

# Evaluation of Application Value of mRNA Vaccines

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**Abstract.** With the prevalence of various diseases, there are many newly developed drugs and treatment methods. Vaccine is one of the widely used methods to prevent and treat some diseases including some infectious diseases and cancer. These days, there is a promising research field that has significant therapeutic benefits called messenger RNA vaccine (mRNA). mRNA vaccine has a prominent treatment efficacy which uses mRNA to trigger the immune response of the human body. Currently, the development of the mRNA vaccine has already reached many aspects, especially in treating COVID-19 and pancreatic cancer. At present, although mRNA vaccines have significant advantages over other vaccines, there are still some gaps in their side effects and development prospects. This review summarizes the current application of the mRNA vaccine and evaluates its efficacy and future development in order to have a comprehensive understanding of the current situation and a clear plan for future research and how to solve some tough issues.

**Keywords:** mRNA vaccine; COVID-19; Pancreatic cancer; side effects; development.

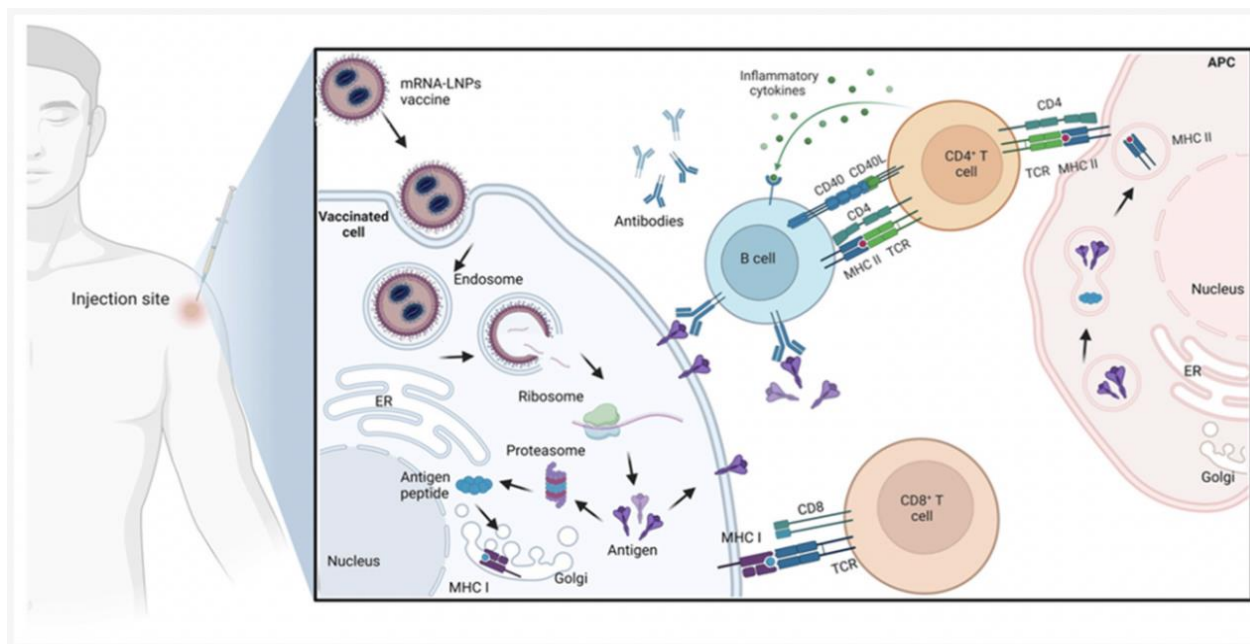
## 1. Introduction

A vaccine is a biological procedure that has the potential to initiate active acquired immunity against a specific infectious disease or cancer. Typically, vaccines include just the surface protein of pathogens or their weakened or dead versions. They trigger the immune system to react to these microorganisms or surface proteins when they are introduced to the human body. Consequently, when humans encounter this toxin a second time in the future, it will further attack them. [1]. Numerous vaccinations have been developed in recent years, such as live-attenuated vaccines, inactivated vaccines, and genetic vaccines such as messenger RNA (mRNA), DNA, and viral vector vaccines. Among them, the mRNA vaccine has been particularly prominent recently, mRNA vaccine is one newly developed vaccine that uses mRNA to trigger the immune response of cells. Antigen-encoding mRNA molecules are delivered by the vaccine to immune cells, which are used to set a protein produced by some pathogens or cancerous cells. Then the immune system will respond with these proteins by activating the adaptive immune response which will help to recognize and destroy the pathogens and cancer cells [2]. Compared to the traditional vaccine, it is not necessary for the mRNA vaccination to generate a large number of pathogens. As a result, it lowers the chance of viral outbreaks. Furthermore, mRNA vaccines are produced at a faster and more efficient pace than conventional vaccinations. The capacity of mRNA vaccines to stimulate humoral and cellular immunity—because the antigens are synthesised inside the cell—is an additional biological advantage [3]. In contrast to DNA vaccines, mRNA does not require entry into the cell nucleus since it translates only in the cytoplasm, preventing the integration of the host genome and mRNA [4]. Recently, the mRNA vaccine was created for cancer, immunotherapy, genetic abnormalities, infectious diseases, and other conditions for both therapeutic and preventive uses [5]. The research on mRNA vaccine is still in the development stage, there are still some side effects that have not been well controlled, therefore, this kind of vaccine still has a lot of room for tumor treatment. This review is mainly based on current data and new research on mRNA to summarize and evaluate the application and future development of mRNA vaccines.

