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Analysis of the value of genetic engineering technology in the field of biopharmaceuticals

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Abstract: *In recent years, genetic engineering technology has become an indispensable key technology in the field of biopharmaceutical. Genetic engineering technology can significantly improve the production efficiency and efficacy of drugs by manipulating and modifying genes. This paper analyzes the application of genetic engineering technology in the field of biopharmaceutical, introduces its successful cases, and discusses the great value of genetic engineering technology in the field of biopharmaceutical. This paper first summarizes the classification and development of biopharmaceutical field, and then introduces the principle and method of genetic engineering technology in detail. Then the specific application of genetic engineering technology in biopharmaceutical field is analyzed. Finally, the application prospect of genetic engineering technology in biopharmaceutical field is prospected. With the continuous progress of technology and the improvement of regulations, genetic engineering technology will certainly bring revolutionary changes to the field of biopharmaceutical and benefit human health.*

Keywords: *genetic engineering technology; biopharmaceuticals; protein drugs; gene therapy; vaccine production*

1. Introduction

Genetic engineering technology has made great progress in the past few decades. These advances have not only promoted the development of the biotechnology field, but also injected new vitality into the development of the biopharmaceutical industry. Biopharmaceuticals is an emerging interdisciplinary field involving multiple fields such as biotechnology, molecular biology, cell biology, medicine, and engineering [1]. It uses living cells or cell components to produce products for preventing, treating or diagnosing diseases, such as protein drugs, vaccines, gene therapy, etc. [2]. Although traditional small molecule chemical drugs have achieved certain success in treating certain diseases, they also have some limitations, such as poor targeting and high side effects. In contrast, biopharmaceutical products have obvious advantages in efficacy and safety due to their high specificity and biocompatibility [3]. With the continuous in-depth understanding of the molecular mechanisms of diseases and the rapid development of biotechnology, biopharmaceuticals have become one of the most active and promising branches in the field of medicine.

Genetic engineering technology plays an important role as the core of biotechnology, especially in the field of biopharmaceuticals. Genetic engineering technology offers unprecedented flexibility and precision in the development and production of biopharmaceuticals. By altering or regulating the expression of specific genes, scientists are able to synthesize proteins required for drugs in a targeted manner, which not only improves the production efficiency but also reduces the production cost [4]. Genetic engineering technology plays an important role in the field of vaccine development. The preparation of traditional vaccines often requires the use of live viruses or bacteria, with problems of safety and high production costs. Genetic engineering technology, on the other hand, can realize large-scale and efficient production by synthesizing genes for target antigenic proteins and inserting them into safe vectors [5]. In addition, genetic engineering technology has brought hope to areas such as gene therapy. Gene therapy is a cutting-edge therapeutic approach that treats hereditary or other incurable diseases by introducing normal genes into patients and repairing or replacing abnormal genes [4]. The outstanding feature of this technology is that through the manipulation and recombination of genes, scientists are able to synthesize the required proteins or other biologically active molecules in vitro, thus providing a strong guarantee for the development of new biological agents.

Due to the broad application prospects of genetic engineering technology in the field of biopharmaceuticals, it is necessary to conduct an in-depth analysis of its value. A comprehensive

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explanation of the role of genetic engineering technology in the development and production of various biopharmaceutical products will help to better grasp the advantages of this technology and provide theoretical guidance for its future development.

2. Overview of the biopharmaceutical field

2.1 Classification of biopharmaceutical field

The biopharmaceutical field can be divided into several major categories. The first is protein drugs, which are recombinant proteins produced by genetic engineering technology, including vaccines, enzymes, hormones, cytokines, etc. These protein drugs are widely used to treat various diseases, such as cancer, diabetes, autoimmune diseases, etc. [5]. Next are antibody drugs, which are monoclonal antibodies or their derivatives produced by hybridoma cells or genetically engineered cell lines, and are mainly used for targeted treatment of tumors, autoimmune diseases and inflammatory diseases [6]. The third category is cell and gene therapy, which uses genetic engineering technology to genetically modify living cells, and then transports the modified cells into the patient's body to achieve therapeutic purposes. This type of therapy is mainly used to treat cancer, single-gene genetic diseases and some immune diseases [7]. The fourth category is nucleic acid drugs, including antisense oligonucleotide, siRNA, miRNA, etc., which regulate gene expression by binding to target molecules and are used to treat various genetic and acquired diseases [8]. Finally, there are vaccines, which are mainly recombinant vaccines produced using genetic engineering technology, including subunit vaccines, gene vaccines, vector vaccines, etc., used to prevent infectious diseases [9]. In general, the field of biopharmaceuticals covers a wide range of disease areas and provides new and effective means for clinical treatment.

