WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 15, Issue 2, 170-184. Review Article ISSN 2277–7105

NEXT GENERATION MRNA THERAPEUTICS

Ms. S. Subalakshmi*[1], Ms. R. Pirtheeshwari[1], Ms. N. Priyadharshini[1], Ms. K. Narmadha[1], Mr. M. Praveen Kumar[2], Dr. C. Jothimanivannan[3]

[*1]Students, SS Institute of Pharmacy, Sankari, Salem-637301.

[2]Assistant Professor, Department of Pharmacology, SS Institute of Pharmacy, Sankari, Salem 637301.

[3]Professor & Principal, SS Institute of Pharmacy, Sankari, Salem-637301.

Article Received on 15 Dec. 2025,
Article Revised on 05 January 2026,
Article Published on 16 January 2026,
https://doi.org/10.5281/zenodo.18255683

***Corresponding Author**
Ms. S. Subalakshmi
Students, SS Institute of Pharmacy,
Sankari, Salem-637301.

How to cite this Article: Ms. S. Subalakshmi*[1], Ms. R. Pirtheeshwari[1], Ms. N. Priyadharshini[1], Ms. K. Narmadha[1], Mr. M. Praveen Kumar[2], Dr. C. Jothimanivannan[3]. (2026) Next Generation Mrna Therapeutics. "World Journal of Pharmaceutical Research, 15(2), 170–184.

This work is licensed under Creative Commons Attribution 4.0 International license.

ABSTRACT

Messenger RNA (mRNA) therapeutics have emerged as a transformative platform in modern medicine, enabling rapid, flexible, and precise treatment strategies across a wide range of diseases. Building on the success of first-generation mRNA vaccines, next generation mRNA therapeutics focus on improving stability, delivery efficiency, safety, and therapeutic scope. Advances in mRNA engineering, including optimized codon usage, nucleoside modifications, and improved untranslated regions, have significantly enhanced protein expression while minimizing unwanted immune responses. In parallel, innovations in delivery systems—particularly lipid nanoparticles and emerging polymer- and peptide-based carriers—have enabled targeted and tissue-specific delivery, expanding applications beyond infectious diseases. Next generation mRNA therapeutics are being explored for cancer immunotherapy, protein replacement therapies, gene editing, and treatment of rare genetic disorders. Personalized cancer vaccines, for example, use patient-specific tumor antigens encoded in mRNA to stimulate tailored immune responses. Additionally, self-amplifying mRNA and circular RNA platforms offer prolonged protein expression at lower doses, potentially reducing cost and improving safety profiles. Integration with gene-editing technologies such as CRISPR further broadens the therapeutic potential by enabling transient expression of genome-modifying tools without permanent genetic alteration. Despite these advances, challenges remain, including large-scale manufacturing, long-term storage, targeted delivery to difficult tissues, and regulatory considerations. Ongoing research aims to address these limitations while ensuring accessibility and global scalability. Overall, next generation mRNA therapeutics represent a versatile and powerful modality poised to redefine treatment paradigms and accelerate the development of personalized and precision medicine in the coming decades.

KEYWORDS: *mRNA therapeutics, Lipid nanoparticles, Personalized medicine, Cancer immunotherapy, Gene editing, RNA delivery systems.*

INTRODUCTION

Messenger RNA (mRNA) treatments signify a groundbreaking development in contemporary medicine, providing an innovative method for illness therapy and prevention. mRNA therapeutics function by introducing synthetic mRNA into cells, allowing the body's own cellular machinery to create therapeutic proteins, in contrast to traditional therapies that depend on tiny chemicals or recombinant proteins. During the COVID-19 pandemic, this approach garnered international recognition as mRNA vaccines showed previously unheard-of speed, efficacy, and scalability. Building on this achievement, next-generation mRNA therapies are being created to extend their use beyond vaccinations into fields like regenerative medicine, cancer treatment, genetic abnormalities, and infectious diseases.

The shortcomings of first-generation mRNA technologies, such as instability, immunogenicity, and ineffective delivery, are intended to be addressed by next-generation mRNA therapies. The stability, translational efficiency, and safety of mRNA have been greatly enhanced by developments in chemical modifications, delivery technologies, and mRNA sequence engineering. Changes like nucleoside substitutions (like pseudouridine) increase protein expression while lowering undesirable immunological activation. Improved capping and polyadenylation methods, codon optimization, and optimized untranslated regions (UTRs) all support effective and long-lasting protein synthesis.

The creation of sophisticated delivery systems is one of the biggest advances in next-generation mRNA treatments. The most efficient carriers are lipid nanoparticles (LNPs), which shield mRNA from deterioration and make it easier for it to enter target cells. Next-generation LNPs and alternative delivery methods that enable tissue-specific targeting, controlled release, and decreased toxicity are the subject of ongoing study. These developments are essential for extending mRNA uses to organs other than the liver and for long-term medicinal use.

mRNA is a potent platform for personalized treatment due of its adaptability. Next-generation mRNA therapies, which encode tumor-specific antigens to elicit a targeted immune response, are being investigated in oncology for customized cancer vaccines. Unlike DNA-based gene therapies, mRNA therapy provides a transient but repeatable way to repair missing or faulty proteins in genetic and metabolic illnesses without the risk of chromosomal integration. Furthermore, mRNA is being studied for use in regenerative medicine, where it can stimulate growth factor expression to aid in tissue regeneration and repair.

