International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 15, No. 3, 2026

Research Progress of mRNA Vaccines in Disease Prevention and Treatment

Jie Zhou *

Zhejiang Ocean University, Zhoushan, Zhejiang, 316022, China
*** Corresponding author Email:** 2134430533@qq.com

Abstract: mRNA vaccine is a novel category in the medical field. Its core mechanism is to deliver mRNA into cells, and then use the host cell system to produce therapeutic proteins or immunogenic proteins, exerting therapeutic effects on the body or stimulating the body to produce antibodies. In addition to COVID-19, mRNA vaccines' application in targeted tumor therapy is expanding, with numerous clinical trials underway. This review covers the molecular structure of mRNA vaccines, synthesis and purification technologies including nucleoside modification and LNP delivery systems, applications in infectious disease prevention and oncology treatment, and prospects for future development.

Keywords: mRNA Vaccine; Molecular Structure; Synthesis and Purification; LNP Delivery System; Nucleoside Modification; Infectious Disease; Targeted Tumor Therapy; Nucleic Acid Delivery.

1. Introduction

mRNA vaccine is a novel category in the medical field. Its core mechanism is to deliver mRNA into cells, and then use the host cell system to produce therapeutic proteins or immunogenic proteins, exerting therapeutic effects on the body or stimulating the body to produce antibodies[1]. COVID-19,caused by the novel coronavirus SARS-CoV-2,emerged in late 2019.During the vaccine research, mRNA vaccines became an excellent candidate due to their non-toxicity and potent immune response[2]. Meanwhile, mRNA vaccines are mainly synthesized by chemical methods, which are easy for industrialization with a relatively simple production process[3]. In addition to COVID-19, mRNA vaccines' application in targeted tumor therapy is expanding, with numerous clinical trials underway[4]. This review mainly introduces the research progress of mRNA vaccines to support the research and development of mRNA vaccines.

2. Molecular Structure

2.1. Cap Structure

The cap structure of mRNA mainly includes three types: Cap 0, Cap 1 and Cap 2. Among them, the terminal nucleotide ribose of Cap 0 is unmethylated; the ribose of the first nucleotide of Cap 1 is methylated; and the riboses of the first two nucleotides of Cap 2 are both methylated[5]. Selecting an appropriate capping method can ensure normal mRNA expression[6].

2.2. Poly(A) Tail Structure

The poly(A) tail of mRNA can be added either before or after transcription. For a tailing method, a poly(T) sequence needs to be pre-constructed in the 3′ untranslated region of the target DNA to provide a template for the synthesis of the poly(A) tail[7]. The length of the poly(A) tail directly affects the translation and stability of mRNA: a tail that is excessively long cuts down traslation efficiency, while one that is overly short renders mRNA vulnerable to degradation[8]. In practical applications, an appropriate length should be selected to achieve an appropriate balance between mRNA translation efficiency and molecular stability[9].

3. Synthesis and Purification

3.1. mRNA Molecular Modification and Optimization

3.1.1. Nucleoside Modification Technology

Incorporating chemically modified nucleosides into mRNA sequences can effectively resist degradation by intracellular ribonucleases, while improving translation efficiency and enhancing intracellular stability. Uracil analogs are the most commonly used. Replacing all uridines in mRNA with pseudouridine can improve efficiency and reduce immunogenicity. In addition, a variety of base analogs can be used in mRNA sequences to optimize their biological functions. Studies by Kormann et al.[10] have shown that modifying mRNA sequences with different ratios of 5-methylcytidine and 2-thiouridine can effectively reduce the recognition rate of pattern recognition receptors (PRRs), alleviate PRR-mediated immune activation, improve the stability of mRNA and prolong the translation window, providing an important guarantee for the intracellular delivery and functional performance of mRNA.

