The m-RNA Based Therapies on The Different Diseases.

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Abstract: mRNA-based treatments are emerging as powerful tools for managing a wide range of diseases, including cancer, cardiovascular disorders, infections, and certain genetic conditions. These therapies work by delivering laboratory-designed messenger RNA into the body, allowing cells to temporarily produce specific proteins that support healing or trigger an immune response. Because the mRNA remains only for a short period and does not integrate into the patient's DNA, this approach is considered safe and highly adaptable. Initially, mRNA technology was mainly used for ex-vivo transfection of dendritic cells—key immune cells responsible for presenting antigens and activating immunity. Over time, improvements in delivery systems, such as lipid nanoparticles, and advances in mRNA design have significantly enhanced stability, efficiency, and therapeutic potential. Today, mRNA therapies are reshaping modern medicine by enabling precise protein expression and targeted immune modulation. Their flexibility makes them suitable for personalized treatments, rare disease management, and next-generation vaccine development. As research continues, mRNA technology is expected to play an increasingly important role in future clinical care and innovative drug development.

Keyword: m-RNA therapies, Cancer, auto immune disease, Genetic disorder, Crigler -Najjar syndrome**.**

1. INTRODUCTION

Messenger ribonucleic acid (mRNA) is a single-stranded molecule that carries genetic information from DNA in the nucleus to the cytoplasm, where it guides protein synthesis at the ribosomes. Around twenty-five years ago, researchers began exploring mRNA as a tool for anticancer vaccines, but its instability and rapid degradation initially limited its direct therapeutic use. Early work therefore focused on ex vivo transfection of dendritic cells, key antigen-presenting cells involved in immune activation [1].

Since the discovery of mRNA in 1960 [2]. major advances in mRNA design, modification, and delivery have positioned it as an important tool in genetic research. With next-generation sequencing (NGS), mRNA can be accurately analyzed, enabling the development of mRNA-based therapeutics that offer high biocompatibility, controlled dosing, transient expression, and minimal genomic integration risk [9].

The human genome contains nearly three billion nucleotides arranged into 23 chromosome pairs, and gene expression follows the central dogma of DNA–RNA–protein [7]. Therapeutic mRNA utilizes this natural process to produce proteins that prevent or treat disease. Its ability to achieve effective transcription and expression in cells, including skeletal muscle, demonstrates its potential for inducing immune responses. Overall, mRNA therapy leverages the molecule's capacity to direct the synthesis of almost any required protein in vitro or in vivo [8].

Structurally, mRNA therapeutics consist of two key components: the mRNA molecule and the lipid nanoparticle (LNP) carrier that enables its delivery into the cytoplasm. The mRNA strand contains a 5′ cap, 5′ UTR, open reading frame, 3′ UTR, and poly(A) tail, with the 5′ cap providing stability and supporting ribosome binding during translation [6]. Therapeutic mRNA delivers

genetic instructions to produce specific proteins, allowing treatments to replace or supplement defective proteins and achieve targeted biological effects. These therapies are often administered intravenously and can be rapidly designed, making them suitable for developing personalized cancer vaccines tailored to individual tumor profiles—a major step toward precision oncology [10]. mRNA technology is currently being explored for personalized cancer care, autoimmune and genetic diseases, protein replacement therapy, and infections such as influenza, HIV, and malaria. Studies also highlight applications in bone repair, lung diseases, and metabolic disorders [2]. Most therapeutic mRNA is produced through in vitro transcription using linearized DNA templates and RNA polymerases like T7, T3, or SP6 [3]. mRNA-LNP systems have also shown strong safety and immunomodulatory potential, particularly evident during the COVID-19 pandemic [4]. In This review highlights Overall, these advances demonstrate the broad therapeutic promise of mRNA platforms in modern vaccine development and drug discovery.

2.Mechanism Of m-RNA Therapies

mRNA therapeutics function by introducing a synthetic messenger RNA sequence into the body, allowing cells to produce a specific protein needed for treatment. This strategy relies on the cell's natural protein-synthesis machinery to generate the desired therapeutic effect. By delivering mRNA that is translated into defined proteins within targeted cells, the therapy can influence disease-related pathways and restore normal function. Through this mechanism, mRNA can replace missing or defective proteins, making it a promising option for protein-replacement therapy. Although most applications remain in preclinical stages, mRNA technology shows strong potential for treating many conditions, including cancer, neurological diseases, cardiovascular disorders, and metabolic abnormalities [5].

