

New Possibilities for Cancer Immunotherapy Discovered Through Cancer Vaccines

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Abstract. Cancer vaccine, a type of cancer immunotherapy, works by enhancing the identification and eradicating antigens, preventing cancer recurrence and stopping the growth or spread of tumors function. Because cancer vaccines are highly specific and therapeutically effective in preventing and treating cancer, it is gradually becoming the mainstay of cancer immunotherapy. First, some malignancies have relatively poor immunotherapy response rates, thus it's important to talk about ways to boost reactive T cell activity. In addition, how to combine cancer vaccines with other immunotherapies will be a challenge for cancer immunotherapy. In addition, how to apply adjuvants as well as novel materials as cancer vaccine delivery agents will also be the focus of subsequent cancer vaccine research. Currently, scientists aspire to use adjuvants to enhance the immunization effect of cancer vaccines and reduce their cost. This essay will concentrate on the cancer vaccine's mode of action, classification, benefits, and drawbacks, as well as its issues and possible uses. It will also offer suggestions for future cancer vaccine research and development.

Keywords: Cancer immunotherapy, cancer vaccine, adjuvant.

1. Introduction

Cancer immunotherapy is generated to strengthen the immune system to combat cancer. Common immunotherapies currently used in clinical practice include adoptive T-cell therapy (ACT), monoclonal antibodies (mAbs), immune checkpoint blockade, cytokines and cancer vaccines. Cancer vaccines work primarily by producing immunity. The vaccine injects a weakened disease antigen into the body, and the body attacks the antigen by producing antibodies. If this antigen re-enters the body, the body's immune system has the potential to fight it off. A vaccination works on the basis that it is an immunological preparation for the prevention of infectious diseases generated from dangerous microbes and their byproducts that have been genetically changed, artificially attenuated, or inactivated, among other things. Nowadays, cancer vaccines are widely used in clinical practice because of their high specificity, low damage to healthy cells, and good preventive and therapeutic effects. Cancer vaccines are emerging as a new trend in cancer treatment and prevention. However, there are many problems with cancer vaccines, such as the difficulty of research and development, high production costs and uncertainty about toxic side effects. This paper will focus on the classification of cancer vaccines and their advantages and disadvantages, in addition to focusing on the limitations and solutions of cancer vaccines and exploring the role of adjuvants in vaccines.

2. General Introduction to Cancer Vaccines

2.1. Overview of current developments in cancer vaccines

Vaccines are drugs that aid in disease prevention and can train the immune system to identify and destroy dangerous molecules. The clinic offers two main categories of cancer vaccinations: preventive vaccines and therapeutic vaccines. Preventive vaccines are primarily given to healthy people to provide defense against the development of certain cancers. It is crucial to remember that for the vaccine to be effective, a person must be inoculated before contracting the virus. One kind of preventive vaccine is the HPV vaccine, which is currently being utilized in clinical settings. and cancer immunotherapy, which includes therapeutic vaccinations. They function by strengthening the body's anti-cancer defenses. Therapeutic vaccines are used for patients who already have that type of

cancer. Applying cancer treatment vaccines at the right time can effectively prevent the recurrence of cancer and organize the growth and spread of tumors.

Cancer vaccines work primarily by creating immunity. The vaccine injects a weakened form of the disease antigen into the body, and the body attacks the antigen by producing antibodies. If this antigen re-enters the body, The immune system of the body may be able to repel it. Antigens are essentially chemicals seen on the surface of cells that are typically not found in the body. As a result of the immune system's attack and elimination of these antigens, a "memory" is left behind, enabling the immune system to react more swiftly when they recur. The same principles apply to cancer vaccinations. The vaccination injects these molecules into the body to trigger the immune system to recognize and remove the cancer cells because they contain particular antigenic molecules on their surface that healthy cells do not. Individualized cancer vaccines are still employed in the treatment of cancer due to technological advancements. Based on how the given antigen is used in the vaccine, there are several different kinds of cancer vaccines that can be divided into three primary groups: Cellular vaccines, genetic vaccines, and other cancer vaccines are examples of vaccines based on proteins and peptides [1]. To trigger the immune system and combat cancer, scientists employ cancer antigens in the form of proteins or artificial peptides, cellular transportation of tumor antigens, as well as DNA/RNA encoding of cancer antigens [1].