3.1.2. Cap Structure Optimization and Detection

There are two technical routes for 5′-capping of mRNA: co-transcriptional capping by incorporating m7GpppG cap analogs, and post-transcriptional enzymatic capping catalyzed by capping enzymes after transcription[11]. At present, two schemes have been formed for mRNA capping technology: co-transcriptional capping and post-transcriptional enzymatic capping. Post-transcriptional enzymatic capping, which is a mature application method, stably generates the Cap 1 structure through the combined catalysis of vaccinia virus capping enzyme and 2′-O-methyltransferase[12]. Stable and reliable detection methods should be adopted for the 5′-cap structure to evaluate the efficiency and integrity of the capping reaction[13]. Currently, quantitative analysis of 5′-capping efficiency mostly adopts liquid chromatography-mass spectrometry[14].

3.1.3. Poly(A) Tail Design and Stability Regulation

Chemical modification of the 3′ polyadenylation tail provides an effective strategy to inhibit its degradation. At present, a "modular" modification strategy based on click chemistry has been developed, which can introduce modifications on the poly(A) tail, including linking modified oligonucleotides or coupling modified poly(A) tail trimers through branched topological structures[15,16].

3.2. Research and Preparation of Key Delivery Systems

The delivery system is the core support for the application of mRNA technology, playing an important role in protecting mRNA, improving delivery and achieving targeted delivery[12]. Lipid nanoparticles (LNPs) have played a key role,not only protecting mRNA but also enhancing delivery efficiency in Pfizer-BioNTech and Moderna vaccines[17].

LNPs are generally composed of four core components: ionizable lipids, phospholipids, cholesterol and polyethylene glycol (PEG)-modified lipids[12]. Ionizable lipids are electrically neutral under physiological pH and carry positive charges in acidic environments. This characteristic promotes the fusion of LNPs with endosomal membranes, thus facilitating the release of mRNA into the cytoplasm[18].As the core component of the LNP lipid bilayer, phospholipids can mimic the lipid bilayer structure of cell membranes. They enhance the interaction between LNPs and cell membranes and improve delivery efficiency[12].Cholesterol exerts crucial effects on stabilizing LNP structure and increasing membrane fluidity. It facilitates the fusion between LNPs and cell membranes and maintains the stability of LNPs in vivo[12,19].PEG-modified lipids enable LNPs to evade rapid clearance by the immune system and extend their circulation time in the body. In addition, such lipids reduce LNP aggregation in blood and further optimize delivery capacity[12,20].

4. Applications

4.1. Research on mRNA Vaccines Against Influenza Virus

The antigenicity of seasonal influenza viruses mutates rapidly, especially hemagglutinin, the main target, leading to immune escape in the host[21]. An nm-mRNA-LNP vaccine expressing H3 antigen induced neutralizing antibody titers against the 3c.2A H3N2 virus more than 10 times higher than those induced by the MF59-adjuvanted conventional egg-derived vaccine and the mRNA-LNP vaccine encoding egg-adapted H3 antigen[22]. Two other mRNA vaccines (H10N8 and mRNA H7N9) showed excellent effects in preclinical and Phase I clinical trials, with good safety and high immunogenicity[23]. In addition, mice inoculated with LNP-mRNA vaccine encoding H1N1 HA produced a strong immune response, including high HAI titers, IgG, IgG1, IgG2a antibodies, and CD4+ T cells secreting IL-4 and IFN-γ. Importantly, the vaccine provided 100% survival rate for mice under lethal viral challenge and reduced lung viral load by 3 times[24].

4.2. Research on mRNA Vaccines of Oncology

The emergence of mRNA therapy has provided a clinically promising new strategy for the treatment of malignant tumors[25]. With the deepening of relevant research and the advancement of clinical trials, mRNA technology has shown great application potential: it can cover a variety of solid tumors simultaneously, and can target specific tumors such as lung cancer, breast cancer, prostate cancer, melanoma, as well as hematological tumors[26].

