Editorial

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Toward cancer immunoprevention: what are the prospects for therapeutic vaccines?

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Abstract

Therapeutic cancer vaccines represent a promising immunotherapy approach aimed at treating existing cancers by stimulating the patient's immune system to target tumor cells. Unlike prophylactic vaccines, therapeutic vaccines are administered after cancer diagnosis and focus on inducing specific cytotoxic $CD8^+$ T cell responses against tumor-associated antigens or tumor-specific neoantigens. These antigens are presented by antigen-presenting cells, such as dendritic cells, to activate an immune attack. However, the efficacy of therapeutic vaccines is often limited by immune tolerance, tumor heterogeneity, and an immunosuppressive tumor microenvironment, necessitating combination with other treatments like immune checkpoint inhibitors or chemotherapy. Multiple vaccine platforms are under investigation, including peptide/protein-based, DNA/messenger RNA (mRNA)-based, dendritic cell vaccines, viral vector vaccines, and personalized neoantigen vaccines that leverage next-generation sequencing for precision targeting. Clinical trials target a range of cancers, including melanoma, gynecologic, breast, pancreatic, liver, glioblastoma, and lung cancers, with results showing immune activation but modest clinical efficacy. Key challenges include immune evasion, variability in patient response, manufacturing complexities, high cost, and lack of predictive biomarkers. Technological advances in nanoparticle delivery, potent adjuvants, mRNA platforms, and combination immunotherapies are being explored to enhance vaccine performance. In low-resource settings, barriers such as limited access to advanced diagnostics and clinical trials necessitate tailored strategies to ensure equitable vaccine deployment. Overall, therapeutic cancer vaccines hold potential to become integrated into standard oncology protocols, especially for adjuvant therapy and recurrence prevention, with an emphasis on personalized and accessible immunotherapies to transform cancer management globally.

Keywords: immunotherapy, mRNA vaccines, oncology, personalized medicine, tumor antigens

Despite major advances in oncology, conventional cancer treatments such as surgery, chemotherapy, and radiotherapy still face significant limitations, including high toxicity, the emergence of resistance, and a high risk of relapse[1]. The advent of immunotherapy has revolutionized cancer management by harnessing the patient's immune system to recognize and eliminate tumor cells. Among the most innovative strategies in this field, therapeutic cancer vaccines are gaining increasing attention. Unlike prophylactic vaccines that aim to prevent disease, such as those against human papillomavirus or hepatitis B, therapeutic vaccines are administered to individuals already diagnosed with cancer, with the goal of stimulating a targeted immune response against tumor cells[1,2]. This article examines The Prospects for Therapeutic Vaccines Toward Cancer Immunoprevention. This study follows the TITAN 2025 guidelines to ensure 14 transparent and reproducible methods[3].

The development of therapeutic vaccines is based on the identification and presentation of tumor-associated antigens (TAAs). These antigens can be classified into two main types. TAAs are often overexpressed in cancer cells but may also be found in normal tissues, while neoantigens arise from tumor-specific somatic mutations and display higher immunogenicity. These antigens are presented to cytotoxic $CD8^+$ T lymphocytes by antigen-presenting cells (APCs), such as dendritic cells, which play a central role in triggering an immune attack against cancer cells. However, the efficacy of these antigens can be hindered by factors such as immune tolerance, tumor heterogeneity, and the immunosuppressive tumor microenvironment. Consequently, therapeutic vaccines are frequently combined with other strategies, including immune checkpoint inhibitors that reactivate exhausted T cells, or chemotherapy, which enhances antigen release from tumor cells[1,2,4].

A variety of vaccine platforms are currently under investigation. Peptide-or protein-based vaccines are designed to target specific epitopes and are relatively easy to manufacture[2]. DNA and messenger RNA (mRNA)-based vaccines, such as those developed by BioNTech for melanoma and pancreatic cancer, enable rapid and personalized synthesis of tumor antigens. Dendritic cell vaccines, such as Sipuleucel-T approved for prostate cancer, involve the *ex vivo* activation of the patient's own APCs. Other approaches include viral vector-based

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vaccines, using engineered viruses such as vaccinia or adenovirus to deliver antigens to the immune system. Additionally, personalized vaccines based on each patient's neoantigens are gaining interest due to their specificity and potential for strong immune activation[4,5].

Clinical trials of therapeutic vaccines span a wide range of cancers. Melanoma has been a model for development due to its high mutational burden and immunogenicity. Gynecologic cancers, especially cervical and ovarian cancers, are also actively studied due to their association with viral oncogenesis and the availability of well-characterized antigens. Breast and pancreatic cancers are the focus of early phase trials, although challenges related to tumor heterogeneity remain. Liver cancer, particularly in regions with high hepatitis B or C prevalence, is another relevant target. Trials involving glioblastoma and lung cancer face additional challenges due to local immunosuppression and the blood–brain barrier[1–6].

Clinical results have shown that therapeutic vaccines can induce specific immune responses, although their overall clinical efficacy remains modest. Some studies have reported prolonged progression-free survival or improved objective response rates, particularly when vaccines are combined with other treatments. However, several obstacles persist, including tumor heterogeneity[4], immune evasion mechanisms, variability in patient response, and logistical challenges in vaccine manufacturing. The high cost, long production timelines, and lack of reliable biomarkers to predict response also limit the large-scale clinical use of these therapies[2,4,5].

Technological advances offer promising opportunities to improve vaccine efficacy. Nanoparticle-based delivery systems, more potent adjuvants, and flexible platforms like mRNA are being explored to enhance immunogenicity. Combining vaccines with other immunotherapies, such as checkpoint inhibitors or targeted therapies, could further boost therapeutic responses. Personalized approaches based on patient-specific neoantigens, made possible by next-generation sequencing, pave the way for precision oncology. In the future, therapeutic vaccines may be integrated into standard treatment protocols, especially as adjuvant therapies or to prevent recurrence[1,2,4,6].

In low-resource settings, multiple barriers hinder the deployment of therapeutic cancer vaccines. Access to clinical trials and advanced technologies remains limited. Essential infrastructures for molecular diagnostics, which are required to identify neoantigens and monitor immune responses, are often lacking. Prioritizing cancers with high prevalence, such as cervical or liver cancer, could guide research and development toward more locally adapted strategies. It is equally important to promote equitable access to therapeutic innovations by encouraging local production, investing in healthcare professional training, and strengthening international collaboration[3–6].

In conclusion, therapeutic cancer vaccines represent an innovative and promising approach in oncology. By leveraging advances in immunology and biotechnology, these vaccines aim to elicit specific, long-lasting, and better-tolerated immune responses. Although still in the exploratory phase, preliminary results are encouraging. The future of cancer treatment will likely incorporate immunoprevention and personalized immunotherapy, with the goal of transforming certain cancers into manageable or even curable diseases. The major challenge ahead lies in ensuring equitable access to these innovations within a global and inclusive healthcare framework.

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