2.2 Development History of Biopharmaceuticals

Biopharmaceuticals are an emerging industry that uses biotechnological means such as genetic engineering and cell culture to obtain useful proteins, nucleic acids and other products from living cells and process them into medicines. It integrates biotechnology, medicine and modern industrial technology and is one of the most dynamic and promising fields of life sciences today. The development of biopharmaceuticals can be traced back to the 1960s, when scientists successfully extracted human insulin from bacteria and yeast. In the 1970s, the rapid development of molecular biology and genetic engineering technology laid a solid theoretical and technical foundation for the rise of biopharmaceuticals. In 1982, the first human growth hormone obtained through genetic recombinant technology was launched on the market, marking the formal formation of the biopharmaceutical industry [10].

Since the beginning of the 21st century, the biopharmaceutical industry has entered a period of rapid development. Many new biological products are constantly coming out, and the treatment scope has expanded from a single disease to a variety of difficult and complicated diseases. At the same time, the production process and quality control level have also been greatly improved. In recent years, the integration of emerging technologies such as gene editing, cell therapy, protein engineering, etc. is promoting the development of the biopharmaceutical industry in the direction of precision and individualization [11].

3. Principles and methods of genetic engineering technology

Genetic engineering technology refers to the method of in vitro gene manipulation to modify, recombine, and insert the target gene into other cells or vectors to create products with completely new functions [12]. This technology has been widely used in the field of biomedicine, providing strong technical support for the production of protein drugs, vaccines and gene therapy.

Common genetic engineering technologies include gene cloning technology, gene recombination technology, gene transfer technology, and gene editing technology. Gene cloning technology is to isolate the target gene from the donor cell and insert it into a vector (such as plasmid, virus, etc.), and obtain a large number of copies of the desired gene by allowing the vector to replicate in host cells (such as E. coli) [13]. Gene recombination technology splices gene fragments from different sources to form a new recombinant gene [14]. Gene transfer technology is to introduce recombinant genes into target cells so that the target cells acquire new genetic characteristics. Common gene transfer methods

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include viral vector transfer, electroporation, gene gun, etc. [15]. Gene editing technology directly edits and modifies the genome of cells or organisms. For example, the CRISPR/Cas9 system is a revolutionary gene editing technology [16].

Through the application of the above technologies, scientists can efficiently express the required functional genes in cells and obtain recombinant protein drugs with special biological activities; they can also construct recombinant vaccines to improve the immunogenicity and safety of the vaccines; they can also achieve Repair of defective genes provides new therapeutic approaches for gene therapy of genetic diseases. In general, genetic engineering technology has given powerful wings to the field of modern biopharmaceuticals.

4. Specific applications of genetic engineering technology in the field of biopharmaceuticals

4.1 Interferon

Interferon is a protein secreted by cells that has antiviral, antiproliferative and immunomodulatory effects. Traditional interferon preparation methods have shortcomings such as low yield, high cost, and impurity. The development of genetic engineering technology provides new ways for the large-scale production of interferons [17].

As early as the 1980s, scientists used genetic recombination technology to express human interferon α in E. coli, achieving the first large-scale production of interferon. Since then, more types of recombinant interferon preparations, such as human interferon β, γ, etc., have been developed using different host expression systems such as yeast and mammalian cells [18]. In recent years, with the continuous innovation of genetic engineering technology, new progress has been made in the research and development of interferons. In 2021, Merck's long-acting recombinant human interleukin 11 (Lrpldn) was approved for marketing and can be used to treat moderate to severe acne through subcutaneous injection once every 2 weeks. Lrpldn is a long-acting recombinant protein that binds to human interleukin 10 receptor α and has anti-inflammatory and immunomodulatory effects. Its production relies on genetic engineering technology [19]. Researchers from Great Ormond Street Children's Hospital and University College London in the UK used CRISPR/Cas9 technology to genetically modify donor T cells. This phase I clinical trial is the first to use "universal" CRISPR gene-edited T cells in humans. Cells, results showed that two patients required biological intervention due to grade II cytokine release syndrome, one patient experienced transient grade IV neurotoxicity, and one patient developed cutaneous GVHD that resolved after transplantation conditioning. Other complications were expected, and primary safety objectives were met. As part of this clinical trial, they constructed and applied a new generation of more precise “universal” genome-edited T cells [20].