4.3. Research on mRNA Vaccines Against HIV

Globally, human immunodeficiency virus (HIV) currently affects 40.8 million people[27]. After long-term research, an effective vaccine has not been developed, mainly due to the antigenic diversity of HIV protein and glycan shield masking key epitopes of the envelope protein[28]. A novel HIV vaccine strategy is to isolate broadly neutralizing antibodies[29]. Notably, the broadly neutralizing antibody VRC01 has attracted much attention in recent years, which can neutralize 98% of HIV strains and prevent the transmission of antibody-sensitive strains with an efficacy of 75.4%[30]. In one study, a single intravenous injection of 0.7 mg/kg LNP-encapsulated modified mRNA produced antibody concentrations comparable to those achieved by usual injections of 10–20 mg/kg monoclonal antibody proteins[31].

4.4. Research on mRNA Vaccines Against Rabies

Rabies is the most fatal zoonotic disease. The first candidate mRNA rabies vaccine (CV7201) consists of mRNA encoding rabies virus glycoprotein antigen and cationic protein protamine[32]. In BALB/c mice, intradermal injection of this mRNA induced antibody production, thereby providing protection. Notably, rabies mRNA vaccines can induce a stronger cellular immune response compared with approved vaccines[33]. Phase I clinical trials further confirmed that the protamine-formulated rabies mRNA vaccine (CV7201) was immunogenic in most subjects when delivered by a needle-free injector. However, the vaccine required a high dose of mRNA to achieve protective effects[32]. To reduce the dosage, a new formulation encapsulated in lipid nanoparticles containing the same mRNA antigen as CV7201 has been applied in Phase I clinical trials. Recent studies have shown that only two low-dose injections of LNP-encapsulated mRNA can induce neutralizing antibody responses meeting the World Health Organization standards in all subjects[34].

5. Conclusion and Prospect

In summary, mRNA vaccine is a new technology in the biomedical field. With the advantages of non-toxicity, strong immunogenicity and easy industrial synthesis, it has been rapidly applied[35]. The maturity of technologies such as nucleoside modification and enzymatic capping, combined with detection methods such as LC-MS/MS, has improved the modification and quality control system of mRNA, and the application of LNP delivery system can protect mRNA and improve intracellular delivery efficiency[19]. At present, this technology has expanded from infectious disease to targeted tumor therapy[36].

In the future, the development of mRNA vaccines can optimize targeting and explore novel vectors. Conventional lipid nanoparticles face challenges of insufficient targeting accuracy, rapid immune clearance by the mononuclear phagocyte system (MPS), and preferential hepatic accumulation leading to off-target effects. Advanced targeting strategies and innovative vectors can enhance

specific accumulation at lesion sites, reduce healthy tissue damage, and improve delivery efficiency and biosafety [37,38]. It can also accelerate the development of multivalent broad-spectrum vaccines for infectious diseases. Pathogens mutate rapidly, rendering monovalent vaccines ineffective against emerging variants. Multivalent broad-spectrum mRNA vaccines can induce antibodies against multiple subtypes/related pathogens in a single dose, reducing vaccination frequency and enabling rapid response to outbreaks [39,40]. Finally,it can promote the application of tumor vaccines. Tumors exhibit strong individual heterogeneity, limiting universal vaccines' efficacy. Personalized mRNA vaccines targeting unique tumor neoantigens trigger specific anti-tumor immunity, restrain immune escape, and complement surgery/ chemo/ radiotherapy to improve outcomes [41,42,43].

References

[1] Saxena, S., Mandrah, V., Tariq, W., et al. (2025). The future of mRNA vaccines: Potential beyond COVID-19. *Cureus*, *17*(5), e84529. https://doi.org/10.7759/cureus.84529.

[2] Szabó, G. T., Mahiny, A. J., & Vlatkovic, I. (2022). COVID-19 mRNA vaccines: Platforms and current developments. *Molecular Therapy*, *30*(5), 1850–1868. https://doi.org/ 10. 1016/ j. ymthe.2022.03.036.

