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Immunogenicity regulation of genetically engineered vaccine and its potential in tumor treatment

Zhuoran Yang
The Xiuwen International Academy at Jinan, China

Abstract. In this study, the strategy of enhancing immunogenicity of genetically engineered vaccine and its application potential in tumor treatment were discussed. Firstly, the study explained the principle that genetic engineering vaccine designed antigen by gene recombination technology to trigger strong immune response. By adjusting gene combination, improving vaccine delivery system and using adjuvant, the immune stimulation ability and delivery efficiency of vaccine were improved. Especially in tumor therapy, these vaccines stimulate specific immune responses against specific or related tumor antigens. This paper also summarizes the clinical manifestations of mRNA cancer vaccine and individualized cancer vaccine, and discusses the combined application with traditional treatment methods such as chemotherapy, radiotherapy, targeted therapy and immune checkpoint inhibitors, in order to improve the treatment effect and the diversity of patients' treatment options.

Key words: Immunogenicity regulation; genetically engineered vaccine; tumor treatment.

1. Introduction

As a global health problem, tumor's complexity and diversity pose a great challenge to traditional treatment methods. Although surgery, radiotherapy and chemotherapy have achieved certain results in tumor treatment, these methods are often accompanied by significant side effects, and the curative effect on advanced or metastatic tumors is limited. Therefore, it is particularly important to develop new and efficient tumor treatment methods.

As an effective means to prevent diseases, vaccines have achieved remarkable results in the field of infectious diseases. However, the application of traditional vaccines in tumor treatment has been limited, mainly due to the complexity and diversity of tumor antigens and the immune escape mechanism of tumor cells. In recent years, with the development of genetic engineering technology, genetic engineering vaccine, as a new type of tumor immunotherapy, has gradually attracted the attention of researchers [1-2]. Genetic engineering vaccine can accurately design and optimize antigens through gene recombination technology, thus stimulating the body to produce stronger immune response. Compared with traditional vaccines, genetically engineered vaccines have higher specificity and efficacy, so they show great potential in tumor treatment. However, how to regulate the immunogenicity of genetically engineered vaccine to improve its therapeutic effect is still a hot and difficult point in current research.

The purpose of this study is to explore the immunogenicity regulation strategy of genetically engineered vaccine and analyze its application potential in tumor treatment. By adjusting gene combination, improving vaccine delivery system and using adjuvants, we can find effective ways to improve the immunogenicity of genetically engineered vaccines, thus providing new ideas and means for tumor treatment.

2. Overview of genetic engineering vaccine

With the rapid development of biotechnology, the field of vaccine development has ushered in major changes. Genetic engineering vaccine, as an outstanding representative of this change, uses advanced genetic engineering technology to accurately operate and clone the immunogenic genes of pathogens

in vitro, and then produces new vaccines. Compared with traditional vaccines, genetically engineered vaccines have significant advantages in safety, effectiveness and production controllability.

The definition of genetically engineered vaccines includes vaccines produced by gene recombination technology, which can express specific antigens, thus inducing a strong immune response. Its preparation process usually involves cloning, expression and purification of antigen genes, and finally produces vaccine products with high immunogenicity. Compared with traditional vaccines, the advantages of genetically engineered vaccines are obvious. First of all, they can more accurately target specific pathogens and improve the specificity and effectiveness of immune response. Secondly, the production process of genetically engineered vaccine is more controllable and the quality is more stable, thus ensuring the safety and effectiveness of the vaccine. However, this vaccine also faces some challenges, such as the regulation of immunogenicity, that is, how to ensure that the vaccine can stimulate a strong enough immune response without causing excessive immune response.

3. Immunogenicity regulation strategy of genetically engineered vaccine

3.1. Adjusting gene combination to improve immunogenicity

In the research and development of genetic engineering vaccine, improving the immunogenicity of the vaccine is a core goal. Immunogenicity refers to the ability of antigen to stimulate the immune system to produce immune response. In order to enhance this characteristic, researchers optimized the expression of antigen by adjusting the gene combination in the vaccine, thus making the vaccine more immunostimulatory [3].

Accurate selection and combination of antigen genes with strong immunogenicity through genetic engineering technology. These genes usually encode specific proteins or glycoproteins on the surface of pathogens, which play a key role in the process of infection, so they are the main targets of immune system recognition and attack [4]. By inserting these genes into expression vectors, these antigens can be expressed in large quantities in the process of vaccine production, thus stimulating the body to produce a strong immune response.

