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REVIEW ARTICLE

From Vaccines to Therapeutics: The Evolution of mRNA-Based Medicine

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ABSTRACT
Messenger RNA (mRNA) therapy has emerged as a significant innovation in contemporary medicine, providing a novel strategy beyond the traditional vaccine approach. Initially validated in the creation of COVID-19 vaccines, mRNA technology is currently being investigated for a range of therapeutic uses, including oncology, genetic disorders, infectious diseases, and cardiovascular issues. This therapeutic approach delivers synthetic mRNA into cells, guiding them to produce specific proteins that can mend, replace, or regulate abnormal cellular processes. The benefits of mRNA therapy encompass rapid design capabilities, versatility, and the opportunity for personalized treatment. Unlike standard therapies, it minimizes the risks associated with genomic integration and can be quickly developed in response to health emergencies. However, challenges such as instability, managing immune responses, and establishing efficient delivery systems still require attention. Ongoing research is aimed at enhancing lipid nanoparticles and other delivery methods to improve stability and safety. Overall, mRNA therapy signifies a ground-breaking advancement with extensive applications beyond vaccination, promising great potential for addressing intricate and previously untreatable diseases.
***KEYWORDS**: Advantages of mRNA, Applications of mRNA Therapy, Drug Delivery Systems, mRNA Therapy, lipid nanoparticles, protein replacement therapy.*

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INTRODUCTION

The application of messenger RNA (mRNA) in medical studies dates back to 1961 when researchers identified its crucial role in protein production. A major breakthrough in the discipline occurred in 1984 when Krieg and Melton successfully produced functional mRNA in a controlled lab environment. Throughout the 1990s, scientists began preclinical studies on in vitro mRNA synthesis for various uses, including protein therapies, gene editing, and vaccination approaches targeting cancer and infectious diseases [1]. The most effective public health strategy to curb the spread of infectious diseases is vaccination. Life-threatening ailments like smallpox have been nearly eradicated due to successful vaccination campaigns, and the World Health Organization estimates that vaccines prevent 2–3 million fatalities each year from measles, tetanus, pertussis, and influenza. However, conventional vaccines often fail against diseases that elude immune detection, such as the human immunodeficiency virus (HIV), hepatitis C, and the malaria parasite Plasmodium falciparum. Furthermore, they require frequent modifications to combat quickly evolving infections like the influenza virus [2]. The base for mRNA vaccines is the "central dogma," involving the use of mRNAs with specific antigens through purification, chemical modifications, and optimization in molecular biology. There are two main types of mRNA: non-replicating and self-amplifying [3]. This natural process makes mRNA-based therapeutics practical for various biological and therapeutic applications, including vaccines, protein replacement therapy, cancer immunotherapy, genome editing, and cellular reprogramming. Based on traditional criteria for drug properties, mRNAs are typically not ideal drug candidates due to their high molecular weight, negative charge, instability in physiological conditions, and potential to provoke an immune response. To mitigate

these challenges, extensive research has been dedicated to developing mRNA delivery systems and engineering mRNA molecules [4]. As a result, the potential of mRNA-based therapies has gained increased visibility. Fueled by the urgent need for COVID-19 vaccines, mRNA therapy is advancing rapidly. As either a preventive or therapeutic agent, mRNA generates functional proteins across almost all known sequences, demonstrating favorable safety and effectiveness at any target, which holds significant promise in the fields of precision and personalized medicine [5].