[3] Fang, E., Liu, X., Li, M., et al. (2022). Advances in COVID-19 mRNA vaccine development. *Signal Transduction and Targeted Therapy*, *7*(1), 94. https://doi.org/10.1038/s41392-022-00990-x.

[4] Gao, Y., Yang, L., Li, Z., et al. (2024). mRNA vaccines in tumor targeted therapy: Mechanism, clinical application, and development trends. *Biomarker Research*, *12*(1), 93. https:// doi. org/10.1186/s40364-024-00623-7.

[5] Despic, V., & Jaffrey, S. R. (2023). mRNA ageing shapes the Cap2 methylome in mammalian mRNA. *Nature*, *614*(7947), 358–366. https://doi.org/10.1038/s41586-022-05668-7.

[6] Gentry, R. C., Ide, N. A., Comunale, V. M., et al. (2025). The mechanism of mRNA cap recognition. *Nature*, *637*(8046), 736–743. https://doi.org/10.1038/s41586-024-08291-7.

[7] Trepotec, Z., Geiger, J., Plank, C., et al. (2019). Segmented poly(A) tails significantly reduce recombination of plasmid DNA without affecting mRNA translation efficiency or half-life. *RNA*, *25*(4), 507–518. https://doi.org/ 10. 1261/ rna. 069913.118.

[8] Passmore, L. A., & Coller, J. (2022). Roles of mRNA poly(A) tails in regulation of eukaryotic gene expression. *Nature Reviews Molecular Cell Biology*, *23*(2), 93–106. https://doi. org/ 10.1038/s41580-021-00417-7.

[9] Oh, A., Lee, S., Park, H. J., et al. (2025). Loop structure in poly(A) tail of mRNA vaccine enhances antigen translation efficiency and mRNA stability. *npj Vaccines*, *10*(1), 234. https:// doi.org/10.1038/s41541-025-00882-3.

[10] Kormann, M. S., Hasenpusch, G., Aneja, M. K., et al. (2011). Expression of therapeutic proteins after delivery of chemically modified mRNA in mice. *Nature Biotechnology*, *29*(2), 154–157. https://doi.org/10.1038/nbt.1740.

[11] Fechter, P., & Brownlee, G. G. (2005). Recognition of mRNA cap structures by viral and cellular proteins. *Journal of General Virology*, *86*(5), 1239–1249. https:// doi. org/ 10. 1099/ vir. 0. 80848-0.

[12] Pardi, N., Hogan, M. J., Porter, F. W., & Weissman, D. (2018). mRNA vaccines — a new era in vaccinology. *Nature Reviews Drug Discovery*, *17*(4), 261–279. https://doi. org/10. 1038/ nrd. 2017. 243.

[13] Webb, A. L. J., Welbourne, E. N., Evans, C. A., et al. (2025). Characterisation and analysis of mRNA critical quality attributes using liquid chromatography based methods. *Journal of Chromatography A*, *1745*, 465724. https://doi.org/10. 1016/ j. chroma.2025.465724.

[14] Beverly, M., Dell, A., Parmar, P., et al. (2016). Label-free analysis of mRNA capping efficiency using RNase H probes and LC-MS. *Analytical and Bioanalytical Chemistry*, *408*(18), 5021–5030. https://doi.org/10.1007/s00216-016-9601-6.

[15] Chen, H., Liu, D., Guo, J., et al. (2025). Branched chemically modified poly(A) tails enhance the translation capacity of mRNA. *Nature Biotechnology*, *43*(2), 194–203. https://doi.org/ 10. 1038/s41587-024-00782-4.

[16] Croce, S., Serdjukow, S., Carell, T., et al. (2020). Chemoenzymatic preparation of functional click-labeled messenger RNA. *ChemBioChem*, *21*(11), 1641–1646. https:// doi. org/10.1002/cbic.202000136.

[17] Prabhakar, P. K., Khurana, N., Vyas, M., et al. (2023). Aspects of nanotechnology for COVID-19 vaccine development and its delivery applications. *Pharmaceutics*, *15*(2), 451. https:// doi. org/ 10.3390/pharmaceutics15020451.

