out relevant optimization work on CHO cells, and their growth rate was increased. Specifically, the doubling time was successfully shortened to 14 hours. The specific productivity has also been improved, reaching the level of 50 pg/cell/day. The quality of the product has also improved, with the polymer content controlled within the range of less than 2%. Such "super cell lines" have reduced the production cost of monoclonal antibodies by as much as 40%. Combined with the genomic vulnerable sites predicted by machine learning algorithms, the exogenous genes are targeted and integrated to the high-expression sites, which significantly shortens the development cycle of stable strains from the original 6 months to 8 weeks [6].

4. Application of Gene Editing in Cell Therapy

Gene editing technology has achieved breakthrough development, which has brought revolutionary progress to the field of cell therapy. Especially in the optimization of CAR-T cell therapy, the correction of genetic diseases, and the innovation of treatment strategies for solid tumors, considerable potential has been demonstrated. By precisely regulating the functions of immune cells or repairing pathogenic gene mutations, these technologies have opened up brand-new treatment paths for malignant tumors, hereditary blood diseases and immunodeficiency diseases.

4.1 Precise Optimization of CAR-T Cell Therapy

The CRISPR/CAS9 technology, with the aid of multi-gene editing strategies, has effectively enhanced the therapeutic efficacy of CAR-T cells. During the development of allogeneic CAR-T, researchers used CRISPR to simultaneously knockout the TRAC and the CD52 gene, thereby successfully constructing universal UCART19 cells. The related clinical trials have shown that for relapsed/refractory B-cell leukemia, This cell can achieve a complete remission rate as high as 82%. Furthermore, through the biallelic knockout of PD-1, the anti-tumor activity of T cells can be increased to three times the original, and the related therapy has already entered the Phase II clinical stage. The latest research, by introducing base editing technology, can precisely modify the immune checkpoint genes of CD19 CAR-T cells without causing the occurrence of DNA double-strand breaks, thereby reducing the incidence of cytokine release syndrome by 40%.

4.2 Stem Cell Correction for Hereditary Hematological Diseases

Gene editing has achieved a breakthrough in hematopoietic stem cell therapy, enabling lifelong cure with a single treatment. With the help of the CRISPR-based β -globin gene correction technology, the hemoglobin level of patients with β -thalassemia was restored to about 80% of the normal range, and no off-target effects were detected during the follow-up period of up to 3 years. When treating sickle cell disease, electroporation was used to deliver the CRISPR/CAS9 ribonucleoprotein complex, which successfully repaired the c.20A>T mutation of the Hemoglobin subunit beta gene, significantly reducing the incidence of pain crisis in patients after transplantation by 90%. It is particularly worth mentioning that during the application of the new lead editing technology, the efficiency of gene correction has been enhanced, reaching up to 65%. This undoubtedly opens up a brand-new path for the

treatment of single-gene hereditary diseases [7].

4.3 Reprogramming Strategies for the Microenvironment of Solid Tumors

In terms of the immunosuppressive microenvironment of solid tumors, gene editing technology has developed a dual regulatory strategy. With the help of the CRISPRa system, while overexpressing Interleukin-12, the Transforming Growth Factor-β receptor type II gene was knocked out. As a result, the number of tumor-infiltrating lymphocytes in melanoma model mice increased by as much as five times at once, and their complete response rate also improved. It has reached a level such as 70%. When treating pancreatic cancer, the CCR5-deficient CAR-T cells constructed using the TALEN technology are capable of penetrating the rather dense interstitial barrier, thereby prolonging the median survival period of patients up to 14.5 months. Some recent studies have also found that CRISPR-based GPC3-specific Chimeric Antigen Receptor Natural Killer (CAR-NK) cells can achieve a killing efficiency of 95% against liver cancer cells. At the same time, they can significantly reduce the risk of cytokine storm [8-9].

4.4 Technical Challenges and Security Considerations

Although obvious progress has been made, gene editing cell therapy still faces many challenges. The data obtained from whole-genome sequencing indicate that the high-fidelity CAS9 variant, namely HIFI-CAS9, can control the off-target rate at a level of less than 0.05%. However, in order to be smoothly carried out in large-scale clinical applications, a more sensitive off-target detection system still needs to be established. Due to the risk of insertion mutations caused by viral vector delivery, this has prompted the rapid development of non-viral vectors. Take the CAS9 mRNA encapsulated in nano-liposomes as an example. Its delivery efficiency has reached 75%, and its half-life in vivo has been extended to as long as 72 hours. In addition, the problem of immune rejection existing in general-purpose cell therapy has been improved to a certain extent through HLA-I loci directed silencing technology. After transplantation, the incidence of host-versus-graft reactions has also decreased to 15%.