History of mRNA therapy

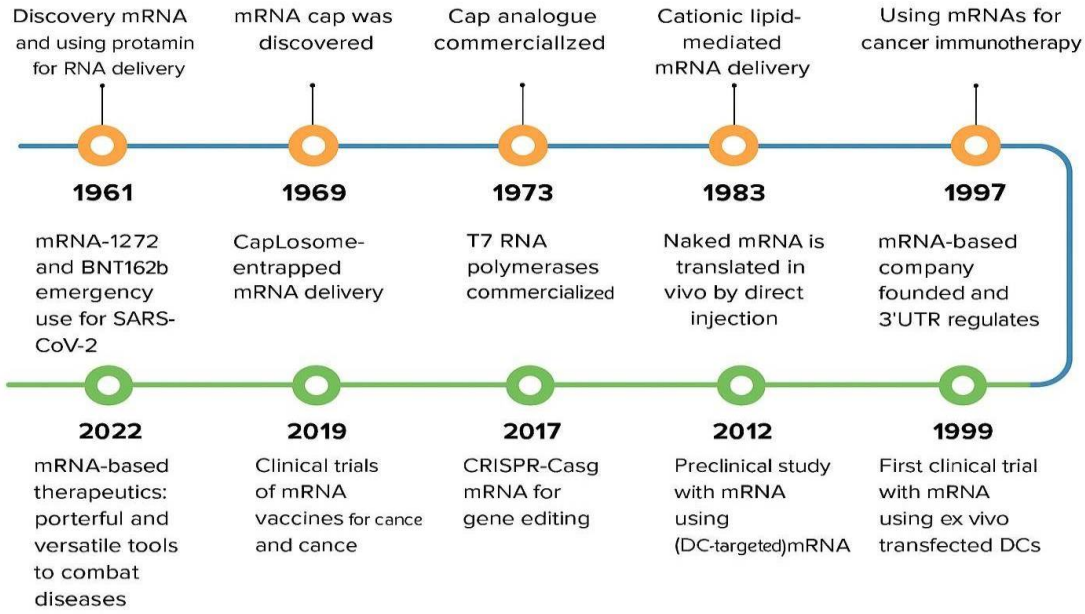

Figure 1: The process of developing mRNA- grounded rectifiers can be distributed into three phases.

Phase 1, which encompasses mRNA discovery, in vitro conflation, and the construction of nucleic acid delivery systems(1961 – 1990), includes the discovery of mRNA523 and the use of protamine for RNA delivery, 526 as well as the in vitro restatement of insulated mRNA, 525 the discovery of the mRNA cap, 526 the delivery of liposome- entangled mRNA, 527 the commercialization of cap analogues, and T7 RNA polymerases, along with cationic lipid- intermediated delivery of mRNA528 and the direct injection of naked mRNA for in vivo restatement.529 In Phase 2, knowledge accumulated through ongoing sweats and varied operations, particularly in protein relief curatives and vaccination strategies for cancer and contagious conditions, which involve using mRNAs for cancer immunotherapy, 5 the establishment of mRNA- grounded companies, and the regulation of mRNA localization by the 3 ′- UTR530, induction of antitumor T cell responses via mRNA531, the first clinical trial exercising mRNA with ex vivo transfected DCs532, mRNA- grounded immunotherapy for mortal cancers, 533 preclinical studies with mRNA targeted to DCs delivered orally534, defensive mRNA vaccines for influenza240 and respiratory syncytial virus98, CRISPR – Cas9 mRNA for gene editing535, and substantiated mRNA cancer vaccines entering clinical trials.330 Phase 3 marks the period of mRNA- grounded rectifiers as a Revolutionary remedial technology that's getting an important and protean tool for Treating conditions, including clinical trials for mRNA vaccines Targeting cancer and contagious conditions like mRNA- 1273536 and the exigency Use of BNT162b for the SARS- CoV- 2 pandemic5[6].

DRUG DELIVERY SYSTEMS OF mRNA THERAPY

Lipid carriers for mRNA delivery

Lipid carriers possess a development history of more than 60 Years, aiming to improve drug delivery and reduce side effects. Lipid carriers for mRNA delivery can be divided into several Types, including liposomes (LPs), liposome-like nanoparticles (LLPs), solid lipid nanoparticles (SLNs), nanostructured lipid Carriers (NLCs), lipid polymer hybrid nanoparticles (LPNs), Nano emulsions, exosomes and lipoprotein particles (LPTs)41. The Characteristics of lipid carriers and their use for mRNA delivery Are summarized in this section and Table 342,43. Meanwhile, the Structures of different lipid carriers [7].

