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The Potential Role of mRNA Vaccine: In treating SARS-CoV-2

Anisha Patil
patilanisha66@gmail.com
New Arts, Commerce and Science College, Ahmednagar, Maharashtra

Dr. Ramneet Kaur
ramneetkaur@rimt.ac.in
School of Biosciences RIMT University, Mandi Gobindgarh, Punjab

ABSTRACT

An effective vaccine is needed to halt the proliferation of SARS-CoV-2 that is: Severe Acute Respiratory Syndrome Coronavirus-2. An RNA vaccine is a type of vaccine that uses a copy of a natural chemical called messenger RNA (mRNA) to produce an immune response. COVID-19 BNT162b1 mRNA vaccine has been proved omnipotent enough for eliciting robust CD4+ and CD8+ T Cell responses and powerful antibody response. COVID-19 mRNA vaccine can make fake versions of the viral protein especially, S antigenic protein but, potent enough to elicit a primary immune response against the COVID-19 virus. T Cells and commendatory cytokine retaliation induced by the BNT162b1 mRNA vaccine propose that it has a future to protect against SARS-CoV-2

Keywords*: SARS-CoV-2; COVID-19 BNT162b1 mRNA Vaccine; Spike Antigenic Protein; Protection Against SARS-CoV-2.*

1. INTRODUCTION

The main cause of the deadly COVID-19 virus outbreak is SARS-CoV-2 that is a severe acute respiratory syndrome. Coronavirus 2 (SARS-CoV-2) has posed a serious threat to human health. SARS-CoV-2 belongs to the Betacoronavirus of the family Coronaviridae, and commonly induces a plethora of respiratory symptoms, such as fever, cough, throat irritation, myalgia, and fatigue. Quest has been going on throughout the globe to develop a successful vaccine against COVID-19, to halt its further proliferation. A brief history of the COVID-19 pandemic can be summarized as: On 31st December 2019, the World Health Organization (WHO) firmly noticed a cluster of cases of pneumonia in Wuhan City, home to approximately 11 million people and the cultural and economic hub of central China. By 5 January, few cases were known and none of them were severe. A few days later, WHO was aware of 282 confirmed cases, of which four were successfully detected in Thailand, South Korea, and Japan. The death rate had been elevated in Wuhan, 51 people were severely ill and 12 were in critical condition. After many clinical testing by scientists, the chief cause behind the outbreak and information about this deadly genome came to be known on 12 January. The cause of severe acute respiratory syndrome that became, known as COVID-19 was a novel coronavirus, SARS-CoV-2. As a result, this virulent history that is constantly been written: as of 12 May, 82,591 new cases of COVID-19 worldwide were being confirmed daily and the death rate was astonishing over 4200 per day and still counting…

1.1 ETIOLOGY

Members of a large family of coronaviruses can cause many respiratory, enteric, hepatic, and neuronal diseases in different animal species including mammalian bats too. To date, seven human coronaviruses have been discovered.

When the virus was viewed under a highly magnified electron microscope it revealed its unique characteristics like it is elliptical or round, and it can exist in different shapes, in short, it is pleomorphic in nature with a diameter of approximately 60-140 nm. Different strains of coronaviruses have been discovered including MERS-CoV, SARS-CoV, and SARS-CoV-2 which are cytoplasmically replicating entities. It looked like a 'virus containing crown' due to the presence of spike (S) protein on its surface. Apart from S protein, it has other structural proteins too, like membrane protein (M), an envelope protein (E), and nucleoplasmid protein (N). S protein plays a crucial role in eliciting the immune response during disease infection. It is also sensitive to heat and ultraviolet radiation like other coronaviruses. Although, high temperature hinders the replication of any species of virus. Currently, the hindering temperature of SARS-CoV-2 must be well explained. It seems that CoV-2 can be inactivated at 27 degrees Celsius. On the contrary, studies reveal that it may resist cold temperatures even below 0 degrees Celsius. Furthermore, viral growth can be hindered by lipid solvents including ether (75%), ethanol, peroxyacetic acid, and chloroform except for chlorohexidine.

In genetic terms, Chan et al. have proven that SARA-CoV-2 is an ssRNA virus that contains 29891 nucleotides, encoding for 9860 amino acids. Although the exact origin of SARS-CoV-2 is not known yet, its genomic studies reveal that it probably evolved from a strain particularly found in mammalian bats. The genome of the virus which has been isolated from humans shows close resemblance with the viral genome isolated from bats that is, beta CoV RaTG13. The proteins which are structural in nature are mainly S, E, M, and N, whereas non-structural proteins, such as 3-chymotrypsin-like protease, papain-like protease, and RNA-dependent RNA polymerase, are encoded by the ORF region.

From deep viral studies, we came to know that, for a virus, to get inside the host cell it requires the assistance of specific receptors which are present on the surface of the host cell. In the case of SARS-CoV-2, this process is favored by receptors of host cells commonly known as angiotensin-converting enzyme2 (ACE2). Once the viral spike protein binds to the host cell surface a special type of serine protease mainly TMPRSS2 checks the entry of the virus into the cell by activating or switching on the spike protein. After entering the host cell viral RNA genome undergoes replication and transcription process to form viral proteins via replicase-transcriptase complex. Thus, viral RNA is replicated, and virulent structural proteins get synthesized, assembled, and packaged inside the host cell.

