CODEN: WJAPAC Impact Factor: 3.87 ISSN: 3049-3013

World Journal of Advance Pharmaceutical Sciences

Volume 2, Issue 2. Page: 151-159 Review Article www.wjaps.com

mRNA-BASED THERAPEUTICS BEYOND VACCINES: APPLICATIONS IN ONCOLOGY

Saravanagiri A.*[1], M. Molungzang Aier[2], Adarsh S. Kumar[3], Debjit Bhakat[4], Anirban Debnath[5], Afrah Fathima[6], R. Roshinee[7], Dr. Gopal Kumar Sunilkumar Singh[8], Mehrosh Sirajoddin Patel[9] and Dr. Darshan Bhuvaneshwari Bhushan Deshmukh[10]

[1]Pharm.D, Saravanagiri8@gmail.com.
[2]Pharm.D, azangaier@gmail.com.
[3]Pharm.D, adarshsk496@gmail.com.
[4]Pharm.D, rijumidnapore@gmail.com.
[5]Pharm.D, anirbandebnath304@gmail.com.
[6]Pharm.D, Afrahshariff.23@gmail.com.
[7]Pharm.D, rroshinee99@gmail.com.
[8]Clinical Pharmacologist, Pharm.D, DNHE, DAFE, dr.gopalsuryavanshi@gmail.com.
[9]Pharm.D, mehroshpatel1@gmail.com
[10]Pharm.D, darshandeshmukh3000@gmail.com

How to cite this Article Saravanagiri A., M. Molungzang Aier, Adarsh S. Kumar, Debjit Bhakat, Anirban Debnath, Afrah Fathima, R. Roshinee, Dr. Gopal Kumar Sunilkumar Singh, Mehrosh Sirajoddin Patel, Dr. Darshan Bhuvaneshwari Bhushan Deshmukh (2025). mRNA-BASED THERAPEUTICS BEYOND VACCINES: APPLICATIONS IN ONCOLOGY. World Journal of Advance Pharmaceutical Sciences, 2(2), 151-159.

Article Info

Article Received: 21 June 2025,

Article Revised: 11 July 2025,

Article Accepted: 31 July 2025.

DOI: https://doi.org/10.5281/zenodo.16738192

***Corresponding author:**

***Saravanagiri A.**

Pharm.D,

ABSTRACT

Messenger RNA (mRNA) therapeutics grabbed the world's attention during the COVID-19 pandemic vaccine development, but the potentials of mRNA vaccines go much beyond infectious diseases and into oncology. The review thus showcases how mRNA technology can revolutionize the field of cancer medicine as well. Applications include therapeutic cancer vaccines, mRNA encoding for immune-modulatory agents such as cytokines and monoclonal antibodies, and the modification of immune cells, such as CAR-T cells. Since mRNA can mount targeted and very powerful immune responses and also has a form of adaptability for personalized medicine, it truly presents mRNA as a suitable tool against a vast range of malignancies. The review further explores new delivery technologies, clinical evaluations, real-world applications, and the current hurdles of stability, delivery, and tumor heterogeneity. With more and more therapeutic mRNA advancing rapidly, oncology is witnessing the coming of a new wave that centers around precision, efficacy, and least system toxicity. Explore further and emphasizes the need for continued investigation and collaboration to harness the mRNA therapeutic potential in cancer therapeutics fully.

KEYWORDS: mRNA therapeutics, cancer immunotherapy, vaccines, tumor suppressor gene, personalized medicine, clinical trials.

INTRODUCTION

Messenger RNA (mRNA) is a single-stranded molecule holding within it the genetic code for proteins laid down by DNA. Once mRNA goes to ribosomes, it directs the process of protein synthesis. It was first discovered back in the early 1960s, but very little research comparatively was done on medicine for decades due to its instability and immunogenicity. Over the last 20 years, however, these newly emerging technologies in molecular biology, synthetic chemistry, and nanotechnology have integrated

to give mRNA-based technologies a revolution. Chemical modifications (such as N1-methyl-pseudouridine) to improve in vitro transcription and efficient delivery vehicles, such as lipid nanoparticles (LNPs), provided mRNA a therapeutically held high for consideration. The sudden rise and success of mRNA-based COVID-19 vaccines brought into limelight how quick, scalable, and efficacious this technology is, thus reviving global interest in its scope beyond infectious diseases, especially toward cancer therapeutics.[1,2]

Conventional cancer treatments, such as chemotherapy, radiotherapy, and surgery, are poorly specific and have an inappropriate amount of toxicity to normal tissues. For chemotherapy, rapid division of cells results in systemic side effects, immunosuppression, and resistance to treatments. Radiotherapy, on the other hand, is limited in the dose it may administer due to the adverse effects it may have on the neighboring normal tissues. Targeted therapy and monoclonal antibodies are somewhat more precise, yet they often tend to be less effective because of tumor heterogeneity and resistance mechanisms. Furthermore, a great majority of these therapies do not provide the proper stimuli for the activation of the host immune system, which is very essential for long-term control of cancer and for keeping it from relapsing. These shortcomings have led to the need for new, adaptive, and personalized cancer treatments.[3,4,5]

