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Research in Biotechnology and Environmental Science. 2023; 2(4): 55-64.
DOI: 10.58803/rbes.v2i4.21
http://rbes.rovedar.com/

Review Article

The Power of Nanovaccines in Immunotherapy of Melanoma, Lung, Breast, and Colon Cancers: A Comprehensive Review

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ARTICLE INFO

Article History:
Received: 14/10/2023
Revised: 14/11/2023
Accepted: 26/11/2023
Published: 25/12/2023

Keywords:
Breast cancer
Cancer immunotherapy
Colon cancer
Lung cancer
Melanoma
Nanovaccines

ABSTRACT

Scientists are exploring new approaches to overcome cancer, and nanovaccines have emerged as one of the most promising tools in the fight against cancer. This review aimed to provide a thorough overview of nanovaccines as potential cancer immunotherapy agents by describing their mechanism of action and potential therapeutic implications. The growing incidence of cancer underscores the urgent need for comprehensive strategies focusing on prevention, early detection, and innovative treatment modalities to control and mitigate the impact of this widespread disease effectively. It is important to note that nanovaccines are a cutting-edge platform with a wide range of applications in immunotherapy for colon, breast, lung, melanoma, and ovarian cancers. Nanoscale formulations of tumor-specific antigens and adjuvants can initiate an efficient and targeted immune response. Research on nanovaccines involving melanoma has shown that they can trigger potent anti-tumor immune responses, which permit prolonged survival and tumor regression. Furthermore, nanovaccines have been effective in treating breast cancer since they can modulate the tumor microenvironment and stimulate the presence of cytotoxic T cells within the tumor. The nanovaccines strategy has enhanced the immune system's recognition of tumor antigens, resulting in tumor cell destruction and effective immune recognition. There have also been studies that have utilized nanovaccines to modify the immune response of tumor cells to immune checkpoint inhibitors, thereby improving the synergistic outcomes of colon cancer treatment. Besides improving the immune response to malignancies, nanovaccines represent a transformative approach to cancer immunotherapy. The presence of compelling results across various cancer types suggests that nanovaccines are a powerful tool in cancer treatment despite further research required to optimize their design and validate their clinical applicability.

1. Introduction

The incidence of various malignant tumors has been steadily increasing, making cancer the leading cause of death in recent years[1,2]. In this regard, immunotherapy has played an important role in cancer treatment, standing as the fourth treatment pathway following surgery, chemotherapy, and radiotherapy as the fourth major

Cite this paper as: Angaji SGh, Salim MA, Azizi A, Amiri N, Rastakhiz S, Jahani N, Akhlaghi B, Ebrahimi Tirtashi P. The Power of Nanovaccines in Immunotherapy of Melanoma, Lung, Breast, and Colon Cancers: A Comprehensive Review. Research in Biotechnology and Environmental Science. 2023; 2(4): 55-64. DOI: 10.58803/rbes.v2i4.21

treatment pathway[3]. *In-vitro* experiments have shown that certain parasites, including the protozoans *Toxoplasma gondii*, *Trypanosoma cruzi*, and the helminths *Trichinella spiralis* and *Echinococcus granulosus* represent anti-cancer activities[4-7]. Nanovaccines are a promising strategy due to their increased lowest immunotoxicity, antigen stability, flexibility of the physical characteristics of nanomaterials, and sustained release. Nano vaccines surpass regular vaccines in efficiency owing to their controllable and flexible physicochemical properties8. Identifying and eliminating neoplasm cells is how the immune system fights tumors. Free cancer cells are eliminated by immunotherapy, thus preventing tumor recurrence and metastasis[9].

An antigen-based vaccine is administered to provoke an immune response against a particular pathogen[9]. Hundreds of millions of lives have been saved since the advent of vaccines in the last century. Since peptide subunit vaccines are safe and easy to produce, they are an excellent option for cancer immunotherapy[11]. However, their immune responses are suboptimal, primarily because they are not co-delivered to lymph nodes (LNs) where B- and T-cells coordinate immune responses[12]. Peptide-based vaccines are frequently combined with adjuvants and administered through delivery systems to enhance their immunogenicity[13]. Although depot-forming immunoadjuvants, like incomplete Freund's adjuvant (IFA), enhance Ag immunogenicity by releasing it sustainably from a depot, evidence suggests that persisting Ag depots may result in T-cell sequestration, exhaustion, and dysfunction. This, in turn, may prevent T cells from infiltrating tumors from vaccination sites. To date, no treatment is compelling for cancer[14].

