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Review Article

mRNA -Based Therapeutics in Pharmacology: A New Frontier in Precision Medicine

Pathruni Hema Geethika*

Department of Pharmacology, KITS College of Pharmacy, Ramachandrapuram

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ABSTRACT

Messenger RNA (mRNA)- based therapeutics have revolutionized the landscape of pharmacology, especially following their success in COVID-19 vaccine development. This review explores the foundational principles, technological advances, clinical applications, and prospects of mRNA therapeutics. It also highlights the challenges related to stability, delivery, immunogenicity, and regulatory approval. The growing relevance of this therapeutic class suggests a paradigm shift in how modern medicine approaches disease prevention and treatment.

INTRODUCTION

The concept of using mRNA as a therapeutic agent has transitioned from theoretical potential to clinical reality. Unlike DNA-based therapies, mRNA does not integrate into the host genome, making it a safer alternative. It enables transient protein expression and is highly customizable, opening avenues for treatment of infectious disease, cancer, genetic disorders, autoimmune conditions, and metabolic syndromes. This flexibility, combined with advances in molecular biology and delivery technologies, has propelled mRNA therapeutics to the forefront of precision medicine.

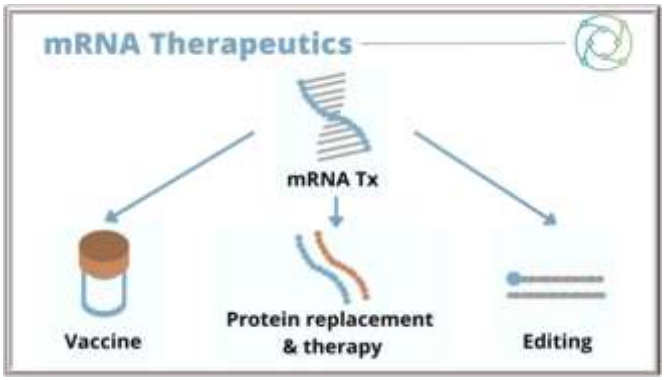

Figure. 1: mRNA Therapeutics

Mechanism of Action

mRNA therapeutics work by delivering synthetic mRNA into cells, typically using nanocarriers. Once inside the cytoplasm, the cellular machinery

***Corresponding Author:** Pathruni Hema Geethika
Address: *Department of Pharmacology, KITS College of Pharmacy, Ramachandrapuram*
Email : geethikahema9162@gmail.com
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translates the mRNA into a functional protein. These proteins can serve various roles- acting as antigens to stimulate immune responses (in the case of vaccines), replacing deficient or dysfunctional proteins, or modulating cellular pathways. The design of the mRNA molecule is critical: codon optimization enhances translation efficiency, while incorporation of modified nucleotides (such as pseudouridine) reduces recognition by innate immune sensors, improving stability and reducing inflammatory responses.

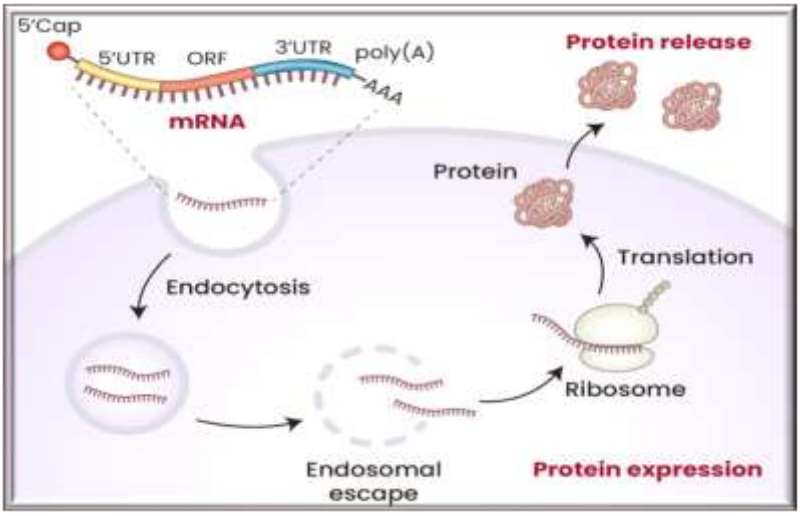

Figure 2. Mechanism of action of mRNA

Types of mRNA Therapeutics

Types	Description	Example Therapies
mRNA vaccines	Induce immune responses against pathogens	Pfizer - BioNTech and Modern COVID-19 vaccines
Cancer Immunotherapy	Personalized vaccines to target tumor antigens	Mrna-4157 (Moderna) for melanoma
Protein Replacement	Encode functional proteins to replace deficient ones	Cystic fibrosis, Fabry disease
Gene Editing Tools	Deliver CRISPR/Cas9 components for gene editing	Ex vivo editing for sickle cell disease

Delivery systems

1. Lipid Nanoparticles (LNPs)

Composed of ionizable lipids, cholesterol, phospholipids, and PEGlylated lipids, LNPs protect mRNA and facilitate its endosomal escape. They have been validated clinically and are currently the gold standard for systemic mRNA delivery.

2. Polymeric Carriers

Biodegradable polymers such as poly (lactic-co-glycolic acid) (PLGA) and polyethyleneimine (PEI) offer customizable release kinetics and have shown promise in targeted delivery.