In order to improve the effect of the vaccine, the strategy of multivalent vaccine will be adopted, that is, the antigen genes of multiple pathogens will be combined into the same vaccine. This method can not only prevent multiple pathogens at the same time, but also enhance the overall immune response through the interaction between different antigens. This strategy is especially suitable for those cases where multiple pathogens coexist in epidemic areas. In addition, researchers will also transform antigens through genetic engineering technology to enhance their interaction with the immune system [5]. For example, changing the specific amino acid sequence of antigen by site-directed mutagenesis can improve its binding ability with immune cells, thus enhancing immune response. Or by adding a specific signal sequence, the antigen can be better recognized and processed by the immune system.

3.2. Improvement of vaccine delivery system

Liposome is a kind of closed vesicle composed of phospholipid bilayer, which can form spontaneously in water. Liposomes can be used as a delivery system for drugs and gene therapy, and can be used for the delivery of anticancer, anti-inflammatory, antibiotic, antifungal, anesthetic and other drugs. In the field of vaccines, liposomes can be used to coat nucleic acid vaccines, such as mRNA vaccines, to improve their stability and immune effect [6]. The size, charge and composition of liposomes can affect their interaction with cells, thus affecting the delivery efficiency and immunogenicity of vaccines.

Nanoparticles are particles with a diameter of 1-100 nanometers and have unique physical and chemical properties. Nanoparticles can be used as carriers of vaccines to improve the stability and targeting of vaccines. Lipid nanoparticles (LNP) have been used to deliver mRNA vaccines, such as COVID-19 vaccine. The particle size distribution of LNP can be controlled by extrusion, ultrasound and homogenization, and microfluidic methods are also used for LNP manufacturing and size control.

The surface charge and composition of nanoparticles can affect their interaction with cells, thus affecting the delivery efficiency and immunogenicity of vaccines [7].

The design of immunogen is the key to improve the immunogenicity of vaccine. Some research teams designed the immunogen (FP8GKLH) of FP8-coupled carrier protein KLH, and the neutralization spectrum of neutralizing antibody was increased from 31% to 59% through the immunization mode of FP8GKLH primary immunization and gp140 trimer enhancement [8]. This shows that the immune effect of the vaccine can be significantly improved through reasonable immunogen design. The delivery mode of immunogen will also affect the immunogenicity of vaccine. For example, an mRNA vaccine induces an immune response by expressing proteins from pathogens. The delivery system of mRNA vaccine needs to be able to protect mRNA from degradation and deliver it into cells effectively. Liposome and nanoparticle technology show great potential in this respect. The strengthening of immunogen refers to improving the immune effect through multiple vaccinations or using different vaccine combinations. The study of influenza recombinant subunit immunogen shows that the rational design idea based on structure can improve the immunogenicity of vaccine. In addition, the immune effect of the vaccine can also be improved by combining different immunogens or using different delivery systems.

3.3. Use of adjuvant

Adjuvants are substances that can enhance or regulate immune response, and they play a role through various mechanisms. Adjuvants can help antigens to be captured and processed by antigen presenting cells (APC) more effectively, thus enhancing the activation of T cells and B cells. Some adjuvants can directly activate immune cells, such as dendritic cells, and promote their maturation and activation, thus enhancing the immune response [9-10]. Adjuvants can induce local inflammatory reaction, attract immune cells to aggregate, and create an environment conducive to immune response.

Cytokines are a kind of protein secreted by immune cells, which play an important role in immune regulation. As adjuvants, cytokines such as IL-2 and IFN-γ can enhance specific immune response and promote the proliferation and differentiation of T cells and B cells [11]. Chemokines are a kind of protein that can guide the migration of immune cells. As an adjuvant, chemokines can attract immune cells to gather at the site of vaccine injection and enhance local immune response. In addition to cytokines and chemokines, there are many other types of adjuvants, such as aluminum salts (commonly used aluminum adjuvants), lipopolysaccharide (LPS), saponins, etc., which enhance the immunogenicity of the vaccine through different mechanisms [12].

In practical application, the choice and use of adjuvants need to be optimized according to the specific type of vaccine and the target population. For the elderly or people with weak immune system, it may be necessary to use more powerful adjuvants to ensure adequate immune response. At the same time, the safety of adjuvants is also an important factor that must be considered. Some adjuvants may cause adverse reactions, and it is necessary to find a balance between effect and safety.

4. Application of genetically engineered vaccine in tumor treatment

4.1. Basic principle and preparation method of genetic engineering tumor vaccine

The basic principle of genetically engineered tumor vaccine is to improve the immune system's ability to recognize and kill tumor cells containing specific antigens by targeting tumor-associated antigens (TAA) or tumor-specific antigens (TSA) [13]. These antigens are unique protein on the surface or inside of tumor cells, and they can be recognized as foreign substances by the immune system. Through vaccination, the body can be induced to produce specific immune responses against these antigens, thus attacking tumor cells.