LNPs for mRNA Delivery

LNPs are the most studied and commonly utilized drug delivery systems for mRNA. The first generation of LNPs, known as liposomes, appeared in the 1960s. These Liposomes were formed in an aqueous environment, showcasing closed bilayer lipid Structures. Due to their ability to increase the aqueous solubility of drugs, liposomes Quickly became recognized as a potential drug delivery method. As advancements in Nanotechnology occurred, smaller liposomes were further developed by attaching Targeting ligands or polymers. This swift evolution in different pharmaceutical Domains led to the development of the "next generation" liposomes, referred to as LNPs, which have assumed a vital role in mRNA delivery. Recently developed LNPs For mRNA application consist of ionizable lipids, helper lipids, cholesterol, Polyethylene glycol (PEG)-lipids, and mRNA. LNPs have been studied as drug delivery Systems for encapsulating small molecules, nucleic acids, small interfering RNA (siRNA), and mRNA. With progress in ionizable cationic lipids, LNPs have recently Been harnessed for mRNA delivery. Ionizable lipids exhibit pH sensitivity, Transitioning from a positively charged form at low pH to neutrality at physiological pH, owing to the capacity of their head groups to exchange charge. This characteristic enables them to create 'mRNA-ionized cationic lipid' complexes that stabilize and protect mRNA in a pH-dependent manner. Since ionizable cationic lipids remain neutral in the bloodstream, the release of mRNA from LNPs can be regulated by pH, helping to alleviate systemic toxicity in vivo. Moreover, in the acidic environment of endosomes, ionizable lipids can protonate, acquiring a positive charge that facilitates membrane destabilization and assists in the escape of nanoparticles from the endosomal compartment. Another essential component, PEG lipid, greatly affects the characteristics of lipid nanoparticles. It guarantees extended systemic circulation and improved stability by preventing opsonisation and Phagocytosis by macrophages. The selection of PEG-lipid, which depends on the Molar mass of PEG and lipid length, can influence overall outcomes, including Targeted delivery and cellular uptake effectiveness. Helper lipids and cholesterol play Crucial roles in LNP formation, impacting their fluidity or rigidity. Polyethylene glycol (PEG)-lipids, along with mRNA, have been explored as drug delivery vehicles for Encapsulating small molecules, nucleic acids, small interfering RNA (siRNA), and mRNA [8].

Polymer-based nonviral vectors for cancer mRNA delivery

Polymer molecules typically bind with mRNA through electrostatic interactions. An ideal polymer-based mRNA delivery system should: (1) effectively encapsulate and shield mRNA from degradation by nucleases; (2) ensure high biocompatibility and safety; (3) facilitate penetration and accumulation in targeted cells, tissues, and organs; (4) evade lysosomal degradation during intracellular transport; and (5) enhance the release of mRNA in the cytoplasm to achieve the desired outcome. This section will discuss various types of polymer base mRNA delivery systems, including polyplexes and lipo-polyplexes.

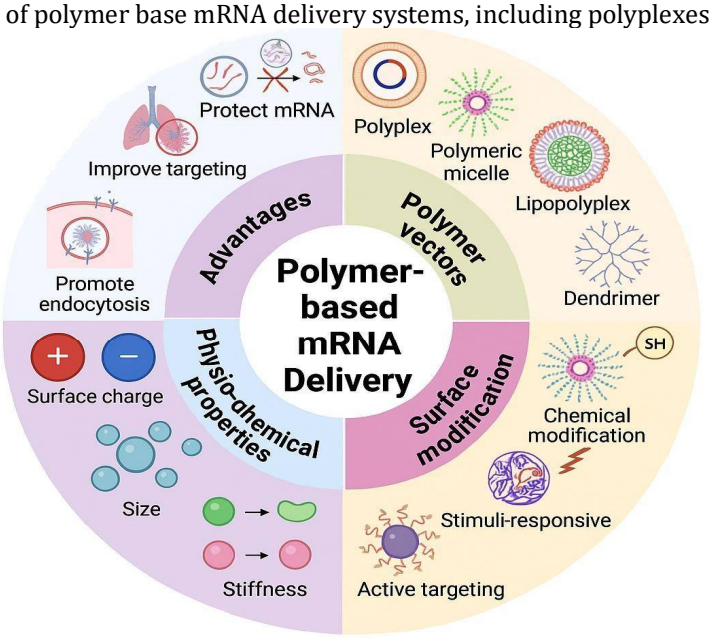

Figure 2: Nanoparticles (PNP) were created by combining the synthesized P[Asp(DET)]91 polymers with EGFP mRNA in a 10 mM HEPES nanoparticles.