All things considered, next generation mRNA therapeutics represent a flexible, scalable, and innovative therapeutic platform with the potential to revolutionize the treatment of a wide range of diseases. As research advances, mRNA-based therapies are expected to play a central role in the future of precision and personalized medicine. However, despite these encouraging developments, challenges like large-scale manufacturing, long-term safety, storage stability, and regulatory considerations remain Rapid technological advancements.

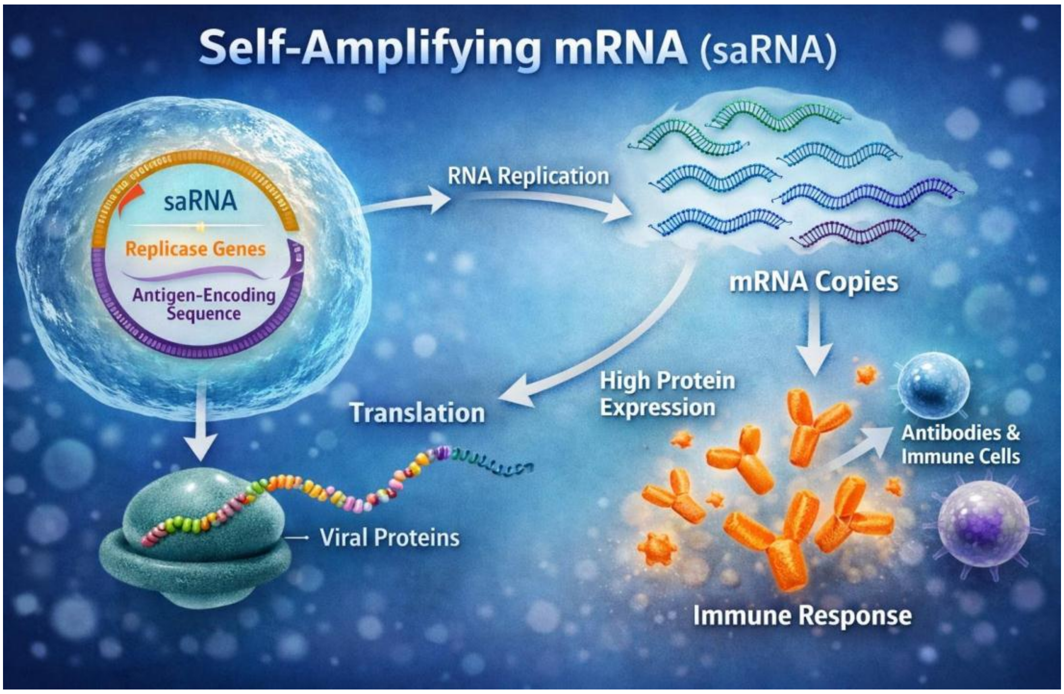
SELF-AMPLIFYING mRNA (saRNA)

A sophisticated type of messenger RNA called self-amplifying mRNA (saRNA) is intended to improve protein expression in host cells. In contrast to traditional mRNA, saRNA includes genetic sequences that encode a viral RNA-dependent RNA polymerase, which is often derived from alpha viruses, in addition to the gene of interest. This polymerase facilitates intracellular amplification of the RNA once it is transported into the cytoplasm of the cell, producing many copies of the target mRNA from a single given molecule.

SaRNA's remarkable efficacy at low doses is its main benefit. Because the RNA repeats itself, far less is needed to reach therapeutic protein levels, which lowers production costs and the possibility of dose-related adverse effects. Additionally, saRNA offers longer protein expression than traditional mRNA, which is advantageous for vaccinations and the treatment of chronic illnesses.

Self-amplifying mRNA has demonstrated promise uses in vaccines, especially for cancer immunotherapy and infectious diseases where robust and long-lasting antigen expression is desired. Additionally, it is being investigated for immune regulation and protein replacement treatments. Lipid nanoparticles (LNPs) are frequently used in saRNA delivery to prevent RNA breakdown and promote cellular absorption.

Controlling innate immune activation, improving delivery methods, and guaranteeing safety are obstacles, nevertheless. All things considered, saRNA is an essential part of next-generation mRNA treatments with substantial therapeutic promise.