mRNA therapeutics act as a promising alternative and adjunct to classical chemotherapeutic approaches. In the preclinical and clinical settings, mRNA has been used to manufacture cancer vaccines through encoding tumor antigens as well as immunomodulatory proteins such as cytokines or checkpoint inhibitors and gene-editing tools for the reprogramming of immune cells. However, unlike DNA approaches that integrate into the genome of the host, mRNA does not insert itself there, thereby making it much safer. It also allows for the fast-track manufacture of personalized treatments. Besides, mRNA for cancer vaccination would seldom express more than one tumor antigen, which poses a big hurdle for combating tumor heterogeneity. In both preclinical and clinical studies, mRNA-based approaches have demonstrated the ability to elicit strong immune responses combined with increased survival rates, while also providing a synergistic function with prevalent antagonist treatments such as checkpoint inhibitors. As the field grows mature, mRNA is inevitably going to change the landscape of cancer treatment by providing a flexible, scalable, and highly customizable platform suited for the paradigms of precision oncology.[6,7,8]

mRNA TECHNOLOGY

Structure and Function of Synthetic mRNA

Synthesized mRNA is a single-stranded nucleic acid molecule contrived to resemble natural mRNAs, putting them in a situation where cells can translate them to carry out the major functionality of producing proteins. From a synthetic point of view, mRNA is designed keeping in mind the enhancement of its stability or translation efficiency and minimization of innate immune activation. Key Structural Components of Synthetic mRNA includes:

1.5′ Cap Structure

The 5′ cap provides protection against mRNA degradation and assists in the initiation of translation by facilitating ribosome binding. Cap modifications called Cap 1 or ARCAs enhance stability and evade immune recognition.

2.5′ Untranslated Region (5′ UTR)

The 5′ UTR is responsible for translation efficiency by way of aiding ribosome recruitment. Sequence optimization would improve protein expression and is, therefore, very important for therapeutic mRNA, especially mRNA targeting cancers.[9,10]

3. Open Reading Frame (ORF)

The ORF produces the therapeutic protein. Translation is enhanced by codon optimization so that the proteins such as tumor antigens, cytokines, or checkpoint inhibitors can be expressed for targeted cancer immunotherapy.

4.3′ Untranslated Region (3′ UTR)

The 3′ UTR stabilizes mRNA and controls its lifespan and translation. A fit design prevents premature degradation and maintains expression for the therapeutic proteins in vivo.

5. Poly(A) Tail

The poly(A) tail is a master stabilizer and enhancer for mRNA translation. It may help with ribosome recycling while guarding against degradation; this ensures sufficient protein production until internalization into a cell.[11]

FUNCTIONS OF mRNA

1. Natural Biological Function of mRNA

Messenger RNA (mRNA) is at the heart of gene expression. It acts as a transient copy of genetic information transcribed off DNA in the nucleus, delivering it to ribosomes in the cytoplasm for translation into a given protein. This process is largely responsible for specifying cellular structures and functions and their responses to environmental signals.

Key functions

- Transmits genetic instructions from DNA to ribosomes
- Produces proteins in accordance with the genetic code
- Controls gene expression by the means of mRNA stability, splicing, and degradation
- Regulates adaptive protein synthesis via cellular signals.[12]

2. Therapeutic Functions of Synthetic mRNA

Directly synthesizing therapeutic proteins within the patient's body using synthetic mRNA, engineered and

delivered, without intervening with the genome, present truly versatile options for mRNA methods-their most considerable application in medicine is in oncology.

Key therapeutic functions

- Production of therapeutic proteins (cytokines, growth factors)
- Cancer immunotherapy by encoding tumor-associated antigens to stimulate the immune system
- Restoration of a missing or defective protein in genetic disease or in cancer
- Induce an immune response by expressing immune regulators (for example, IL-12 or GM-CSF)
- Expressed for a short period of time and without integration; thus, minimizing risk from insertional mutagenesis.[13]

TYPES OF THERAPEUTIC mRNA

1. Non-Replicating mRNA

Non-replicating mRNA is the therapeutic format used most often. It has only the components necessary for translation—5′ cap, 5′ and 3′ UTRs, coding region, and poly(A) tail. It directs transient protein production and is largely used in vaccines and cancer immunotherapies simply because it is safe and easy.[14]

2. Self-Amplifying mRNA (saRNA)

Self-amplifying mRNA codes for both antigen of interest along with viral replicase enzymes, hence engaging into intracellular self-replication. This eventualizes longer and stronger protein expression on smaller doses initially injected. Due to their extra potency and low dose, saRNAs are currently being sought in cancer and infectious diseases.[15]

3. Circular RNA (circRNA)

Circular RNA is one of a covalently closed RNAs with great resistance to exonuclease degradation, rendering it more stable with longer protein expression. It is lacking free ends, unlike the linear mRNA, and so an increased durability in vivo is expected from it. circRNAs are being studied for cancer therapeutics, wherein prolonged protein output is beneficial.[16]

4. Trans-Amplifying mRNA (taRNA)

Trans-amplifying mRNA separates the replicase and antigen-coding sequences into two molecules co-delivered into the cell. The modular approach affords some control over expression and can enhance the safety aspect in that long replicase sequences are avoided. It is this combination of flexibility and improved expression that renders it the method of choice in advanced mRNA therapies.[17]