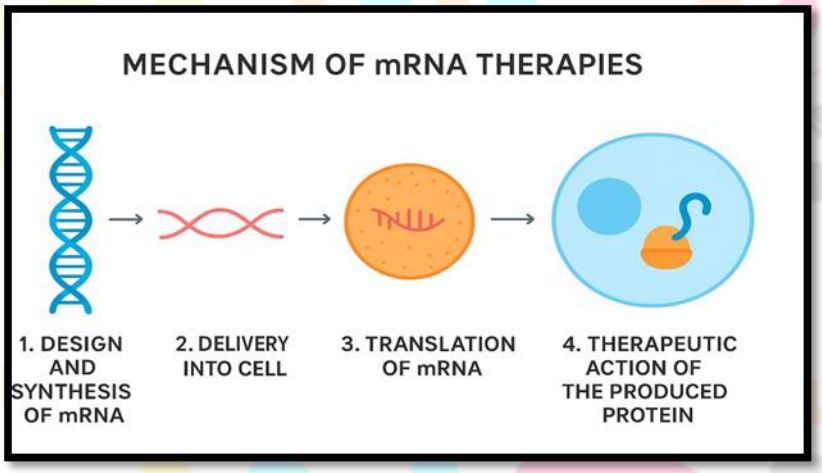

Fig No. 1: Mechanism Of m-RNA Therapies.

3.Application Of mRNA Therapies.

mRNA therapies are used in many medical areas, such as vaccines for infectious diseases and treatments for genetic disorders, cancer, and protein-deficiency conditions. Because mRNA can instruct cells to make specific proteins, it can either activate a strong immune response or replace missing proteins. This flexibility gives mRNA therapies clear advantages over many conventional treatments.

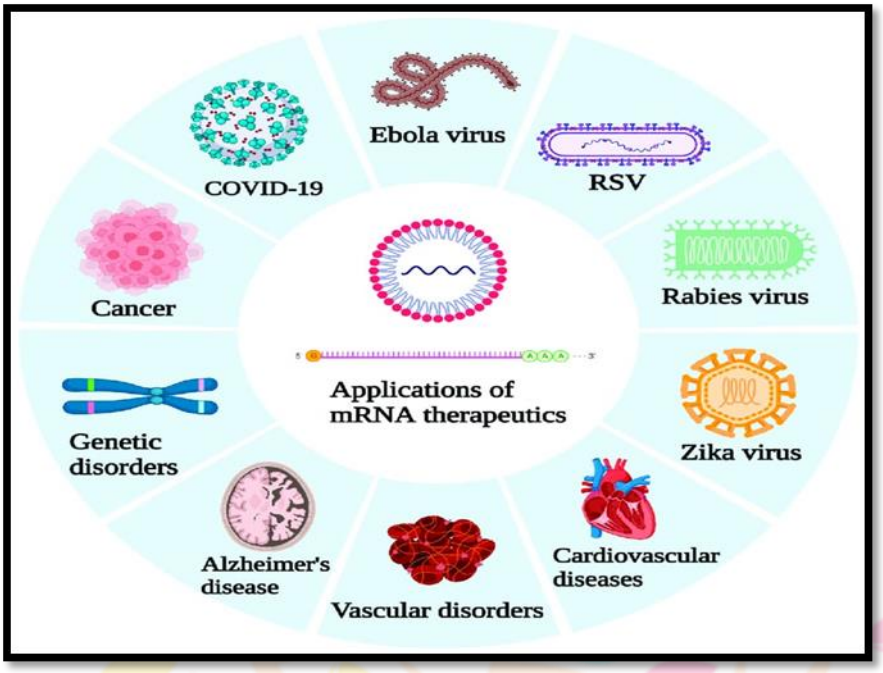

Fig No. 2: Application Of m-RNA Therapies

4. Advantage Of m-RNA Therapies.

A. Rapid development – mRNA can be designed quickly for fast responses to new diseases.

B. Strong immune activation – stimulates both antibody and T-cell responses.

C. No genomic integration – does not enter the nucleus or alter DNA.

D. Highly flexible – can be adapted to produce many therapeutic proteins.

E. Efficient production – uses a common platform, reducing time and cost.

F. Transient expression – temporary protein production lowers long-term risks.

G. Broad applications – effective for infections, cancer, genetic and autoimmune diseases.

5. m-RNA Therapies for the Treatment of Cancer

Cancer is a disease characterized by uncontrolled and abnormal cell growth in the body. According to global cancer statistics, an estimated 10.3 million people died from cancer in 2020, and about 19.3 million new cases were reported worldwide [3]. Cancer typically progresses through four stages, during which abnormal cells grow, form Tumors, and may spread to other parts of the body. In cancer therapy, mRNA can be used to produce proteins that help train the immune system to recognize and destroy cancer cells. Over the last two decades, advances in mRNA technology have opened new possibilities for developing innovative treatments and improving existing approaches. Its flexibility allows support for multiple anti-cancer strategies, including tumour antigens, monoclonal antibodies, and immunomodulators [3]. Although some cancer patients naturally develop T-cell responses, these cells are often suppressed by the tumour and its microenvironment, reducing their effectiveness [1]. With its adaptable design, mRNA technology can contribute to a wide range of therapeutic options and also supports precision oncology by enabling treatments tailored to individual patient profiles [3]. mRNA cancer therapies work by delivering synthetic mRNA into the body, allowing a patient's own cells to produce tumor-specific antigens. These antigens help trigger a focused immune response. After administration—usually through lipid nanoparticles—the mRNA enters cells, especially dendritic cells, which translate it into antigen proteins. These antigens are then displayed to T cells, enabling them to identify and destroy cancer cells carrying the same markers. This process creates a targeted and personalized immune attack against the tumor.