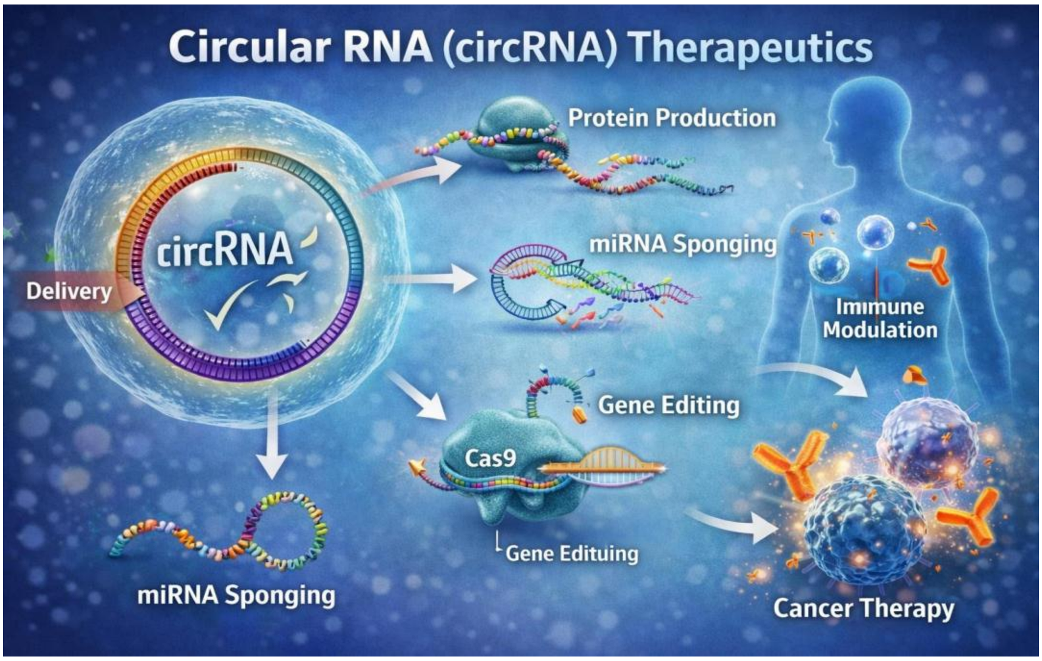
CIRCULAR RNA (circRNA) THERAPEUTICS

A covalently closed, circular structure devoid of 5′ and 3′ ends characterizes circular RNA (circRNA) therapies, a next-generation RNA-based therapeutic platform. Compared to linear mRNA, circRNA has more stability and longer protein expression because of its special shape, which renders it extremely resistant to exonuclease-mediated breakdown. Long-term therapeutic effects benefit from circRNA's capacity to continue translation within cells due to its increased stability.

To start cap-independent translation, CircRNAs are modified with internal ribosome entry sites (IRES) or N6-methyladenosine (m6A). CircRNA serves as a template for ongoing protein production without quickly degrading after it is transported into the cytoplasm. Because of these characteristics, circRNA treatments can be administered less frequently and at lower concentrations.

Promising uses for circRNA treatments include cancer immunotherapy, vaccinations, and protein replacement therapy for metabolic and genetic diseases. They are especially well suited for chronic illnesses that need continuous protein production because of their extended expression. Lipid nanoparticles (LNPs) or other sophisticated delivery systems are frequently used to accomplish delivery.

Despite these benefits, there are still issues with maximizing translation effectiveness, producing on a big scale, and reducing undesirable immunological reactions. However, in next-generation RNA medicine, circRNA treatments are becoming a potent and long-lasting substitute for traditional mRNA platforms.



