BPR MCS Bulletin of Pioneering Researches of Medical and Clinical Science

Bulletin of Pioneering Researches of Medical and Clinical Science

Available online: https://bprmcs.com
2023 | Volume 2 | Issue 1 | Page: 9-16

Comprehensive Overview of Vaccines and Theirtypes for Human Immunization

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Abstract

Prevention is better than cure. Vaccines are one category of medicine. The purpose of vaccines is to mitigate the spread of infectious diseases. They work by boostingthe body's immune response to specific infections that can cause illness. This is an important weapon in fighting against infections that cause disease. Since they have been around for a while, vaccines have aided humanity in preventing many infectious diseases. Vaccines come in many different types, including mRNA vaccines, subunit, recombinant, or conjugate vaccines, live attenuated vaccines, and inactivated or dead vaccines. Many infectious illnesses, including smallpox, polio, and measles, have been successfully stopped from spreading thanks to vaccinations, which have also saved countless lives. Vaccines work like drugs in such a way that they trigger an immune response against a specific organism that causes a particular disease. This response results in the development of memory cells that can recognize and fight pathogens if they reoccur, thus providing immunity to disease. Vaccines have prevented the spread of many infectious diseases and saved countless lives.

Keywords: Vaccines, Attenuated, Immunization, Antibody, Inoculation

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How to Cite This Article: Burghate S, Mundada A. Comprehensive Overview of Vaccines and Theirtypes for Human Immunization. Bull Pioneer Res Med Clin Sci. 2023;2(1):9-16.

Introduction

The use of vaccines is essential in combating the spread of infectious illnesses. They work by triggeringan immune response from the body's immune system against a specific disease-causingpathogen (virus or bacteria). As a result of this immune response, memory cells develop so thatthey can identify and fight pathogens in the future, giving the patient immunity to the disease. The history of the smallpox vaccination can be summarized byreplacing the human smallpox injection with cowpox inoculation, a process developed by an English doctor named Edward Jenner. Smallpox is a contagious illness that affects humans but has no known animal reservoir (1749-1823) [1]. Vaccines come in a variety of forms, each of which has advantages and disadvantages. The most common kind of vaccination is the inactivated or killed vaccine, which is created by eradicating or inactivating the disease-causing bacteria. The polio vaccination, the hepatitis A vaccine, and the influenza vaccine are a few examples of inactivated vaccines. The extension of life expectancy in high-income nations is one of contemporary society's greatest achievements [2]. The average lifetime in the nations with the longest life expectancies was 35 years in 1750 and 45 years in 1840 [3]. Since then, it has climbed by roughly 2.5 years every ten years, reaching 55 years in 1900 and 65 years in 1950 [4, 5]. Given that estimates of a life expectancy threshold have consistently proven false, the current life expectancy is above 80 years, and we can predict that it will exceed 100 years in six decades [6].

To produce a live attenuated vaccine, the pathogen must be weakenedso that it can grow but not spread disease. Compared to inactivated vaccines, this kind of vaccine

