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A REVIEW OF mRNA VACCINES IN PROSTATE AND LUNG CANCER THERAPY: MECHANISMS, CLINICAL APPLICATIONS AND DEVELOPMENT DIRECTIONS

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ABSTRACT

mRNA vaccines constitute a new class of anticancer therapy, enabling precise stimulation of the immune system through the expression of tumour antigens. The success of COVID-19 vaccines has accelerated their development and has opened up new therapeutic possibilities in oncology. The aim of the review is to discuss the current state of knowledge on the mechanisms of action, clinical applications, and directions for the development of mRNA vaccines in cancer therapy. The study reviews scientific literature on the therapeutic use of mRNA vaccines in the treatment of prostate and lung cancer. The data include scientific publications from 2003 to 2025, published in the PubMed and Scopus databases. mRNA vaccines have shown promising efficacy in the treatment of advanced prostate cancer (CV9103, CV9104), non-small cell lung cancer (CV9201, CV9202, mRNA-5671/V941). The use of lipid nanocarriers (LNPs) significantly improves vaccine stability and immunogenicity. Combination therapies with immune checkpoint inhibitors (ICIs) demonstrate synergistic effects. mRNA vaccines present a promising strategy in cancer immunotherapy but require further research into formulation stability, the accuracy of antigen selection, and the predictability of immune responses. Furthermore, advancements in LNP technology and personalised medicine supported by artificial intelligence could markedly enhance the clinical efficacy of mRNA therapies.

KEYWORDS

mRNA-Based Cancer Vaccines, Clinical Trials, Prostate Cancer, Lung Cancer, Neoantigen, Lipid Nanoparticles

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1. Introduction

mRNA vaccines, previously known mainly for their use in the fight against COVID-19, have gained enormous interest in the field of oncology in recent years. Technology based on synthetic messenger RNA (mRNA) enables encoding of tumor antigens in human host cells, which leads to a targeted immune response directed against tumor cells (Pardi et al., 2018). Thanks to the possibility of designing a product of high purity and due to the lack of risk of interference with the host genome, vaccines based on mRNA technology provide a great alternative to classical forms of immunotherapy (Li et al., 2024). There are currently approximately over 120 ongoing RNA cancer vaccine trials in various malignancies, including lung, breast, prostate, melanoma, pancreatic, and brain cancers, representing a significant increase compared to previous years (Yaremenko et al., 2025). mRNA vaccines allow for the presentation of common tumor antigens (TAA) as well as individual neoantigens, which is a new path of development for personalized therapy (Sahin & Türeci, 2018). Tumour-Associated Antigens (TAA) therapy has shown effectiveness; however, this therapy is associated with a high risk of autoimmunity because TAA are also present in healthy cells of the body (Fan et al., 2023).

Tumor-Specific Antigens (TSA) are tumor-specific mutations, making them more attractive targets for therapy (Buonaguro & Tagliamonte, 2023). Currently, intensive ongoing clinical trials on the use of vaccines in the treatment of cancers, including prostate, lung and breast cancer, show high safety in the mechanism of action and the ability to induce a T lymphocyte response, especially in combination therapy with checkpoint inhibitors (Ribas & Wolchok, 2018; Sahin et al., 2017). Despite its numerous advantages, this technology faces challenges such as low particle stability, the need for carrier systems, including lipid nanoparticles, and the need to optimize antigen selection (Hou et al., 2021). Bioinformatics and artificial intelligence, which support the vaccine design process today, enable better therapeutic matching to a specific type of cancer (Klingemann, 2022).. The aim of this article is to review the current data on mRNA vaccines used in cancer therapy, taking into account their mechanisms of action, the results of selected clinical trials, and the prospects for further development of this promising technology.

2. Materials and methods

The paper presents a narrative review supplemented with elements of systematic literature analysis. The literature search was conducted in PubMed, Scopus, and Web of Science databases using the keywords: “mRNA vaccine”, “cancer immunotherapy”, “clinical trial”, “LNP”, “prostate cancer”, “lung cancer”. Studies published between 2000 and 2025 were considered, including phase I–II clinical trials, systematic reviews, and original research articles presenting data on mRNA vaccines in cancer therapy. Furthermore, documents from clinicaltrials.gov and EMA registries were also included. This review discusses the range of available mRNA vaccines in the treatment of prostate and lung cancer. The studies were analysed and synthesised to provide a comprehensive overview of the field.