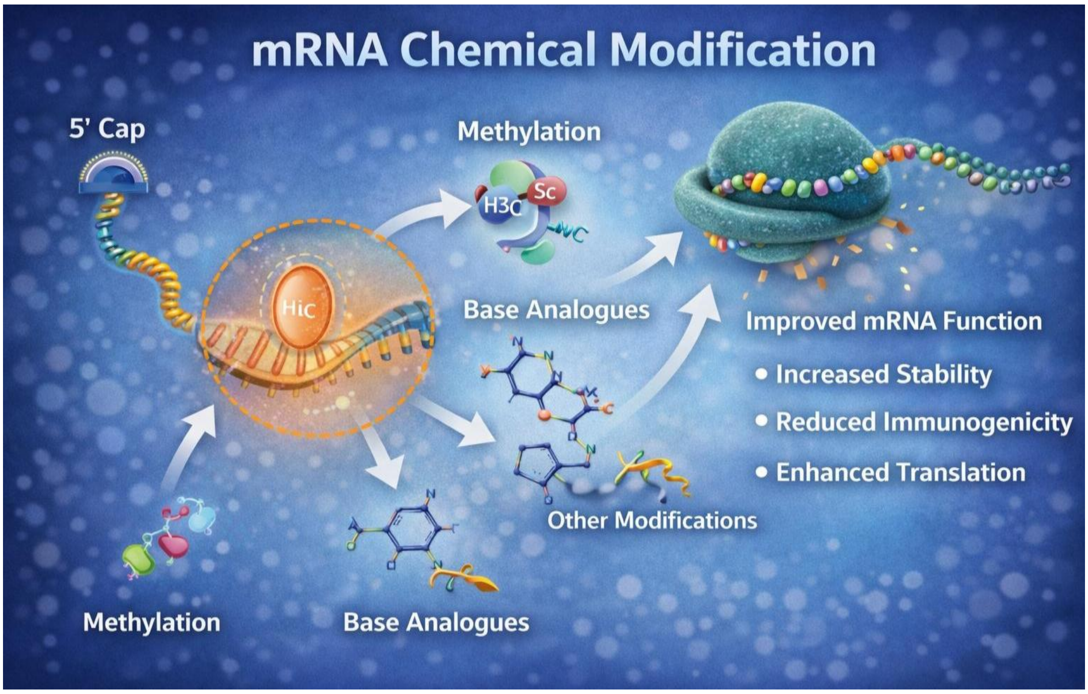
mRNA CHEMICAL MODIFICATION

In order to improve molecular stability, translational efficiency, and safety, next- generation mRNA treatments rely heavily on mRNA chemical alterations. Natural, unaltered mRNA can significantly trigger innate immune responses via pattern-recognition receptors like Toll-like receptors (TLRs) and is very vulnerable to enzymatic destruction. Certain modified nucleosides are added to synthetic mRNA to get around these restrictions.

Pseudouridine (Ψ) and its derivative N1-methylpseudouridine are among the most significant changes. These altered nucleosides take the place of uridine in the mRNA sequence, which lowers immunogenicity by decreasing immune sensor detection. Consequently, the generation of inflammatory cytokines is reduced, enhancing the safety and tolerance of mRNA treatments. Pseudouridine also improves ribosome binding and mRNA stability, which leads to more effective and long-lasting protein translation.

5-methylcytidine and 2-thiouridine are two further chemical changes that increase translational precision and resistance to ribonuclease destruction. Optimization of the poly(A) tail length and 5′ cap structure, in addition to nucleoside changes, enhances mRNA performance.All things considered, the clinical effectiveness of mRNA vaccines and treatments depends on the chemical modification of mRNA, which permits efficient protein production with less immunological activation and enhanced pharmacological characteristics.

Type of Modification	**Location on mRNA**	**Chemical Change**	**Purpose / Function**	**Example**
5′ Cap Modification	5′ end	Addition of 7-methylguanosine	Protects mRNA from degradation and helps ribosome binding	m^7 G cap
Poly(A) Tail	3′ end	Addition of adenine nucleotides	Increases stability and regulates translation	Poly(A) tail
Base Modification	mRNA bases	Chemical alteration of nucleotides	Reduces immune response and improves stability	Pseudouridine
Sugar Modification	Ribose sugar	Modified hydroxyl groups	Enhances translation efficiency	2′-O-methylation
Backbone Modification	Phosphate backbone	Chemical substitutions	Improves resistance to enzymes	Phosphorothioate

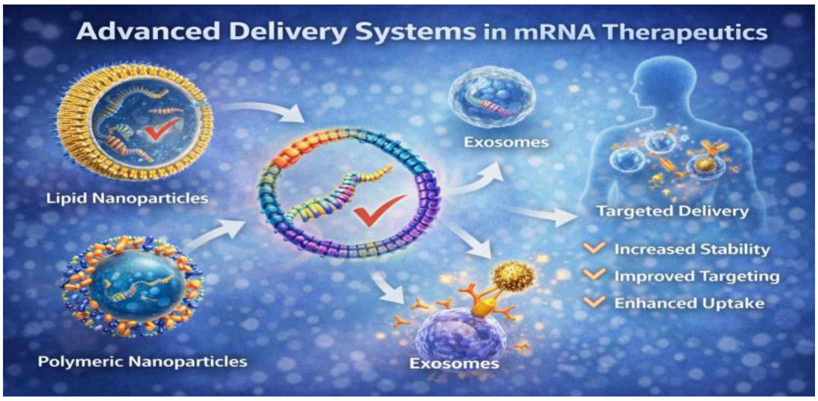


ADVANCED DELIVERY SYSTEM

By safeguarding delicate mRNA molecules and guaranteeing effective transport into target cells, sophisticated delivery methods are essential to the success of mRNA therapies. Specialized carriers are necessary because naked mRNA cannot easily pass through cell membranes and is quickly broken down by nucleases. The most popular delivery method for mRNA vaccines and treatments nowadays is lipid nanoparticles (LNPs). LNPs enhance cellular uptake by endocytosis, encapsulate mRNA, and shield it from enzymatic destruction. By rupturing the endosomal membrane, ionizable lipids in LNPs aid in the release of mRNA into the cytoplasm.

Another significant class of delivery technologies are polymeric carriers, such as biodegradable polymers and polyethyleneimine (PEI). These carriers can enhance intracellular transport, enable regulated release, and form stable complexes with mRNA. Although toxicity and biocompatibility must be carefully adjusted, their chemical plasticity allows customisation for various therapeutic purposes.

The next development in mRNA therapy is targeted delivery systems. These technologies reduce off-target effects and improve therapeutic efficiency by selectively delivering mRNA to particular tissues or cell types using ligands, antibodies, or aptamers linked to carriers. For applications including gene editing and cancer treatment, targeted distribution is especially crucial. All things considered, sophisticated delivery methods greatly improve the efficacy, safety, and stability of mRNA-based treatments.