induces a more potent and durable immune response. The measles, mumps, and rubella (MMR) vaccine, varicella (chickenpox) vaccine, and yellow fever vaccine are a few examples of live attenuated vaccinations. Live vaccines have been effective in treating a variety of bacterial and viral illnesses in humans and animals. Because the smallpox vaccine was not developed from variola and was not technically speaking an attenuated vaccine, the final incidence of rinderpest was discovered in Kenya in 2001, making the rinderpest vaccine possibly the most successful live attenuated vaccine to date [7]. Subunit, recombinant, or conjugate vaccines are prepared using pathogen components such as proteins and sugars, to elicit an immune response. These vaccines are less dangerous than live attenuated vaccines because they only contain a fraction of the. The meningococcal vaccination, the HPV vaccine, and the Haemophilus influenza type B (Hib) vaccine are a few examples of subunit vaccines. The creation of less reactogenic, more potent, safer, and better-defined vaccines as well as vaccinations that offer broader protection against several lies ahead of bacteria are the key drives for recombinant protein-based vaccine research. The first of these vaccines were made using yeast-expressed, very pure hepatitis B surface antigen [8, 9]. A novel type of vaccine known as an mRNA vaccine works by initiatingan immune response using a genetic component known as messenger RNA (mRNA). The body's production of a protein that is present on the surface of the disease-causing bacteria is directed by instructions found in the mRNA. The immune system mounts an immune reaction after identifying this protein as foreign. The Pfizer-BioNTech and Moderna COVID-19 vaccines are mRNA vaccines. The idea of genetic (DNA and RNA) vaccines was first proposed decades ago to develop a versatile, easy-to-manufactured, safe, and efficient class of vaccines. Until the late 2000s, the focus was on developing DNA-based technologies because of the challenges posed by RNA instability, ineffective in vivo delivery, and the promotion of excessive inflammatory responses [10]. Making in vitro-transcribed (IVT) messenger RNA (mRNA) is a very simple process [11, 12], but until recently, it was exceedingly difficult to produce high-quality "therapeutic" mRNA that is highly translatable and does not cause significant inflammation [13]. Vector vaccines use benign viruses, known as vectors to deliver antigens of disease-causing microorganisms to the body’s cells. Although the vector virus has been altered to prevent sickness, it can still transmit the antigens to the cells, which in turn triggers an immunological response. The Ebola vaccine and the Johnson & Johnson COVID-19 vaccine are two examples of vector vaccines. DNA vaccines instruct the body to produce a protein that elicits an immune response by using a small fragment of DNA. The development of DNA vaccines is still in its early stages, and none have been given the go-ahead for use in people. DNA vaccines offer a fresh method of expressing antigens in living organisms to trigger cellular and humoral immune reactions. They have also induced a protective immune response in several disease-related preclinical models. Instead of employing the proteins themselves, a live replicating vector, or an attenuated version of the pathogen itself, DNA vaccines use genes that encode the proteins of infections or cancers. DNA vaccines are made up of the target gene, a polyadenylation/transcriptional termination sequence, and a bacterial plasmid with a potent viral promoter [14].

Most vaccines are given via injection, while some can also be taken orally or nasally. Although vaccinations are often advised for children, adults can also get protection against infectious diseases including the flu, pneumonia, and shingles. Although vaccinations are mostly safe and effective, they might have negative effects like any other medical procedure. Serious adverse effects are infrequent, but most of them are mild and fade away on their own. The hazards of vaccination are significantly outweighed by its advantages in preventing serious illness and slowing the spread of infectious illnesses. One of the best ways to stop contagious diseases and safeguard the public's health is through vaccinations. Millions of lives have already been saved, and millions more could be. The success of efforts to guarantee that everyone gets access to vaccines will depend on continuous investment in research, delivery methods, and public health education.

Inactivated or killed vaccines

Inactivated or killed vaccines use dead forms of viruses or bacteria to elicit an immune response. Unlike live-attenuated vaccines. Which use an attenuated version of a virus or bacteria, inactivated or dead vaccines are made by irradiating, heating or chemically poisoning the virus or bacterium.the bacteria or virus are removed, they cannot spread disease. Antigens, the building blocks of viruses and bacteria that can trigger animmune reaction, are still evident in the dead pathogen. These antigens are utilized to activate the immune system of the body, which creates antibodies to combat bacteria or viruses. Using vaccines that have been inactivated or killed has several benefits. As there is no chance of the pathogen causing disease, this is one of their key advantages over live attenuated vaccines. Also, since they don't contain live viruses or bacteria that could spread disease, inactivated or dead vaccinations can be administered to patients with compromised immune systems. Inactivated or dead vaccinations have the added benefit of being easier to produce than live attenuated vaccines. There is no need to be concerned about retaining the weakened form of the pathogen, as is the case with live attenuated vaccines