Among the many therapies available, chemotherapy is widely used throughout the world[15]. Patients suffer from side effects from chemotherapy, which cause inconvenience for them[16]. Therapeutically potent drugs are destroying the rapidly multiplying cells. In addition to killing the malignant cells, chemotherapy induces several side effects[17]. Due to its oppressive side effects, chemotherapy is often avoided by patients. The non-targeted distribution of chemotherapeutic drugs in the body as 'free drugs' limits the drug concentration at impaired organ sites due to non-targeted distribution throughout the body. These obstacles might hamper degenerative diseases, which are closely related to their clinical failure. Chemotherapy could be improved with site-specific targeted drug delivery. Nanotechnology involves chemistry, physics, engineering, biology, and medicine[15,17]. It is a significant technique for treating degenerative diseases, detecting tumors early, acting specifically on them, reducing multidrug resistance, reducing toxicity, discovering cancer biomarkers, and developing novel treatments. Drug molecules have been successfully delivered to targeted sites/cells using nanocarriers[18]. Furthermore, nanotechnology and nanocarrier-based drug delivery systems offer improved healing efficacy and decrease undesirable side effects associated with conventional drugs, introducing new classes of therapeutics and persuading the development of biologically active molecular new entities previously considered undevelopable due to pharmaceutically suboptimal properties[19,20]. Nanotechnology has introduced peptide-based subunit called nanovaccines, where antigens and adjuvants are co-delivered. This innovative approach aims to optimize peptide-based subunit vaccines by leveraging various nanocarriers designed to efficiently deliver epitopes and enhance the effectiveness of nanovaccines.

In addition to offering the capability to modify their surface for functionalization and charge delivery, nanocarriers are also helpful in encapsulating loaded charges and being able to be accepted by antigen-presenting cells (APCs)[21]. Nanovaccines that deliver antigens/adjuvants promote maturation and APC activation, resulting in active T lymphocytes that attack cancer cells[22]. As a result of engineering approaches to the co-delivery of antigens/adjuvants to immune cells, robust immune responses can be stimulated, which in turn increases the speed and duration of immune responses, intensifies weak antigen immunogenicity, and modulates Ag-antibody responses. The first part of this study will focus on cancer vaccines and adjuvants in immunotherapy for cancer. The second part will discuss the strategies for designing and developing nanovaccines, emphasizing the interactions between epitopes and adjuvants.

2. Methods and materials

A thorough literature search, encompassing PubMed, Scopus, and Web of Science databases, was conducted between 2015 and 2023 to identify studies on nanovaccines in cancer immunotherapy. Inclusion criteria comprised research articles and reviews in English, focusing on nanovaccines development for breast cancer, colon cancer, lung cancer, melanoma, and relevant cancer types. Exclusion criteria included studies not directly related to nanovaccines or not in English. Data on nanovaccines formulations, mechanisms of action, and therapeutic outcomes were extracted, and the quality of the derived articles was checked. Due to the qualitative nature of this review, there was no need to perform statistical analysis. The review was structured to provide insights into mechanisms and implications of nanovaccines across various cancers, acknowledging potential limitations, such as variability in study designs and evolving nature of the field.

3. Cancer immunotherapy

As cancer therapy advances, immune checkpoint-based therapies, including immune checkpoint blockade, are ideal strategies for making fantastic progress[22]. Nevertheless, these immunotherapies are only effective for a small percentage of patients. The selection of patients is, therefore, an essential factor in preventing the harmful

effects of treatment and avoiding unnecessary costs. An early indication of response and clinical benefit will be required by identifying and validating reliable surrogate biomarkers. There is evidence that immunotherapy is particularly effective in highly mutagenized tumors[23]. Mutational load contributes to the clinical response to immunotherapy via neo-antigen-specific responses[24]. It has been reported by two independent groups that anti-CTLA-4 treatment correlated with mutational frequency in melanoma tumors[25].