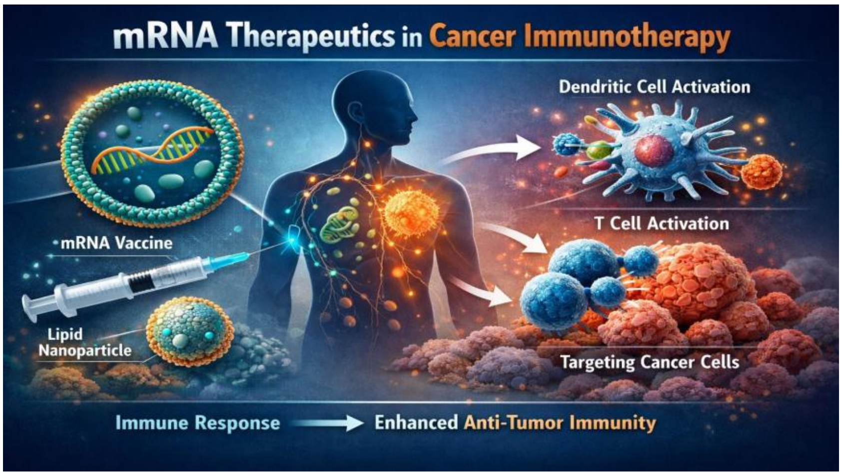


mRNA THERAPEUTICS IN CANCER IMMUNOTHERAPY

By using the body's immune system to identify and eliminate tumor cells, mRNA therapies in cancer immunotherapy offer a potential and cutting-edge method of treating cancer. Personalized cancer vaccines, in which mRNA is engineered to express tumor- specific antigens or neoantigens particular to each patient's cancer, are one significant use. Following delivery, antigen-presenting cells absorb the mRNA, generate the encoded antigens, and display them on major histocompatibility complex (MHC) molecules. This triggers a tailored immune response against cancer cells while protecting healthy tissues by activating cytotoxic T lymphocytes.

Immune modulators based on mRNA are another significant use. These mRNAs produce immunostimulatory proteins that boost anticancer immunity, including as cytokines, co-stimulatory molecules, or immunological checkpoint regulators. Interleukin-encoding mRNA, for instance, can increase T-cell activity in the tumor microenvironment, enhancing immune cell infiltration and function.

In cancer immunotherapy, mRNA therapies provide a number of benefits, such as quick design, scalability, and the capacity to elicit humoral and cellular immune responses. Lipid nanoparticles are frequently used for delivery in order to guarantee effective cellular absorption. All things considered, mRNA-based cancer immunotherapy offers a versatile, accurate, and customized therapeutic approach with substantial clinical potential.



mRNA FOR GENE EDITING APPLICATIONS

mRNA for gene editing applications is a new approach that uses sophisticated genome-editing technologies to precisely and temporarily modify genetic material. This method involves delivering guide RNA and CRISPR-Cas components, like Cas9 or Cas12 nucleases, into target cells using messenger RNA.

After entering the cytoplasm, the mRNA is translated into the Cas protein, which combines with the guide RNA to modify the particular DNA sequence.

The transitory expression of mRNA-based delivery is a major benefit. Since mRNA does not integrate into the host genome like DNA-based delivery systems do, there is less chance of insertional mutagenesis and long-term off-target consequences.

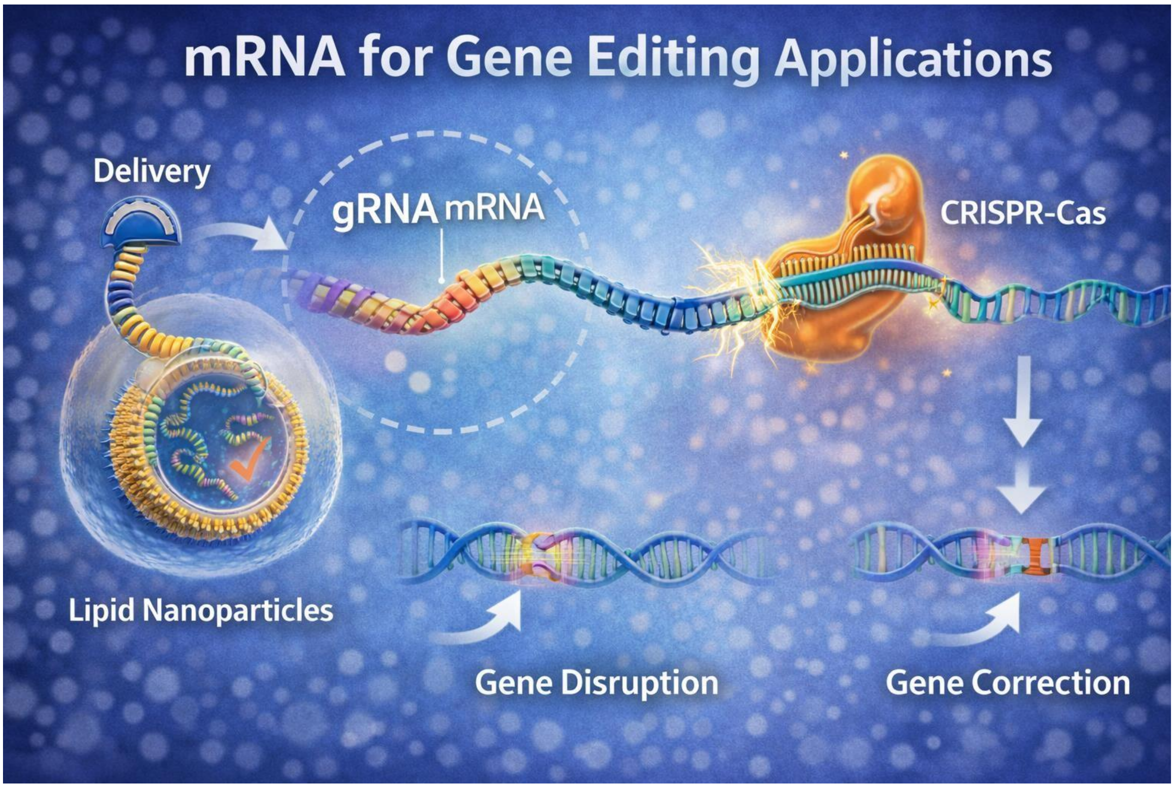
Controlled gene editing with better safety profiles is made possible by the Cas protein's transient presence. Furthermore, mRNA distribution allows for effective editing in both dividing and non-dividing cells as well as quick beginning of action.

