Proceedings of the 3rd International Conference on Environmental Geoscience and Earth Ecology
DOI: 10.54254/2753-8818/2025.24402

The Application of mRNA Vaccines in Cancer Therapies

Chenyu Zhang

Wuxi Dipont School of Arts and Sciences, Wuxi, China
13306161064@163.com

Abstract. mRNA immunotherapy works by presenting tumor-associated antigens to the patient's immune system, thereby training it to recognize and target cancer cells th at express these antigens. mRNA cancer vaccines have shown remarkable tolerability and safety in both clini cal and preclinical trials. mRNA cancer vaccines produce fewer adverse reactions compared to traditional ca ncer treatments such as chemotherapy and radiotherapy. These vaccines elicit a memory immune response, thereby significantly reducing the risk of cancer recurrence. Notably, in contrast to peptide-based cancer vaccines, mRNA vaccines circumvent the necessity for human leukocyte antigen (HLA) haplot ype matching, offering a broader applicability across diverse patient populations. mRNA vaccines can initiat e antigen expression more rapidly, and they do not carry the genetic risks associated with insertional mutage nesis, which is a concern with DNA vaccine. The therapeutic efficacy of mRNA-based cancer vaccines is fundamentally dependent on their ability to precisely target tumor-associated antigens, consequently eliciting robust cellular immune responses. Tumor antigens can be system atically classified into two distinct categories: tumor-specific antigens (TSAs), which are exclusively expressed on malignant cells and absent in normal tissues, and tumor-associated antigens (TAAs), which exhibit differential expression patterns between neoplastic and normal ce llular populations. Many different types of vaccines were developed to address multiple cancer types, includi ng melanoma, breast cancer, and pancreatic cancer.

Keywords: mRNA vaccine, cancer therapies, translation, nucleotide, protein

1. Introduction

Cancer is always a serious worldwide challenge, giving rise to countless illness and death worldwide, causing around 10 million deaths each year [1]. Cancer is resulted from the malignant proliferation of cells, it is very aggressive and pervasive. The main type of cancer include hematologic (blood) cancers and solid tumor cancers. Cancer is usually caused by undesirable behavior or lifestyle, such as smoking, radiation, un healthy diet and excessive alcohol consumption, which will lead to mutations in genes. Cancer is very different from other diseases, which generally do not kill patients quickly. It can be controlled with medication. However, if the cancer is progressing, then it is not enough in the case of taking medication. The most common methods used to treat cancer are surgery, radiation and chemotherapy, and targeted therapy. But those traditional methods are often accompanied by severe side effects and have limited effect on advanced cases.

DOI: 10.54254/2753-8818/2025.24402

These drawbacks highlight the need for innovative and effective treatment strategies. Due to vast increase in technology, there are many new strategies approaching, mRNA immunotherapy is one of several cancer vaccines currently entering clinical trials globally. This therapeutic approach works by presenting tumor-associated antigens to the patient, which triggers the immune response of the immune system, thereby training it to recognize and target cancer cells that express these antigens [1].

Additionally, this therapy has the potential to neutralize immune-suppressive cells, enhancing the overall antitumor immune response [1]. The mRNA technology has already demonstrated its effectiveness during the pandemic by successfully producing vaccines to combat COVID-19. mRNA vaccines are a piece of mRNA from a viral protein which can introduce exogenous target antigen gene sequences into cells by a specific method, and they will undergo translation and transcription. Those proteins synthesized will stimulate bodies immune system and cause particular immune responses, thereby conferring immune protection. mRNA vaccines are considered to be a new technology to treat tumor. mRNA vaccines can target multiple array of tumor antigens while eliciting a broader spectrum responses from T cells by concurrently delivering human leukocyte antigen (HLA) class I and HLA class II molecules, leading to a more general and multi-faceted attack. Consequently, mRNA vaccines show great potential on treating cancer. Currently, numerous clinical trials worldwide are investigating mRNA tumor vaccines, encompassing cancers such as melanoma, pancreatic cancer, and colorectal cancer. In some trials, mRNA vaccines are being used in combination with other immuno-oncology agents. Notably, the recently developed mRNA-4157 vaccine has received Breakthrough Therapy Designation from the US Food and Drug Administration (FDA) and Priority Medicines status from the European Medicines Agency, positioning it as a frontrunner to be the first mRNA tumor vaccine on sale [2]. There are several advantages of using mRNA vaccines over traditional strategies including less side effect and more effective, mRNA vaccines introduces mRNA from viral proteins into the body to stimulate immune system to respond to the specific antigen. It is very safe because of the low infection risk.