In general, genetic engineering technology has played an important role in improving the production capacity and reducing production costs of interferons and other protein drugs, and has made outstanding contributions to the development of the biopharmaceutical industry.

4.2 Antibiotics

Antibiotics are one of the important drugs produced using genetic engineering technology. The traditional fermentation method for producing antibiotics has problems such as low yield and high cost, but the application of genetic engineering technology has greatly improved the production efficiency and quality of antibiotics [21].

In recent years, researchers have used genetic manipulation and metabolic engineering technologies to optimize and transform antibiotic biosynthetic pathways, greatly increasing the production of antibiotics. For example, in 2023, Professor Li Jian's team at Shanghai University of Science and Technology used synthetic biology and metabolic engineering to reconstruct the erythritol metabolic pathway isolated from the natural environment in E. coli and obtained erythritol. Escherichia coli with sugar alcohol (C4) as the only carbon source for growth. This is also the first time that the carbon source available for E. coli has been expanded to C4 [22]. In addition, scientists have also used genetic engineering technology to develop new antibiotic molecules. In 2019, Professor Kim Lewis' team once again discovered a new antibiotic - darobactin, a metabolite of Photobacterium photobacterium. It contains a short peptide of 7 amino acids and can selectively kill Gram-negative bacteria by binding to a key outer membrane protein bamA. bacteria. This brings new light to deal with the increasingly serious problem of drug resistance [23].

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In general, the application of genetic engineering technology in the field of antibiotics continues to break new milestones, providing us with more and better antibacterial drugs and helping mankind overcome the challenge of drug resistance.

4.3 Insulin

Insulin is a protein drug with important therapeutic significance and is widely used to treat diabetes. Traditional insulin is extracted from animal pancreas, which has problems such as low purity and limited sources. The development of genetic engineering technology has brought new opportunities for the production of insulin.

In 1982, American scientists used genetic recombination technology to successfully express the human insulin gene in E. coli for the first time, marking the birth of the world's first recombinant protein drug. This technology has greatly improved the purity and production efficiency of insulin, and also laid the foundation for meeting the clinical needs of insulin. In recent years, scientists have continued to work on using genetic engineering technology to transform and optimize insulin molecules [24]. In 2023, Denmark's Novo Nordisk developed icodec insulin injection (icodec), a long-acting insulin designed to treat patients with type 1 and type 2 diabetes with a frequency of subcutaneous injection once a week [25]. In addition, genetic engineering technology has also been used in the development of insulin analogs. In 2019, Sanofi's ultra-long-acting insulin analog Toujeo was approved for marketing, which has a gentler blood sugar control effect [26]. The advent of these innovative insulin preparations not only meets the individual needs of different patients, but also further promotes the development of diabetes treatment.

In general, genetic engineering technology has played an irreplaceable role in the production and optimization of insulin, greatly promoted the clinical treatment of diabetes, and brought good news to many diabetic patients.