[18] Zong, Y., Lin, Y., Wei, T., et al. (2023). Lipid nanoparticle (LNP) enables mRNA delivery for cancer therapy. *Advanced Materials*, *35*(51), e2303261. https://doi. org/ 10. 1002/ adma. 202303261.

[19] Knaggs, K. L. M., Sun, Y., Walz, B. A., et al. (2025). The role of excipients in lipid nanoparticle metabolism: Implications for enhanced therapeutic effect. *Therapeutic Delivery*, *16*(7), 687–700. https://doi.org/10.1080/20415931.2025.2461238.

[20] Semple, S. C., Akinc, A., Chen, J., et al. (2010). Rational design of cationic lipids for siRNA delivery. *Nature Biotechnology*, *28*(2), 172–176. https://doi.org/ 10. 1038/ nbt. 1608.

[21] Petrova, V. N., & Russell, C. A. (2018). The evolution of seasonal influenza viruses. *Nature Reviews Microbiology*, *16*(1), 47–60. https://doi.org/10.1038/nrmicro.2017.118.

[22] Pierce, S. R., Shi, H., Caetano, C., et al. (2025). Self-amplifying mRNA expressing COBRA hemagglutinin elicits long-lasting, broadly reactive antibodies against seasonal influenza A viruses. *Vaccine*, *62*, 127449. https://doi.org/10. 1016/j. vaccine. 2025.127449.

[23] Lee, I. T., Nachbagauer, R., Ensz, D., et al. (2023). Safety and immunogenicity of a phase 1/2 randomized clinical trial of a quadrivalent, mRNA-based seasonal influenza vaccine (mRNA-1010) in healthy adults: Interim analysis. *Nature Communications*, *14*(1), 3631. https://doi.org/10.1038/s41467-023-38924-9.

[24] Cargnin Faccin, F., & Perez, D. R. (2024). Pandemic preparedness through vaccine development for avian influenza viruses. *Human Vaccines & Immunotherapeutics*, *20*(1), 2347019. https://doi.org/10.1080/21645515.2024.2347019.

[25] Rojas, L. A., Sethna, Z., Soares, K. C., et al. (2023). Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer. *Nature*, *618*(7963), 144–150. https://doi.org/ 10.1038/s41586-023-06061-3.

[26] Lorentzen, C. L., Haanen, J. B., Met, Ö., et al. (2022). Clinical advances and ongoing trials on mRNA vaccines for cancer treatment. *The Lancet Oncology*, *23*(10), e450–e458. https://doi.org/10.1016/S1470-2045(22)00477-2.

[27] Dugdale, C. M., Ufio, O., Giardina, J., et al. (2025). Estimating the effect of maternal viral load on perinatal and postnatal HIV transmission: A systematic review and meta-analysis. *The Lancet*, *406*(10501), 349–357. https://doi.org/10.1016/S0140-6736(25)01183-0.

[28] Doores, K. J. (2015). The HIV glycan shield as a target for broadly neutralizing antibodies. *The FEBS Journal*, *282*(24), 4679–4691. https://doi.org/10.1111/febs.13563.

[29] Mu, Z., Haynes, B. F., & Cain, D. W. (2021). Strategies for eliciting multiple lineages of broadly neutralizing antibodies to HIV by vaccination. *Current Opinion in Virology*, *51*, 172–178. https://doi.org/10.1016/j.coviro.2021.101564.

[30] Zhou, T., Georgiev, I., Wu, X., et al. (2010). Structural basis for broad and potent neutralization of HIV-1 by antibody VRC01. *Science*, *329*(5993), 811–817. https://doi. org/10. 1126/ science.1192819.