2. The overview of mRNA vaccine

Messenger RNA, also known as mRNA, is a type of RNA transcribed from a strand of DNA which carries genetic information which lead protein synthesis. mRNA was first extracted by a group of scientist in a laboratory at the California Institute of Technology in 1961 [3]. Messenger RNA is a type of RNA which will transcribe genetic information from DNA and carry it to ribosome, in the ribosome, it will act as a proteins synthesis template and will determine the amino acids sequence of the proteins . Proteins were translated by mature processed mRNA which is transcribed from primary mRNA by RNA polymerase. mRNA is a naturally occurring molecule that encodes the genetic instructions for human cells, enabling the synthesis of target proteins or immunogens that elicit an immune response in the body to combat various pathogens. mRNA vaccines leverage the virus's genetic sequence rather than the virus itself, ensuring that these vaccines contain no viral components and pose no risk of infection [4]. Additionally, mRNA vaccines benefit from a shorter research and development cycle, allowing for the rapid development of new vaccine candidates to address viral mutations. The dual mechanisms of humoral and T cell immunity, combined with strong immunogenicity, eliminate the need for adjuvants, and facilitate large-scale production, which are key advantages supporting global supply. The way mRNA vaccines work is by introducing the mRNA from viral proteins and send it into the body though a specific delivery system and express the protein to stimulate a specific immune response by the body, so the body will have specific immune protection [5].

DOI: 10.54254/2753-8818/2025.24402

Between transcription and translation, mRNA serves as an intermediary that carries genetic information essential for guiding protein synthesis. mRNA vaccines codes for more than one immunogens, which are then translated into immunogenic proteins inside the host cells' cytoplasm, and initiate both active and passive immune responses [1]. Moreover, mRNA vaccines fall under the category of immunizations based on nucleic acid. These vaccines can be categorized into two types: self-amplifying mRNA vaccines (saRNAs) and non-replicating mRNA vaccines [3]. Self-amplifying mRNA vaccines contain a sequence encoding the RNA-dependent RNA polymerase (RdRp) complex and subgenomic promoter within the 5' ORF, in addition to ordinary components like cap, 5' UTR, 3' UTR, and poly(A) tail [6]. The gene sequence encoding the target vaccine antigen is typically located downstream of the subgenomic promoter. Alphavirus genomes, including those of Semliki Forest virus (SFV), Sindbis virus (SINV), and Venezuelan equine encephalitis virus (VEEV), are frequently utilized in the design of self-amplifying mRNA vaccines [7]. When the self-amplifying mRNA enters the host cell, it will be translated by the host ribosomes to form replicase complex. Since the self-amplifying mRNA sequence is a positive-sense (+) strand RNA, it can serve as a template for the replicase to generate complementary negative-sense (-) strand mRNA, it results in two types of strand RNA synthesis: one is a full-length copy of the original genomic RNA, and the other is a subgenomic RNA that encodes for the target antigen [8]. With the presence of gene of interest in self-amplifying mRNA sequences and subgeneric promotors, viral replicases recognize these promoters in the (-) strand mRNA, leading to the production of large quantities of (+) strand mRNA containing the target gene sequences, thereby achieving high levels of target protein expression even at low doses. A typical non-replicating mRNA comprises a 5′ cap, 5′-untranslated regions (UTRs), an open reading frame (ORF) encoding the vaccine antigens, 3′- untranslated regions (UTRs), and a poly(A) tail [9]. Collectively, these components enhance mRNA stability and prolong its half-life in vivo. Specifically, the 3′-UTR and poly(A) tail influence mRNA stability and translation efficiency, while the cap structure and 5′-UTR are crucial for efficient translation initiations. Modifications to these structural elements have facilitated clinical application of routine mRNA vaccine [10].

3. The history of mRNA vaccine development

mRNA was first extracted by a group of scientists at the California Institute of Technology in 1961. In 1990, Wolff et al. from the University of Wisconsin reported for the first time that immune responses can be generated by injecting mRNA into mouse skeletons muscles and can also express corresponding proteins, which proved that mRNA technology can be used for vaccine development [11]. Two years later, another scientist found that the hormone-encoding mRNA can alleviate diabetes insidious by injecting it directly into the brain of mice, suggesting that mRNA could be used as a therapeutic drug [12]. The first mRNA vaccine was developed by intra hypothalamic injection of vasopressin mRNA to treat diabetes insipidus in rat. mRNA vaccines offer several advantages over traditional vaccines, primarily due to their non-infectious and non-integrative properties within the human body [13]. Furthermore, the half-life of mRNA can be precisely modulated within cells through targeted modifications to the mRNA molecule. Vaccines based on nucleic acid can mimic the infections of live pathogens, thus stimulating the immune response of follicular T helper cells and germinal center B cells [14].