There are already cancer vaccines being used in the clinic. For example, the vaccine for The human papillomavirus (HPV)-related cancer is now common. The recent studies showed the correlation between human papillomavirus and the development of cervical cancer, further started to develop and research and develop the vaccine for HPV. Currently available preventive HPV vaccine forms are virus like particles (VLPs) assembled from L1 proteins using different expression systems, which can induce viral neutralizing antibodies and memory effects in vivo to protect the body from HPV infection [2]. VLPs are non-enveloped virus like particles with neutralizing antigenic epitopes on their surface, which induces the production of high titer anti-L1 antibodies IgG and IgA to protect the body from viral infection [3]. Meanwhile, the therapeutic HPV vaccine currently used in clinical settings refers to an immune agent that can clear the virus and virus-infected cells by stimulating a specific T-cell-mediated immune response in an organism that has been infected with the virus. The oncogenic proteins HPV E6 and E7 are constantly produced in infected cells and can promote cervical epithelial cells' malignant transformation [4]. Therapeutic HPV vaccines transmit different E6 and E7 antigen forms to cells that present antigens, for example, DCs to trigger an immune response specific for the antigen in order to stimulate CD8⁺ CTL responses or CD4⁺ helper T-cell responses specific for HPV antigen [5]. And CD4⁺ helper T-cell responses to identify and eradicate E6- and E7-expressing cells, respectively, to eradicate the virus. The virus and infected cells are eliminated as a result of the recognition and destruction of E6- and E7-expressing cells [3]. Currently, most cancer treatment of vaccines are still in clinical trials. Research on preventive and therapeutic vaccines for lung, bone marrow, and colorectal cancers is also underway. In short, cancer vaccines will be more and more widely used in cancer immunotherapy.

2.2. Cancer Vaccine Classification

Cancer vaccines are categorized in various ways and can be divided into preventive and therapeutic vaccines according to their therapeutic effect on cancer. Preventive vaccines include cervical cancer vaccine, melanoma cell vaccine and breast cancer vaccine. At this stage, there are fewer therapeutic vaccines, For cervical cancer, however, there are clinically effective vaccinations (Table. 1).

2.2.1 Preventive vaccines

Since human papillomavirus infection is the primary cause of most cases of cervical cancer, the term "cervical cancer vaccine" is used to describe the HPV vaccination, which is intended to prevent infection with the virus. Generally through the antigen into the body and neutralization of viral antibodies for prevention. It mainly targets high-risk types of human papillomavirus, including bivalent vaccine, quadrivalent vaccine and nine-valent vaccine, which covers different types of preventable human papillomavirus and has been widely used clinically.

As the fourth most prevalent malignant neoplasm among females and a "killer" of women's health, cervical cancer incidence rates have been rising in recent years. The World Health Organization (WHO) reported 528,000 new cases and 266,000 fatalities from cervical cancer in 2012 [4]. Globally, it is predicted that there would be 310,000 fatalities and 570,000 new cases in 2018 [5]. In underdeveloped nations, cervical cancer accounts for 85% of cases. As a member of the developing world, China likewise faces a very dire position. In China, cervical cancer incidence rates have increased since 2000, although fatality rates have remained largely unchanged. In 2015, there was a total of 98,900 newly diagnosed cervical cancer cases reported in China, and the mortality rate was relatively stable. In the year 2015, China witnessed a total of 98,900 newly reported cases along with 30,500 fatalities [6]. With such a high incidence of cervical cancer, HPV becomes very important. First of all, the cervical cancer vaccine can effectively HPV infection, thus reducing the incidence of cervical cancer. Secondly, through the cervical cancer vaccination, the body's immune system is stimulated to improve the body's resistance to HPV and prevent HPV infection.