4.4 mRNA vaccines

mRNA vaccines are an example of a major breakthrough in biopharmaceuticals made possible by genetic engineering technology. After the outbreak of the new coronavirus pneumonia in 2020, scientists used mRNA technology to quickly develop a variety of mRNA vaccines. The first batch of vaccines approved for marketing include Pfizer/BioNTech's Comirnaty vaccine and Moderna's Spikevax vaccine. At the end of 2020, the mRNA vaccines Comirnaty and Spikevax developed by Pfizer/BioNTech and Moderna respectively were approved for emergency use, making great contributions to preventing the spread of the epidemic. This is the first large-scale application of mRNA technology to produce vaccines in human history. Compared with traditional vaccines, these genetically engineered vaccines have the advantages of high efficiency, renewability, and no potential infection risk [27,28]. The working principle of the mRNA vaccine is that after the mRNA molecules encoding viral proteins are injected into human cells, the cells will "read" the information and synthesize the corresponding viral proteins, thus inducing the body to produce an immune response. Compared with traditional vaccines, mRNA vaccines do not contain active viruses, are safer, and have a shorter manufacturing cycle [27]. According to the latest research, the Pfizer vaccine is 95% effective against symptomatic COVID-19 after 14 days [29]. The effectiveness of the Moderna vaccine is around 94.5%. A 2022 study showed that Moderna was slightly effective in preventing symptomatic infection and hospitalization [30]. During the COVID-19 epidemic, mRNA vaccines showed excellent protective efficacy. The development process of anti-COVID-19 vaccines fully reflects the power of genetic engineering technology. In 2023, the health department approved CSPC Pharmaceutical Group (1093.HK) to announce that the company's new coronavirus mRNA vaccine (SYS6006) would be included in China for emergency use. SYS6006 is well tolerated and highly immunogenic, producing stronger and more durable immune responses against different variants of SARS-CoV-2 [31].

It is worth noting that the protective power of these two vaccines against mutated virus strains such as Omicron has declined but can still be maintained at a certain level. In addition to the new coronavirus vaccine, scientists are currently developing mRNA vaccines to treat other diseases. For example, in 2022, Pfizer announced that its mRNA influenza vaccine has entered Phase III clinical trials [32]. In addition, many pharmaceutical companies are also developing mRNA vaccines to treat HIV, respiratory syncytial virus, etc. mRNA technology has brought hope to mankind in defeating many diseases.

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5. Prospects for the application of genetic engineering technology in the field of biopharmaceuticals

Genetic engineering technology has broad application prospects in the field of biopharmaceuticals. In the future, genetic engineering technology will continue to promote innovation and development in the biopharmaceutical industry. Among them, synthetic biology and gene editing technology are considered to be the two key driving forces for the future development of genetic engineering technology. Synthetic biology aims to design and build new biological systems from scratch, and in the future is expected to design and manufacture new therapeutic proteins, vaccines and gene therapy drugs. Gene editing technologies such as CRISPR/Cas9 make it possible to precisely modify the genome, bringing new potential to the treatment of genetic diseases, cancer and other diseases. In addition, the rapid development of technologies such as high-throughput sequencing and bioinformatics will also greatly improve the efficiency and accuracy of genetic engineering technology. With the power of these emerging technologies, the application of genetic engineering in the field of biopharmaceuticals will be more personalized and precise in the future. At the same time, as technology continues to mature, the decline in production costs is also a major trend in the future. For example, the advent of mRNA vaccines is believed to make vaccine production faster and cheaper. Therefore, the products of genetic engineering technology are expected to benefit more people in the future.

Genetic engineering technology, the term occupies a pivotal position in the field of contemporary science and technology. Since its inception, this revolutionary branch of science has deeply influenced the trajectory of the global scientific community. Especially in the biopharmaceutical industry, the breakthrough and application of genetic engineering technology has become a key force to promote the rapid development of this field. This paper demonstrates the potential and prospect of genetic engineering technology in biopharmaceutical field through specific cases. The first is interferon, a new antiviral treatment that uses gene editing technology to give the body the ability to resist disease. The second is the improvement of antibiotics, which utilizes synthetic biology and genetic engineering to revolutionize traditional medications and provide more efficient and safer treatments. And the third is insulin, a genetically engineered protein that is widely used in the medical care of diabetic patients and greatly improves their outcomes. Finally, mRNA vaccines, which are produced using genetic material encoded by mRNA, offer a new solution to prevent infectious diseases. With the continuous progress and improvement of genetic engineering technology, it is expected that the biopharmaceutical field will usher in more diverse and innovative treatment options in the near future. These therapies may include gene editing, synthetic biotechnology, and personalized medicine to provide patients with a wider range of effective treatment options. For example, gene editing technology will allow doctors to precisely modify an individual's genome to treat genetic diseases, while synthetic biotechnology promises to develop unprecedented new types of biomaterials for use in a variety of medical devices and drug carriers.