Further, patients with colon and non-small cell lung cancer (NSCLC) treated with anti-PD1 inhibitors exhibited higher numbers of mutations, including mutations in DNA repair pathways[26]. The anti-PD1 treatment has practical clinical effects on some kidney cancer patients with low mutational frequencies, and this is not true for all tumor types[27]. There is a correlation between lymphocyte infiltrates and improved survival for many types of cancer[28]. The expression of PD-L1 on tumor cells can be considered a valuable biomarker to determine which patients would benefit from immune checkpoint blockade monotherapy in addition to the use of PD-L1 on tumor cells. It has been found that some patients with high levels of PD-L1 are not responsive to programmed cell death protein 1 (PD1) pathway blockade, in contrast to those with PD-L1-negative tumors[29]. Therefore, the lack of PD-L1 expression around the tumor microenvironment cannot reliably exclude patients from PD1 pathway blockade treatment. Therefore, PD-L1 is not an optimal biomarker for patient selection[30]. Murine models have indicated that the combination of immune checkpoint inhibitors can overcome the exhausted phenotype in several tumors by characterizing TILs, including overexpression of exhaustion markers such as PD1, LAG3, and TIM3 [31]. Different immunotherapeutic combinations may also respond differently based on the patient's immune system[32]. A system that considers the immune milieu in addition to PD-L1 status and lymphocyte profile will be essential to guide therapeutic combinations. Moreover, immunohistochemistry and genetic profiling of the tumor microenvironment could be combined to improve biomarker algorithms by classifying cancers according to their immunoevasion strategies[33].

4. Immunotherapy by vaccines

The development of vaccines and the creation of vaccines against various diseases have significantly impacted global health since the invention of vaccines[34]. Aside from its role in protecting the body from parasites, viruses, and bacteria, the immune system also protects against cancer through its relentless fight against infections[35]. The Food and Drug Administration (FDA) has approved five cancer vaccines up to this point; they protect against virus-induced cancers, specifically cervical cancer caused by human papillomavirus (HPV) and liver cancer caused by hepatitis B virus (HBV)[36]. Additionally, therapeutic vaccines targeting existing tumors are being studied along with prophylactic vaccines.

Therapeutic cancer vaccines aim to regulate tumor growth, , initiate tumor regression, and eradicate existing tumors by provoking acquired immune responses in patients against specific tumor antigens[37]. High-quality antigens must be delivered to dendritic cells (DCs) 38 as a significant component of effective therapeutic cancer vaccination[38]. These DCs must be optimally activated to generate persistent and robust responses from CD4+ helper T cells and cytotoxic T lymphocytes, infiltration and recruitment into tumor microenvironments, and maintenance and durability of their effects[39]. However, despite the difficulties in producing vaccines and their low clinical response rates, they remain attractive due to their specificity, safety, tolerability, and ability to provide long-lasting memory responses among the several strategies in cancer immunotherapy[40]. The vaccine platform employed in cancer vaccines could be one reason for low response rates. A cancer vaccine can be made from various platforms, including whole cells, nucleic acids (DNA and RNA), bacterial and viral vectors, and proteins/peptides[41]. Constructing DNA vaccines by cloning plasmids that encode tumor antigens to elicit and enhance CD8+ and CD4+ T-cell responses is possible. Apoptosis or exosomes release transgenes in transfected cells after DNA plasmids are administered to them[42]. To amplify adaptive immune responses, DCs endocytose released transgenes and present them with Major Histocompatibility Complex I (MHC) and MHC II to CD4+ and CD8+ T-cells, respectively. A phase III trial evaluates VGX-3100 against high-grade cervical intraepithelial neoplasia by combining it with electroporation against HPV-16/HPV-18 E6 and E7 coding DNA vaccines. The phase 2b trial results showed that 49.5 % of treated women regressed their lesions, while 30.6% of placebo patients wholly regressed[43].