The COVID-19 pandemic speeds up the research process and significantly increased researcher's interest towards mRNA vaccines on infectious disease, which have developed for many year. Notably, the Pfizer-BioNTech and Moderna COVID-19 vaccines, which encode for the spike protein of SARS-CoV-2, have been instrumental in generating a robust immune response toward the virus.

DOI: 10.54254/2753-8818/2025.24402

The mRNA vaccine encodes for the spike protein antigens or its receptor-binding domain, thereby eliciting an immune response that protects individuals from severe infection. In late 2020, the U.S. Food and Drug Administration (FDA) granted emergency approval for two groundbreaking mRNA-based vaccines designed to combat COVID-19: Pfizer and BioNTech's BNT162b2 and Moderna's mRNA-1273. Both vaccines utilized lipid nanoparticles to deliver their genetic payload, with the ionizable lipids playing a key role in protecting and transporting the mRNA. Clinical trials showed that two doses of the Pfizer-BioNTech vaccine were highly effective, reducing COVID-related hospitalizations by 87%, preventing symptomatic infections in 94% of cases, and demonstrating an overall efficacy rate of 95% [15]. These vaccines marked a major milestone in both pandemic response and vaccine technology. In December 2020, a pivotal moment in medical history occurred when the FDA authorized the first mRNA vaccines for COVID-19. Developed independently by Pfizer-BioNTech and Moderna, these revolutionary vaccines employed advanced lipid nanoparticle technology to deliver their genetic material safely into cells. Clinical data revealed the Pfizer BioNTech formulation exhibited remarkable protection, showing 95% effectiveness against infection overall, while specifically preventing 94% of symptomatic cases and reducing hospitalization risk by 87%. These authorizations not only provided crucial tools against the pandemic but also validated mRNA as a transformative vaccine platform [4].

4. The impact of mRNA vaccines on cancer treatment

mRNA cancer vaccines have demonstrated excellent tolerability and safety in both clinical and preclinical trials. Unlike traditional cancer treatments such as chemotherapy and radiotherapy, they produce less side effects and the immune response generated has equal effect on metastatic lesions and primary tumors. mRNA cancer vaccines can be mass-produced in a relatively short period of time. A significant advantage of this vaccine platform is its flexibility in designing multiple tumor antigens (TAs) and granulocyte-macrophage colony-stimulating factor (GM-CSF). Additionally, they induce a memory immune response, which helps reduce the likelihood of recurrence. Importantly, unlike peptide-based cancer vaccines, the development of mRNA vaccines does not require human leukocyte antigen (HLA) haplotype matching [10]. mRNA vaccines also have several advantages compared to DNA vaccines. mRNA vaccines can initiate antigen expression faster because they do not undergo transcription process that DNA vaccines need Furthermore, they do not carry the genetic risks associated with insertional mutagenesis, which is a concern with DNA vaccines. Although mRNA has been discovered long time ago, and the idea of mRNA vaccines is widely known, the application is very limited. One reasons for this limitation is their strong intrinsic immunogenicity. Specific mRNA motifs and phage-derived double-stranded RNA (dsRNA) can activate the innate immune system through pattern recognition [5]. The efficacy of mRNA cancer vaccines is contingent upon their ability to target tumor antigens, thereby stimulating cellular immunity.

Tumor antigens are broadly categorized into two groups: tumor-specific antigens, which are only present on tumor cells, and tumor-associated antigens, which are expressed on both normal and tumor cells. An illustrative example of an mRNA cancer vaccine is the FixVac BNT111 vaccine developed by BioNTech. This vaccine targets four melanoma-associated TAAs: tyrosinase, melanoma antigen family A3 (MAGE A3), New York esophageal squamous cell carcinoma 1 (NY-ESO-1), and transmembrane phosphatase with tensin homology (TPTE) . Preclinical studies have demonstrated that BNT111 elicits a robust immense response against tumor. In a phase 1/2 trial, after receiving eight injections, 75% of patients showed an immune response to at least one of the four TAAs, with CD8 T cells playing a key role in the T cell response. The year 2020 witnessed a