3.1 Antigens in Prostate and Lung Cancer

Antigens can be divided into two categories: self-antigens and non-self-antigens. Antigens are molecules naturally found in the body that the immune system recognizes as "self." They play a key role in maintaining immune tolerance and preventing autoimmune reactions. Non-self antigens are molecules originating from outside the body that the immune system recognizes as "non-self" and trigger an immune response. Unlike prophylactic vaccines, self-antigens are typically more suitable for the development of mRNA-based cancer vaccines. Tumor-associated antigens are often proteins that have mutated or are overexpressed within the tumor microenvironment. Self-antigens are unique to a given patient's tumor, so their use in vaccines increases selectivity while simultaneously reducing the risk of off-target adverse reactions.

Tumor antigens are degraded by the proteasome, leading to the formation of epitopes presented on major histocompatibility complex (MHC) molecules. These epitopes are targeted to MHC class I—present on most cells—or to MHC class II, which are found exclusively on antigen-presenting cells (APCs), such as macrophages, B cells, and dendritic cells. APCs transmit information about the antigens to helper T cells, while antigens originating from within the cells are presented to cytotoxic T cells. These epitopes are then recognized by the T cell receptor (TCR), leading to the activation of CD4+ or CD8+ T cells and the initiation of an immune response aimed at eliminating cancer cells (Qin et al., 2022). Currently, the identification of cancer antigens relies on bioinformatic technologies, including genome sequencing, proteomic studies, antibody screening, and detailed assessment of tumor material (Asplund et al., 2012; Lu et al., 2014). An optimal cancer antigen should demonstrate high specificity, the ability to induce a strong immune response, and stable expression (Srinivasan & Wolchok, 2004).

3.2 Key Factors Influencing Immunotherapy and Vaccine Selection in Prostate Cancer

Prostate cancer (PC) is one of the most common cancers in men worldwide and a leading cause of cancer-related deaths. In 2022, 1.4 million cases and 390 thousand deaths were reported worldwide (Bray et al., 2024). Patients with localized prostate cancer are typically considered for radical prostatectomy or radiotherapy, and low-risk patients may also be candidates for active surveillance, which generally has a good prognosis (Cornford et al., 2024). Twenty per cent of patients are diagnosed with locally advanced or metastatic disease and require treatment with androgen deprivation therapy (ADT), but all these patients eventually develop castration-resistant prostate cancer that continues to grow despite testosterone suppression (CRPC) within 2–3 years (Lowrance et al., 2023; Tilki et al., 2024). In recent years, significant progress has been made in the treatment of prostate cancer, mainly due to the development of new drugs that additionally inhibit androgen receptor signalling (Bernal et al., 2024; Raychaudhuri et al., 2025). Synergistic effects have been observed when combining therapeutic cancer vaccines with immunotherapy using immune checkpoint inhibitors, leading to increased vaccine efficacy (McNeel et al., 2018; McNeel et al., 2022). The tumour antigens used in mRNA vaccines against prostate cancer include: PSA, PSMA, PAP, six-transmembrane prostate epithelial antigen 1 (STEAP1), and mucin 1 (MUC-1), which are present in both prostate cancer and healthy prostate tissue (Rausch et al., 2014). Since the prostate is not a vital organ that can be entirely removed, the immune response elicited by the vaccine can target any prostate tissue (Pardi et al., 2024).

It is worth noting that the use of modified nucleotides (e.g., pseudouridine, 5-methylcytosine, N6-methyladenosine and 2-thiouridine) allows avoiding TLR receptor activation and the innate immune response, which led to the initiation of research on mRNA vaccines since 2005 (Karikó et al., 2005).