However, the cervical cancer vaccine currently has some disadvantages, such as its higher cost and lower penetration rate, making it difficult to achieve universal vaccination. Secondly, it cannot achieve 100% prevention of cervical cancer. People who have been vaccinated against HPV are still at risk of developing cervical cancer. In addition, although the cervical cancer vaccine has now been subjected to scientific research and safety trials, there may still be unknown toxic side effects [7].

(1) Melanoma cell vaccine

Melanoma is usually a relatively high probability of cancer, so researchers are gradually developing melanoma cell vaccine according to the cause of melanoma and antigen and other methods, so as to inhibit the angiogenesis in melanoma, as well as melanoma cell breeding and other effects.

Melanoma is a serious malignant tumor of the skin. In the early stages of melanoma, surgery has a high cure rate with a good prognosis, but in the advanced stages of the disease, there is currently no effective treatment. Immunotherapy, as an emerging therapeutic modality, has also shown good results in the treatment of melanoma. Among them, tumor vaccines play their therapeutic role by reactivating the anti-tumor immune function of the body. However, most of the current vaccines have not achieved the expected results.

(2) Breast cancer vaccine

Breast cancer vaccine is a preventive vaccine, through the injection of anti-cancer vaccine and activate the immune cells in the body, through the body's immune response and rejection of the tumor cell foreign objects to attack and destroy, so as to achieve the role of breast cancer prevention.

A part of the endeavor to prevent breast cancer with immunization includes optimizing vaccine regimens and administration techniques. There exists a wide range of breast cancer vaccines available. However, enable the autoimmune system to recognize the target antigen in order to have a therapeutic effect [8]. Currently, peptides made from tumor antigens are used as the most popular type of breast cancer vaccination. Peptide vaccines, As a popular therapeutic approach for breast cancer, MHC class I-restricted peptide epitopes play a crucial role in stimulating immune responses against specific tumor antigens [8]. The primary immune effector cells will receive the processed injectable peptide from the apc and use it to search for and destroy cancer cells that display the shared antigen. Peptide vaccines, which give MHC class i-restricted peptide epitopes to induce immune responses against certain tumor antigens, are one of the most widely used therapy strategies for breast cancer [8]. The primary immune effector cells will receive the processed injectable peptide from the apc and use it to search for and destroy cancer cells that express the shared antigen [9]. Short amino acid peptides are easy, inexpensive, and reasonably stable to synthesize in comparison to other forms. For breast cancer vaccines, for instance, the following seven categories can be used to classify the vaccines: peptide vaccine, carbohydrate antigen vaccine, tumor cell vaccine, tumor cell vaccine, and DC-based vaccine [8].

Table1. types of canner vaccines

types	synopsis	advantage	disadvantage
Peptide Vaccine	breast cancer, use peptides that restrict MHC Class I epitopes to stimulate an immune response against a specific tumor antigen. The primary immune effector cells will process the injected peptide and then present it to the cancer cells that express the common antigen, which the immune system will then seek out and destroy. [7]	Cost-effective Easily manufacturable, Relatively higher stability. Enables large-scale manufacture and transportation [8].	Not effective for without HLA subtypes [9]. May result in restricted activation of CD8+ cytotoxic T cells and a transient immune response [8].
Peptide Vaccine	Protein-based vaccines are developed using entire or truncated fragments of tumor antigen proteins [8].	Efficiently internalizing, and processing [8].	Challenging due to the absence of specific biomarkers [11].
Carbohydrate Antigen Vaccine	targeting aberrantly expressed carbohydrate antigens on neoplastic cells		
Tumor Cell Vaccine	The vaccine is formulated using autologous or allogeneic tumor cells derived antigens, to induce a polyvalent immune response. [12,13].		Eliciting a polyvalent immune response. Secrete cytokines or express co-stimulatory molecules [12,13].
Tumor Cell Vaccine	Expression antigens, typically delivered as plasmids or vectors subsequently conjugated and translated by APCs into tumor antigens, for the stimulation of antigen-specific immune responses [14].	Can be easily scaled up to produce large quantities and they can be stored at a low cost.	The immunogenicity is constrained [9].