The formation of PNP occurred through electrostatic interactions between the positively charged polymer and the negatively charged mRNA. The ratios of amine groups in the DET component of the

polymer to the phosphate groups in the mRNA (N/P) were assessed, ranging from 4 to 32. At an N/P ratio of 32, the hydrodynamic diameter of PNP was found to be 179 ± 1 nm (with a polydispersity index (PDI) of 0.20). Z potential measurements revealed that PNP possesses a positive surface charge of 13.2 ± 1.49 mV. The encapsulation efficiency of the mRNA was 99.7%. To improve colloidal stability and reduce non-specific interactions in biological environments, we functionalized the surface of PNP with 2 kDa poly (ethylene glycol) (PEG) via a reaction between NHS ester and amine groups, leading to the formation of an amide bond. PEG was incorporated into PNP at 1:1 and 10:1 molar ratio relative to the polymer, corresponding to 11.5% and 23% of the amine groups in the polymer, respectively. PEG-PNP exhibited decreased zeta potentials, measuring 7.35 ± 1.37 mV for the 1:1 ratio (PEG(1x)-PNP) and 3.22 ± 0.74 mV for the 10:1 ratio (PEG (10x)-PNP). The zeta potential values diminished as the PEG to polymer ratio increased, as the positively charged amine groups were utilized for the conjugation of PEG. Dynamic light scattering (DLS) analysis indicated that the average hydrodynamic diameters for PEG(1x)-PNP (215 ± 3 nm, PDI = 0.28) and PEG (10x)-PNP (220 ± 5 nm, PDI = 0.29) were marginally greater than those of PNP [9].

Exosome-liposome hybrids

It is well-established that mRNA and DNA can be effectively integrated into liposomal structures; however, liposomes face challenges in delivering these therapeutic agents to target cells. In contrast, exosomes excel at transporting their contents to cells and facilitating their release due to their unique transmembrane proteins that enable attachment to the cell and enhance endocytosis. Lin Y. et al. demonstrated that the exosome-liposome hybrid could efficiently transfect target cells with plasmid DNA. While this technique has not yet been applied to mRNA loading, it can be inferred that, similar to how a DNA molecule is incorporated into the hybrid structure, mRNA can also be encapsulated. Thus, after binding mRNA to cationic liposomes and incubating these liposomes with exosomes, an exosome liposome hybrid can be generated that effectively delivers mRNA to cells. Some combinations of liposomes and mRNA may not interact with the exosomes, necessitating a separation step. Based on these strategies, exosome-liposome hybrids have been shown to yield structures exceeding 200 nm in size, making ultrafiltration a feasible method for separating them from a mixture of smaller exosomes and liposomes [10].

ROLE OF PROTEIN-BASED NANOPARTICLES IN IMMUNOTHERAPY AND DRUG DELIVERY SYSTEMS

The human immune system is crucial for many essential functions within the body, including homeostasis, defined mechanisms, tissue repair, and the elimination of dead cells. This system consists of cells that continuously circulate throughout the body, assessing every individual cell for abnormalities. These cells identify and promptly eliminate invading pathogens and cancerous or dysfunctional cells. Immune cells can be categorized into two main branches of the immune system: innate and adaptive. Innate immune cells provide an immediate response to pathogen invasion, utilizing receptors that recognize pathogens through specific molecular patterns. These cells then engulf pathogens and secrete substances that initiate a swift response. Key players in innate immunity include neutrophils and macrophages. In contrast, the adaptive immune system consists of B and T cells, including CD4+ helper T cells and CD8+ cytotoxic T cells. Cytokines released by CD4+ helper T cells regulate the functions of natural killer cells, B cells, and components of the innate immune system, while CD8+ killer cells target and destroy infected cells. T and B lymphocytes possess a clonal characteristic upon Encountering an antigen, activating an immune response and supporting innate Defences to eliminate invading pathogens. Cancer is a leading cause of death worldwide, and despite extensive efforts, it remains challenging to treat. It is characterized by the uncontrolled multiplication of abnormal cells. Traditional cancer treatments, such as radiotherapy, surgery, and chemotherapy, often fall short due to poorly targeted drug accumulation, significant side effects, and drug resistance, leading to the progression of cancer and subsequent treatment failure. [11].