There are differences between RNA-based vaccines and DNA-based vaccines as far as their susceptibility to degradation by RNases is concerned. However, modified nucleosides incorporated and applied can protect RNA-based vaccines[43]. DNA vaccines require transcription through the nuclear membrane barrier, whereas RNA vaccines do not[44]. One clinical trial examines the tolerability, effectiveness, and safety of a personalized mRNA vaccine for advanced esophageal and non-small cell lung cancer. In a recent study, A—using an *in-vitro* transcribed (IVT) mRNA vaccine encoding four antigens failed to demonstrate satisfactory anti-tumor activity despite remarkable innovations in the design and development of mRNA-based vaccines[45]. The recognition of receptors on immune cells makes vector-based vaccines an attractive delivery system for antigens and immunomodulatory molecules, resulting in the development of both acquired and innate immune systems[46]. Despite this, antiviral immune responses limit the efficacy of repeated vaccinations by limiting vaccination frequencies. To address this limitation, various strategies have been employed, such as heterologous

prime-boost administration and surface coating strategies[47]. RNA-based vaccines in cancer treatment are currently being evaluated through many clinical trials. Three major categories of tumor antigens can be used to develop anti-tumor vaccines, such as Tumor-Specific Antigens (TSA), which are specifically expressed in cancer cells, and Tumor-Associated Antigens (TAAs) that are expressed both on average and in cancer cells but are overexpressed on cancer cells; neoantigens that are derived from tumor cells and have unique epitopes of self-antigens. Numerous clinical trials have examined peptide-based vaccines, yet no substantiated evidence has emerged to support their remarkable advantages. In the realm of cancer vaccines, the utilization of short peptides, comprising fewer than 15 amino acids, has proven unsuccessful in eliciting robust immune responses.

Moreover, short peptides cannot fully activate CD4+ helper T-cells, which are necessary for optimal CTL activation. Several methods for overriding these limitations include combining immunostimulatory molecules with peptides, combining other adjuvants with peptides, and synthesizing long peptides (SLPs) of multiple lengths[48,49]. Due to the tedious and expensive process of producing neoantigen-based peptide vaccines, advances in databasing, software predictions, and sequencing have shed light on overcoming the difficulties[50,51].

5. Nanovaccines

There are several advantages to nanoparticle (NP)-based vaccines compared to subunit Ag-based vaccines. Antigens are either encapsulated within the NPs or decorated on the surface of the NPs[52]. NPs could elicit robust immune responses due to long-term bioavailability and sustained release of Ag in contrast to soluble Ag-based vaccines. Also, NPs allow antigens to be uptaken and processed by APCs, resulting in the maturation of APCs[53]. This further promotes Ag cross-presentation by MHC class I to CD8+ T-cells, which determines innate and adaptive immune responses through the production of cytokines[22].

Furthermore, NPs serve as delivery mechanisms for cytokines and activate innate immune receptors to produce them. In addition to their composition, nanoparticles' physical characteristics, such as charge, pore size, and charge density, may affect their immunogenicity[54]. Nanoparticles made of mesoporous silica with extensive pores have the potential to enhance DC activation and Ag presentation, leading to the stimulation of immune responses and the inhibition of tumor growth. The utilization of nanoparticles with spacious pores holds promise in clinical applications, as it facilitates the introduction of minimal quantities of antigens and immunostimulatory molecules into the body[55].

Additionally, the size of NPs has a significant influence on immune responses. A study has shown that NPs with smaller sizes (20–30 nm) are endocytosed by DCs, whereas macrophages phagocytose those with larger sizes (less than 0.5 mm) [56]. Additionally, the size of nanoparticles influences the efficacy of nanovaccines by determining the leakiness of tumor vasculatures and their pore sizes. The microparticle forms of alum-based adjuvants promote Th2-biased immune responses, while their nanoparticulated forms can stimulate Th1-biased immune responses to develop cancer vaccines[57]. Additionally, the surface charge of nanoparticles plays a essential function in the internalization and trafficking of antigens. The electrostatic interaction between cationic NPs and the oppositely-charged cellular membrane makes them more efficient at being taken up by the APCs. The positive charges also aid in cationic NP escape from the lysosome. The blood circulation time of slightly negatively charged nanoparticles is longer than that of cationic nanoparticles of the same size[58].

Another factor that stimulates immune solid responses is the morphology of nanovaccines. According to Gong et al., the tumor antigens are trapped in endosomes and have a low immunogenicity[59]. The vaccine is configured with proton-driven nanotransformers capable of altering the morphology of the endosome in an acidic environment. In response to the morphological change in nanovaccines from nanosphere to nanosheet, the endosomal membrane was disrupted, which allowed the antigenic peptide to be released into the cytoplasm. As a result, inflammation pathways were activated, and tumor growth was suppressed in HPV-induced cancer and mice models of melanoma[56].

