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Emerging Role of Vaccines in Breast Cancer

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Abstract:

Breast cancer is a serious threat to women's health. It can metastasize to vital organs, causing complications and endangering lives. Early detection and treatment can prolong survival. Although existing treatments such as chemotherapy, targeted therapy, and endocrine therapy have improved the overall cure rate of breast cancer, they are ineffective for patients with advanced metastatic breast cancer. Tumor vaccine therapy is expected to solve this problem by inducing the activation of the body's immune system, precisely killing cancer cells, and reducing the chance of cancer recurrence. There are two types of breast cancer vaccines: preventive vaccines and therapeutic vaccines. Preventive vaccines are designed to activate the immune system in high-risk individuals, targeting specific antigens commonly found on breast cancer cells. Several ongoing clinical trials are testing these vaccines. Therapeutic vaccines are designed to treat patients already diagnosed with breast cancer by activating their immune system to recognize and attack cancer cells. Examples of therapeutic vaccines include peptide-based vaccines, whole-cell lysate vaccines, viral or DNA-based vaccines, and dendritic cell vaccines. This review introduces the types, mechanisms, and ongoing clinical trials of breast cancer vaccines, including preventive and therapeutic vaccines, and discusses the future research directions in this field.

Keywords: Breast cancer; preventive vaccine; therapeutic vaccine.

1. Introduction

As a malignant tumor that seriously threatens women's health, the harm of breast cancer should not be underestimated. Breast cancer not only affects the physical and mental health of patients but also affects the aesthetics of breasts after undergoing surgical treatment, leading to anxiety and other negative emotions and damaging psychological health. At the same time, breast cancer is a systemic disease that can metastasize to lungs, bones, and liver through blood, causing serious complications and even en-

dangering lives. According to statistics, if breast cancer can be detected early, diagnosed early, and treated in time, the survival period can be effectively prolonged.

Breast cancer vaccine research and development are very significant because of the catastrophic consequences of the disease. At present, although chemotherapy, targeted therapy, and endocrine therapy have constituted the cornerstones of non-surgical treatment of breast cancer in clinical practice and the overall cure rate of breast cancer has been significantly improved, the existing treatments are ineffective for patients with advanced metastatic breast cancer. The emergence of tumor vaccine therapy is expected to solve this clinical problem by inducing the activation of the body‘s immune system, precisely killing cancer cells, and reducing the chance of cancer recurrence.

2. Mechanism of Vaccines in Breast Cancer

2.1 Principle of Immune Activation

The GP2 breast cancer vaccine, a kind of breast cancer vaccine under development‘s preventive principle, is to stimulate cellular immunity and humoral immunity to produce antibodies to fight against breast cancer cells. GP2, as a fragment of the human HER2 protein, can be captured by antigen-presenting cells, which can stimulate the antigen-presenting cells to find the T cells that specifically bind to GP2. These T cells are stimulated to proliferate into specific effector T cells that bind to the HER2 protein indicated by the tumor, thereby killing the tumor cells. Another example is the HER-vaxx vaccine, which stimulates the anti-cancer immune system in breast cancer patients who have an excess of HER-2 protein, improving their chances of survival. In addition, scientists are working on a new dendritic cell vaccine that can target the her2 protein on the surface of breast cancer cells, collect dendritic cells from the patient‘s body, and expose the dendritic cells to fragments of the her2 protein to create an individualized vaccine that can be injected into the patient‘s lymph nodes to activate the immune response of the patient‘s body [1].

2.2 Targeting Specific Proteins

Vaccines targeting breast cancer-associated proteins work primarily by recognizing and attacking specific proteins. For example, HER-2 is an important tumor-associated antigen associated with the pathogenesis of breast cancer, and NeuVaxTM is a HER-2 protein vaccine in clinical trials. HER2/neu is a cell surface receptor protein usually expressed in HER2-positive breast cancer and a variety of other common malignant tumors, and GP2 and AE37 are both short peptide vaccines derived from HER2/neu. vaccines that improve disease-free survival. In triple-negative breast cancer, the alpha-lactalbumin vaccine prevents it by activating the immune system, so that when alpha-lactalbumin-expressing cancer cells are present in the body, they are immediately “seized” by the immune cells and eliminated before they can develop into cancer. The adagloxad simolenin vaccine targets Globo-H and, together with the saponin adjuvant OBI-821, induces an immune response against breast cancer [1].