5.1. Creation of Vaccine for Cancer Diseases based on mRNA.

mRNA vaccine technology has become a major advancement in modern medicine. Instead of using whole pathogens, mRNA vaccines deliver genetic

instructions that prompt host cells to make antigenic proteins, generating a protective immune response. For more than 25 years, mRNA has been explored as a tool for anti-cancer vaccines, and today it is regarded as an effective platform for inducing strong immune activity against Tumors [1]. Therapeutic vaccination remains the most established mRNA-based anti-tumor strategy, using ex vivo or in vivo loading of antigen-presenting cells—mainly dendritic cells—with whole tumor mRNA or synthetic mRNA encoding tumor-associated and tumor-specific antigens [3]. Early development faced issues with instability and low expression, and unmodified mRNA triggered innate immunity through TLR3, TLR7, TLR8, and TLR9.

5.1.2: Personalized cancer vaccines: mRNA provides essential information for designing individualized cancer vaccines, and customized neoantigen vaccines have shown clinical benefits. A key milestone is the phase III trial of mRNA-4157 with pembrolizumab for melanoma. Current goals focus on improving delivery systems and advancing personalized mRNA cancer vaccines.

5.1.3: CAR-T cell therapy: CAR-T technology engineers' patient-derived T cells to express synthetic receptors targeting tumor antigens without relying on MHC presentation. This approach has achieved high remission rates, reaching up to 80% in hematologic cancers.

6. m-RNA Therapies for the treatment Of Autoimmune Disease.

Autoimmune diseases occur when the immune system mistakenly targets the body's own healthy cells, tissues, or organs. Instead of defending against infections, the immune system fails to recognize what belongs to the body, leading to abnormal responses that cause inflammation, tissue injury, and reduced organ function. These conditions often arise from a combination of genetic susceptibility and environmental triggers such as viruses or certain chemicals. Autoimmune diseases (ADs) are a growing health challenge caused by the immune system attacking the body's own tissues. [3] Current treatments are mostly non-specific and can lead to major side effects, highlighting the need for more targeted and early interventions. [12] Several mRNA-based strategies have shown encouraging preclinical results, including vaccines using self-antigens without co-stimulation, approaches that remove autoreactive lymphocytes, methods to boost regulatory T-cell activity, and delivery of anti-inflammatory cytokines to reduce inflammation [3]. In autoimmune diseases, mRNA therapies work by producing proteins that reduce excessive immune activity or by acting as vaccines that promote tolerance to self-antigens. These approaches can deliver mRNA that helps neutralize autoantibodies, regulate immune cells, or enhance regulatory T-cell (Treg) function. mRNA vaccines targeting autoantigens aim to retrain the immune system to recognize self-proteins safely, lowering harmful autoimmune responses.

6.1: Creation of vaccine for autoimmune diseases based on mRNA.

The U.S. Code (26 USC § 4132(a)(2)) defines a vaccine as any preparation used to prevent disease, and under this definition, products that stimulate immune responses to manage autoimmune disorders may also be considered vaccines [13]. The success of COVID-19 mRNA vaccines has accelerated the use of this technology in other fields, with several candidates now in phase 1–3 trials, especially for respiratory pathogens. Current mRNA research is being tailored for patients with autoimmune inflammatory rheumatic diseases (AIIRD) [14]. Individuals with AIRD receiving glucocorticoids or other immunosuppressants face a higher risk of severe COVID-19, making effective prevention essential [15]. The use of mRNA in autoimmune diseases includes the development of anti-idiotypic mRNA vaccines, which are designed to regulate harmful autoantibodies and help restore immune balance. Anti-idiotypic vaccines use Ab2 antibodies that mimic the original antigen, stimulating Ab3 antibodies against the true target. This approach is useful when natural antigens are scarce or difficult to isolate and has applications in infectious diseases, cancer, and autoimmune disorders. These antibodies can neutralize harmful autoantibodies by binding to their idiotype, a concept based on the idiotypic network theory. Their ability to block autoreactive antibodies offers a promising immunotherapy with potentially longer-lasting benefits and fewer side effects [13].

7. m-RNA Therapies for the treatment of Genetic Disorder

Genetic disorders are health conditions caused by changes in DNA, including single-gene mutations, chromosomal defects, or interactions between genetic and environmental factors. These alterations disrupt normal biological processes and may appear at birth or develop later in life. Human genetic information is stored in 23 chromosome

pairs, containing about 25,000 protein-coding genes [16]. mRNA is emerging as a promising therapeutic platform, with research and clinical trials focusing on vaccines, protein replacement, and treatments for genetic disorders. Advances in mRNA synthesis and delivery have supported its progress, though effective delivery systems remain a major challenge. mRNA therapy offers a safer alternative for monogenic diseases compared with gene therapy, which can pose risks due to permanent genetic modification. Instead, mRNA enables temporary production of therapeutic proteins, providing a balance between long-lasting gene therapy and short-acting protein drugs. It can also encode genome-editing nucleases like ZFNs, TALENs, and Cas9 for limited activity, reducing unintended genetic changes [12, 17].