1.1.1 Nucleic acid vaccines

All life forms are known to exist on Earth today and all life for there is, evidence in the geological records seems to be of the same form based on DNA genomes and protein. A plethora of scientific studies have revealed that, somehow, DNA-dependent life was once preceded by simple, innocuous, and undecorated RNA-dependent life. This earlier era is referred to as the 'RNA world', which played a crucial role in determining the various phenotypic characteristics of life.

Genome-based vaccines are brought into existence and use since it combines the excellent attributes of both attenuated, live and subunit vaccines. Recently, mRNA vaccines have emerged as an alternative approach. Ribonucleic Acid (RNA) is believed to be the pioneer molecule contributing to modern-day vaccinations. Enthusiasm has elevated in these vaccines because they can be synthesized in undemanding and uncomplicated ways in a laboratory easily. They are non-infectious, non-integrating, cell-free, and offer both rapid responses and high productivity.

1.1.2 Role of mRNA vaccine in treating SARS-CoV-2 and its target antigens

Coronaviruses, including SARS-CoV, MERS-CoV, and SARS-CoV-2, contain four structural proteins (S, E, M & N). Generally, the spike protein or S protein contributes most towards eliciting a strong immune response during exposure to disease. With a size of 180-200kDa, the S protein consists of an extracellular N-terminus, a transmembrane domain anchored in the viral membrane, and a short intracellular C-terminal segment. S normally exists in a metastable, prefusion conformation; once it captures the host cell, S protein undergoes several conformational modifications which helps it to enter the host cell. Spikes are covered with polysaccharide molecules to camouflage them, this helps them to avoid being noticed by the host immune system.

The trimeric S protein contains two subunits, S1 and S2, which facilitate viral entry into the host cells. S1 subunit contains a fragment called the receptor-binding domain or in simple words RBD, that can bind with ACE2. The binding of spike protein to the ACE2 gives rise to complex conformational modifications, driving the S protein from a prefusion conformation to a post-fusion conformation. This post-fusion conformation with N-linked glycans has been proved as a master strategy to evade the host immune response. Studies reported that vaccines encoding SARS-CoV S protein have the potency in eliciting a cellular and human immune response. That's why the S gene is regarded as the main target for the SARS-CoV-2 vaccine that is the BNT162b1 mRNA vaccine. The S protein of the COVID -19 virus especially the receptor-binding domain is potent enough to induce neutralizing antibodies (Nabs) and T-cell immune responses.

When an mRNA vaccine is injected into a person's upper arm, tiny lipid vesicles containing the mRNA molecule travels through the body fluids, and merge with a special type of immune cells called antigen-presenting cells (APCs). Inside the cell mRNA molecule bounce around and meets the ribosome that is, the protein-making machinery in the cytoplasm of our cells. The ribosome produces a final protein known as antigen which is based on mRNA sequence. In short, the antigen protein mimics those proteins found in a specific virus. This antigenic protein is what will ultimately stimulate the immune system. In the case of the COVID-19 mRNA vaccine which will be the coronavirus spike protein. There are mainly two trajectories for Spike protein antigen in being getting introduced to the immune machinery.

PATHWAY-I

In this pathway, the antigenic protein is broken into fragments that are bound to another protein called MHC-I. Once the fragment is bound to the MHC-I molecule, the complex leaves the ER (endoplasmic reticulum) through the secretory pathways to reach the cell surface. The complex is transported to the surface of the cell where it is recognized by the cytotoxic T-cells. This enables cell-mediated immunity against future infection.

PATHWAY-II

The S antigenic proteins or their fragments are transported to the surface of the cells, and it is released which is taken up by the other antigen-presenting cells and degraded into fragments which forms a complex with MHC-II protein. This complex is transported to the cell surface where it is recognized by the helper T-cells which neutralize the virus in any future infections. This pathway is called the antibody-mediated immune process. This helps in eliciting an advanced immune response against the virus to protect our body when it is introduced to the actual and virulent COVID-19 virus.

1.1.3ADVANTAGES OF mRNA VACCINE

-Stimulates both types of immunities that are, cell-mediated and antibody-mediated immunity.
-There are no traces of a real viral entity in it.
-Low risk of integrating into the genome.
-Makes mRNA vaccines considerably safer than conventional attenuated or killed vaccines. CONCLUSION

The pandemic of SARS-CoV-2 and its widespread effects has spawned challenges to discover a safe and effective anti-viral drug throughout the globe. Scientists around the globe are working to develop an effective vaccine against it. Till now many antibodies have been discovered or identified to specifically target various domains of COVID-19, and are effective in neutralizing SARS-CoV-2. For developing an excellent and effective vaccine, it is of great importance to generate quick and protective T and B-cell immune responses. From our studies, we came to know that the S protein or the spike protein plays a pivotal role in binding and penetrating the host cell. As a result, this gave rise to the development of the BNT162b1 SARS-CoV-2 mRNA vaccine. This vaccine helps in making fake version viral antigenic proteins but, potent enough for eliciting a primary immune response to protect from future real-time exposure to the COVID-19 virus. Though it's a race against time to develop an effective vaccine, the mRNA vaccine helps in developing antibodies specific to the COVID-19 virus.

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