3.3 mRNA vaccines for prostate cancer in clinical trials

Compared to DNA vaccines, mRNA only needs to enter the cytoplasm and then be translated into target proteins. Therefore, the rate of protein expression by mRNA is usually faster than in DNA vaccines. Unlike DNA vaccines, mRNA acts exclusively in the cytoplasm, does not require transport to the nucleus, and poses no risk of integration into the genome, making this technology safer (Miao et al., 2021). The Phase I/IIB clinical trial of the mRNA vaccine in patients with mCRPC is called CV9104 (Kübler et al., 2015). In the study involving 197 patients, 134 patients received intradermal administration of the CV9104 mRNA vaccine, while 63 patients received a placebo (Kübler et al., 2015). Their analysis showed no significant difference in median overall survival (OS) between the groups: 35.5 months in patients treated with CV9104 and 33.7 months in the placebo group. Additionally, the rate of grade ≥3 adverse events was similar in both groups: 51.1% in patients receiving the CV9104 vaccine and 59.7% in the placebo group. Similarly, in another study, the rate of serious adverse events was comparable, reaching 44.5% in the treatment group and 43.5% in the control group (Miao et al., 2021). The lack of vaccine efficacy may be due to the use of unmodified mRNA, which has limited immunogenicity and simultaneously stimulates the innate immune response by activating Toll-like receptors (TLRs), which can lead to undesirable side effects (Kübler et al., 2015). Another important aspect is the method of vaccine administration, as intradermal administration may not ensure the appropriate number of dendritic cells (DCs) necessary for effective antigen presentation. Another Phase I/IIa study used intravenous administration of an unmodified RNA vaccine encoding, among others, kallikrein-2, kallikrein-3, prostatic acid phosphatase, HOXB13, and NK3 homeobox 1, in the treatment of metastatic castration-resistant prostate cancer (mCRPC) (Linch et al., 2021). Although the study is still ongoing, results to date indicate a good safety profile in the five patients included in the second part of the study, as well as a significant immune response and a reduction in PSA levels (Linch et al., 2021). The vaccine contains sequences encoding multiple antigens, and its key feature is systemic administration via the intravenous route, which enables the activation of an adaptive immune response and stimulation of the patient's immune system. Furthermore, intravenous administration promotes selective delivery of the vaccine to dendritic cells located in the spleen and systemic lymph nodes, leading to a stronger immune response compared to other routes of administration (Saxena et al., 2021). BNT162b2 and mRNA-1273 preparations, containing modified nucleotides in the form of N1-methylpseudouridine, achieved very high clinical efficacy of 95% and 94.1%, respectively (Baden et al., 2021; Polack et al., 2020). Unlike unmodified mRNA, N1-methylpseudouridine has a limited ability to stimulate the innate immune response, or to a much lesser extent, and is also more efficient in translation (Mulroney et al., 2024). Recent research has shown that mRNA containing N1-methylpseudouridine can induce a +1 frameshift in vitro. Furthermore, in both mice and humans, after administration of the BNT162b2 vaccine, a cellular response directed against translation products resulting from this shift was observed (Mulroney et al., 2024). The +1 frameshift by ribosomes may be caused by their arrest during translation, particularly in sequence regions that promote ribosomal slippage. Although other nucleotide modifications, such as m5C, reduce the risk of this phenomenon, they may also reduce translation efficiency, limiting their clinical potential. However, N1-methylpseudouridine, although it promotes ribosomal shifts of +1, has not been associated with adverse effects in clinical trials so far (Mulroney et al., 2024).

mRNA vaccines have shown great potential, mainly in the treatment of advanced prostate cancer. The CV9103 and CV9104 vaccines developed by CureVac encoding prostate cancer-associated antigens such as PSA, PSMA, PSCA and STEAP1. In the phase I study of CV9103, good tolerability and T cell activation were demonstrated in most patients (Alberts et al., 2020). Table 1 summarises the studies on mRNA-based vaccines conducted between 2009 and 2024, along with their results. The CV9104 vaccine was tested in a randomized phase II study, but no statistically significant difference in overall survival was achieved, indicating the need for combination therapy (Heidenreich et al., 2017). In addition, combining mRNA vaccines, such as BNT112, with checkpoint inhibitors (e.g., anti-PD-1) is the subject of research, and the results suggest a synergistic effect (Kranz et al., 2016).

Summary of clinical trials evaluating mRNA-based vaccines in prostate cancer patients. Table 1 summarises clinical trials evaluating mRNA-based vaccines in prostate cancer patients, including vaccine types, targeted antigens (PSA, PSMA, PSCA, STEAP, PAP, MUC-1), disease stages (CRPC, mCRPC, PCa), clinical outcomes and trial identifiers (NCT numbers).