Compared with rod-like and spherical particles, cylindrical hydrogel nanoparticles can present antigens to APCs for lasting periods, which results in robust immune responses. In a study, softer NPs showed increased circulation and targeting compared to harder ones. Also, the softer nanoparticles significantly reduced tumor cell uptake, endothelial cell uptake, and immune cell[60].

6. Mechanisms of action of nanovaccines

6.1 Antigen presentation

Nanovaccines enhance cancer immunotherapy by optimizing antigen presentation. Some nanovaccines carry antigens specific for tumors or antigenic peptides that mimic antigens present in tumors[61]. Antigen-presenting cells, such as dendritic cells, present the antigens to antigen-presenting cells. Nanoparticles facilitate antigen uptake and processing by APCs through various mechanisms, including receptor-mediated endocytosis. These APCs present antigens on their cell surfaces through their MHC molecules once they have internalized the antigens. By presenting antigens efficiently, T cells, specifically CD8+ cytotoxic T cells, are primed to recognize and attack cancer cells with the same antigen. A successful immune response against a tumor depends on this process[62].

6.2 Immune cell activation

Besides delivering antigens, nanovaccines are designed to contain immune-stimulating molecules and adjuvants[63]. These components potently activate the immune system. The adjuvant may consist of a toll-like receptor agonist, cytokines, or other immunomodulators. They activate APCs and subsequent immune responses in nanovaccines when co-delivered with antigens[64]. Antigen-presenting cells release many pro-inflammatory cytokines and costimulatory molecules during activation that stimulate the activation and proliferation of effector T cells, especially CD8+ cytotoxic T cells[65]. When these activated T cells are transported to the tumor site, they can kill tumor cells.

6. 3 Tumor microenvironment modulation

Tumor microenvironments are often immunosuppressive environments, hindering immune responses to cancer[66]. Nanovaccines may be essential in modulating the tumor microenvironment to encourage an immune response against the tumor. It is possible to manufacture nanovaccines that contain agents capable of targeting immune suppressive cells within the TME, such as myeloid-derived suppressor cells (MDSCs) and regulatory T cells (Tregs) [67]. Nanovaccines can improve anti-tumor responses by reducing the presence or activity of immunosuppressive cells. Additionally, some nanovaccines may have components that promote better immune surveillance and tumor cell recognition by infiltrating immune cells into tumors [68].

6.4 Role of adjuvants and immune-stimulating molecules

Nanovaccines comprise immune-stimulating molecules and adjuvants[69]. The purpose of adjuvants is to enhance vaccine immunogenicity. Activating pattern recognition receptors (PRRs) on APCs triggers signaling pathways that induce stimulation and pro-inflammatory responses [65]. For example, toll-like receptor agonists, such as lipopolysaccharides or CpG oligonucleotides, can activate TLRs on APCs, enhancing cytokine production and antigen presentation. The immune system can also be stimulated by encapsulating cytokines such as tumor necrosis factor-alpha (TNF-A) and interleukin-12 (IL-12)[70] (Figure 1).