## 2. Mechanism of mRNA vaccines

mRNA vaccine is a newly developed and promising way to prevent and treat some diseases. The mRNA vaccination stimulates the immune system by introducing a single coded RNA sequence of

the targeted pathogen into the human body [6]. As shown in figure 1, Individuals will pick a single antigen and then accurately produce its mRNA outside of their bodies. The encoded antigen has to be placed into a DNA template in order for the mRNA to be transcribed in vitro and used to make mRNA vaccines [7]. Following introduction of the produced mRNA vaccine, the vaccine uses the host cell's protein machinery to establish an environment conducive to viral infection. Subsequently, the mRNA is transformed into a particular antigen, which triggers a strong humoral and cellular immune response [6]. Additionally, mRNA is transiently active and not integrated into the genome, therefore, it is less dangerous than viral vectors and DNA.



**Fig. 1** The mechanism of mRNA vaccine [8]

To properly and efficiently deliver and operate in vivo, a complete system of delivery is required for mRNA in order to both cross the cell membrane and stop nucleic acid breakdown. Among the most practical methods of introducing mRNA into the human body are lipid nanoparticles. A liposome is a kind of vesicle that possesses the elements of both a cell membrane and a phospholipid bilayer. As a result, liposomes may pass through the membrane while transporting certain materials. The mRNA is shielded from biological and hazardous surroundings by the liposome's outer coat, which also gives them a stable environment in which to perform their role. Furthermore, the liposome is easily broken down and expelled from the body, therefore it has little effect on the in vivo environment.[9].

One of the most potent antigen-presenting cells is the dendritic cell (DC), which may trigger antigen-specific immune responses in lymphoid tissues upon sensing pathogenic pathogens. After introducing the mRNA vaccine, these mRNA fragments will be engulfed by dendritic cells through phagocytosis. Then the viral antigens that the mRNA encodes are produced by dendritic cells using ribosomes to decode the mRNA. When the viral antigens are created by the host cells, the dendritic cells have already been activated. Once activated, the dendritic cell will move to the lymph node to carry out the next step of the immune response. The T-cell and B-cell will produce a huge number of antibodies to target the specific antigens which will cause the immunity to happen [10].

In conclusion, according to current research, mRNA vaccine is more secure because it is not necessary for the mRNA vaccination to generate a large number of pathogens and not integrate into the original genome. Additionally, lipid nanoparticles are an effective way to deliver mRNA vaccines, which needs to be further studied and developed in order to find more effective and more secure way. Dendritic cell acts as an antigen-presenting cell which helps to trigger the ultimate immune response.

### 3. Classification of mRNA Vaccines

#### 3.1. Prophylactic Vaccine

Over the past 10 years, there has been a remarkable increase in the development of mRNA vaccines for both therapeutic and preventive purposes. As a routine preventative vaccination, mRNA vaccines are used to treat respiratory illnesses [8]. The most effective and well-known mRNA vaccine is COVID-19. Numerous tactics, including the mRNA vaccine, DNA vaccine, live attenuated virus, recombinant protein, and adenovirus vector, have been developed to limit the COVID-19 pandemic. The largest contribution to yet has come from the mRNA vaccine [11]. For attacking the virus and triggering the immune system, COVID-19 encodes the S protein on the surface of SARS-CoV-2. The virus that causes severe acute respiratory syndrome called SARS-CoV-2. With 29,881 nucleotides, it is an enclosed, single-stranded RNA virus. Selecting an immunogenic target for the mRNA vaccine that can trigger a protective immune response is crucial. A target known as the spike (S) glycoprotein usually selected as an antigen for COVID-19 vaccine development, because it is the primary surface protein of SARS-CoV-2 and facilitates viral entry by interacting to the host cell's ACE2 receptor [12].

Based on their genetic properties, mRNA vaccines are classified as unable replication mRNA, saRNA, or circRNA. However, most COVID-19 mRNA vaccines under clinical study or presently on sale are non-replicating vaccinations. In contrast to another kind of vaccination, saRNA vaccines may transport two or more genetic information into the human body. This vaccine only imparts the genetic information of the target antigen. The COVID-19 vaccine exhibits extraordinary clinical effectiveness, potentially preventing hospitalizations and severe symptom rates as well as preventing coronavirus infection [11].