3. Exosomes

Naturally secreted vesicles, exosomes have the advantages of low immunogenicity and inherent targeting capabilities, through large scale manufacturing remains a challenge.

Table.1: Comparison of major mRNA delivery systems

Delivery System	Advantages	Limitations
LNPs	High efficiency	Cold chain required
Polymers	Tunable properties	Potential toxicity
Exosomes	Biocompatible	Scale up challenges
Hybrids	Targeted delivery	Complex formulation

Advantages of mRNA Therapeutics

- Rapid development and scalability: m RNA constructs can be rapidly synthesized based on genetic sequences, facilitating swift responses to emerging infectious diseases or mutations.
- Avoids genomic integration: Unlike DNA-based gene therapies, mRNA functions in the cytoplasm and poses minimal risk of insertional mutagenesis.
- Controlled and transient expression: This allows for precise dosing and reversibility, reducing the potential for prolonged side effects.
- Modifiable for personalized medicine: mRNA can be engineered to encode patient- specific antigens or therapeutics proteins, enhancing precision.
- Non – infectious and cell free production: mRNA drugs do not rely on live cells or viruses, reducing biosafety concern.

Challenges

- Stability: mRNA is inherently unstable and requires protection from enzymatic degradation.
- Delivery: Effective intracellular delivery is complex and requires carefully designed carriers that balance efficacy and safety.
- Immunogenicity: While mRNA modifications reduce immune activation, some individuals may still experience.
- Storage and Transportation: Most mRNA formulations require ultra -low temperatures storage, complicating global distribution- especially in low – resource settings.
- Regulatory Hurdles: Being a relatively new therapeutic class, mRNA drugs face evolving regulatory landscapes with limited long -term safety data.

Clinical Applications and Trials

The clinical pipeline for mRNA therapeutics is expanding rapidly. As of 2025, over 150 candidates are in various stages of development. They include:

- **Infectious Diseases:** COVID – 19, influenza, cytomegalovirus, HIV and Ebola antibodies, and cytokine therapies.
- **Oncology:** Personalized neoantigen vaccines, mRNA – encoded monoclonal antibodies, and cytokine therapies.
- **Genetic Disorders:** Ornithine trans carbamylate deficiency, methylmalonic acidemia, and Fabry disease.
- **Autoimmune and Inflammatory Disease:** Modulating immune responses in conditions like multiple sclerosis and type 1 diabetes.

Example: Moderna's mRNA -4157/V940is in Phase 2/3 trials for melanoma, in combination with immune checkpoint inhibitor.

Table. 2: Selected mRNA therapeutics in clinical trials (2024–2025).

Disease	Therapy	Developer	Phase
Melanoma	mRNA-4157	Modern	Phase 2/3
Influenza	mRNA-1010	Modern	Phase 3
HIV	mRNA-1644	Modern /IAVI	Phase 1
RSV	mRNA-1345	Modern	Phase 3

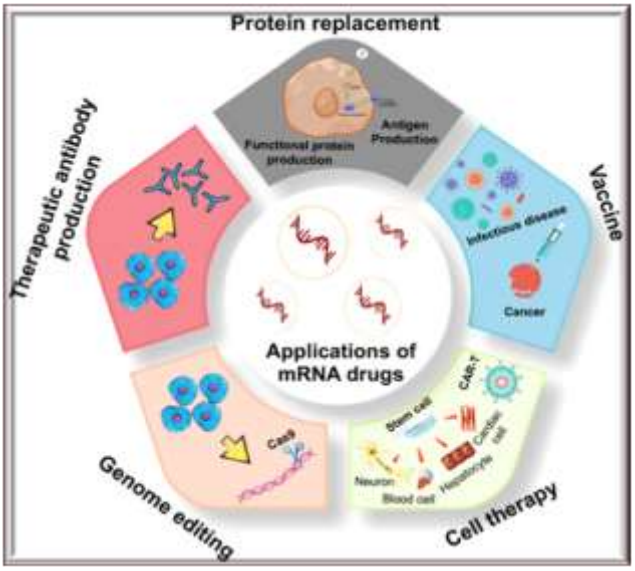

Figure.2: Applications of mRNA

FUTURE PROSPECTS

- **Next-generation mRNA platforms:** Self - amplifying RNA (saRNA) and circular RNA (circRNA) offer improved expression efficiency and longer durability with lower doses.
- **Broder delivery innovations:** Targeted delivery to specific tissues (e.g., lungs brain) is being explored through ligand- conjugated nanoparticles and peptide- base vectors.
- **Global accessibility:** Development of thermostable mRNA formulations that remain stable at room temperature could revolutionize distribution in remote or underdeveloped regions.
- **Combination therapies:** Co- delivery of mRNA with other therapeutics, such as adjuvants, check out inhibitors, or small molecules, may enhance efficacy and broaden treatment paradigms.
- **AI and silico design:** Machine learning is being used to optimize mRNA sequences, predict immune responses, and accelerate candidates screening.

CONCLUSION

mRNA -based therapeutics have established themselves as a transformative tool in modern pharmacology, redefining the possibilities of disease prevention, treatment, and personalized medicine. While challenges related to stability, delivery and regulation remain, ongoing research and technological advancements are poised to overcome these hurdles. Continued collaboration across academia, industry, and regulatory agencies will be essential in realizing the full therapeutics potential of mRNA

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