3. Preventive vaccines

Preventive breast cancer vaccines are designed to activate the immune system in individuals who are at high risk of developing breast cancer, such as those born with BRCA1 or BRCA2 mutated genes or individuals with a strong family history of the disease. These vaccines work by targeting specific antigens that are commonly found on breast cancer cells, enabling the immune system to recognize and attack any precancerous or early cancerous cells before they can develop into full-blown malignancies.

A target in preventive breast cancer vaccines is the HER2 (human epidermal growth factor receptor 2) protein, which is overexpressed in about 20% of breast cancers. HER2-positive breast cancers tend to be more aggressive, making them an attractive target for vaccine development. MUC1, a glycoprotein often found in higher levels on the surface of breast cancer cells, is another target. MUC1-targeted vaccines aim to disrupt the formation and growth of tumors by interfering with cancer cell communication and survival mechanisms [2].

Several ongoing clinical trials are testing preventive breast cancer vaccines. One example is the GP2 peptide vaccine, which targets the HER2 protein and is being tested in patients who have undergone surgery and are at risk of recurrence. The goal is to boost the immune system‘s ability to eliminate any remaining cancer cells and prevent the disease from returning. Another trial is exploring a vaccine targeting MUC1 in individuals with a high risk of developing breast cancer, seeking to generate a strong immune response before cancer can form [3].

4. Therapeutic Vaccines

Therapeutic breast cancer vaccines are designed to treat patients already diagnosed with breast cancer by activating their immune system to recognize and attack cancer cells. These vaccines are often used in combination with other treatments to improve outcomes.

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Therapeutic vaccines work by using specific antigens associated with breast cancer cells to trigger an immune response. For example, vaccines like E75 target the HER2 protein. When administered with an immunoadjuvant, the antigen is processed by antigen-presenting cells, which activate cytotoxic T-lymphocytes. These CTLs are trained to recognize and destroy cancer cells displaying the HER2 antigen. Therapeutic vaccines aim to create immune memory, similar to traditional vaccines, to lower the risk of cancer relapse [4].

4.1 Peptide-based Vaccines

One notable example of a therapeutic vaccine is NeuVax (E75), a peptide-based vaccine that targets the HER2 protein, a protein that is overexpressed in HER2+ breast cancer patients. HER2+ breast cancer, along with triple-negative breast cancer (TNBC), represents one of the more aggressive breast cancer phenotypes, with a particularly poor 4-year survival rate [2]. E75 works by training the immune system‘s T-cells to recognize and destroy cells that overexpress HER2. E75 demonstrated its potential in clinical trials, especially when used in patients with low-to-intermediate HER2 expression, helping to reduce the risk of recurrence after initial treatment.

Two concurrent Phase II trials were conducted, enrolling 186 disease-free breast cancer patients with node-positive and node-negative disease. These patients received the E75 vaccine combined with GM-CSF (granulocyte-macrophage colony-stimulating factor). The trials aimed to assess the vaccine‘s safety, immune response, and clinical effectiveness in preventing recurrence. The results showed that the vaccine was safe, with patients exhibiting a measurable immune response, and findings indicated a reduced recurrence rate in vaccinated patients [4].

4.2 DNA Vaccines

DNA vaccines are a type of vaccine that uses plasmid DNA encoding tumor-associated antigens to deliver the vaccine antigen to the immune system. These vaccines have the potential to induce strong immune responses and offer long-term immunity. In the context of breast cancer research, DNA vaccines targeting HER2 and other antigens are being explored. For example, in a certain clinical trial, the safety and immunogenicity of a plasmid-based vaccine encoding the ERBB2 intracellular domain (ICD) were evaluated in patients with advanced-stage ERBB2-positive breast cancer. The results showed that the vaccine had the potential to generate ERBB2-specific type 1 T cells in most patients, and further research is being conducted to assess its effectiveness. Overall, DNA vaccines represent a promising avenue in the development of breast cancer vaccines [5].