Promising uses for mRNA-based gene editing include cancer treatment, hereditary diseases, and regenerative medicine. Additionally, it is useful for ex vivo modification of patient-derived cells, including stem cells or T cells, prior to reinfusion.

To protect mRNA and improve cellular uptake, delivery methods including electroporation and lipid nanoparticles are frequently employed.

All things considered, mRNA-mediated delivery of CRISPR-Cas systems provides a secure, effective, and adaptable platform for next-generation gene editing treatments.

Step	Stage Name	Explanation
1	mRNA Design	mRNA is designed to encode a gene-editing protein (e.g., Cas enzyme).
2	mRNA Synthesis	The designed mRNA is synthesized in the laboratory.
3	Delivery into Cell	mRNA is delivered into target cells using lipid nanoparticles or other methods.
4	Translation	Ribosomes translate mRNA into the gene-editing protein.
5	Target Recognition	The gene-editing protein locates the specific DNA sequence.
6	Gene Editing	The DNA is cut or modified at the target site.
7	mRNA Degradation	mRNA naturally breaks down after protein production.
8	Edited Gene Expression	The corrected or modified gene functions normally.

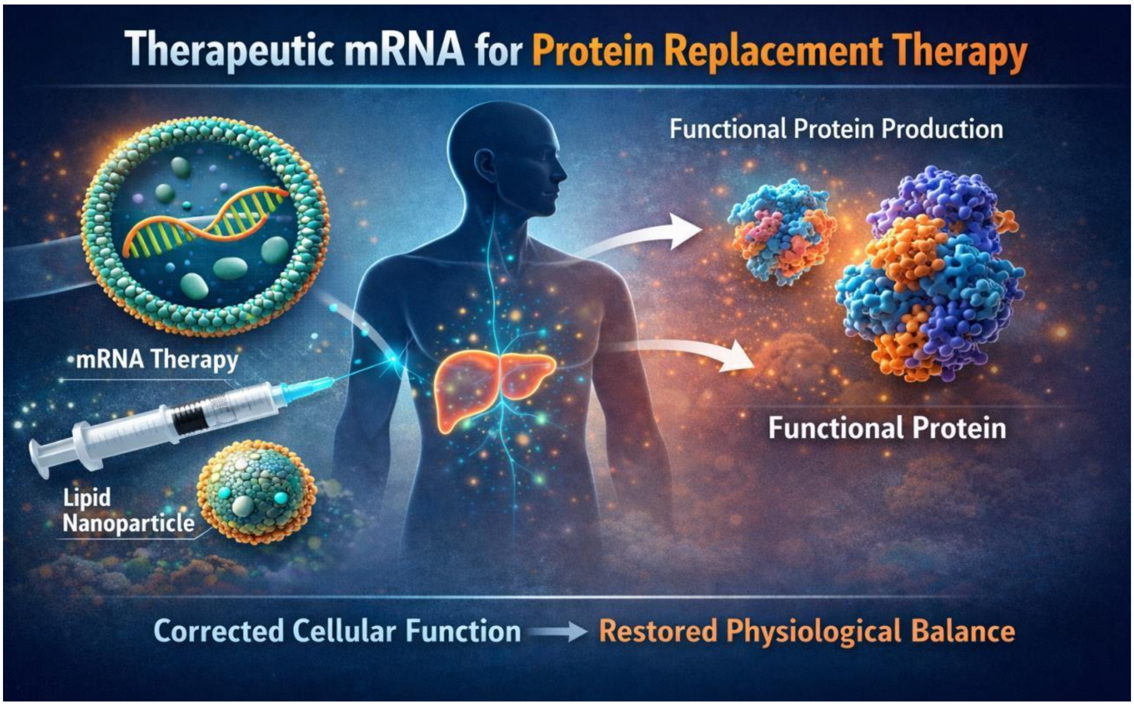


THERAPEUTIC mRNA FOR PROTEIN REPLACEMENT THERAPY

A unique strategy for treating genetic and metabolic diseases brought on by the lack or deficiency of particular proteins is therapeutic mRNA for protein replacement therapy. This method involves delivering synthetic mRNA that codes for the functional protein into patient cells, where the biological machinery translates it to create the necessary protein. This approach offers a transient but efficient source of protein expression without requiring long-term genetic alteration.