DC-Based Vaccine	Diversity efficiently capture antigens and subsequently eliciting an immune response. DCs possess the ability to activate NK cells and B cells [15].		technical complexities.
DC-Based Vaccine	The fusion of tumor cells with DCs. The generation of hybrids between DCs and tumor cells can be achieved by subjecting them to polyethylene glycol [16]		This vaccine is more difficult to produce.

2.2.2 Therapeutic vaccines

For instance, the primary function of a vaccine for treating cervical cancer is to stimulate the immune system's reaction within the body, leading to the elimination of mutated cells caused by viral infection. So as to get the effect of cervical cancer treatment. Its specific therapeutic effect is also different from person to person, so it is also necessary to actively cooperate with the doctor for treatment. Until now, cancer therapeutic vaccines have been in the research stage, with few actual clinical applications.

2.3. Cancer Vaccine Advantages and Disadvantages

Cancer vaccines have many advantages over other cancer immunotherapies: they are safe, do not suffer from off-target toxicity. Furthermore, they have demonstrated efficacy in inducing T-cell immune responses. Additionally, when combined with other forms of immunotherapy, cancer vaccines exhibit enhanced efficacy not only can solve the problem of low activity of T cell immune response, but also overcome the tumor immunosuppressive microenvironment. However, most cancer vaccines are currently in the development stage, and there are still some limitations

2.3.1 The difficulty of further application

There are a number of hurdles that need to be overcome in the further application of vaccines. First, some cancers have relative low response rates to immunotherapy, and further research is needed on how to use personalized cancer vaccines and increase reactive T-cell activity in order to combine other immunotherapies with a synergistic therapeutic effect on them [17]. In addition, the future development of cancer vaccines will witness a significant trend towards integrating them with other immunotherapies. There are also promising applications for combining cancer vaccinations with other traditional treatments such as targeted medicines, chemotherapy, and radiotherapy. Cancer vaccinations and targeted therapy complement each other's effects. Furthermore, the effectiveness of immunotherapy can be enhanced through a combination with chemotherapy, as it promotes T-cell response, and facilitates increased synthesis of antigens [17]. Moreover, the combination of PD-1/PD-L1 inhibitors and cancer vaccines exhibits promising potential. To address the problem of immune escape of tumor cells, PD-1 inhibitors have been developed, which can activate T-cell activity and induce the secretion of immunogenic factors. This solves the problem that it is difficult for cancer vaccines to activate the immune response of T cells.

Additionally, the complex tumor microenvironment contains a variety of immunosuppressive mechanisms that help the tumor avoid the immune system. As a result, the combination use of the cancer vaccine will emerge as a fresh approach to treating cancer [18].

Second, the inclusion of adjuvants creates fresh opportunities for the creation of cancer vaccines. Adjuvant, which is often referred to as an immunomodulator or an immunopotentiator, is a crucial component in the creation of cancer vaccines. It is a substance that is used in combination with an antigen to produce better immunity than the antigen alone. Nowadays, immune adjuvants can be understood as a class of substances that bind or mix with antigens non-specifically to enhance the immunogenicity and immunoprotective effect of the antigen. With the development of modern anti-infection immunology technology, a large number of recombinant vaccines, subunit vaccines, synthetic peptide vaccines, and anti-unique antibody vaccines with high purity and high specificity have appeared. However, most of these vaccines have small antigenic molecules and weak immunogenicity, which make it difficult to induce an effective immune response when used alone, and require immune adjuvants to enhance their immunogenicity, prolong their retention time and immunostimulatory effect, and enhance the protective immune response of the body [18]. The mechanism of action of immunoadjuvants has the following five general points:

(1) Immunomodulation involves the modulation of immune system function and the production and activity of cytokines. Certain adjuvants have a positive impact on overall immune system function, whereas most adjuvants specifically enhance the production and activity of particular cytokines

(2) Promote antigen presentation: Adjuvants can interact with antigen or with antigen-presenting cells, B cells, dendritic cells, etc., to promote antigen presentation or longer-term reserve antigen.