The use of mRNA as a preventative vaccination has shown notable benefits and advancements in illness prevention. It must yet be developed in the future, though. Nevertheless, the logical design and optimization of the epitope or antigen-specific sequence require careful consideration.

#### 3.2. Therapeutic Vaccine

mRNA vaccines are currently used therapeutically, particularly in the treatment of cancer. Activating the immune system against tumors is the goal of cancer immunotherapies. Tumor microenvironment modifications and inhibitions can increase the survival rate by halting the development of the tumor and the spread of malignancy. The vaccine will target tumor-specific and tumor-associated antigens once it is injected into the human body.

Therapeutic vaccinations come in a range of forms, such as DNA, mRNA, dendritic cell, and antigen vaccines. The vaccination offers a more secure, specific, and more effective means of preventing the spread of cancer than current forms of cancer immune therapy [13]. Therapeutic cancer vaccines are thought to selectively target tumor cells and stimulate the immune system in addition to surgery, radiation, and chemotherapy [14].

mRNA is a strand like molecule which is related to the DNA, when it enters the ribosomes, the protein will be produced. The mRNA vaccination introduces the selected encoded antigen into the cytoplasm of the host cells. Then the cancer cell will trigger an immunological reaction of human body. Additionally, after injection, the mRNA vaccine can be adapted to the unique antigen repertoire of each patient's tumor, potentially causing the patient's cells to express the chosen neoepitopes and resulting in elimination [14].

Currently, pancreatic cancer is the primary condition for which mRNA vaccines are employed. Among the most fatal malignancies is pancreatic cancer, only around 12% of individuals with this cancer will be alive five years after being diagnosed, even with contemporary treatments. At present, surgical therapy is the most effective method in the treatment of pancreatic cancer. However, the disadvantage of surgery is that it has side effects and a certain risk of recurrence. The use of mRNA vaccines can effectively improve these defects.

Encode the antigen of pancreatic cancer cells to elicit a more focused and efficient immune response. Different types of vaccines have been developed to treat pancreatic cancer, including

vaccines based on microorganisms, peptides, and DNA. Therefore, vaccine selection needs to be developed based on the needs of individual pancreatic cancer patients.

Additionally, the mRNA vaccine offers some benefits over other therapeutic vaccine forms. Unlike DNA vaccines, which need many steps to translate an antigen from mRNA into cytoplasm, antigen translation from mRNA may occur in a single step in cells that are proliferating or not. However, because mRNA also significantly contributes to high-level protein production, mRNA vaccinations cannot be included into the genetic code [15].

#### 4. mRNA Vaccine Side Effects

Despite mRNA's clear therapeutic benefit, there are still certain adverse effects that require improvement. Thrombosis, thrombocytopenia, and myocarditis are among the potentially catastrophic cardiovascular complications, in addition to usual side symptoms including headache, fever, and exhaustion.

One of the most frequent adverse effects is thrombosis. It can happen in several bodily locations, such as the pulmonary vein, splanchnic vein, cerebral vein, and artery. The symptom of thrombosis is life-threatening, for mild cases like headaches, fatigue while for severe case like respiratory failure, visual impairment. Thrombocytopenia, another cardiovascular complication, usually occurs with the thrombosis. Thrombocytopenia is a disease that cause the decrease of blood platelet which will cause bruise and abnormal bleeding. Mild cases of thrombocytopenia may show minimal signs or symptoms. Rarely, there may be hazardous internal bleeding due to a low platelet count. The last CV complication is myocarditis, which is inflammation of the heart muscle, it could cause chest pain, respiratory failure, and rapid or irregular heart rhythms. Additionally, too little blood flow to the body can lead to organ failure [16].

#### 5. Conclusion

According to recent advances in mRNA vaccines, this therapy has already dominated the field of treatment and prevention. It is undeniable that the mRNA vaccine has unique advantages over other types of vaccines. It could induce the immune response directly without producing pathogens and also trigger the working of the immune system without entering the cell nucleus. However, there are still some unsolved side effects like CV complications including thrombosis, thrombocytopenia, and myocarditis which are life-threatening. This article provides a comprehensive description of mRNA vaccines in prophylactic and therapeutic fields including the COVID-19 vaccine and pancreatic cancer vaccine, and also analyzes the side effects and development gaps. It gives a clear current situation about this newly developed field provides ideas for following treatments and gives them some ways and directions for the treatment of different kinds of diseases.

However, the review does not describe the mechanism of side effects or treatment options for these side effects. They play a decisive role in the future development of mRNA vaccines. In the future, mRNA vaccines need to be further studied, on the premise of ensuring its safety to develop this vaccine into different aspects to treat more diseases.

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