For disorders where conventional enzyme replacement therapies are hindered by poor tissue penetration, short half-lives, or immunological responses, mRNA-based protein replacement therapy is very helpful. mRNA therapies can accomplish more natural protein folding and post-translational changes by permitting endogenous protein creation within target cells. Promising targets for this strategy include rare genetic illnesses, enzyme shortages, and inherited metabolic abnormalities.

Therapeutic mRNA is frequently delivered safely and effectively using lipid nanoparticles (LNPs), which shield it from deterioration and promote uptake by target tissues, particularly the liver. Since mRNA is spontaneously broken down following protein synthesis, the temporary nature of mRNA expression further lessens long-term safety issues. Therapeutic mRNA represents a significant leap in next-generation medicine by providing a versatile, scalable, and accurate platform for protein replacement treatment, despite ongoing issues such immune activation and recurrent dosage.



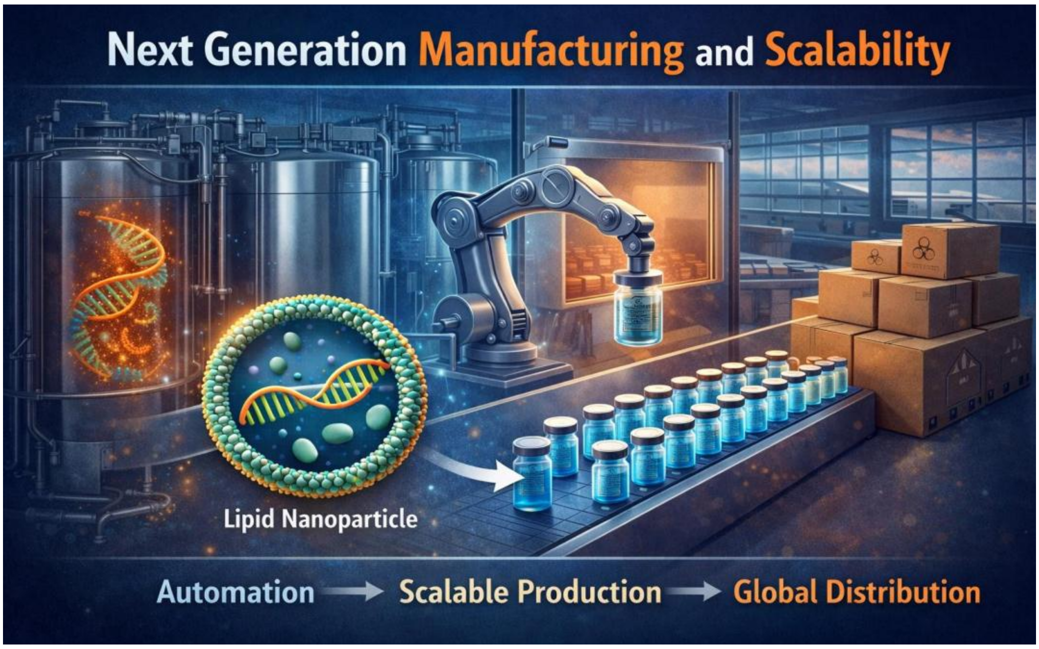
NEXT-GENERATION MANUFACTURING AND SCALABILITY

The widespread clinical and economic success of mRNA therapies depends on next-generation manufacturing and scalability. In contrast to conventional biologics, mRNA is made using cell-free synthesis, which does not require fermentation systems or living cells. This procedure uses DNA templates, RNA polymerase enzymes, nucleotides, and capping chemicals to create mRNA through in vitro transcription. This method ensures constant product quality by providing exact control over mRNA sequence, length, and changes.

Rapid production is a key benefit of cell-free mRNA manufacture. mRNA can be created and produced in a matter of weeks if a therapeutic target's genetic sequence is determined. This speed is particularly useful for reacting to rare genetic illnesses, customized cancer vaccinations, and newly developing infectious diseases. Different mRNA products can be produced on the same platform, increasing scalability and versatility.

Another significant development is better purifying techniques. Impurities, such as leftover DNA, enzymes, and double-stranded RNA that can cause immunological reactions, are eliminated using methods including tangential flow filtration and high-performance liquid chromatography (HPLC). Safety, stability, and translational efficiency are all enhanced by these purification techniques.

All things considered, next-generation manufacturing makes it possible to produce mRNA therapies on a big scale, at a reasonable cost, and with high quality, supporting their widespread clinical use.



SAFETY, STABILITY AND REGULATORY ADVANCES

The development and clinical uptake of next-generation mRNA therapies depend heavily on safety, stability, and regulatory advancements. Rapid disintegration, unintentional immune activation, and formulation-related toxicity were among the major issues with early mRNA formulations.