MECHANISM OF ACTION OF THERAPEUTIC mRNA

Therapeutic mRNA works by delivering synthetic genetic instructions that do not integrate into the host genome for the expression of a protein of interest. Usually, mRNA is loaded into lipid nanoparticles which gain entry into the cell by endocytosis and subsequently escape into the cytosol, where ribosomes translate the mRNA to synthesize the protein. Depending on the therapeutic intent, this protein can be tumor antigen, cytokine, or regulatory molecule. Tumor-antigen mRNAs are conveyed in oncology by APCs via MHC class I and II pathways to activate cytotoxic and helper T cells to mount an anti-tumor immune response. Because mRNA is expressed only transiently and does not interfere with the host genome, this constitutes a highly safe, flexible, and tightly regulated therapeutic platform. The capability of mRNA to generate immune activation and harbor targeted protein payloads has fueled its use in cancer immunotherapy and personalized medicine.[18,19]

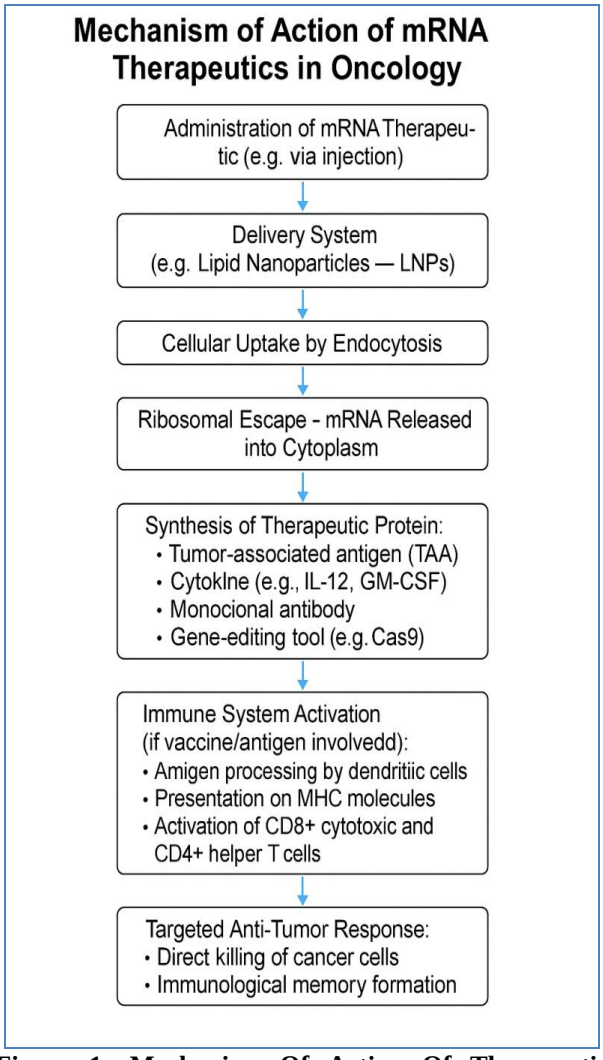

Figure 1: Mechanism Of Action Of Therapeutic mRNA.

DELIVERY SYSTEMS FOR THERAPEUTIC mRNA

An effective delivery of synthetic mRNAs into the target cells is critical in obtaining the desired therapeutic effects. Because naked mRNA is in an unstable state and is quickly degraded in biological environments, an array of delivery systems has been designed to shield the mRNA, favor its uptake into cells, support the escape

from the endosomes, and provide availability in the cytoplasm for translation.

1. Lipid Nanoparticles (LNPs)
Lipid systems represent the most commonly used mRNA therapeutic agents. LNPs consist of ionizable lipids, cholesterol, phospholipids, and PEG-lipids that encapsulate mRNA to shield it from degradation. The LNP would support cellular endocytosis along with endosomal escape so that mRNA can be efficiently delivered inside the cytoplasm. LNPs have been validated clinically for vaccines and therapies in cancers.

2. Polymer-Based Nanoparticles
Cationic and biodegradable polymers including polyethyleneimine (PEI), poly(lactic-co-glycolic acid) (PLGA), and chitosan can complex with mRNA to form a stable nanoparticle. Such systems increase mRNA stability and cellular uptake, yet they might induce cytotoxicity. Polymer carriers provide flexibility in both structure and functionalization for targeted use in cancer therapy.[20,21]

3. Lipoplexes and Polyplexes
Lipoplexes result from the electrostatic interaction between cationic lipids and mRNA, whereas polyplexes include cationic polymers with mRNA. Such systems are simple to prepare and are thought to offer enhanced cellular uptake, yet their efficiencies and stabilities appear diminished compared to those of LNPs. They are investigated for localized and intratumoral delivery.

4. Exosomes
Exosomes are extracellular membranes of natural origin secreted by cells, which may be engineered to deliver therapeutic mRNA. They are known to be highly compatible biocompatible materials and have the potential to evade the immune response due to their endogenous nature. While still being explored in the nascent stages, they have good possibilities for target delivery of mRNA in anticancer and regenerative medicine.