Of course, the development of genetic engineering technology in the field of biopharmaceuticals also faces some challenges, such as outdated regulatory policies, and urgent safety and ethical issues to be addressed. But overall, we have reason to believe that genetic engineering technology will play an increasingly important role in the biopharmaceutical industry in the near future, benefiting more patients.

6. Summary

Genetic engineering technology plays a great value and role in the field of biopharmaceuticals. With the continuous progress of science and technology, the application of genetic engineering technology in the field of biopharmaceuticals is also expanding and deepening. Genetic engineering technology plays a key role in the production of protein drugs, vaccine production, gene therapy and so on. In addition, genetic engineering technology has made significant achievements in many fields such as antibiotics, growth hormone, insulin, etc., which has greatly promoted the development of the biopharmaceutical industry. It is foreseeable that with the continuous progress of science and technology, the application of genetic engineering technology in the field of biopharmaceuticals will become more and more extensive, and make greater contributions to the cause of human health.

References

[1] Barolo L, Abbriano R M, Commault A S, et al. Perspectives for glyco-engineering of recombinant

ISSN 2706-6819 Vol.6, Issue 5: 41-47, DOI: 10.25236/IJFM.2024.060507

biopharmaceuticals from microalgae[J]. Cells, 2020, 9(3): 633.
[2] Han X, Alu A, Liu H, et al. Biomaterial-assisted biotherapy: A brief review of biomaterials used in drug delivery, vaccine development, gene therapy, and stem cell therapy[J]. Bioactive Materials, 2022, 17: 29-48.
[3] Madhavan A, Arun K B, Sindhu R, et al. Customized yeast cell factories for biopharmaceuticals: from cell engineering to process scale up[J]. Microbial Cell Factories, 2021, 20(1): 124.
[4] Jin F J, Hu S, Wang B T, et al. Advances in genetic engineering technology and its application in the industrial fungus Aspergillus oryzae[J]. Frontiers in Microbiology, 2021, 12: 644404.
[5] Roesch A, Zölls S, Stadler D, et al. Particles in biopharmaceutical formulations, part 2: an update on analytical techniques and applications for therapeutic proteins, viruses, vaccines and cells[J]. Journal of pharmaceutical sciences, 2022, 111(4): 933-950.
[6] Suh K, Kyei I, Hage D S. Approaches for the detection and analysis of antidrug antibodies to biopharmaceuticals: A review[J]. Journal of separation science, 2022, 45(12): 2077-2092.
[7] Cring M R, Sheffield V C. Gene therapy and gene correction: targets, progress, and challenges for treating human diseases[J]. Gene therapy, 2022, 29(1): 3-12.
[8] Chakraborty C, Sharma A R, Sharma G, et al. Therapeutic advances of miRNAs: A preclinical and clinical update[J]. Journal of advanced research, 2021, 28: 127-138.
[9] Matić Z, Šantak M. Current view on novel vaccine technologies to combat human infectious diseases [J]. Applied microbiology and biotechnology, 2022, 106: 25-56.
[10] Akram M, Jabeen F, Daniyal M, et al. Genetic engineering of novel products of health significance: Recombinant DNA technology[J]. Functional Foods and Nutraceuticals: Bioactive Components, Formulations and Innovations, 2020: 595-611.
[11] Shanmugaraj B, I. Bulaon C J, Phoolcharoen W. Plant molecular farming: A viable platform for recombinant biopharmaceutical production[J]. Plants, 2020, 9(7): 842.
[12] Kowalczyk T, Merecz-Sadowska A, Picot L, et al. Genetic manipulation and bioreactor culture of plants as a tool for industry and its applications[J]. Molecules, 2022, 27(3): 795.
[13] Gutiérrez S, Lauersen K J. Gene delivery technologies with applications in microalgal genetic engineering [J]. Biology, 2021, 10(4): 265.
[14] Ahmar S, Saeed S, Khan M H U, et al. A revolution toward gene-editing technology and its application to crop improvement[J]. International Journal of Molecular Sciences, 2020, 21(16): 5665.
[15] Jeong B, Jang J, Jin E S. Genome engineering via gene editing technologies in microalgae[J]. Bioresource Technology, 2023, 373: 128701.
[16] Jin F J, Hu S, Wang B T, et al. Advances in genetic engineering technology and its application in the industrial fungus Aspergillus oryzae[J]. Frontiers in Microbiology, 2021, 12: 644404.
[17] Soldi M, Sergi L S, Unali G, et al. Laboratory-scale lentiviral vector production and purification for enhanced ex vivo and in vivo genetic engineering[J]. Molecular Therapy-Methods & Clinical Development, 2020, 19: 411-425.
[18] Das P K, Sahoo A, Veeranki V D. Current status, and the developments of hosts and expression systems for the production of recombinant human cytokines[J]. Biotechnology Advances, 2022, 59: 107969.
[19] Meng Huan, Su Yifan, Wang Sa, Zhang Shuwen, Zheng Yongxiang, Yu Rong, Zhang Chun. Prokaryotic soluble expression, purification, characterization and preliminary activity evaluation of recombinant albumin-binding peptide fused human interleukin-11 [J]. Chinese Journal of Bioengineering, 2023,43(7):44-52.
[20] Ottaviano G, Georgiadis C, Gkazi S A, et al. Phase 1 clinical trial of CRISPR-engineered CAR19 universal T cells for treatment of children with refractory B cell leukemia[J]. Science translational medicine, 2022, 14(668): eabq3010.
[21] Jin F J, Hu S, Wang B T, et al. Advances in genetic engineering technology and its application in the industrial fungus Aspergillus oryzae[J]. Frontiers in Microbiology, 2021, 12: 644404.
[22] Ba F, Ji X, Huang S, et al. Engineering Escherichia coli to utilize erythritol as sole carbon source[J]. Advanced Science, 2023, 10(14): 2207008.
[23] Imai Y, Meyer K J, Iinishi A, et al. A new antibiotic selectively kills Gram-negative pathogens[J]. Nature, 2019, 576(7787): 459-464.
[24] Battineni J K, Boggula N, Sirikonda S, et al. Recombinant DNA Technology in Previous, Present and Future with Examples[J]. Advances in Multidisciplinary Research and Development, 2021: 1.
[25] Mathieu C, Ásbjörnsdóttir B, Bajaj H S, et al. Switching to once-weekly insulin icodec versus once-daily insulin glargine U100 in individuals with basal-bolus insulin-treated type 2 diabetes (ONWARDS 4): a phase 3a, randomised, open-label, multicentre, treat-to-target, non-inferiority trial[J]. The Lancet, 2023, 401(10392): 1929-1940.
[26] Porcellati F, Lucidi P, Candeloro P, et al. Pharmacokinetics, pharmacodynamics, and modulation