because the virus or bacteria is destroyed before it is utilized in the vaccine. Three essential conditions must be met to produce inactivated viral vaccines. For the vaccine to be effective, each dosage must contain a significant amount of inactivated virus, which necessitates the production of huge quantities of the viral antigen. Second, the virus preparation must be rendered inactive while maintaining the immunogenicity of the virus's surface proteins. This ensures that there is no residual infectivity. Thirdly, the vaccine must contain an adjuvant to boost the immune system's reaction to viral proteins [15]. Moreover, utilizing inactivated or killed vaccinations has certain drawbacks as well. They might not be as effective as live attenuated vaccines because the immunological response they elicit might be less robust. In addition, since the immune response produced by inactivated or dead vaccinations may not endure as long as that of live attenuated vaccines, booster shots are frequently needed to maintain immunity.

Vaccines that have been inactivated or destroyed are used to prevent a variety of infectious diseases, including pertussis, rabies, polio, hepatitis A and B, and influenza (whooping cough). To boost the efficacy of a live attenuated vaccine, inactivated or killed vaccines are occasionally used as a booster. Many inactivation methods employ chemical or physical processes. Many chemicals are utilized in the chemical procedures for viral inactivation. Although aldehydes such as formaldehyde are the most prevalent, a rising number of patented substances and patented treatment combinations are successful at inactivating viruses and may therefore be acceptable for vaccine development [16]. In the physical inactivation of viruses, virus inactivation by heat must nearly always be paired with another therapy, typically a chemical one. While using a chemical ingredient ensures complete virus inactivation, it may also make the vaccination more hazardous. A temperature of about 37°C is employed for heat inactivation. To avoid the need for a combination of heat and aggressive chemical treatment, higher temperatures have also been used. The influenza virus was rendered at least 99% inactive when exposed to temperatures between 45 and 59°C for 25 to 180 minutes. Ultraviolet (UV) irradiation is another method that is commonly utilized. The covalent bonds of the cyclic molecules of the purine and pyrimidine bases are broken by the excitation energy of the UV radiation, causing damage to the nucleic acids of viruses and other microbes. This process is known as UV action. The virus is instantly rendered inactive when exposed to UVC radiation that is effective (100 to 280 nm) [16]. Hepatitis A vaccines are produced utilizing inactivated hepatitis A virus, whereas hepatitis B vaccines are produced using the surface antigen of the hepatitis B virus. To fully protect against the disease, both vaccines need to be administered in multiple doses. Vaccines that have been inactivated or killed can also be used to prevent polio. The inactivated polio vaccine (IPV), which is administered in a series of doses, is created using inactivated poliovirus. The live attenuated oral polio vaccine (OPV), which was previously used in many regions of the world, is currently being phased out due to the extremely unlikely possibility that it could result in polio in certain recipients. In summary, Inactivated or killed vaccines, as the name suggests, use a dead form of a virus or bacteria to elicit an immune response. They are less dangerous and easier to make than live attenuated vaccines, but they may not be as effective and may call for booster shots. Vaccines that have been inactivated or destroyed are used to protect against a variety of infectious illnesses and are a key component of public health initiatives to stop the spread of disease.