Since early studies in the 1990s, improvements in mRNA design and intracellular delivery have accelerated its development as a treatment platform. Optimizing stability, translation efficiency, and immune activation is essential for therapeutic use [17]. A major advantage over gene therapy is that mRNA does not integrate into the genome, lowering risks such as mutagenesis. Because monogenic disorders often require repeated dosing, mRNA also avoids the limitations of viral vectors, which can trigger immune responses that block future treatments [12]. mRNA therapies work or treat genetic disorders by supplying cells with synthetic mRNA that instructs them to make the functional protein missing or defective due to a mutation. Instead of altering DNA, it provides a temporary blueprint that helps restore normal cellular function. In conditions like cystic fibrosis or haemophilia, this approach can enable cells to produce the protein that the mutated gene fails to generate.

7.1 Creation of Vaccine for Genetic Disorder based on mRNA.

mRNA therapy can help replace or supplement missing or faulty proteins in genetic disorders such as haemophilia, cystic fibrosis, and muscular dystrophy [18]. Haemophilia results from defects in clotting-factor genes, cystic fibrosis from CFTR gene mutations, and muscular dystrophy from dystrophin gene errors. Delivering mRNA that encodes the needed proteins to affected tissues offers a way to restore normal function [18].

8. m-RNA Therapies for the treatment of Infection Diseases.

The 1918 influenza pandemic, later called the Spanish flu, spread rapidly during the final phase of World War I, infecting over a quarter of the world's population and causing an estimated 30–100 million deaths—surpassing the combined toll of both World Wars [19]. Today, more than 1,400 infectious agents are linked to human disease, with around 347 posing ongoing clinical concern and generating essential diagnostic and epidemiological data for healthcare use [20]. Despite past successes, global health systems continue to face major challenges from emerging and re-emerging threats such as Ebola, Zika, dengue, MERS, SARS, and influenza, all of which carry significant public-health and socio-economic risks [19] mRNA technology offers strong potential against infectious diseases because it can be rapidly redesigned to target new variants, making it especially valuable during fast-evolving pandemics. Once the genetic sequence of a new pathogen is known, mRNA vaccines can be created and produced within weeks. The field has also expanded to include therapeutic vaccines, such as the Epstein–Barr virus candidate mRNA-1189 (NCT05164094), which contains four mRNAs encoding proteins needed
for viral entry and aims to prevent infectious mononucleosis. Its Phase I clinical trial was

Table No.1: mRNA Therapies On infection diseases.

expected to finish in 2023 [3]. The mRNA therapies work by infectious diseases, mainly through vaccines—delivers synthetic mRNA
that encodes a pathogen-specific antigen. After cells translate this mRNA into protein, the immune system identifies it as foreign and activates both antibody and T-cell responses, preparing the body to fight the real infection. A major advantage is the ability to design and produce mRNA vaccines quickly once a pathogen's genetic sequence is known.

Sr. No	Infection Diseases	mRNA Strategy	Target Antigen	Mechanism Of Action	Stage/ Example
1.	COVID 19(SARS -Cov -2	mRNA vaccine	Spike(S)gly coprotein	mRNA encode (s) protein host cell produce antigen immune system generated neutralization antibodies Tcell response	Approved Pfizer BioNTech (BNT162b2), moderna and (mRNA)
2.	Influenza	mRNA Vaccine	Hemogglitinin (HA) Neuraminidase (NA)	Stimulates antibody and T-cell responses against flu surface proteins, providing protection across multiple strains	Clinical trials of modern mRNA vaccines (mRNA-1010, mRNA-1020).
3.	Rabies	mRNA vaccine	Glycoproteins (G)	Generates virus-neutralizing antibodies and blocks CNS infection.	Phase-1 curevac (CU7202)
4.	Zika Virus	mRNA vaccine	Envelope (E) protein	Antibody-mediated neutralization blocks mosquito-borne infection and maternal-fetal transmission."	Early clinical trial moderna (mRNA-1893)
5.	Respiratory Syncytial virus (RSV)	m-RNA vaccine	Fusion glycoprotein (Prefusion form)	Antibodies prevent viral fusion with host cells."	Approved (2023) moderna (m-RNA-1345)
6.	HIV	mRNA vaccine (Immune therapy)	Enu and Gap Protein bnAbs via mRNA	Trains the immune system to produce broad neutralizing antibodies and cytotoxic T-cells.	Phase-1 moderna IVAI (mRNA)
7.	Cytomergalo Virus (CMS)	Multivalent mRNA Vaccine	gB Protin+pentameric (gH/g4 UL128/130/131)	Induces neutralizing antibodies that block viral entry into cells	Phase 2 moderna (mRNA-1647)
8.	Tuberculous	mRNA Vaccine	Ag85B, ESAT-6 fusion antigen	Induces Th1 immunity, activating macrophages to kill bacteria."	Preclinical BioNTech Collaborate ion
9.	Malaria (plasmodium falciparum)	mRNA Vaccine	Circumporozoite protein (CSP)	"Generates antibodies that block sporozoite entry into liver cells."	Preclinical BioNTech
10.	Epstein Barr virus (EBS)	mRNA vaccine	Gp350, gh/glgp42	Induces antibodies that block B-cell and epithelial infection."	Phase-1 moderna (mRNA)
11.	Herpes simplex Virus (HSV)	mRNA vaccine	Glycoproteins gD2, gc2, gE2	Antibody and T-cell responses prevent viral latency and reactivation."	Preclinical moderna
12.	Lyme diseases	mRNA vaccine	Outer surface protein	Blocks Borrelia transmission from tick to human.	Preclinical moderna