5. Application of Gene Editing in Drug Development

Gene editing technology has achieved breakthrough development, which has opened up a brand-new paradigm for the research and development of innovative drugs. Its most crucial value is concentrated in three major areas: the construction of precise disease models, the discovery and validation of targets, and the development of gene therapy drugs. By using tools such as CRISPR-CAS9 to implement targeted regulatory operations, researchers can systematically analyze the internal mechanisms of diseases and also develop highly targeted related therapies, thereby strongly promoting the biomedical field to take a big step into the era of precision.

5.1 Construction of Precise Disease Models and High-Throughput Screening

Traditional drug screening often relies on two-dimensional cell models or animal models, which have many limitations, such as significant species differences and a relatively low degree of restoration of pathological features. CRISPR technology can induce pluripotent stem cells, through targeted editing, thereby constructing humanized disease models. It has successfully simulated the process of neuronal degeneration in Huntington's disease, and the similarity of its pathological protein aggregation characteristics to the patient's brain tissue can reach 92%. In the field of organoids, after simultaneously knocking out the Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS), Tumor Protein P53 (TP53) and SMAD Family Member 4 (SMAD4) genes in the pancreatic cancer model, the tumor interstitial fibrosis microenvironment was re-presented, increasing the efficacy prediction accuracy of the chemotherapy drug gemcitabine to 87%. In addition, based on CRISPRa, that is, the gene circuit technology of activated CRISPR, the Wnt/β-catenin signaling pathway can be dynamically regulated in organoids, thereby enabling real-time observation of the epithelial-mesenchymal transition, that is, the molecular timing of Epithelial-Mesenchymal Transition (EMT), during the metastasis of colorectal cancer. On the one hand, these models accelerate the screening of lead compounds. On the other hand, they can also achieve personalized drug testing by introducing patient-specific mutations, which can reduce the preclinical research cycle by

40%-60%.

5.2 Target Discovery and Functional Genomics Verification

The CRISPR whole-genome screening technology has truly transformed the traditional target discovery model in the past. Specifically, systematic knockout screening operations were carried out on non-small cell lung cancer cells using the Genome-scale CRISPR Knockout library, and as a result, as many as 37 novel drug resistance-related genes were identified. Among them, once the amino acid transporter solute carrier family 1 (neutral amino acid transporter), member 5 is inhibited, the sensitivity of osimertinib-resistant cells can be restored to as much as 6.8 times the original. In the field of epigenetic regulation, the dCAS9-SunTag system successfully activated the expression of the tumor suppressor gene Cyclin-Dependent Kinase Inhibitor 2A (CDKN2A) by recruiting histone acetyltransferase, significantly reducing the proliferation rate of hepatoma cells by 72%[10]. In addition, the single-base editing technology has achieved precise simulation of the glycine and arginine polymorphisms at site 16 of the G Protein-Coupled Receptor (GPCR) family member Adrenoceptor Beta 2, Membranous (ADRB2) during its practical application, thereby providing a new basis for the personalized medication of beta-blockers. These highly breakthrough advancements have enabled the efficiency of drug target discovery to increase by 5 to 10 times, and have also significantly reduced the risk of failure that may be faced during the clinical development stage.

5.3 Innovation in Gene Therapy Drug Development and Delivery Systems

Gene editing technology has actually promoted therapeutic nucleic acid drugs to the stage of clinical transformation. Take the CRISPR-CAS9 system delivered based on the Adeno-Associated Virus serotype 9 vector as an example. In the bodies of patients with transthyretin amyloidosis, it successfully achieved an 85% knockout efficiency of the liver Transthyretin (TTR) gene. Meanwhile, the level of abnormal proteins in the serum has been continuously decreasing, with a reduction rate of up to 90%. Looking at the in vivo editing therapy for hereditary eye diseases again, it successfully repaired the c.2991+1655A>G mutation existing in the Centrosomal protein of 290 kDa (CEP290) gene through subretinal injection. After such treatment, the visual acuity of the patient increased by 0.3 logMAR units within 12 months. In the field of delivery systems, by encapsulating the mrNA-encoded CAS9/gRNA complex with lipid nanoparticles, its targeting efficiency to liver cells can reach 78%, and its half-life in vivo is also extended to 72 hours. This undoubtedly opens up a brand-new path for the treatment of systemic genetic diseases. It is also worth mentioning that when the gold nanoclusters in the new non-viral vectors are covalently coupled with CRISPR, not only is the editing efficiency increased by 3.2 times, but the incidence of immunogenic events can also be controlled below 5%.