5. Peptide-Based Carriers
Cell-penetrating peptides are capable of transporting mRNA either through the formation of non-covalent complexes or through conjugation with nanoparticles. They facilitate crossing through the cellular membrane and intracellular delivery. Thus, peptide systems could be made tunable as needed for tumor targeting. However, problems remain with the stability of these systems and the loading of their cargo.

6. Virus-Like Particles (VLPs)
VLPs (Virus-like particles) are constructed to resemble viruses but lack infective material. They can encapsulate mRNA into the cell by natural viral methods. Though VLPs have good transfection efficiency and immune activation, their immunogenicity and complexities of manufacture are some of our concerns.[22,23]

mRNA THERAPEUTICS IN ONCOLOGY: MECHANISMS OF ACTION

Immunotherapy-Based Mechanisms

1. Inducing Tumor-Specific Cytotoxic T Cells
mRNA is designed to encode tumor-associated antigens (TAAs) or tumor-specific antigens (TSAs). After delivery, host cells—generally dendritic cells (DC)—translate the mRNAs into protein fragments; those antigens are then displayed by MHC class I molecules for the priming of CD8+ cytotoxic T lymphocytes (CTLs). Activated CD8+ CTLs then migrate to the tumor site, recognize the cancer cells that express the same antigens, and kill them specifically. This is as per the normal functioning of the immune system; however, here, it targets cancer cells, not normal tissues.[24]

2. Neoantigen mRNA Vaccines
Neoantigens arise via tumor-specific mutations and do not occur in normal cells, thus making them ideal immunotherapy targets. The patient's tumor is sequenced, and selected neoantigens are encoded in synthetic mRNA aimed at developing a patient-specific mRNA vaccine. Post-administration, the host APCs express and present the neoantigens to both the CD8+ and the CD4+ T cells. In this manner, a strong immune response that is unique against each patient's tumor is generated, and thus, a strong success has been observed in melanoma and NSCLC clinical trials.[25]

Non-Immunotherapy-Based Mechanisms

1. mRNA-Encoded Cytokines (e.g., IL-2, GM-CSF)
While systemic administration of cytokines can cause toxic side effects, mRNA therapeutics provide a method of gene expression for cytokines like IL-2, IL-12, or GM-CSF at the tumor site. The expressed cytokines then act on the tumor microenvironment, boosting immune cell infiltration, antigen presentation, and T-cell activation. Specifically, IL-2 supports cytotoxic T-cell and NK-cell proliferation, while GM-CSF helps recruit and mature dendritic cells for enhanced antigen presentation. Cast in the tumor area, a strong immune response is generated while limiting systemic toxicity.[26]

2. Checkpoint Blockade via mRNA (e.g., anti-PD-1)
Any immune checkpoint, such as PD-1/PD-L1 or CTLA-4, is used to suppress T-cell activation within a tumor environment. Essentially, this mRNA can be designed to express monoclonal antibodies inside the body (such as anti-PD-1 or anti-CTLA-4 monoclonal antibodies). The mRNA will then be translated into functional checkpoint inhibitor proteins that recognize and bind to their specific targets expressed on either immune or tumor cells. This would then keep immune suppression hidden, while revitalizing exhausted T cells and giving them a greater tumor-killing capability. Some think mRNA-based checkpoint blockade is cheaper and quicker to manufacture versus the classic antibody therapy.[27]

3. Oncolytic mRNA Constructs

Oncolytic therapy with mRNA involves the expression of proteins that selectively cause the death of tumor cells, or which allow viral replication to occur in cancer cells. For instance, it may be an mRNA encoding enzymes to disrupt the membranes of tumor cells or that trigger apoptosis of the tumor cells. In others, mRNA expresses proteins that induce lysis of cancer cells, releasing tumor antigens and damage-associated molecular patterns (DAMPs), which directly kill the cancer cells but also convert the dying tumor into an antigenic source for the secondary immune response.[28]

4. Tumor Suppressor Gene Restoration

Cancer is frequently related to the inactivation of tumor suppressor genes such as TP53 or PTEN. Restoration of their expression can be accomplished by the use of mRNA to deliver synthetic mRNA that encodes the functional versions of those proteins. Inside the cells, translation of mRNA produces tumor suppressor proteins that serve as regulators of the cell cycle and mediator of apoptosis and inhibition of angiogenesis. This would then reactivate the internal contraption of the cell to stop uncontrolled growth and henceors to directly control tumor cells in an immune-independent manner.[29]