8.1 Creation of Vaccine for Infection Diseases based on mRNA.

Vaccines are essential for protecting humans from infectious diseases and have helped control or eliminate illnesses like smallpox and polio. Traditional vaccines were produced through chemical or heat inactivation or by using live attenuated pathogens grown in cells or animals [21].

In the past two decades, mRNA technology has become a major focus for developing prophylactic vaccines. Advances in mRNA modification,

stability, and delivery have enabled fully synthetic vaccines that can be designed and produced rapidly in response to emerging infections [22].
Compared with traditional platforms, mRNA vaccines are safer because they are non-infectious and do not integrate into the human genome [21]. They also offer advantages over plasmid DNA and viral vector vaccines by avoiding genomic integration, enabling direct antigen production in the cytoplasm, and allowing fast, synthetic manufacturing once the target sequence is known [22]
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9. m-RNA Therapies for the treatment of Influenza.

Influenza is caused by viruses from the Orthomyxoviridae family, which are negative-sense, single-stranded RNA pathogens [22]. This virus leads to a highly contagious respiratory illness that can range from mild symptoms to severe complications such as pneumonia, especially in vulnerable groups.
mRNA-based approaches are being explored to prevent and treat influenza by encoding viral antigens that train the immune system or by targeting harmful inflammatory responses. These mRNA therapies work or offer rapid production and easier adaptation to new strains, with ongoing research focusing on vaccines that provide broad and long-lasting protection. mRNA therapy for influenza delivers coded instructions that allow host cells to make harmless viral proteins like hemagglutinin (HA). These proteins trigger immune responses from T cells and B cells. The mRNA is protected inside lipid nanoparticles, which help it enter cells. Once the proteins are produced, the immune system learns to recognize them, creating immunity against future influenza infection.

9.Creation of Vaccine for Influenza Diseases based on mRNA.

Human influenza A and B viruses cause major respiratory illness similar to SARS-CoV-2, and the 1918 pandemic, which caused over 40 million deaths, shows the need for effective vaccines. Currently, inactivated, live attenuated, and recombinant HA-based vaccines are used in clinics [21]. The first human trial of an mRNA influenza vaccine used an LNP-formulated, nucleoside-modified mRNA encoding the H10N8 HA antigen (NCT03076385) [22]. Early mRNA vaccine candidates, mRNA-1440 (NCT03076385) and mRNA-1851 (NCT03345043), encoded full-length HA and were well tolerated in studies, producing strong antibody responses but limited T-cell activity, suggesting HA may not be an ideal T-cell target [3]. Traditional FDA-approved influenza vaccines require at least six months to develop during a pandemic, leaving a window of vulnerability [22].

10. m-RNA Therapies for the treatment of HIV

HIV stands for Human Immunodeficiency Virus and remains a major global concern, affecting about 38 million people and causing roughly 1.7 million new infections in 2019 [23].
H: The virus infects only humans and spreads from person to person, not through animals or insect bites.
I: It weakens the immune system, reducing the body's ability to fight infections.
V: It is a small virus that stays inactive outside the body but becomes active once inside a human host mRNA-based therapy is being investigated as a new approach for HIV treatment by stimulating immune defense or producing therapeutic proteins. mRNA vaccines are being developed to encode HIV antigens that help the immune system target the virus. Experimental methods also use mRNA to generate broadly neutralizing antibodies (bNAbs) capable of blocking different HIV strains. This approach allows fast development and avoids genome integration, but major challenges include HIV's rapid mutation rate and achieving long-lasting protection. The m-RNA therapies work to the once delivered into host cells, the mRNA is translated into viral proteins that are displayed on the cell surface through MHC molecules. These antigens activate immune responses, including antibody production, apoptosis of infected cells, and the development of memory cells, while the mRNA is naturally broken down by nucleases due to its short lifespan [25].