[31] Pardi, N., Secreto, A. J., Shan, X., et al. (2017). Administration of nucleoside-modified mRNA encoding broadly neutralizing antibody protects humanized mice from HIV-1 challenge. *Nature Communications*, *8*(1), 14630. https://doi. org/ 10. 1038/ncomms14630.

[32] Fang, Z., Yu, P., & Zhu, W. (2024). Development of mRNA rabies vaccines. *Human Vaccines & Immunotherapeutics*, *20*(1), 2382499. https://doi.org/ 10.1080/ 21645515. 2024. 238 2499.

[33] Liu, J., Sun, J., Ding, X., et al. (2024). A nucleoside-modified mRNA vaccine forming rabies virus-like particle elicits strong cellular and humoral immune responses against rabies virus infection in mice. *Emerging Microbes & Infections*, *13*(1), 2389115. https://doi.org/10.1080/22221751.2024.2389115.

[34] Wang, Y., Yu, T., Zhang, S., et al. (2025). A lyophilized anti-rabies mRNA-LNP vaccine induces early and robust immune responses from a single-dose subcutaneous administration. *Veterinary Microbiology*, *307*, 110612. https://doi.org/ 10. 1016/ j. vetmic.2025.110612.

[35] Kaushik, M., Madeswaraguptha, P., Vanangamudi, M., et al. (2025). Recent progress, challenges (stability and in vivo distribution), and opportunities of DNA & mRNA vaccine in cancer immunotherapy. *Advances in Immunology*, *166*, 211–258. https://doi.org/10.1016/bs.ai.2025.04.002.

[36] Shemesh, C. S., Hsu, J. C., Hosseini, I., et al. (2021). Personalized cancer vaccines: Clinical landscape, challenges, and opportunities. *Molecular Therapy*, *29*(2), 555–570. https://doi.org/10.1016/j.ymthe.2020.12.035.

[37] Dalabehera, M., Ghosh, A., Mohanty, S., et al. (2025). mRNA delivery systems 2.0: Engineering extrahepatic delivery for non-vaccine therapeutics. *Materials Today Bio*, *35*, 102584. https://doi.org/10.1016/j.mtbio.2025.102584.

[38] Sui, Y., Hou, X., Zhang, J., et al. (2025). Lipid nanoparticle-mediated targeted mRNA delivery and its application in cancer therapy. *Journal of Materials Chemistry B*, *13*(33), 10085–10117. https://doi.org/10.1039/D5TB00620A.

[39] Wang, Y., Ma, Q., Li, M., Mai, Q., Ma, L., Zhang, H., Zhong, H., Mai, K., Cheng, N., Feng, P., Guan, P., Wu, S., Zhang, L., Dai, J., Zhang, B., Pan, W., & Yang, Z. (2024). A decavalent composite mRNA vaccine against both influenza and COVID-19. *mBio*, *15*(9), e00668-24. https://doi.org/ 10.1128/ mbio. 00668-24.

[40] Muodiaju, J. C., & Madu, C. S. (2025). Messenger ribonucleic acid (mRNA)-based universal vaccines: Engineering broad-spectrum immunity against future pandemics. *Cureus*, *17*(5), e84821. https://doi.org/10.7759/cureus.84821.

[41] Sahin, U., Schmidt, M., Derhovanessian, E., et al. (2026). Individualized mRNA vaccines evoke durable T cell immunity in adjuvant TNBC. *Nature*, *651*(8107), 1088–1096. https:// doi. org/ 10.1038/s41586-026-07401-7.

[42] Li, X., Jabbarzadeh Kaboli, P., Roozitalab, G., et al. (2026). Next-generation neoantigen mRNA vaccines: Immuno-engineering strategies for precision cancer immunotherapy. *Cell Oncology*, *49*(2), 72. https://doi.org/10.1007/s13402-025-01087-9.

[43] Srivastava, R. (2026). AI-powered mapping of tumor immunity for optimized mRNA vaccine engineering. *Frontiers in Oncology*, *16*, 1766201. https://doi.org/ 10.3389/ fonc. 2026. 1766201.