(3) Promote the production of cytotoxic lymphocytes (CTL).

(4) Targeting: the adjuvant delivers the antigen to specific immunologically effective cells, or the adjuvant interacts with the antigen in some way to form a polymer, so that it can be easily phagocytosed and absorbed by macrophages and DC cells.

(5) Depot effect: the adjuvant will short-term or long-term storage of antigen in the inoculation site, slowly release the antigen, so as to play a long-term role in stimulating immunity.

2.3.2 The delivery of cancer vaccine

Currently, the most common mode of vaccine delivery is still direct injection. Injecting in vitro transcribed mRNA directly into the human body as a transdermal injection can increase the capture of nascent antigens by antigen-presenting cells, which can effectively induce anti-tumor immune responses. Therefore, direct injection is the most convenient and effective delivery method for cancer vaccines, and it is also the most widely used in clinical practice [19].

However, delivering a cancer vaccine as a simple injection does not maximize its effectiveness. Therefore, scientists are investigating biomaterials and nanomaterials to assist in cancer vaccine delivery. Biomaterials can protect antigens from degradation. DNA-RNA nanocapsules (iDR-NC), which can transfer DNACpG and short hairpin RNA (shRNA) as well as tumor-specific antigens into lymphatic antigen-presenting cells (APCs), triggering immune responses in specific peripheral CD8T cells and significantly inhibiting tumor growth [19]. In addition, responsive nanovaccines have been developed, which generate response signals in response to pH changes in vivo, enabling antigen cross-positive delivery, resulting in better anti-tumor effects [19].

However, there are some issues with biomaterials and nanomaterials as delivery agents for cancer vaccines. Firstly, the biggest problem is the too high production cost and technical requirements, secondly, the therapeutic effect of the vaccine can be easily affected due to the possible reaction of the biomaterials in the organism, in addition, it is not certain that the biologic or nanomaterials are suitable for all patients due to the large individual differences of patients. Nowadays, nanoparticles have emerged as the optimal choice for transporting cancer vaccines. These water-based particles imitate PAMP (pathogen-associated molecular pattern), a signal of potential danger that cells can detect and be assimilated by the nanoparticles. Consequently, they serve as an excellent medium for delivering cancer vaccines. They can be effective in eliciting antigen recognition and stimulating the immune system to generate an immune response. In addition, some nanomaterials exhibit inherent adjuvant-like immunostimulatory properties that can further contribute to the efficacy of cancer vaccines [19].

3. Summary

This article focuses on the mechanism of action of cancer vaccines, how it acts on the immune system, and why it can prevent and treat cancer. It also lists cancer vaccines that have been used in the clinic. In addition, cancer vaccines are categorized into preventive and therapeutic vaccines, which are further subdivided according to their mechanism of action, and their advantages and disadvantages are listed. The high cost, difficulty in research and development, and uncertainty of effectiveness in the development of cancer vaccines are discussed. In order to address these issues, there is an optimistic outlook towards utilizing cancer vaccine adjuvants for augmenting the immune response. Additionally, their potential integration with other cancer immunotherapies like PD-1 and PD-L1 monoclonal antibodies holds promise in the context of cancer treatment. In addition, the utilization of biomaterials and nanomaterials as delivery systems for cancer vaccines further enhances the efficacy of cancer immunization. In conclusion, cancer vaccines will be one of the main ways of cancer prevention and treatment in the future. Further studies are needed on the development of vaccine adjuvants. Also, further researches could focus on how cancer vaccines wider prevention and treatment of cancer, make it more effective and reduce its cost.

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