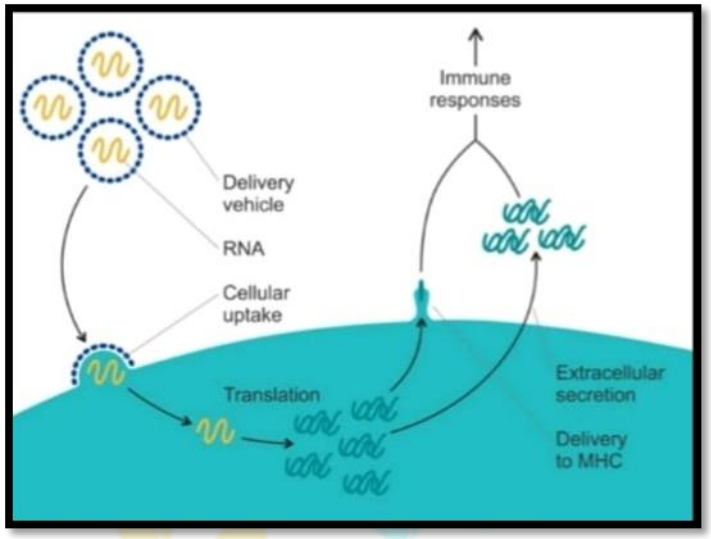

Fig No .3 Working Mechanism of m-RNA based Vaccine.

The mRNA encoding a viral antigen is enclosed in lipid nanoparticles (LNPs) to support cellular uptake. Inside the cell, it is translated into the target protein, which is presented on MHC molecules or released extracellularly, triggering immune cell activation.

10.Creation of Vaccine for HIV Diseases based on mRNA.

Developing a universal HIV vaccine remains difficult because the virus shows high genetic diversity, with strains differing by about 20% in conserved proteins and up to 35% in the Env protein, making broad protection hard to achieve [23]. Most vaccine efforts focus on inducing antibodies that block viral entry, mainly through protein subunit vaccines designed to trigger strong and durable broadly neutralizing antibodies (bnAbs) against multiple Env epitopes. Some studies indicate that pairing bnAb-based vaccination with $CD8^+$ T-cell–stimulating immunogens may reduce the bnAb levels needed for protection [26].

10(C1): Induction of Broadly Neutralizing Antibodies:

HIV-neutralizing antibodies prevent the virus from binding and fusing with $CD4^+$ cells. Although less potent, non-neutralizing Env-

specific antibodies can still help through Fc-mediated actions such as ADCC [26].

10(C2): Activation of $CD8^+$ T-Cell Immunity:

$CD8^+$ CTLs are essential for controlling HIV, as shown by their rise during early infection, viral escape mutations, and slower disease progression linked to protective HLA class I alleles. Animal studies also show that removing $CD8^+$ T cells cause rapid viral rebound, while CMV-based SIV vaccines can clear early infection. Although CTLs cannot entirely prevent HIV, vaccination aims to create long-lasting memory CTLs that eliminate newly infected cells and restrict viral spread [26].

11. m-RNA Therapies for the treatment of COVID

COVID-19, caused by SARS-CoV-2, was first detected in Wuhan, China in December 2019 and quickly spread worldwide, leading the WHO to declare it a Public Health Emergency on January 30, 2020 and a pandemic on March 11, 2020 [26]. SARS-CoV-2 is an enveloped, positive-sense, single-stranded RNA virus of the Betacoronavirus genus. By February 9, 2022, the disease had affected 227 countries, with over 399 million cases and about 5.75 million deaths. The genome of the Wuhan-Hu-1 strain (GenBank: MN908947) consists of 29,881 nucleotides and encodes 9,860 amino acids, forming 16 nonstructural proteins, 9 accessory proteins, and 4 structural proteins [27]. mRNA technology enabled the rapid development of COVID-19 vaccines by using modified messenger RNA to instruct cells to make a harmless viral protein. This protein triggers an immune response that helps the body recognize and fight SARS-CoV-2 in future infections, demonstrating the speed and potential of mRNA platforms for global health emergencies. mRNA

Therapies work on COVID-19 mRNA vaccines use synthetic mRNA to instruct cells to make a harmless spike-protein fragment, which triggers antibody and T-cell responses. The mRNA, delivered in lipid nanoparticles, never enters the nucleus and is quickly degraded. This immune training allows the body to rapidly recognize and neutralize SARS-CoV-2 if exposed, preventing severe infection.

11.1 Creation of Vaccine for COVID-19based on mRNA.

mRNA vaccines offer major advantages, including rapid design, scalable production, and strong potency. Although previously tested for cancer, their capabilities became clear during COVID-19, when mRNA candidates quickly entered clinical trials and gained accelerated approval, supported by decades of prior research [28]. Dosage comparisons show Moderna's mRNA-1273 uses 100 µg and Pfizer's BNT162b2 uses 30 µg, while the sa-RNA vaccine ARCT-154 requires only 5 µg, suggesting effective single-dose potential [3]. Progress in delivery systems—from concerns about liposome toxicity to the successful use of LNP-formulated siRNA—led to highly efficient ionizable LNPs for mRNA vaccines. The combination of LNPs with modified mRNA created a reliable vaccine platform with improved stability, immune activation, safety, and efficacy [28].