Table 1. Examples of mRNA vaccines for prostate cancer treatment in clinical trials

Vaccine name	NCT trial no.	Inclusion criteria	Target antigens	Phase	Clinical trial design	Key outcomes	Number of participants	Duration and status
CV9103	NCT00906243	CRPC	PSA, PSMA, PSCA, STEAP	Phase I/II	CV9103 single arm	Good safety and tolerability	6	May 2009 - December 2010 (terminated)
CV9103	NCT00831467	CRPC	PSA, PSMA, PSCA, STEAP	research Phase I/II	CV9104 single arm	Good tolerated, with 26 of 33 evaluable patients developing immune responses to multiple antigens. One patient confirmed a PSA response. The median overall survival time for 36 mCRPC patients was 31.4 months.	48	January 2009 - September 2013 (completed)
CV9104	NCT01817738	mCRPC	PSA, PSMA, PAP, MUC-1	Phase I/II	CV9104 vs placebo	The median overall survival time for the CV9104 group was 35.5 months (95% CI, 28.0-NA) compared to 33.7 months (95 %CI,28.7 - NA) for placebo, with no statistical difference (HR =1.1;95% CI, 0.70 - 1.76; p =0.33)	197	August 2012 - January 2017 (terminated)

CV9104	NCT02140138	Intermediate-to high-risk non-metastatic PCa	PSA, PSMA, PAP, MUC-1	Phase II	CV9104 vs placebo	Undisclosed data	35	June 2014 - April 2016 (terminated)
BNT112	NCT04382898	CPRC and high-risk localized PCa	5 antigens	Phase I/II	BNT112 vs BNT112 + cemiplimab	Test interrupted	75	December 2019 - January 2024 (terminated)

Legend: PSA – Prostate-Specific Antigen; PSMA – Prostate-Specific Membrane Antigen; PSCA – Prostate Stem Cell Antigen; STEAP – Six-Transmembrane Epithelial Antigen of the Prostate; MUC-1 – Mucin-1 (mukina-1,Tumor-associated glycoprotein); PAP – Prostatic Acid Phosphatase; RPC – Castration-Resistant Prostate Cancer; mCRPC – Metastatic Castration-Resistant Prostate Cancer; PCa – Prostate Cancer; NCT trial no. – unique identifier of a clinical trial registered in the ClinicalTrials.gov database; BNT112 – mRNA vaccine developed by BioNTech; CV9103 / CV9104 – mRNA vaccines for prostate cancer developed by CureVac; NA -Not Available; CI – Confidence Interval; HR – Hazard Ratio; p – p-value.

4. Factors influencing the choice of mRNA vaccine for lung cancer due to pathogenesis

Lung cancer is the most prevalent and lethal form of cancer. According to data from 2022, there will be 2.5 million cases and 1.8 million deaths due to lung cancer (Bray et al., 2024). The main risk factors responsible for the development of the disease include: smoking (80% of cases), environmental and occupational factors, genetic factors and a history of other lung diseases. However, the exact causes have not yet been identified; we observe an increase in LC cases among non-smokers, which accounts for approximately 25% of all cases (Bhopal et al., 2019; Zhang et al., 2021). Histopathological classification of tumors, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), and molecular characterization, especially in NSCLC, is crucial in deciding on further treatment based on targeted genetic therapies (Jamal-Hanjani et al., 2015; Marino et al., 2019). Cancer cells evade the immune system using a variety of strategies, including downregulating surface antigens to reduce visibility to immune cells, secreting immunosuppressive factors such as TGF-β, IL-10, CXCL, and expressing immune checkpoint molecules such as PD-L1 and CTLA-4, which bind to T cells and inhibit their activity (Mundhara & Sadhukhan, 2024). In the case of lung cancer, immunotherapy is already an approved treatment approach, while new technical advances have helped to better understand the immunogenicity of lung cancer (Lahiri et al., 2023). Therapeutic vaccines, including mRNA vaccines, currently represent a promising treatment option.