Peptides as carriers for mRNA delivery

Multifunctional peptides, created from various amino acid sequences, provide the potential to enhance efficient cell penetration or to target nucleic acid drugs to specific tissues or organelles. Protamine, cell-penetrating peptides (CPPs), and peptides that target cell membrane proteins have all been shown to be effective for mRNA delivery. Peptide-based carriers for mRNA delivery can be classified into two types based on the role of peptides within the delivery system: (I) mRNA delivery carriers that utilize single-component peptides specifically for aiding mRNA transmission; (ii) carriers where peptides are combined with additional materials to enhance mRNA delivery capabilities and address the shortcomings of the original carriers. Notably, peptide-dominant mRNA delivery can be categorized into cationic peptide-facilitated delivery, amphipathic peptide-mediated delivery, mRNA-peptide covalent conjugate delivery,

and phase separation-mediated delivery, reflecting the latest advancements in peptide use for effective mRNA transport.[12]

Delivery of oligonucleotides to the brain and eye.

A) ONs cannot passively verbose into the central nervous system (CNS) because of the vascular blood-brain barrier (BBB). (B) ONs that do not have a delivery agent need to be directly administered into the brain or spinal cord. The most generally used route for CNS administration in humans is intrathecal (IT) injection, which involves delivering ONs into the subarachnoid space of the spinal cord to bypass the pia mater and reach the parenchyma. This results in a rapid-fire elevation of ON attention in the cerebrospinal fluid, allowing for a lower needed dose and minimizing side effects. Also, the BBB hinders ON transport into the supplemental rotation, leading to sustained high ON situations. © The eye is a localized, vulnerable, privileged part of the CNS that facilitates targeted delivery. ONs are effective and well-permitted when introduced through intravitreal injections [13].

Applications of mRNA Therapy Beyond Vaccines

Gene Editing

Gene editing represents a promising therapeutic domain for utilizing mRNA technology that expresses programmable nucleases, such as zinc-finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs), or CRISPR-Cas. These genome-engineering instruments allow for the replacement or modification of gene expression by making site-specific changes within the cellular genome, which includes correcting harmful mutations or introducing beneficial ones. Editing with ZFNs, TALENs, and CRISPR-Cas happens after the cellular DNA repair mechanisms address the DNA double-stranded break (DSB) via non homologous end joining (NHEJ), potentially resulting in insertions or deletions, or through homology-directed repair (HDR), with a donor sequence available at the break site. ZFNs and TALENs achieve sequence recognition through protein-DNA interactions; however, the intricate protein engineering needed to develop specific DNA-targeting protein domains limits their widespread use. The realization of RNA-guided DNA endonucleases provides an easily accessible platform for modifying genomic information. Furthermore, catalytically inactive Cas9 variants like dead Cas9 (dCas9) have been combined with various functional domains to reach targeted genetic and epigenetic changes in DNA sequences, including base editing. Recently, the novel nuclease Cas13a has been indicated to preferentially attach to and cleave RNA instead of DNA substrates, broadening the CRISPR toolbox [14].