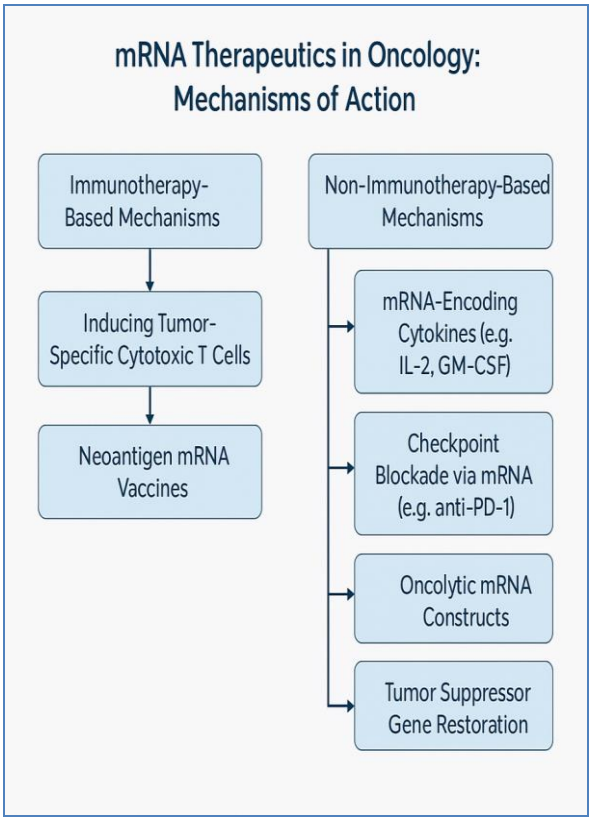

Figure 2: mRNA Therapeutics In Oncology: Mechanisms Of Action.

ADVANTAGES OF mRNA-BASED THERAPEUTICS IN ONCOLOGY

1. Rapid and Scalable Production

Among the multiple advantages mRNA therapeutics offer, top in the list would be rapid design and manufacturing. Once the target antigen or therapeutic protein is identified, mRNA sequences can be synthesized in a matter of days through in vitro transcription. This allows rapid response to tumor mutations or patient-specific antigens, especially under platforms for personalized cancer vaccines. Also, the production process is cell-free and can be scaled up for the production of large batches without compromising the quality.

2. Non-Integrating and Transient Expression

In contrast to DNA-based therapies, mRNA does not need to gain entry into the nucleus or integrate into the host genome. This lowers the carcinogenic risks associated with insertional mutagenesis and long-term genomic imbalance. The transient nature of expression mediated by mRNA ensures that expression of the therapeutic protein is only from a short period and therefore could help in avoiding problems related to overexpression, toxicity, or chronic immune activation.[30]

3. High Safety Profile

mRNA therapeutics are generally accepted to be safer than gene therapies employing viral vectors. There is no chance of replication-competent viruses being produced or of autoimmune reactions triggered by persistent protein expression. Further, modern mRNA platforms incorporate chemically modified nucleosides and implement other advanced purification processes to minimize unwanted innate immune activation and consequent side effects.

4. Potent Immune Activation

These are potent immunizers in case of mRNA vaccine initiation of the immune system in cancer immunotherapy. They activate both arms of innate and adaptive immune responses to help make cytotoxic T lymphocytes (CD8+) and helper T cells (CD4+) against tumor-associated antigens. Due to this dual activation of the immune system, the immune system has enhanced potentiality to kill tumors, thereby imparting long-term protection from recurrence.[31]

5. Flexibility in Antigen Design

This mRNA system allows for easy design customization to encode a wide array of tumor-associated antigens (TAAs) or neoantigens. Multiple antigens can be encoded in the same construct, leading to a multivalent vaccine that could address tumor heterogeneity. Such flexibility allows for much more targetting within the cancer cells in even highly heterogeneous tumor microenvironments.

6. Compatibility with Personalized Medicine

mRNA cancer therapeutics lend themselves very much to a personalized approach. Tumor biopsy and next-generation sequencing to find mutations of the given patient allow for rapid manufacturing of an individualized neoantigen-encoding mRNA vaccine.

Personalized mRNA vaccines are already in clinical trials and represent a targeted approach that could potentially yield response rates and outcomes superior to whatever is less effective versus conventional treatment on cancers.

7. Re-dosability and Combination Potential
Its transient nature and relative lack of anti-vector immune response means that mRNA can be administered repeatedly without loss of efficacy. This re-dosability would be an opportunity to combine with other therapies, such as immune checkpoint inhibitors (anti-PD-1/PD-L1), chemotherapies, or radiation therapy. The combination synergism might further increase the response to the treatment and overall survival.[32]

8. Improved Control over Expression Levels
Engineered mRNA confers tight control on protein expression by manipulating UTRs, codons, and nucleotide modifications. Such tunable expression assists in maximizing therapeutic action while minimizing unwarranted activity or side effects. Short-term expression is, for instance, encouraged where prolonged exposure to a protein-IL-12 or IFN-γ-might cause systemic toxicity.

9. Applicability Beyond Vaccines
While therapeutic cancer vaccines constitute a major focus area of mRNA therapeutics, it also allows in vivo delivery of other proteins, namely monoclonal antibodies, bispecific T-cell engagers, cytokines, and immune checkpoint blockers. This ability to encode functional proteins in situ shall open the door to new possibilities in cancer immunotherapy, gene correction, and tumor reprogramming.