4.1 mRNA Vaccines for Lung Cancer

In recent years, numerous studies have been conducted to test the efficacy and safety of mRNA vaccines in monotherapy and in combination (Kiousi et al., 2023). Initially, DC-based vaccines containing mRNA encoding CEA were evaluated in a Phase I clinical trial involving patients with metastatic cancers that expressed CEA, including lung cancer. The results showed that this vaccine was safe, and no toxicities were observed (Morse et al., 2003). Of all the cancer vaccines studied in lung cancer to date, mRNA vaccines have shown the most promising results, overcoming many of the previous limitations of this technology (Sanaei et al., 2024). Despite previous attempts to increase the efficacy of mRNA vaccines against lung cancer, new approaches are currently being developed to further improve their performance. These include the use of lipid nanoparticles (LNPs), the use of multiple lung cancer-associated antigens, and the combination of mRNA vaccines with other immune therapies. An example of such an approach is the Phase I trial (NCT03948763)

evaluating the LNP-formulated mRNA-5671/V941 vaccine, administered alone or in combination with pembrolizumab, in patients with KRAS-mutated non-small cell lung cancer (NSCLC) and other solid tumors. The trial is completed, but the results have not yet been published. Another mRNA vaccine, CV9201, developed for patients with stage IIIB/IV lung cancer, contains mRNA encoding five NSCLC-associated antigens (NY-ESO-1, MAGE-C1, MAGE-C2, survivin, and 5T4). In a Phase I/II study, the vaccine was well tolerated, and the recommended dose for Phase IIa was set at 1600 μg. Although immune activation was rare, some signs of an immune response were observed (Sebastian et al., 2019). The next step was the CV9202 vaccine, which contains six NSCLC antigens (MUC1, survivin, NY-ESO-1, 5T4, MAGE-C2, MAGE-C1) and was studied in combination with local radiotherapy in patients with stage IV lung cancer (NCT01915524). The treatment was well tolerated, and patients showed antigen-specific responses (Papachristofilou et al., 2019). Encouraging results led to further investigation of CV9202 in combination with immune checkpoint inhibitors (ICIs). A Phase I/II study (NCT03164772) evaluated the safety and efficacy of CV9202 when used with the anti-PD-L1 antibody durvalumab or in combination with durvalumab and the anti-CTLA-4 tremelimumab. Results showed that patients treated with the triple regimen (CV9202 + durvalumab + tremelimumab) experienced more disease progression (59.3%) compared to those treated with CV9202 and durvalumab alone (36.8%). In contrast, the latter group had a higher rate of partial responses (26.3% vs. 11.1%) (Kübler et al., 2015; Baden et al., 2021). Currently, the BNT116 vaccine is also being studied in combination with the PD-1 inhibitor cemiplimab in patients with advanced NSCLC (NCT05142189, NCT05557591) (Mulroney et al., 2024; Kim et al., 2021). A parallel study (NCT03908671) is evaluating a personalized vaccine containing mRNA encoding individual neoantigens, aimed at improving the safety and tolerability of the treatment (Ramos et al., 2024).

5. Discussion

5.1 Development of mRNA-lipid nanoparticles (mRNA-LNPs)

mRNA vaccines have a simple structure and are more immunogenic than DNA vaccines. More importantly, they cannot interfere with genome sequences and are free from insertional mutagenesis. mRNA must enter the cell, where it undergoes a single-step translation in the cytoplasm to produce the desired antigen (Miao et al., 2021; Pardi et al., 201; Vishweshwaraiah & Dokholyan, 2022). The ability of mRNA to encode multiple antigens increases the overall efficacy of the vaccine and increases the possibility of creating personalized cancer therapies. Temporary mRNA expression limits antigenic stimulation, reducing chronic inflammation and increased autoimmune response (Weissman & Karikó, 2015). However, mRNA vaccines have disadvantages, such as RNA instability and rapid degradation by extracellular RNases, insufficient in vivo delivery, and high intrinsic innate immunogenicity (Son et al., 2020). Over the years, research has been conducted to improve the stability of mRNA and its delivery to cells in vivo. Dendritic cells were the main carriers in older studies. Recently, other systems have been developed, including carriers in the form of lipid nanoparticles (LNPs), which are currently most often used for vaccine production, as well as polymers and peptides (Lorentzen et al., 2022; Miao et al., 2021; Perez & De Palma, 2019). The most important role of LNP-based mRNA vaccines is their function as adjuvants, which act as potent immunostimulators, improving the quality and adaptive response of the immune system, which has been proven in many clinical studies. LNPs significantly increase the activity of T-follicular helper cells and humoral immunity (Alameh et al., 2021; Alameh, Weissman, & Pardi, 2022). Hollow LNPs can elicit a therapeutic response by enhancing antibody production, releasing chemokines, and promoting neutrophil and monocyte infiltration at the injection site (Anindita et al., 2024). Amino groups contained in lipid compounds of the particles interacted with immune cells, activating both innate and adaptive immune responses and increasing proinflammatory cytokines. It should be noted that this interaction can also lead to the release of compounds that reduce the effectiveness of mRNA-LNPs (Chaudhary et al., 2024). It is important to highlight that LNPs not only serve as delivery agents for mRNA vaccines but also act as immunostimulatory agents. Their design must ensure favorable immunological profiles for their efficacy (Ramos et al., 2023). Additionally, LNPs serve as immunostimulating agents alongside their role as vaccine delivery vehicles. Their structure must promote beneficial immunological responses for optimal efficacy (Ramadan et al., 2024). The mRNA-LNP vaccine can provoke an immune response, including MHC-I presentation, because it can express intracellular antigens that are processed and presented on the surface of antigen-presenting cells (APC). This MHC-I–peptide complex is recognised by CD8+ T cells, which can subsequently target and eliminate tumor cells (Ramadan et al., 2024)