Although gene-edited drugs have made considerable progress in development, there are still many challenges, such as issues with delivery efficiency, off-target effects, and long-term safety problems. The new generation of lead editing technology fuses reverse transcriptase and CAS9. As a result, it enables the conversion of any base without causing double-strand breaks, thereby reducing the Insertion/Deletion (INDEL) mutation rate to below 0.01%. With the continuous optimization of gRNA design algorithms assisted by artificial intelligence and the gradual development of real-time in vivo monitoring technology, gene-edited drugs are very promising to become the first-line treatment options for major diseases such as malignant tumors and genetic diseases in the next decade [11].

6. Conclusion

Gene editing technology has become the core driving force in the modern biotechnology revolution and is reshaping the innovation landscape of the biopharmaceutical industry to a large extent. This technology has undergone three generations of evolution during its development process, namely ZFN, TALEN and the CRISPR-CAS9 system. Among them, CRISPR technology has many advantages, such as being relatively simple to design, having a relatively low cost, and having a relatively high editing efficiency. With these advantages, CRISPR technology has developed into the mainstream technology in the field of gene editing.

In the field of biopharmaceuticals, gene editing technology holds extremely important core value, which is mainly reflected in three

different dimensions. From the perspective of cell engineering, the expression level of therapeutic proteins can be increased by 30% to 50% by precisely regulating the metabolic pathways of CHO cells. In terms of the innovation of treatment methods, the universal CAR-T cells developed with the help of CRISPR technology have reduced the treatment cost by 60%, thereby greatly enhancing the possibility for patients to obtain treatment. In the process of reconstructing the drug research and development system, by using base editing technology to create disease models, the accuracy rate can be as high as 95%, and it also greatly accelerates the entire process of target validation.

At present, globally, 12 gene therapy drugs have been approved and thus put on the market. Among them, CRISPR therapy has achieved an extremely significant breakthrough in the treatment of thalassemia, that is, it has realized the effect of lifelong cure through a single treatment. However, at the level of technology transformation, there are still many challenges to be overcome, such as effectively controlling off-target effects, how to improve the efficiency of in vivo delivery, and how to achieve large-scale production, etc. The new generation of base editing systems, with its unique "lock-key" mechanism, has successfully reduced the off-target rate to less than 0.01%. As a result, a more secure and reliable technical platform has been constructed for clinical transformation. Looking ahead, gene editing technology holds great promise for achieving brand-new breakthroughs in cutting-edge fields such as the innovation of delivery systems and artificial intelligence-assisted design.

References

[1] Khan, S. H. Genome-editing Technologies: Concept, Pros, and Cons of Various Genome-editing Techniques and Bioethical Concerns for Clinical Application.Molecular Therapy Nucleic Acids, 2019, 16, 326-334.

[2] Mudziwapasi, R., Chekera, R., Ncube, C. Z., et al., Genome Editing Tools and Gene Drives: A Brief Overview. CRC Press. 2021.

[3] Gaj, T., Sirk, S. J., Shui, S. L., et al., Genome-editing Technologies: Principles and Applications. Cold Spring Harbor perspectives in Biology, 2016, 8(12), a023754.

[4] Tamura, R., & Toda, M. Historic Overview of Genetic Engineering Technologies for Human Gene Therapy. Neurologia Medico-chirurgica, 2020, 60(10), 483-491.

[5] Li, H., Yang, Y., Hong, W., 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),

[6] Llargués-Sistac, G., Bonjoch, L., & CAStellvi-Bel, S. HAP1, A New Revolutionary Cell Model for Gene Editing Using CRISPR-CAS9. Frontiers in Cell and Developmental Biology, 2023, 11, 1111488.

[7] Maeder, M. L., & Gersbach, C. A. Genome-editing Technologies for Gene and Cell therapy. Molecular therapy, 2016, 24(3), 430-446.

[8] Moradi, V., Khodabandehloo, E., Alidadi, M., et al., Progress and Pitfalls of Gene Editing Technology in CAR-T Cell Therapy: A State-of-the-art Review. Frontiers in Oncology, 2024, 14, 1388475.

[9] Atsavapranee, E. S., Billingsley, M. M., & Mitchell, M. J. Delivery Technologies for T Cell Gene Editing: Applications in Cancer Immunotherapy. EBioMedicine, 2021, 67.

[10] Liu, W., Li, L., Jiang, J., Wu, M., et al., Applications and Challenges of CRISPR-CAS Gene-editing to Disease Treatment in Clinics. Precision clinical medicine, 2021, 4(3), 179-191.

[11] Karagyaur, M. N., Efimenko, A. Y., Makarevich, P. I., et al., Ethical and Legal Aspects of Using Genome Editing Technologies in Medicine. Modern Technologies in Medicine, 2019, 11(3 (eng)), 117-132.