ISSN 2706-6819 Vol.6, Issue 5: 41-47, DOI: 10.25236/IJFM.2024.060507

of hepatic glucose production with insulin glargine U300 and glargine U100 at steady state with individualized clinical doses in type 1 diabetes[J]. Diabetes Care, 2019, 42(1): 85-92.
[27] Durand J, Dogné J M, Cohet C, et al. Safety Monitoring of COVID-19 Vaccines: Perspective from the European Medicines Agency[J]. Clinical Pharmacology & Therapeutics, 2023, 113(6): 1223-1234.
[28] Consoli S, Dono F, Evangelista G, et al. Status migrainosus: A potential adverse reaction to Comirnaty (BNT162b2, BioNtech/Pfizer) COVID-19 vaccine—A case report[J]. Neurological Sciences, 2021: 1-4.
[29] Wang X. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine[J]. N Engl J Med, 2021, 384(16): 1577-1578.
[30] Oliver S E. Use of the Janssen (Johnson & Johnson) COVID-19 vaccine: updated interim recommendations from the advisory committee on immunization practices—United States, December 2021[J]. MMWR. Morbidity and Mortality Weekly Report, 2022, 71.
[31] Gui Y, Cao Y, He J, et al. Safety and immunogenicity of a modified COVID-19 mRNA vaccine, SYS6006, as a fourth-dose booster following three doses of inactivated vaccines in healthy adults: an open-labeled Phase 1 trial[J]. Life Metabolism, 2023, 2(3): load019.
[32] Pecetta S, Rappuoli R. mRNA, the beginning of a new influenza vaccine game[J]. Proceedings of the National Academy of Sciences, 2022, 119(50): e2217533119.