12. m-RNA Therapies for the treatment of Crigler-Najjar Syndrome

Crigler–Najjar syndrome (CNS) is a rare autosomal recessive disorder characterized by very high levels of unconjugated bilirubin, causing non-haemolytic jaundice and risking neurological injury when bilirubin crosses the blood–brain barrier. There are two type of Crigler-Najjar Syndrome type-1 it also knows as CNS-1 they severe from nearly complete absence of the UGT enzyme and a high risk of brain damage and death in childhood, often requiring liver transplantation for survival and more severe than CNS-2 and it also treats that phototherapy and later LTX. Type-2 Crigler-Najjar syndrome is also known as aa CNS-2 type 2 (CN2), a milder form with a partial deficiency of the enzyme, where phenobarbital can help reduce bilirubin levels and prevent neurological complications and less severe than CNS-1and also treats phenobarbital. It results from mutations in the UGT1A1 gene, leading to deficiency of the UGT enzyme required for bilirubin metabolism. Affected individuals must inherit the mutated gene from both parents. Current treatments include phototherapy, phenobarbital, and liver transplantation, with options such as liver cell transplantation and gene therapy also being explored [29]. A mRNA therapy called mRNA-3351 is being developed for Crigler–Najjar syndrome (CNS) to correct the UGT1A1 gene defect that prevents bilirubin clearance. The treatment uses lipid nanoparticles (LNPs) to deliver modified mRNA encoding the UGT1A1 enzyme directly to liver cells. After uptake, the mRNA guides the cells to produce the missing enzyme, restoring bilirubin processing and lowering toxic levels. Preclinical studies have shown promising results in animal models. mRNA therapies for Crigler–Najjar syndrome works by giving liver cells the instructions to make the missing UGT1A1 enzyme. In this disorder, mutations in the UGT1A1 gene prevent normal bilirubin conjugation, causing toxic buildup that leads to severe jaundice and risk of brain damage. The treatment uses LNP-packaged mRNA to deliver the code for UGT1A1 directly to the liver. Once inside the cells, the mRNA is translated into functional enzyme, restoring bilirubin conjugation and helping the body clear excess bilirubin, reducing life-threatening symptoms.

12.1 Creation of Vaccine for Crigler Najjar Syndrome based on mRNA. mRNA therapy for Crigler–Najjar syndrome is progressing from early research to clinical testing, with groups like Moderna and partner organizations aiming to bring new options to patients with this ultra-rare disorder. Current treatments are limited, but mRNA offers a way to temporarily replace the missing enzyme without the risks of gene therapy or liver transplantation. Because mRNA does not integrate into DNA, it can be given repeatedly with fewer long-term immune concerns, though ongoing dosing is needed to maintain its therapeutic effect.

13.Future Perspective of m-RNA therapies. Advances in nanoparticles, chemical modifications, and targeted delivery are improving mRNA stability, efficiency, and safety. Integrating mRNA with CRISPR, cell therapy, and AI-powered drug design will greatly expand its future applications, despite challenges like immune reactions, large-scale production, and long-term safety.

1. Next-generation vaccines: Universal flu, HIV vaccines, and heat-stable formulations.
2. Cancer treatment: Personalized mRNA cancer vaccines becoming routine.

3. Rare diseases: Broader use for enzyme and metabolic disorders.
4. Regenerative medicine: mRNA-driven tissue and organ repair.
5. Lower production cost: Improved technologies enabling affordable mass manufacturing.
6. Global access: Wider use in developing countries as storage issues are resolved.

Summary: mRNA-based therapies are transforming modern medicine by delivering genetic instructions that help the body produce therapeutic proteins. Their success was highlighted by the rapid creation of COVID-19 vaccines. Beyond infectious diseases, showing strong potential in cancer immunotherapy, rare genetic disorders, and autoimmune conditions. The molecule's design—consisting of the 5′ cap, UTRs, coding region, and poly(A) tail—supports its stability and protein production. Global research is expanding quickly, with more than 150 clinical trials investigating mRNA applications in cancer, infectious diseases, and genetic medicine.

Conclusion: mRNA-based therapies are revolutionizing medicine by using the body's own protein-making machinery to prevent and treat diseases. From COVID-19 vaccines to cancer and rare genetic disorders, these therapies show great promise. While challenges like instability, delivery, and cost remain, advances in formulation and manufacturing are expanding their potential. Their adaptability and personalized approach position mRNA therapies as key players in the future of medicine.

Reference:

1.Sandra Van Lint, Dries Renmans, The ReNAissanCe of mRNA-based cancer therapy Expert Rev,2014. Vaccines Early online, 1–17.

2. Mudassir Khan, Messenger RNA (mRNA) based therapeutics in transforming cardiovascular care: Progress, regulatory challenges and future perspectives, 2025 Journal of Pharmacological Research 218 (2025) 107847, 1043-6618

3. Rohan Deyhimfar, The clinical impact of mRNA therapeutics in the treatment of cancers, infections, genetic disorders, and autoimmune diseases. Journal homepage: www.cell.com/heliyon 10 ,2024, e26971, 1-28

4. Rose Razavi, Harnessing mRNA- lipid nanoparticles as innovative therapies for auto immune diseases, 2025 Journal of molecular therapy: method and clinical development Vol 33, 1-22.