5.2 Comparison of mRNA vaccines with peptide vaccines

Peptide vaccines targeting TSA are safe, specific, and easy to produce. However, to be effective, these vaccines require high doses, potent adjuvants for efficient delivery, and prolonged presence in the body (Buonaguro & Tagliamonte, 2023; Liu et al., 2024). The mRNA-lipid nanoparticle (mRNA-LNP) platform addresses this problem by offering easy delivery, intrinsic adjuvant properties, extended duration of action, and increased TSA expression (Thundimadathil, 2012; Wang et al., 2023). A large number of studies have demonstrated the efficacy of TSA in both peptide and mRNA forms in inhibiting tumor growth (Biswas et al., 2023; Li et al., 2023). Although peptide vaccinations using neoantigens have the potential to induce a strong antitumor response, their clinical efficacy remains limited (Rossino et al., 2023).

6. Development Directions

The use of artificial intelligence and CRISPR technology is a breakthrough in the development of RNA cancer vaccines. Combining these techniques allows for precise selection of neoantigens and improved immune response. AI-based platforms now include multi-omics data analysis to identify optimal tumor-specific targets. Furthermore, these platforms predict immune escape mechanisms and immunogenicity (Alburquerque-González et al., 2022; Zhang et al., 2017). There are currently around 100 clinical trials underway worldwide using CRISPR, combining modified CAR-T cells and gene editing methods with RNA vaccine strategies (Henderson, 2024; Barrangou, 2024). Combining CRISPR gene editing with RNA vaccine platforms offers the potential for immune system programming. Genetic modifications can optimize T cell responses to tumor antigens delivered in vaccines. Machine learning algorithms have reached remarkable levels of sophistication in neoantigen prioritization, encompassing HLA binding prediction, T cell receptor recognition modeling, and tumor clonality analysis to select optimal vaccine targets. These systems can process whole-exome sequencing data in hours, generating ranked lists of potential neoantigens that contribute to streamlining the vaccine design process (Alburquerque-González et al., 2022; Zhang et al., 2017). The use of CRISPR editing tools in RNA vaccine design allows for dynamic refinement of mRNA sequences, including the selection of optimal codons, modification of secondary structure, and integration of immunostimulatory sequences. This strategy accelerates the vaccine design and testing cycle, increasing their potential immunogenicity and shortening the time required to achieve an optimized formulation (Young et al., 2022). Predictive modeling platforms increasingly leverage individualized immune profiling data to anticipate patient-specific responses to vaccination and refine dosing strategies. By evaluating key biomarkers—such as tumor mutational burden, immune infiltration signatures, and cytokine expression patterns—these AI-driven systems enable precise customization of both vaccine design and administration protocols tailored to each patient's immunological landscape (Blass & Ott, 2021).

Integrated therapeutic platforms combining different types of RNA represent a promising direction for cancer vaccine development. This comprehensive approach aims to more effectively address tumor heterogeneity, immune evasion mechanisms, and treatment resistance by simultaneously targeting multiple key biological pathways (Bloom et al., 2021; McKay et al., 2020).