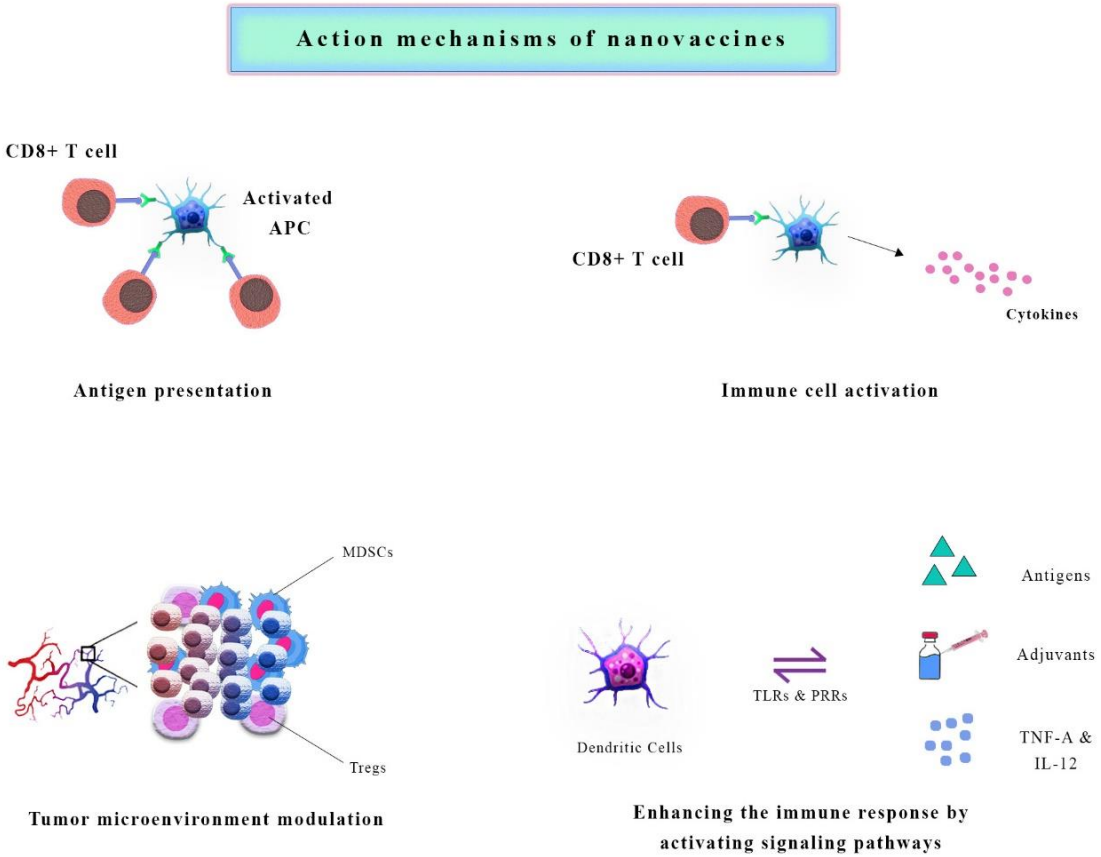

Figure 1. This figure shows the key elements of nanovaccines, highlighting the role of adjuvants and immune-stimulating molecules. The nanovaccines consist of antigens and adjuvants. The adjuvants activate pattern recognition receptors (PRRs) on antigen-presenting cells (APCs) such as dendritic cells (DCs). This interaction triggers signaling pathways leading to stimulation and pro-inflammatory responses. Toll-like receptor (TLR) agonists, like lipopolysaccharides and CpG oligonucleotides, activate TLRs on APCs, enhancing cytokine production and antigen presentation. Additionally, cytokines such as tumor necrosis factor-alpha (TNF-A) and interleukin-12 (IL-12) are encapsulated within the nanovaccines to stimulate the immune system. These components collectively enhance vaccine immunogenicity.

7. Clinical trials

Clinical trials using nanomaterials for cancer treatments mainly focus on camptothecin, paclitaxel, and monoclonal antibodies that block immune checkpoints (ICBs)[71]. In clinical trials, the results of nanomaterials used in cancer vaccines have been less promising than those of traditional cancer drugs. Nanomaterials are often complex in design and need modification, resulting in difficulty in mass production and quality control[72]. The clinical trial of a nanoparticle vaccine against Epstein-Barr virus (EBV) gp350 is noteworthy[73]. Animal studies have shown that the vaccine induces high neutralizing antibodies in nonhuman primates and mice[74]. Many cancers are associated with EBV, including non-Hodgkin's lymphoma, Hodgkin's lymphoma gastric cancer, and nasopharyngeal cancer[75]. Therefore, it was included in clinical trials related to cancer vaccines as a preventive vaccine. The effects of treating advanced solid tumors with Poly(lactic- co -glycolic) Acid (PLGA) nanoparticles containing antigens and adjuvants are also being evaluated in phase I clinical trials [76]. These vaccine components include antigens derived from the NY-ESO-1 cancer-testis antigen peptide and the alpha-galactosylceramide-derived iNKT cell activator IMM60. Phase II clinical trials (NCT00199901) have previously combined NY-ESO-1 with ISCOMATRIX® adjuvant for treating melanoma, a cellular target found in many cancers[77]. Although the survival period for most patients had not improved, significant antibody responses had been induced among them, which is encouraging for future research [78]. A novel cancer vaccine based on NY-ESO-1-derived peptides and IMM60 was developed using polymer PLGA nanoparticles.