DOI: 10.54254/2753-8818/2025.24402

groundbreaking advancement in vaccinology with the U.S. regulatory approval of two innovative immunization solutions against COVID-19 [11]. These pioneering mRNA-based formulations, developed through separate research initiatives by pharmaceutical leaders Pfizer-BioNTech and Moderna, introduced a novel approach to vaccine delivery using specialized lipid-based encapsulation systems [12]. Clinical evaluations demonstrated exceptional performance of the Pfizer-BioNTech candidate, with trial data indicating a 95% success rate in preventing COVID-19 infection, 94% effectiveness against symptomatic manifestations, and 87% protection against severe outcomes requiring hospitalization. This regulatory milestone not only addressed urgent public health needs but also established mRNA technology as a viable platform for future vaccine development, opening new possibilities for rapid response to emerging pathogens [13]. The achievement represented a significant leap forward in biomedical science and pandemic preparedness. This vaccine is now under clinical evaluation to determine its tolerability, safety, and effectiveness in treating cancer . Collectively, these vaccine candidates are being developed and can address multiple cancer types.

5. Future prospect for mRNA vaccine development

Self-amplifying RNA (saRNA), also referred to as replicons, represents the next generation of mRNA vaccine technology. These saRNA constructs are typically extracted from alphaviruses, including the Venezuelan equine encephalitis virus (VEEV), Sindbis virus (SINV), and Semliki Forest virus (SFV). The saRNA is engineered by removing genes that codes for viral structure proteins, thereby rendering the mRNA to be non-infectious and incapable of producing viable virions. In place of these deleted genes, the saRNA incorporates target gene(s) that encode the desired vaccine antigens [14]. This innovative approach enhances the immunogenicity and efficacy of the vaccine by enabling sustained antigen expression within the host cells. Self-amplifying RNA (saRNA) shares structural similarities with conventional non-replicating mRNA, including the presence of 5' and 3' untranslated regions, a 5' cap, and a polyadenylated (polyA) tail. However, saRNA is notably larger in size, typically ranging from 9 to 12 kDa, due to the inclusion of an extended open reading frame (ORF). This ORF contains one subgenomic promoter and four genes that codes for non-structural proteins (nsP1–nsP4), which are essential for the package of a functional RNA-dependent RNA polymerase (RDRP) complex [15]. The RDRP complex binds with subgenomic promoter located immediately upstream of the antigen sequence. Utilizing the saRNA as a template, the RDRP synthesizes a complementary negative-sense RNA strand. This negative-sense RNA subsequently serves as a template to produce positive-sense genomic and subgenomic RNA strands, facilitating robust and sustained antigen [6].

In the future, research about mRNA vaccines for cancer should consider improving prophylactic and therapeutic vaccine formulations. Specialized mRNA vaccines represent a promising therapeutic strategy, particularly for malignancies such as pancreatic cancer that exhibit resistance to conventional treatments. Furthermore, mRNA technology holds significant potential for the development of vaccines targeting oncogenic viruses, such as human papillomavirus (HPV) and hepatitis B virus (HBV). Preclinical studies have demonstrated that HPV mRNA vaccines elicit superior antitumor efficacy compared to HPV recombinant protein vaccines and HPV DNA vaccines in animal models. These findings underscore mRNA-based prophylactic vaccines have great potential in cancer prevention, warranting further evaluation in clinical trials to assess their safety and efficacy [7].

DOI: 10.54254/2753-8818/2025.24402

6. Conclusion

Cancer remains one of the most challenging and deadly clinicopathological conditions worldwide due to its high prevalence, complexity, and significant impact on patients and healthcare systems. Although the current antitumor medications therapies helped increase the survival rate of patients with cancer, they also result in several issues, including tumor drug resistance, side effects and toxicity, high cost and other issues keep on bring new challenges. However, recent breakthroughs in molecular medicine, particularly in the fields of mRNA vaccines and cancer immunotherapy, have opened new avenues for effective treatment and management. Although current mRNA cancer vaccines have not yet demonstrated the ability to elicit a clinically significant immune response, their potential has been substantiated through extensive clinical trials, warranting continued investment and development. To address existing limitations and enhance therapeutic efficacy, multiple innovative strategies are being actively explored. Key areas requiring further clinical investigation include the optimization of tumor antigen selection based on immunogenicity prediction, refinement of delivery systems, development of combination therapies, and optimization of administration routes. Comprehensive reviews such as this contribute significantly to expanding our understanding of this platform, while providing valuable insights into the future development and clinical application of mRNA-based cancer vaccines.