4.3 Dendritic Cell Vaccines

Dendritic cell vaccines represent an innovative approach to breast cancer immunotherapy by leveraging the antigen-presenting capabilities of dendritic cells to activate a robust immune response against tumors. These cells are essential for initiating immune reactions, as they process and present antigens to T-cells, triggering an immune attack. In the case of dendritic cell vaccines, a patient‘s dendritic cells are extracted, loaded with specific cancer antigens, and reintroduced into the body to activate T-cells that target tumor cells expressing those antigens. One example is DCVax, which has been tested across multiple cancer types, including breast cancer. In this strategy, dendritic cells are often loaded with tumor-specific antigens like HER2 protein fragments, aiming to direct T-cells to attack and destroy cancer cells [6].

Dendritic cell vaccines offer several advantages, particularly their ability to induce a broad immune response by activating multiple arms of the immune system, including cytotoxic T-cells and natural killer (NK) cells. This multifaceted activation increases the likelihood of eliminating tumor cells, even in advanced or metastatic disease. Furthermore, dendritic cell vaccines may address limitations seen in other immunotherapies like immune checkpoint blockades (ICBs) and adoptive cell transfer therapies (ACTs), which struggle with cold tumors, immunosuppressive environments, and immune-related side effects. While ICBs and ACTs have gained attention, dendritic cell vaccines could help overcome these barriers by enhancing the immune system in a more targeted manner [7]. However, despite their promise, dendritic cell vaccines face several challenges. Ensuring that dendritic cells are loaded with the right antibodies to generate a strong and specific immune response is difficult. Additionally, tumors often evolve mechanisms to avoid immune detection, further reducing vaccine effectiveness. While the first generation of dendritic cell vaccines, such as the FDA-approved Provenge, represented significant progress, there are still unresolved issues. Researchers are now developing newer generations of dendritic cell vaccines that incorporate new techniques such as biomaterial-based vaccines, mRNA-pulsed vaccines, and small extracellular vesicle (sEV)-based vaccines, aiming to enhance dendritic cell function and improve clinical outcomes [8].

5. Conclusions

In conclusion, the development of breast cancer vaccines is significant, as current treatments have limitations, especially for advanced metastatic cases. These vaccines aim

to activate the immune system to fight cancer cells more effectively. While there are challenges, ongoing research in areas like mRNA vaccines and dendritic cell technology offers hope for future treatments. Through technology integration and international collaboration, these vaccines have the potential to transform breast cancer care and the field of cancer immunotherapy, providing more personalized and effective solutions.

In the future, the research on breast cancer vaccines can be carried out in the following aspects: First, further optimize the technical route. For example, in the case of mRNA vaccines, the loading system of lipid nanoparticles should be improved to enhance the stability and delivery efficiency of mRNA and, at the same time, reduce the production cost. For self-replicating mRNA vaccines, the advantages and disadvantages of different viral structures can be studied in depth, and safer and more effective viral structures can be selected. In the selection of vaccine carriers, new carrier materials can be explored to improve the immunogenicity and safety of vaccines. Secondly, research on vaccine targets should be strengthened. Dig deeper into the tumor neoantigens of triple-negative breast cancer to improve the precision and effectiveness of the vaccine. At the same time, combine technologies such as artificial intelligence and big data analysis to predict and screen potential vaccine targets. Further, conduct large-scale clinical trials. Recruit more subjects for long-term follow-up observation to further validate the safety and effectiveness of the breast cancer vaccine. At the same time, explore the differences in response to the vaccine among different populations and subtypes of breast cancer, so as to provide a basis for personalized treatment.

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