Clinical trials are anticipated to demonstrate a better immune response when vaccines are nanosized, and new adjuvants are added. The mRNA-2752 and mRNA-2416 were encapsulated in lipid nanoparticles in these two clinical trials to be administered intratumorally alone or combined with Durvalumab to treat relapsed or refractory solid tumors and lymphomas[79,80]. A recent clinical study was conducted to determine whether corresponding mRNA vaccines would be safe and tolerable for cancer patients [81]. Vaccines for cancer are most likely to be used as adjuncts to surgery or chemotherapy in the clinic. Preparing cancer nanovaccines formulations is time-consuming and labor-intensive in most preclinical studies. Because cancer patients' disease progression is rapid, lead times for treatment should not be too long, and cancer vaccines prepared by overly complex methods are rarely clinically useful. The immunogenicity and toxicity of vaccines with mature preparation processes are disappointing in clinical settings. In order to optimize drug delivery, FDA-approved biocompatible materials should be used, and processes should be simplified. Additionally, laboratory animal models differ significantly from the human immune system, which makes preclinical findings challenging to translate into human studies[82]. Despite the current negative clinical results of cancer nanovaccines, as the preparation of complex nanoparticles is simplified and matured, more and more effective nanovaccines will enter clinical trials and prove effective.

8. Future perspectives

Many successful cases of immunotherapy in cancer treatment have occurred recently, including immune checkpoint blockade and chimeric antigen receptor cells. Cancer vaccines induce an anti-tumor immune response effectively and safely as part of immunotherapy. As an adjuvant therapy, cancer vaccines enhance the efficacy of other immunotherapies. A more significant potential for cancer immunotherapy can be realized by developing nanotechnology[83]. Various bio-based and synthetic nanocarriers have been discussed as potential cancer vaccine carriers. Through interactions between TAAs and adjuvants, they are encapsulated in nanocarriers and subsequently targeted to APCs, significantly increasing their immunogenicity[84]. Vaccine components are controlled in their release by selecting the appropriate carrier or modifying it chemically. Preclinical and clinical studies are already attracting much attention in preclinical and clinical settings. Cancer nanovaccines have shown promising results in recent years as a possible therapeutic approach, but translational research still faces many challenges[85]. Several challenges need to be tackled. For instance, in preclinical investigations, the majority of vaccines demonstrated positive outcomes but encountered setbacks in clinical trials. This discrepancy could be attributed to variations in the immune systems between laboratory animal models and humans, although the use of humanized mice can help mitigate some of these differences.

Developing new experimental animal tumor models that mimic human disease mechanisms is critical for a successful clinical translation of cancer vaccines[86]. The selection of tumor animal models must also be based on the specific scientific question since there is a large variety of them. As cancer treatments become increasingly personalized, it is imperative to establish xenograft models derived from patients. For cancer nanovaccines to exert their efficacy, nanoparticles should be resistant to non-specific protein binding, non-toxic, and rapidly cleared by the body. Mass production and inter-batch quality controls are also essential for vaccines to reach clinical practice and be widely commercialized. Recent years have increased interest in neoantigen-based cancer vaccines due to tumor heterogeneity and individual differences[87]. A critical step in developing personalized vaccines is optimizing the identification of tumor-specific antigens. Despite this, it may still be challenging to sequence antigens efficiently and accurately with the available technology. To achieve more precise sequencing and identification of novel antigens, it is imperative to integrate biological sciences with artificial intelligence and computer simulation