Genetic engineering subunit vaccine is a vaccine made by cloning tumor antigen gene, expressing it in host cells and then extracting and purifying antigen protein. This method can avoid using live tumor cells and reduce the potential risk [14]. Genetic engineering vector vaccine is to insert tumor antigen

gene into virus or bacterial vector, infect host cells with vector, and make host cells express tumor antigen. This method can use the immunogenicity of the vector itself to enhance the effect of the vaccine. Nucleic acid vaccines, such as DNA vaccines and mRNA vaccines, directly inject nucleic acid sequences encoding tumor antigens into patients, and patients' cells are responsible for expressing the antigens [15]. The advantage of this method is that it can be designed and prepared quickly and has strong adaptability. Gene deletion live vaccine is to knock out some key genes in tumor cells, so that they lose tumorigenicity, but still retain immunogenicity. This vaccine can be directly injected into patients to activate the immune system.

MRNA cancer vaccine is a new type of genetic engineering vaccine, which is activated by synthetic mRNA encoding tumor-related or tumor-specific antigens [16]. After the mRNA vaccination, the encoded protein will be translated and presented to the immune system to stimulate adaptive immunity. Protein encoded by mRNA is absorbed by APC through endocytosis or phagocytosis, and they may form phagocytic vesicles or endosomes containing antigenic proteins, which are presented through major histocompatibility complexes on dendritic cells (Figure 1).

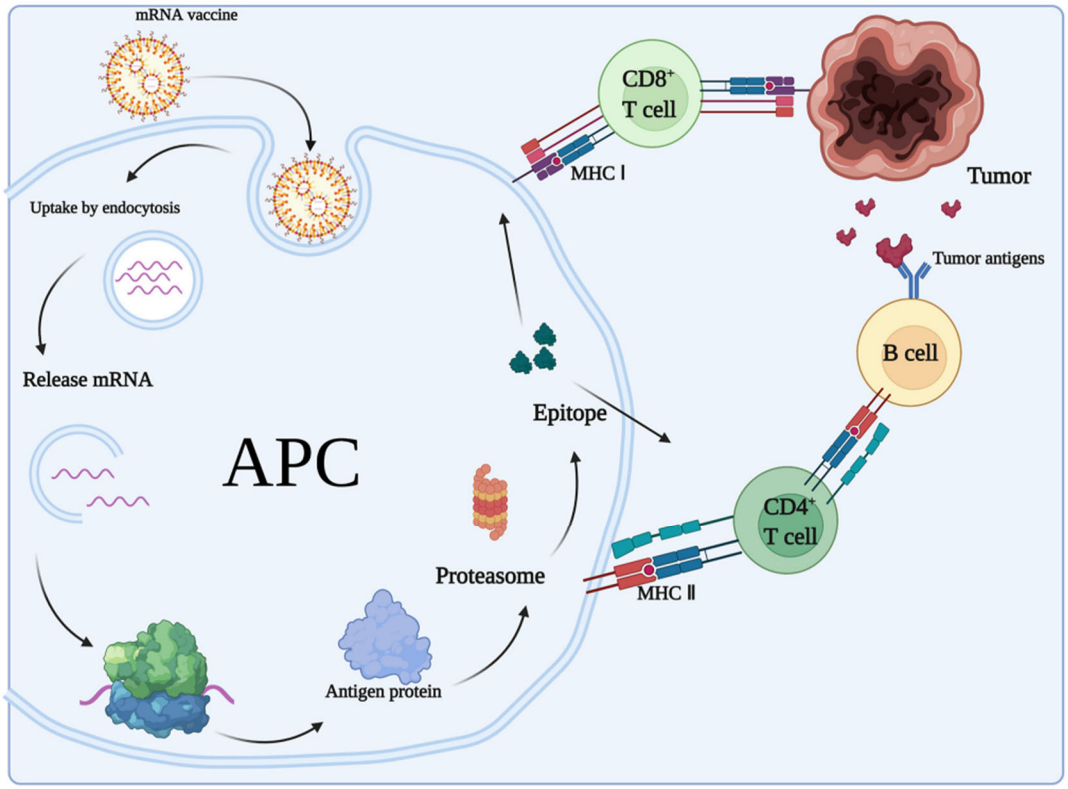

Figure 1 Induce adaptive immune response

Individualized cancer vaccines are customized vaccines based on the genome sequencing results of patients' tumors [17]. This vaccine contains a new antigen specific to the patient's tumor, which can activate the immune system to attack tumor cells more accurately. Genetic engineering tumor vaccine provides a new way for tumor treatment, which attacks tumor cells by activating patients' immune system. With the progress of molecular biology and immunology, the research and development of genetically engineered tumor vaccine will continue to make breakthroughs, bringing more treatment options for tumor patients.