10. Compatibility with Novel Delivery Systems
The mRNA therapeutics present a huge applicability because of innovative delivery systems and this would include lipid nanoparticles (LNPs), polymeric carriers, and tumor-targeting ligands. These protect against mRNA degradation, mediate efficient uptake into cells, and target delivery of the drug into tumor cells or immune cells such as dendritic cells. This ensures greater therapeutic precision, with the implication of fewer off-target effects.[33]

CURRENT mRNA CANCER THERAPIES IN DEVELOPMENT[34,35]

Therapy Type	Example	Developer	Target Cancer
Neoantigen mRNA Vaccine	mRNA-4157 (V940)	Moderna & Merck	Resected high-risk melanoma; planned NSCLC, HNSCC, RCC, urothelial carcinoma
Shared Antigen Vaccine	BNT111 (FixVac)	BioNTech	Advanced melanoma
mRNA-Encoded Cytokines	mRNA-2752	Moderna	Solid tumors, lymphomas
Immune Checkpoint + mRNA	Combination V940 + Pembrolizumab	Moderna & Merck	Melanoma, NSCLC, RCC, urothelial carcinoma, cutaneous SCC
Oncolytic mRNA Constructs	Experimental	Various academic/industry teams	Various solid tumors
Tumor Suppressor Gene mRNA	Experimental	Preclinical research groups	Pancreatic, liver, ovarian cancers

CHALLENGES AND LIMITATIONS

1. mRNA Instability and Degradation: mRNA molecules due to their characteristic instability undergo rapid nuclease-mediated degradation in vivo. Protection and stability of the molecule during delivery is thus very important for a therapeutic application.

2. Delivery System Barriers: Efficient delivery into target cells remains a major hurdle. While lipid nanoparticles (LNPs) are widely used, they can cause off-target effects, toxicity, or induce unwanted immune responses. Targeted delivery to tumor tissues is still under refinement.

3. Immunogenicity and Inflammation: Unmodified mRNA elicits undesirable innate immune activation, which leads to systemic inflammation. Modifications to nucleosides, such as pseudouridine, lower the immunogenicity, but figuring out the correct balance of immunogenicity to therapeutic effect is a tricky thing.

4. Manufacturing and Storage Constraints: mRNA therapeutics need to be maintained in cold chain logistics for storage and transportation, thus creating barriers for global distribution, especially in resource-poor settings. Scale-up manufacturing also requires high precision and consistency.

5. Tumor Heterogeneity: The inherent genetic and antigenic heterogeneity within cancer can limit a single mRNA construct's efficacy. Tumors may lead to mutating or downregulating of antigens for therapeutic resistance or immune escape.[36,37]

6. Short-lived Expression: The mRNA causes transient expression of proteins, which might require repeated applications. This might hamper in oncology the long-byte effect of antitumor unless associated with the formation of immune memory or some other long-term strategy.

7. Regulatory and Cost Hurdles: The new mRNA platform must prove to fall under explicit regulatory pathways that have no precise precedents. Though it is quite expensive to develop mRNA, production, and clinical trials become especially prohibitive in personalized or combination therapies.

FUTURE PERSPECTIVES AND RESEARCH DIRECTIONS

1. Personalized Cancer Vaccines: mRNA allows individualized cancer vaccines to be developed against unique tumor-specific neoantigens. Further advances in AI and sequencing will increase precision, enabling much more personalized immunotherapies so that the clinical outcome may further be improved.

2. Combination Therapies: mRNA cancer vaccines can be combined with immune checkpoint inhibitors, chemotherapy, or radiotherapy. This synergistic method could help to increase response rates while lowering resistance in cancers such as melanoma or NSCLC.

3. Next-Generation Delivery Systems: As lipid nanoparticles and targeted delivery systems progress, so too will mRNA uptake into tumors. This means a self-amplifying RNA would allow for longer expression with less dosing and toxicity.[38,39]

4. In Situ Tumor Editing: mRNAs can provide gene-editing tools such as CRISPR directly into tumor cells, to transiently modulate genes in a targeted manner. Oncogene silencing or reversal of immune evasion may be feasibly achieved without permanently altering the genome.

5. Universal Cancer Vaccines: The use of mRNA-based vaccines targeted against shared tumor-associated antigens could possibly offer protection across different tumor types. This approach is bound to eventually present off-the-shelf, pan-cancer vaccines in clinical settings.

6. Immunomodulatory and Oncolytic Applications: mRNA could work intratumorally to express cytokines, antibodies, or molecules that provide co-stimulation, thereby locally increasing immune responses. The approach sets the bar for low systemic immune-related adverse effects in the modulation of the tumor microenvironment.

7. Global Accessibility and Scalability: mRNA therapeutics are easily scalable and manufactured within days. In the distant future, decentralized production units such as BioNTainers may guarantee worldwide access to personalized cancer treatment, particularly in low- and middle-income regions.

8. Regulatory and Manufacturing Innovations: Regulatory frameworks may offer platform approval for mRNA backbones, speeding up the approval phase of personalized vaccines. Upgrades in the manufacturing sector will improve clinical translation, giving it a better time-to-market and drastically reducing development costs.[40]

CONCLUSION

mRNA-based therapeutics represent a revolutionary change in oncology, imparting ever greater versatility in terms of rapid development and tumor-specific pathway targeting. Beyond their use as vaccines, mRNA technologies supply immune checkpoint modulation, cytokine delivery, oncolytic activity, and tumor suppressor gene restoration-all of which scaffold more personalized and more powerful cancer treatments. Common challenges include stability, targeted delivery, and immune-related adverse events. However, through continued innovation in delivery systems and molecular engineering, the limitations are progressively being addressed. With the increasing conduct of clinical trials and parallel development of technologies, mRNA-based therapies stand to be implemented as the toolkit for the future generation of cancer treatment that, besides bearing the promise of survival extension, can also proclaim patient quality of life through precision medicine.