6.1 Approaches to enhance the effectiveness of mRNA vaccines

Currently, mRNA for vaccines is produced by in vitro transcription (IVT) using T7 polymerase [77]. Key elements influencing mRNA stability and immunogenicity include the 5' Cap structure, UTR regions, coding sequence (CDS), and poly(A) sequence.

6.1.1 5' Cap Optimization

Natural mRNA has a Cap 0 (m7GpppN) cap, however, Cap 1 (m7GpppN1m) and Cap 2 (m7GpppN1mN2m) better protect the mRNA from degradation and unwanted activation of innate immune receptors (Drazkowska et al., 2022). Cap 1 is currently the standard in mRNA vaccines because it mimics natural cellular mRNA and reduces PRR activation (Kim et al., 2021). In mouse studies, mRNA with Cap 1 generated a stronger response against influenza virus compared to Cap 0 (Wang et al., 2023). CleanCap technology enables direct synthesis of Cap 1 with approximately 95% efficiency (Corbett et al., 2020). The CleanCap M6 variant additionally increases protein expression by up to 30% thanks to the presence of m6A, which protects the mRNA from decapping (Bollu et al., 2022).

6.1.2 Optimization of the 5' and 3' UTRs

UTR regions regulate the stability and efficiency of mRNA translation. The 5' UTR is responsible for translation initiation (Qin et al., 2022), while the 3' UTR influences the stability and half-life of the mRNA (To & Cho, 2021). α- and β-globin sequences are often used as UTRs, which enhance protein stability and expression (Kesch et al., 2021). The addition of Kozak sequences further improves translation initiation, as utilized in the BNT162b2 and CvnCoV vaccines (Fang et al., 2022; Zhao et al., 2023).

6.1.3 Poly(A) Tail Optimization

The poly(A) tail is responsible for mRNA stability and translation efficiency (Blanchard et al., 2019). Two polyadenylation methods are most commonly used: enzymatic – less controlled (To & Cho, 2021) designing a DNA template with a specific poly(A) length, which ensures reproducibility (Polack et al., 2020; Zhao et al., 2023).

6.1.4 mRNA Purification

IVT generates contaminants, including dsRNA, which activates TLR3 and can trigger undesirable reactions (Baiersdörfer et al., 2019).HPLC effectively removes dsRNA, improving translation by up to 10–1000-fold, but is expensive and difficult to scale (Miao et al., 2021). Alternative methods include: cellulose purification – which removes over 90% of dsRNA (Baiersdörfer et al., 2019) and RNase III – which selectively degrades dsRNA and improves the efficiency of both modified and unmodified mRNA (Baiersdörfer et al., 2019) Currently, mRNA for vaccines is produced by in vitro transcription (IVT) using T7 polymerase. (Foster et al., 2019). The key elements affecting the stability and immunogenicity of mRNA are: the 5' cap structure, untranslated regions (UTRs), coding sequence (CDS), and the poly(A) tail (Jarvis et al., 2000).

7. Conclusions

Cancer is one of the leading causes of death worldwide. The immune system is playing an increasingly important role in treatment. Contemporary challenges include resistance to treatment and disease progression. Numerous clinical trials are currently investigating mRNA-based vaccines, particularly in the treatment of NSCLC, with promising initial results. The possibility of treating the therapy and its synergistic effect with radiotherapy or other methods is giving encouraging results. Nevertheless, in order to properly use the potential of mRNA vaccines, more detailed studies are required, and it is important to remember the problems we face, such as individual variability, adverse effects, or long-term efficacy of vaccines based on mRNA technology. Further research is required on ways to enhance the cytotoxic T lymphocyte response induced by mRNA vaccines.

In the coming years, it will be crucial to conduct randomized trials, larger patient populations, and precise analysis of biomarkers to enable the introduction of mRNA vaccines into standard medical practice. A key advance in mRNA cancer vaccines is their ability to encode antigens specific to a selected tumor, which allows the immune system to recognize and attack cancer cells. The next goal is to further improve mRNA-LNP by modifying the formulation and vaccination strategy, especially for patients with advanced cancer. These results highlight the promising potential of mRNA vaccines as a more effective therapeutic strategy for treating aggressive cancers and provide important data to support the further development of neoantigen-targeted cancer vaccines.

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