4.2. Performance and effect evaluation of genetically engineered tumor vaccine in clinical trials

Genetic engineering tumor vaccine is a kind of vaccine designed and prepared by using modern molecular biology technology, especially recombinant DNA technology. This vaccine aims to activate the patient's immune system so that it can recognize and attack tumor cells. The research and

development of genetically engineered tumor vaccine provides new hope for tumor treatment, especially in the fields of personalized medicine and precision medicine (Table 1).

Table 1 Clinical trial performance and effect evaluation of genetically engineered tumor vaccine

Vaccine name	type	Clinical trial stage	Main results
BNT122	MRNA cancer vaccine	Phase I	T cell reaction rate of 50%
New mRNA antigen vaccine cevumeran	MRNA cancer vaccine	Not clear	Clinical reactions related to vaccine were observed in 2 cases (40%).
Personalized cancer vaccine	Personalized cancer vaccine	Not clear	Good safety and immunogenicity, and can induce patients to produce specific immune responses against new tumor antigens.

MRNA cancer vaccine has shown good safety and immunogenicity in clinical trials. BNT122 is a personalized cancer vaccine based on mRNA, which shows 50% T cell response rate in phase I clinical trials, and is considered as the responder of cevumeran, a new mRNA antigen vaccine [18]. In addition, the clinical trials of mRNA vaccine in melanoma patients also showed positive results, among which 2 cases (40%) observed clinical reactions related to the vaccine [19].

Individualized cancer vaccine is a customized vaccine based on the genome sequencing results of patients' tumors. This vaccine contains a new antigen specific to the patient's tumor, which can activate the immune system to attack tumor cells more accurately. In clinical trials, individualized cancer vaccine shows good safety and immunogenicity, and can induce patients to produce specific immune responses against new tumor antigens.

4.3. Combined application of genetic engineering tumor vaccine and traditional tumor treatment methods

Genetic engineering tumor vaccine has shown great potential in the field of tumor treatment because of its unique characteristics of targeting, safety and personalization. These vaccines can accurately target specific antigens on the surface or inside of tumor cells and effectively trigger immune responses, thus attacking tumor cells. Compared with traditional chemotherapy and radiotherapy, genetically engineered vaccine has lower toxic and side effects, providing patients with safer treatment options. In addition, genetically engineered vaccines can be customized according to the characteristics of patients' tumors to achieve precise treatment, which brings new hope to cancer patients.

Traditional tumor treatment methods mainly include surgery, chemotherapy, radiotherapy and targeted therapy [20-21]. These methods have their own advantages and disadvantages, but they may cause damage to normal tissues during the treatment, or the effect is limited because of the drug resistance of tumor cells. The combination of genetic engineering tumor vaccine and traditional tumor treatment methods mainly includes the combination with chemotherapy, radiotherapy, targeted therapy and immune checkpoint inhibitors. Chemotherapy can destroy the DNA of tumor cells, make them easier to be recognized and cleared by the immune system, and enhance the immune effect of the vaccine. Radiotherapy can kill tumor cells locally, release tumor antigens, enhance the immunogenicity of vaccines, and change tumor microenvironment to facilitate the infiltration of immune cells. Targeted therapeutic drugs can specifically act on the signal transduction pathway of tumor cells and cooperate with vaccines to improve the therapeutic effect. Immune checkpoint

inhibitors can relieve the inhibition of tumor cells on the immune system, and when combined with vaccines, they can further enhance the immune response.

A clinical trial studied the effect of combining mRNA vaccine with PD-1 inhibitor (an immune checkpoint inhibitor) [22]. The results show that this combination therapy can significantly improve the progression-free survival and overall survival of patients. The combination of genetic engineering tumor vaccine and traditional tumor treatment methods provides new ideas and methods for tumor treatment. By comprehensively using the advantages of different treatment methods, the treatment effect can be improved and the quality of life of patients can be improved. With the deepening of research and the progress of technology, it is expected to develop more effective combined treatment schemes in the future.

5. Conclusion

By accurately designing and optimizing antigens, genetically engineered vaccines can stimulate the body to produce a stronger immune response. These vaccines use advanced gene recombination technology to improve the specificity and efficacy, and provide a new idea for tumor treatment. The study emphasized the importance of adjusting gene combination, improving vaccine delivery system and using adjuvants to enhance immunogenicity. In addition, the research and development of individualized cancer vaccine, based on the genome sequencing of patients' tumors, can induce specific immune response to new tumor antigens, showing great potential of precision medicine. Clinical trials show that mRNA cancer vaccine has good safety and immunogenicity, and the combined application with traditional treatment methods, such as chemotherapy, radiotherapy, targeted therapy and immune checkpoint inhibitors, can significantly improve the therapeutic effect. In a word, the genetic engineering vaccine shows unique characteristics of targeting, safety and personalization in tumor treatment, which brings new hope to tumor patients, and with the deepening of research and the progress of technology, it is expected to develop more effective combined treatment schemes in the future.

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