REFERENCES

1. Gote V, Bolla PK, Kommineni N, Butreddy A, Nukala PK, Palakurthi SS, Khan W. A Comprehensive Review of mRNA Vaccines. Int J Mol Sci., 2023 Jan 31; 24(3): 2700.
2. Khurana A, Allawadhi P, Khurana I, Allwadhi S, Weiskirchen R, Banothu AK, Chhabra D, Joshi K, Bharani KK. Role of nanotechnology behind the success of mRNA vaccines for COVID-19. Nano Today, 2021 Jun; 38: 101142.
3. Li Q, Lei X, Zhu J, Zhong Y, Yang J, Wang J, Tan H. Radiotherapy/Chemotherapy-Immunotherapy for Cancer Management: From Mechanisms to Clinical Implications. Oxid Med Cell Longev, 2023 Feb 2; 2023: 7530794.
4. Liu YP, Zheng CC, Huang YN, He ML, Xu WW, Li B. Molecular mechanisms of chemo- and radiotherapy resistance and the potential implications for cancer treatment. MedComm (2020)., 2021 Jun 10; 2(3): 315-340.
5. Kaczmarek M, Poznańska J, Fechner F, Michalska N, Paszkowska S, Napierała A, Mackiewicz A. Cancer Vaccine Therapeutics: Limitations and Effectiveness-A Literature Review. Cells, 2023 Aug 28; 12(17): 2159.
6. Sun H, Zhang Y, Wang G, Yang W, Xu Y. mRNA-Based Therapeutics in Cancer Treatment. Pharmaceutics, 2023 Feb 13; 15(2): 622.
7. Paczkowska A, Hoffmann K, Andrzejczak A, Pucek WF, Kopciuch D, Bryl W, Nowakowska E, Kus K. The Application of mRNA Technology for Vaccine Production-Current State of Knowledge. Vaccines (Basel), 2025 Apr 4; 13(4): 389.