Through the use of chemically modified nucleosides, tailored lipid nanoparticles, and better dosage techniques, recent developments have dramatically decreased toxicity. These developments maintain high treatment efficacy while reducing excessive innate immune responses.

The expansion of mRNA applications has also been greatly aided by stability advancements. Optimized buffer systems, cryoprotectants, and better lipid compositions are examples of formulation science advancements that have improved mRNA stability during storage and transport.

This has resulted in looser cold-chain regulations, allowing storage at higher temperatures for extended periods of time and enhancing accessibility, especially in environments with limited resources.

From a regulatory standpoint, mRNA-based product approval and oversight have increased because to changing regulatory frameworks. Regulatory bodies now offer more precise guidelines for mRNA therapeutics-specific quality control, manufacturing standards, and clinical evaluation.

Once the delivery system's safety has been verified, platform-based regulatory procedures enable new mRNA products to be approved more quickly. Together, these developments in safety, stability, and regulation are bolstering trust in mRNA treatments and encouraging their wider clinical application in a variety of disease domains.

CONCLUSION

A significant development in contemporary medicine, next-generation mRNA therapies provide a secure, adaptable, and effective platform for the treatment of a variety of illnesses. Stability, protein expression, and safety have all been greatly enhanced by innovations like self-amplifying mRNA, circular RNA, chemical modifications, and sophisticated delivery systems. These treatments have a lot of potential for use in gene editing, protein replacement, cancer immunotherapy, and customized medicine. Even though there are still issues with long-term stability, targeted distribution, and large-scale manufacturing, research is still being done to find solutions. All things considered, precision medicine and future healthcare could be revolutionized by next-generation mRNA therapies.

REFERENCES

1. Knipe, D. M., & Howley, P. M. (2020). Fields Virology (7th ed.). Wolters Kluwer Health.
2. Lodish, H., Berk, A., Kaiser, C. A., et al. (2021). Molecular Cell Biology (9th ed.). W.H. Freeman & Company.
3. Alberts, B., Johnson, A., Lewis, J., et al. (2022). Molecular Biology of the Cell (7th ed.). Garland Science.
4. Weissman, D. (2015). mRNA transcript therapy. Expert Review of Vaccines, 14(2): 265–281.
5. Pardi, N., Hogan, M. J., Porter, F. W., & Weissman, D. (2018). mRNA vaccines — a new era in vaccinology. Nature Reviews Drug Discovery, 17: 261–279.
6. Sahin, U., Karikó, K., & Türeci, Ö. (2014). mRNA-based therapeutics — developing a new class of drugs. Nature Reviews Drug Discovery, 13: 759–780.
7. Karikó, K., Buckstein, M., Ni, H., & Weissman, D. (2005). Suppression of RNA recognition by Toll-like receptors. Immunity, 23(2): 165–175.
8. Zhang, C., Maruggi, G., Shan, H., & Li, J. (2019). Advances in mRNA vaccines for infectious diseases. Frontiers in Immunology, 10: 594.
9. Hou, X., Zaks, T., Langer, R., & Dong, Y. (2021). Lipid nanoparticles for mRNA delivery.
10. Nature Reviews Materials, 6: 1078–1094.
11. Cullis, P. R., & Hope, M. J. (2017). Lipid nanoparticle systems for enabling gene therapies. Molecular Therapy, 25(7): 1467–1475.
12. Verbeke, R., Lentacker, I., De Smedt, S. C., & Dewitte, H. (2019). Three decades of messenger RNA vaccine development. Nano Today, 28: 100766.
13. Blakney, A. K., Ip, S., & Geall, A. J. (2021). An update on self-amplifying mRNA vaccine development. Vaccines, 9(2): 97.
14. Beissert, T., et al. (2020). Self-amplifying RNA vaccines. Molecular Therapy, 28(5): 1196–1210.
15. Qu, L., Yi, Z., Shen, Y., et al. (2022). Circular RNA vaccines against SARS-CoV-2. Cell, 185(10): 1728–1744.

16. Wesselhoeft, R. A., Kowalski, P. S., & Anderson, D. G. (2018). Engineering circular RNA for potent and stable translation. Molecular Cell, 70(6): 1086–1095.
17. Kowalski, P. S., Rudra, A., Miao, L., & Anderson, D. G. (2019). Delivering the messenger: advances in technologies for therapeutic mRNA delivery. Molecular Therapy, 27(4): 710–728.
18. Liu, J., Orkin, S. H., & Shen, S. (2021). CRISPR–Cas systems delivered by mRNA.
19. Nature Reviews Genetics, 22: 145–159.
20. Rurik, J. G., et al. (2022). mRNA cell therapies and protein replacement strategies.
21. Nature Reviews Drug Discovery, 21: 369–388.
22. Schlake, T., Thess, A., Fotin-Mleczek, M., & Kallen, K. J (2012). Developing mRNA-vaccine technologies. RNA Biology, 9(11): 1319–1330.
23. Dolgin, E. (2021). The tangled history of mRNA vaccines. Nature, 597: 318–324.