5.Sora Son and Kyari Lee, Development of m-RNA Vaccine /Therapeutic and Their Delivery System. Molecules and Cell 2023: 46(1): 41-47
6.Pedro Berranodo, Messenger RNA therapy for rare genetic metabolic diseases guts first published as 10.1136/ gutjnl- 22 February 2019, Vol 68, e7 1323-1330.

7. Ming- Jen-Lee, Recent advances in RNA therapy and its carries to treat the single- gene neurological disorder. Biomedicine 2022, Journal of MDPI VOL 10, 158.https: 11doi.org/ 10.3390/biomedicine 10010158.1-22

8. Shugang Qin, Xiaoshan Tang, Xiangrong Song, mRNA- based therapeutics: powerful and versatile tool to combat disesaes single transduction and Targeted therapy 2022 7:166.
9.Guobo Shen, mRNA therapies: Pioneering a new era in rare genetic diseases treatment journal of controlled releases 369(2024),696-721.

10. Ruhui Yao, Recent progress in mRNA cancer vaccine Human vaccine and Immunotherapeutic 2024, VOL 20, NO 1, 2307187, 1-22.

11.Young- Kook Kim, RNA therapy: rich history, various applications and unlimited, future prospects, Experimental & Molecular Medicine (2022) 54:455–465

12.Lars Fugger, Challenges, Prograss and Prospects of Developing Therapies to Treat Auto immune diseases, cell 181, April 2, 2020,03.007, 63-80

13.Sarfaraz K. Niazi, Anti idiotypic mRNA vaccine to treat autoimmune disorders. Vaccine 2024, Journal of MDPI,12,9. https://doi.org/10.3390/ vaccines12010009 ,1-18.

14.Jin Kyun Park, E what rheumatologist need to know about mRNA vaccine: current status and future of mRNA vaccine in autoimmune inflammatory rheumatic diseases 2024 ;83:687-695.

15.Yasuhiro Kato, Efficacy and risk of mRNA vaccination in patients with autoimmune

inflammatory rheumatic diseases. Kato et al Inflammation and regeneration, 2023 43:1, 1-6.

16. Tatjana Michel, Next- Generation Therapeutics: mRNA as a novel therapeutics option for single gen disorder.

17.Piotr S. Kowalski, Delivering the Messenger: Advances in technologies for therapeutic mRNA delivery, 4 April 2019, Molecular Therapy Vol.27 No.

18.Nojound Al Fayez, Recent Advancement in mRNA vaccine Development and Application. Journal of multidisciplinary Digital Publishing Institute of Pharmaceutics 2023, 15, 1972. https:// doi.org 1972. https:// doi.org/10.3390/ pharmaceutics15071972, 1-24.

19. David E. Bloom and Daniel Cadarette, Infection Diseases threats in the twenty first century: strengthening the global response. March 2019, Vol 10, doi: 10.3389/fimmu.2019.00549, 1-12.

20.Simon l. Hay, Global mapping of infection disease 2025. (Rstb. Royalsocietypublishing.org),368:20120250

21.Nikita, The Development of mRNA vaccine for Infection Diseases: Recent Updates 2021, ISSN: 1178-6973(online) Journal homepage: www. Tandfonline.com/ journals/ didr20.5271-5285.

22.Giulietta Maruggi, mRNA as a Transformative Technology for Vaccine Development to Control Infection Diseases. Molecular Therapy Vol. 27 (4) April 2019, The American Society of Gene and cell therapy,757-772.

23.Jias Kim, current approaches to HIV vaccine development: a narrative review, Kim Jetal Journal of the international AIDS Society 2021, 24 (S7): e25793.

24.Sankalp Chaudhary, A Review ON: HIV AIDS Indian J. Pharma. Biol. Res ,2016 CODEN(USA): IJPB07, ISSN: 2320-9267, Indian Journal of Pharmaceutics and Biological Research (IJPBR),69-73.

25.Andra Fortner, Octavian Bucur: mRNA-based vaccine technology for HIV, 2022 Discoveries Journals, e150. DOI: 10.15190/d.2022.9,1-16

26.Zekun Mu, HIV mRNA vaccines- Progress and Future Paths, Vaccines 2021, 9,134. Journal of MDPI, https:/ / doi.org / 10.3390 / vaccines 9020134, 1-22.

27.Enyue Fang, Advances in COVID-19 mRNA vaccine development, published online: 23 March 2022. 7:94(single Transduction and Targeted Therapy) www.nature.com/ sigtrans.

28.Gabor Tamas Szabo, COVID -19 mRNA vaccines: Platforms and current development 2022, Molecular Therapy Vol 30,1850-1868.

29. Vanessa Sambati, Therapeutic Options for Crigler–Najjar Syndrome: A Scoping Review, Int. J. Mol. Sci. 2024, 25, 11006, International of molecular science.