8. Zhang G, Tang T, Chen Y, Huang X, Liang T. mRNA vaccines in disease prevention and treatment. Signal Transduct Target Ther., 2023 Sep 20; 8(1): 365.
9. Wang YS, Kumari M, Chen GH, Hong MH, Yuan JP, Tsai JL, Wu HC. mRNA-based vaccines and therapeutics: an in-depth survey of current and upcoming clinical applications. J Biomed Sci., 2023 Oct 7; 30(1): 84.
10. Rhoads RE. Synthetic mRNA: Production, Introduction into Cells, and Physiological Consequences. Methods Mol Biol., 2016; 1428: 3-27.
11. Vishweshwaraiah YL, Dokholyan NV. mRNA vaccines for cancer immunotherapy. Front Immunol, 2022 Dec 14; 13: 1029069.
12. Sahin, U., Karikó, K. & Türeci, Ö. mRNA-based therapeutics — developing a new class of drugs. *Nat Rev Drug Discov*, 2014; **13:** 759–780.
13. Qin S, Tang X, Chen Y, Chen K, Fan N, Xiao W, Zheng Q, Li G, Teng Y, Wu M, Song X. mRNA-based therapeutics: powerful and versatile tools to combat diseases. Signal Transduct Target Ther., 2022 May 21; 7(1): 166.
14. Chaudhary N, Weissman D, Whitehead KA. mRNA vaccines for infectious diseases: principles, delivery and clinical translation. Nat Rev Drug Discov., 2021 Nov; 20(11): 817-838.
15. Vallet T, Vignuzzi M. Self-Amplifying RNA: Advantages and Challenges of a Versatile Platform for Vaccine Development. Viruses, 2025 Apr 14; 17(4): 566.
16. Shafaghat Z, Radmehr S, Saharkhiz S, Khosrozadeh A, Feiz K, Alkhathami AG, Taheripak G, Ramezani Farani M, Rahmati R, Zarimeidani F, Bassereh H, Bakhtiyari S, Alipourfard I. Circular RNA, A Molecule with Potential Chemistry and Applications in RNA-based Cancer Therapeutics: An Insight into Recent Advances. Top Curr Chem (Cham), 2025 May 9; 383(2): 21.
17. Perkovic M, Gawletta S, Hempel T, Brill S, Nett E, Sahin U, Beissert T. A trans-amplifying RNA simplified to essential elements is highly replicative and robustly immunogenic in mice. Mol Ther., 2023 Jun 7; 31(6): 1636-1646.
18. Son S, Lee K. Development of mRNA Vaccines/Therapeutics and Their Delivery System. Mol Cells, 2023 Jan 31; 46(1): 41-47.
19. Hınçer A, Ahan RE, Aras E, Şeker UÖŞ. Making the Next Generation of Therapeutics: mRNA Meets Synthetic Biology. ACS Synth Biol., 2023 Sep 15; 12(9): 2505-2515.
20. Wang Y, Zhang Z, Luo J, Han X, Wei Y, Wei X. mRNA vaccine: a potential therapeutic strategy. Mol Cancer, 2021 Feb 16; 20(1): 33.
21. Jung HN, Lee SY, Lee S, Youn H, Im HJ. Lipid nanoparticles for delivery of RNA therapeutics: Current status and the role of *in vivo* imaging. Theranostics, 2022 Oct 24; 12(17): 7509-7531.
22. Alfagih IM, Aldosari B, AlQuadeib B, Almurshedi A, Alfagih MM. Nanoparticles as Adjuvants and Nanodelivery Systems for mRNA-Based Vaccines. Pharmaceutics, 2020 Dec 30; 13(1): 45.
23. Yokoo H, Oba M, Uchida S. Cell-Penetrating Peptides: Emerging Tools for mRNA Delivery. Pharmaceutics, 2021 Dec 29; 14(1): 78.
24. Chen W, Zhu Y, He J, Sun X. Path towards mRNA delivery for cancer immunotherapy from bench to bedside. Theranostics, 2024 Jan 1; 14(1): 96-115.
25. Peng M, Mo Y, Wang Y, Wu P, Zhang Y, Xiong F, Guo C, Wu X, Li Y, Li X, Li G, Xiong W, Zeng Z. Neoantigen vaccine: an emerging tumor immunotherapy. Mol Cancer, 2019 Aug 23; 18(1): 128.
26. Beck JD, Reidenbach D, Salomon N, Sahin U, Türeci Ö, Vormehr M, Kranz LM. mRNA therapeutics in cancer immunotherapy. Mol Cancer., 2021 Apr 15; 20(1): 69.
27. Topalian SL, Drake CG, Pardoll DM. Immune checkpoint blockade: a common denominator approach to cancer therapy. Cancer Cell., 2015 Apr 13; 27(4): 450-61.
28. Kaufman HL, Kohlhapp FJ, Zloza A. Oncolytic viruses: a new class of immunotherapy drugs. Nat Rev Drug Discov., 2015 Sep; 14(9): 642-62.
29. Kong N, Tao W, Ling X, Wang J, Xiao Y, Shi S, Ji X, Shajii A, Gan ST, Kim NY, Duda DG, Xie T, Farokhzad OC, Shi J. Synthetic mRNA nanoparticle-mediated restoration of p53 tumor suppressor sensitizes *p53*-deficient cancers to mTOR inhibition. Sci Transl Med., 2019 Dec 18; 11(523): eaaw1565.
30. Vélez DE, Torres BL, Hernández G. The Bright Future of mRNA as a Therapeutic Molecule. Genes (Basel)., 2025 Mar 26; 16(4): 376.
31. Chehelgerdi, M., Chehelgerdi, M. The use of RNA-based treatments in the field of cancer immunotherapy. *Mol Cancer*, 2023; **22:** 106.
32. Zhang, G., Tang, T., Chen, Y. *et al.* mRNA vaccines in disease prevention and treatment. *Sig Transduct Target Ther*, 2023; **8:** 365.
33. Wang J, Ding Y, Chong K, Cui M, Cao Z, Tang C, Tian Z, Hu Y, Zhao Y, Jiang S. Recent Advances in Lipid Nanoparticles and Their Safety Concerns for mRNA Delivery. Vaccines (Basel)., 2024 Oct 8; 12(10): 1148.
34. Weber JS, Carlino MS, Khattak A, Meniawy T, Ansstas G, Taylor MH, Kim KB, McKean M, Long GV, Sullivan RJ, Faries M, Tran TT, Cowey CL, Pecora A, Shaheen M, Segar J, Medina T, Atkinson V, Gibney GT, Luke JJ, Thomas S, Buchbinder EI, Healy JA, Huang M, Morrissey M, Feldman I, Sehgal V, Robert-Tissot C, Hou P, Zhu L, Brown M, Aanur P, Meehan RS, Zaks T. Individualised neoantigen therapy mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab monotherapy in resected melanoma (KEYNOTE-942): a randomised, phase 2b study. Lancet, 2024 Feb 17; 403(10427): 632-644.

35. Li X, You J, Hong L, Liu W, Guo P, Hao X. Neoantigen cancer vaccines: a new star on the horizon. Cancer Biol Med., 2023 Dec 29; 21(4): 274–311.
36. Wadhwa A, Aljabbari A, Lokras A, Foged C, Thakur A. Opportunities and Challenges in the Delivery of mRNA-based Vaccines. Pharmaceutics, 2020 Jan 28; 12(2): 102.
37. Youssef M, Hitti C, Puppin Chaves Fulber J, Kamen AA. Enabling mRNA Therapeutics: Current Landscape and Challenges in Manufacturing. Biomolecules, 2023 Oct 9; 13(10): 1497.
38. Li Y, Wang M, Peng X, Yang Y, Chen Q, Liu J, She Q, Tan J, Lou C, Liao Z, Li X. mRNA vaccine in cancer therapy: Current advance and future outlook. Clin Transl Med., 2023 Aug; 13(8): e1384.
39. Kumar A, Dixit S, Srinivasan K, M D, Vincent PMDR. Personalized cancer vaccine design using AI-powered technologies. Front Immunol, 2024 Nov 8; 15: 1357217.
40. Li D, Liu C, Li Y, Tenchov R, Sasso JM, Zhang D, Li D, Zou L, Wang X, Zhou Q. Messenger RNA-Based Therapeutics and Vaccines: What's beyond COVID-19? ACS Pharmacol Transl Sci., 2023 Jul 3; 6(7): 943-969.