CORONAVIRUS

In the past two decades, there have been three significant coronavirus outbreaks (severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2), all of which have posed severe health pitfalls and caused substantial profitable damage, without any established curatives or restorative vaccines for the ailments. <en-us-grammar>Among all vaccine-related patents, the majority pertain to SARS and MERS, with only three patents specifically concentrated on mRNA vaccines to date.</en-us-grammar> In the wake of the unanticipated new coronavirus outbreak, the speed of vaccine development is critical for timely life-saving interventions. Therefore, it's ineluctable that mRNA vaccines, with their rapid-fire product processes, will be integral to coronavirus vaccine development. COVID-19, a performance from SARS-CoV-2 infection, has been spreading worldwide, with over 23.51 million verified cases and further than 810,000 losses as of August 25, 2020 (according to data from the World Health Organization). An effective vaccine is urgently demanded. Lin et al. reported on two non-replicating mRNA vaccines that render the receptor-binding sphere of the shaft protein and contagion-like patches (VLPs) of SARS-CoV-2; ongoing optimization of antigen sequences and evaluations of safety and efficacy are in progress. Moderna first introduced a seeker mRNA vaccine, mRNA-1273, for SARS-CoV-2 and commenced Phase I clinical trials for safety and immunogenicity assessment on March 16, 2020. This vaccine encodes the shaft (S) protein of SARS-CoV-2 in a stabilized prefusion form. According to interim data released on May 18, 2020, mRNA-1273 was set up to be generally safe and well-tolerated; two weeks after the alternate cure, indeed at a low vaccination cure of 25 μg, the situations of both binding antibodies and neutralizing antibodies in serum were similar to those observed in individuals who had recovered from COVID-19. A cooperative effort to develop a new mRNA vaccine targeting SARS-CoV-2 was blazoned by Sanofi Pasteur and Translate Bio on March 27, 2020. Pfizer and BioNTech reported positive issues from their ongoing phase I/II clinical trials of BNT162b1, which is a modified mRNA vaccine seeker designed using LNP and garbling the trimerized receptor list sphere of the SARS-CoV-2 S protein. The applicable cure situations for BNT162b1 were originally determined to be between 10 μg and 30 μg. After administering two boluses of 10 μg and 30 μg of BNT162b1, the mean titers of specific neutralizing antibodies increased by 1.8-fold and 2.8-fold, independently, compared to those from convalescent individuals [15].

mRNA Vaccines Targeting Cancer

The focus of mRNA cancer vaccines hinges on expressed antigens that elicit cellular immunity. There are two orders of excrescence antigens: excrescence-specific antigens (TSA), which are simply present on excrescence cells, and excrescence-associated antigens (TAA), which are set up on either normal or excrescence cells. An illustration of an mRNA cancer vaccine is the FixVac BNT111, being developed by BioNTech, which targets four carcinoma TAAs, including tyrosinase, carcinoma antigen family A3 (voodoo A3), New York esophageal scaled cell melanoma 1 (NY-ESO-1), and transmembrane phosphatase with tensin homology (TPTE). According to a preclinical study, BNT111 has been set up to evoke a strong antitumor vulnerable response in a phase ½ trial, where 75 of actors showed vulnerable responses against at least one of the four excrescence-associated antigens (TAAs) after entering a series of eight injections, with CD8 T cells playing a pivotal part in these T-cell responses. Other mRNA vaccine exemplifications include BNT112 and BNT113, which are substantiated vaccines acclimatized to the unique mutations present in each case's excrescence and render five prostate cancer-specific antigens (PAP, PSA, and three undisclosed antigens) and HPV16-deduced excrescence antigens (HPV16 E6 and E7 oncoproteins), independently. Also, BNT122 is a combination vaccine designed to render specific excrescence mutations along with a substantiated array of pre-manufactured non-mutated participated TAAs (BNT114), presently witnessing clinical trials to assess its safety, tolerability, and efficacy in treating different types of cancer. These different vaccine campaigners target a range of cancers, including carcinoma, bone cancer, pancreatic cancer, and others [15].

mRNA Vaccines Against Infectious Diseases

Vaccines against infectious pathogens have always been the most effective way to prevent and limit infectious diseases, a classic example of which is the complete eradication of the smallpox virus. Unfortunately, traditional strategies of vaccines, such as non-live freeze-dried vaccines and live attenuated vaccines, underperform against some chronic or recurrent pathogenic infections with a long duration of disease, such as AIDS and tuberculosis (TB). Traditional vaccines' lack of adequate speed, owing to the relatively slow process of development, would not be able to address outbreaks of virulent pathogens such as Zaire ebolavirus, Zika virus (ZIKV), and coronavirus. mRNA vaccines against infectious diseases have made promising accomplishments, and some products have entered human clinical trials. <en-us-grammar>Overall development steps of those vaccines are constructing the core antigen-encoding mRNA sequence optimized or combined based on selected antigen(s) from the target pathogen; trying and choosing a proper combination of mRNA construction type, adjuvants, carrier materials, and the route of administration; detecting in vivo expression of the encoded antigen and the level of elicited immune responses; and providing research and demonstrations of immune induction mechanisms.</en-us-grammar> Here we have reviewed some recently published promising studies related to mRNA vaccine application trials [16].