References

[1] Zong, Y., Lin, Y., Wei, T. and Cheng, Q. (2023) Lipid Nanoparticle (LNP) Enables mRNA Delivery for Cancer Therapy. Advanced Materials, 35, e2303261.
[2] Huang, X., Kong, N., Zhang, X., Cao,Y., Langer, R. and Tao, W. (2022) The landscape of mRNA nanomedicine. Nature Medicine, 28, 2273-2287.
[3] Xiao,Y., Tang, Z., Huang, X., Chen,W., Zhou, J., Liu, H., Liu, C., Kong, N. and Tao, W. (2022) Emerging mRNA technologies: delivery strategies and biomedical applications. Chemical Society Reviews, 51, 3828-3845.
[4] Fan,T., Xu,C., Wu,J., Cai,Y., Cao,W., Shen,H., Zhang,M., Zhu,H., Yang,J., Zhu,Z., Ma,X., Ren,J., Huang,L., Li, Q., Tang,Y., Yu,B., Chen,C., Xu,M., Wang,Q., Xu,Z., Chen,F., Liang,S., Zhong,Z., Jamroze, A., Tang, D.G., Li,H. and Dong, C.(2024) Lipopolyplex-formulated mRNA cancer vaccine elicits strong neoantigen-specific T cell responses and antitumor activity. Science Advances, 10, eadn9961.
[5] Estapé Senti, M., García Del Valle, L. and Schiffelers, R.M. (2024) mRNA delivery systems for cancer immunotherapy: Lipid nanoparticles and beyond. Advanced Drug Delivery Reviews, 206, 115190.
[6] Tilsed, C.M., Sadiq, B.A., Papp,T.E., Areesawangkit, P., Kimura, K., Noguera-Ortega, E., Scholler, J., Cerda, N., Aghajanian, H., Bot,A., Mui,B., Tam,Y., Weissman, D., June, C.H., Albelda, S.M. and Parhiz, H. (2024) IL7 increases targeted lipid nanoparticle-mediated mRNA expression in T cells in vitro and in vivo by enhancing T cell protein translation. Proceedings of the National Academy of Sciences of the United States of America, 121, e2319856121.
[7] Li,W., Li,Y., Li, J., Meng, J., Jiang, Z., Yang, C., Wen,Y., Liu,S., Cheng,X., Mi,S., Zhao,Y., Miao, L. and Lu,X. (2024) All-Trans-Retinoic Acid-Adjuvanted mRNA Vaccine Induces Mucosal Anti-Tumor Immune Responses for Treating Colorectal Cancer. Advanced Science, 11, e2309770.
[8] Guasp,P., Reiche,C., Sethna, Z. and Balachandran, V.P. (2024) RNA vaccines for cancer: Principles to practice. Cancer Cell, 42, 1163-1184.
[9] Qi,S., Zhang,X., Yu,X., Jin,L., Yang,K., Wang,Y., Feng,Y., Lei,J., Mao,Z. and Yu,G. (2024) Supramolecular Lipid Nanoparticles Based on Host-Guest Recognition: A New Generation Delivery System of mRNA Vaccines For Cancer Immunotherapy. Advanced Materials, 36, e2311574.
[10] Masum, M.H.U., Wajed,S., Hossain, M.I., Moumi, N.R., Talukder, A. and Rahman, M.M. (2024) An mRNA vaccine for pancreatic cancer designed by applying in silico immunoinformatics and reverse vaccinology approaches. PLoS One, 19, e0305413.
[11] Al Fayez, N., Nassar, M.S., Alshehri,A.A., Alnefaie, M.K., Almughem, F.A., Alshehri, B.Y., Alawad, A.O. and Tawfik, E.A. (2023) Recent Advancement in mRNA Vaccine Development and Applications. Pharmaceutics, 15, 1972.

DOI: 10.54254/2753-8818/2025.24402

[12] Karam, M. and Daoud, G. (2022) mRNA vaccines: Past, present, future. Asian Journal of Pharmaceutical Sciences, 17, 491-522.
[13] Wu,L., Yi,W., Yao, S., Xie, S., Peng, R., Zhang, J. and Tan, W. (2024) mRNA-Based Cancer Vaccines: Advancements and Prospects. Nano Letters, doi: 10.1021/acs.nanolett.4c03296, Online ahead of print.
[14] Chen,B., Yang,Y., Wang, X., Yang, W., Lu,Y., Wang, D., Zhuo, E., Tang, Y., Su, J., Tang, G., Shao,S. and Gu, K. (2024) mRNA vaccine development and applications: A special focus on tumors (Review). International Journal of Oncology, 65, 81.
[15] Zhao, H., Li, M., Zhou, J., Hu, L., Lu, S. and Li, P. (2024) The Recent Research Progress of the Tumor mRNA Vaccine. Vaccines, 12, 1167.