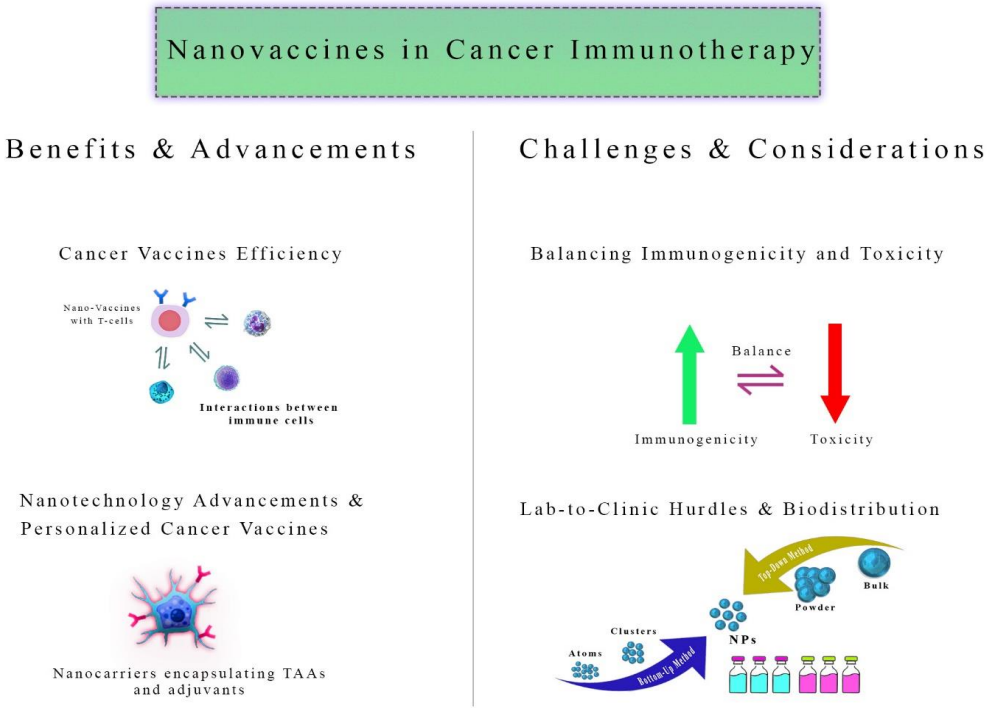

Figure 2. The benefits and advancements: Depicting the effectiveness of cancer vaccines, nanotechnology contributions, and the concept of personalized treatment. Challenges and considerations: Emphasizing the need to balance immunogenicity with potential toxicity and the hurdles in translating laboratory research into clinical applications.

techniques. This fusion of disciplines enhances the leveraging of cross-disciplinary advantages for optimal results[88]. Some nanomaterials are intrinsically immunogenic, allowing them to act as carriers and adjuvants simultaneously. Thus, it is also essential to balance immunogenicity with toxicity when choosing materials. Nanoparticles can also cause problems with immune response and cytotoxicity. The use of advanced emerging technologies in cancer treatments is promising. It is possible to explore a wide range of possibilities. These emerging technologies may produce unexpected results when combined with chemotherapy or immunotherapy[89] (Figure 2)

9. Conclusions

Preclinical studies have shown that cancer vaccines are integral to immunotherapy and can be administered as single drugs or combined with other agents. Nanomaterial-based cancer vaccines are at the beginning of their development, and they still face obstacles in clinical settings. Nanovaccines have the potential to emerge as the next generation of cancer immunotherapy, evolving alongside advancements in diverse fields such as immunology, materials science, and biology. . In the future, advancing interdisciplinary collaboration among immunologists, materials scientists, and biologists is crucial to overcoming challenges and accelerating the clinical translation of nanomaterial-based cancer vaccines. Additionally, exploring synergistic combinations with other immunotherapeutic agents may enhance the efficacy of these vaccines in treating a broad spectrum of cancers.

Declarations

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Parsa Ebrahimi Tirtashi led the conceptualization, while Seyedeh Ghazaleh Angaji, Mohammad Amin Salim, Alireza Azizi, and Negin Amiri contributed to the methodology. Saeede Rastakhiz, Negar Jahani, and Behnaz Akhlaghi conducted the formal analysis and investigation. The initial draft of the manuscript was prepared by Seyedeh Ghazaleh Angaji, Mohammad Amin Salim, Alireza Azizi, and Negin Amiri, with subsequent review and editing carried out by Saeede Rastakhiz, Negar Jahani, and Behnaz Akhlaghi. Parsa Ebrahimi Tirtashi provided supervision throughout the research process. All authors checked and approved the final version of the manuscript for publication in the present journal.

Funding

No funding was received for conducting this study.

Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical considerations

The authors checked for plagiarism and consented to publish the article. The authors have also reviewed the article for data fabrication, double publication, and redundancy.

Acknowledgments

Not applicable.

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