Advantages of mRNA vaccines in cancer treatment

- Generally well-permitted adverse goods are generally manageable and short-lived.
- No integration into the genome eliminates the eventuality for insertional mutagenesis.
- Non-infectious doesn't involve any pathogenic viral factors.
- Fluently degraded minimizes the threat of toxins.
- Stimulates both humoral and cellular immunity essential for initiating and maintaining antitumor responses.
- Quick and cost-effective product conducted in a lab-grounded and cell-free [14].

Challenges

- Insecurity
- Single-stranded and negatively charged
- Rapid declination
- Need strict cold-chain operation
- ingrain impunity
- Stimulate ingrained and adaptive vulnerable responses
- Lotentinial for out-target goods needed for protein-relief curatives
- Immunogenicity
- threat for autonomous responses
- Modulation needed [16].

Clinical Trials of mRNA Vaccines

mRNA vaccines have the potential to manage the spread of various life-threatening conditions, such as infectious diseases and cancer, and can also be employed in immunotherapies. However, the mRNA

vaccine field is predominantly focused on infectious diseases, with approximately 70% of ongoing trials directed at this area. The number of clinical trials utilizing mRNA vaccines has significantly increased in recent years as a result.

of the COVID-19 pandemic and the success of mRNA vaccine technology. The recent FDA approval of two rapid-response mRNA vaccines for COVID-19 represents a significant milestone that has opened the door for additional mRNA-based vaccines to enter clinical trials for various medical applications. mRNA vaccines targeting infectious diseases are typically administered through bolus injection, where they translate into antigens after being absorbed by both immune and non-immune cells. Numerous mRNA vaccine candidates have been submitted for clinical trials against infectious diseases and cancers, with the most notable examples outlined in the following. One infectious disease that surfaced as a global health emergency was the Zika virus outbreak in 2015. This infection led to symptoms ranging from mild to severe, such as fever and fatigue, which could escalate to fatal death during pregnancy. It has been established that immunization against an antigen (the prM-E protein) from any Zika virus strain could provide protection against all Zika virus infections since the disease is caused by a single serotype. Utilizing lipid-based nanocarriers to encapsulate modified mRNA encoding Zika virus structural genes presents a flexible platform for developing an mRNA-based Zika vaccine. The administration of a prime-boost vaccine consisting of modified mRNA encoding Zika prM-E genes, which produced virus-like particles, resulted in increased levels of Zika virus-neutralizing antibodies (nAbs) that protect both immunocompromised and immunocompetent mice. Consequently, the mRNA Zika vaccine administered induced protective antibody responses against the Zika virus. It has been reported that doses of 30 μg or 50 μg of the mRNA vaccine, comprising lipid nanoparticles loaded with prM-E mRNA, produced neutralizing antibodies at levels 50–100 times greater than those generated by traditional inactivated virus methods. By leveraging the mRNA platform as a Zika vaccine candidate, a strong neutralizing antibody response to the Zika virus was achieved, providing proof of concept for rapid protective measures against this infection. Despite the vaccine's effectiveness, it is considered poorly designed, as it potentially activates dengue viral infection through the creation of cross-reactive antibodies. A new Zika virus vaccine is currently in clinical trials, developed by Moderna, which incorporates a mutated fusion loop epitope within the E protein into the modified prM-E mRNA (mRNA1893). The immunization of mice with this mRNA-based vaccine demonstrated its ability to protect against the Zika virus without generating dengue-enhancing antibodies [17].

CONCLUSION

mRNA therapy marks a significant advancement in biomedical science, extending well beyond its initial application in vaccines. Its capability to guide cells in generating therapeutic proteins opens new avenues for tackling cancers, infectious diseases, and genetic disorders. This technology offers notable benefits, including accelerated development, versatility, and the promise of personalized treatment. However, challenges related to delivery efficiency, mRNA stability, and reactions from the immune system must be addressed before it can be widely implemented in clinical settings. Ongoing progress in nanotechnology, formulation science, and clinical studies will be vital for ensuring that mRNA-based therapeutics are both safe and accessible. Overall, mRNA therapy holds the potential to transform medicine by providing innovative, targeted, and patient-specific treatments that could significantly change the management of numerous life-threatening diseases in the future.

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