Live-attenuated vaccines

A live attenuated vaccine is a special type of vaccine that uses a weakened or attenuated virus or microorganism to stimulate an immune response. This type of vaccine is made by modifying the disease-causing virus or bacterium to reduce toxicity while maintaining itsability to elicit an immuneresponse. A vaccine that may be administered to fight back the disease is then created using this pathogen that has been weakened. The fact that live attenuated vaccines elicit a potent and durable immune response is one of their main benefits. As the bacterium or virus used in the vaccine is still alive, it can reproduce and create antigens inside the body, which prompts a strong immune response. Hence, booster doses are often not required because this immune response frequently offers lifelong protection against the disease. As they promote both humoral and cellular immunity, live attenuated vaccines are also very efficient at stopping the spread of disease. Cellular immunity involves the activation of immune cells that can go after infected cells directly, whereas humoral immunity involves the creation of antibodies. Live attenuated vaccines offer a thorough defense against the pathogen because they promote both forms of immunity. Vaccines now in use are developed from naturally occurring, attenuated versions that appear at random and have limited control over the combination of abnormalities that reduce survival [17]. Contrarily, research identifying the function of certain genes in the survival and virulence of the organism mesh well with current and future vaccine development [18, 19]. These methods often entail the targeted or random inactivation or removal of a gene, followed by the measurement of immune response after the vaccine candidate has left the body. These methods often entail the targeted or random inactivation or removal of a gene, followed by the measurement of immune response after the vaccine candidate has left the body. Although simple in concept,

the approach necessitates a lot of experimental trial and error. First, mutations that have a significant impact on survival may weaken the organism to the point where the amount of defense immunity it offers is insufficient [20].

To make live, attenuated vaccines, a variety of techniques can be used. One typical method involves exposing the virus or bacterium to a series of animal or human cells, which over time gradually weakens the infection. The live attenuated MMR (measles, mumps, and rubella) vaccine was developed using this method. Another strategy is to genetically modify the disease to lessen its virulence. The live attenuated varicella (chickenpox) vaccine was developed using this method by modifying the virus to lessen its capacity to cause disease.

When smallpox was declared extinct in 1980, vaccination was likely the most effective human vaccine ever. Most first-time receivers experienced substantial adverse effects, and a fraction of people experienced major, occasionally fatal, side effects. In the 18th century, it was well known in rural areas of the UK that people who had cowpox were resistant to smallpox, thus the farmer Benjamin Jesty purposefully immunized farm workers as a preventative measure. He never published a record of the experience, and unlike Edward Jenner, he never threatened to infect the receivers with smallpox [7]. A typical illustration of a live attenuated vaccination is the MMR (measles, mumps, and rubella) vaccine. The live attenuated versions of the measles, mumps, and rubella viruses are mixed into a single vaccination to create the MMR vaccine. Two doses of the vaccination are normally administered, the first between 12 and 15 months of age and the second between 4 and 6 years of age. The varicella (chickenpox) vaccine is another illustration of a live attenuated vaccination. The varicella-zoster virus, which causes chickenpox, was modified to create the vaccine. The vaccine is normally administered in two doses, the first dosage being administered between the ages of 12 and 15 months and the second dose being administered between the ages of 4 and 6 years.

Live attenuated vaccines have a lot of benefits, but they also have significant drawbacks. One drawback is that they might not be safe for those with compromised immune systems because the pathogen utilized in the vaccine, despite being weaker, may still be able to harm them. Moreover, live attenuated vaccines might not work as well in patients who have taken certain medications, like immunosuppressive ones that can compromise the immune response to the vaccine.

mRNA vaccines

A minor genetic component known as messenger RNA (mRNA) is used in mRNA vaccines, a relatively new type of vaccination, to stimulate an immunological response. These vaccines function by instructing cells to produce a protein that is present on the surface of a pathogen, which then prompts an immune response against the disease. Due to its inclusion in the COVID-19 vaccines created by Pfizer-BioNTech and Moderna, mRNA vaccines have attracted considerable attention lately. In place of traditional vaccine strategies, nucleic acid therapies have shown promise. In 1990, when reporter gene mRNAs were injected into mice and protein synthesis was discovered, the first report of the successful use of in vitro transcribed (IVT) mRNA in animals was published [21]. In a later investigation conducted in 1992, it was shown that delivery of mRNA encoding vasopressin in the hypothalamus might cause a physiological reaction in rats [22]. These early, encouraging discoveries, however, did not result in a significant investment in the development of mRNA therapies, mostly because of worries about mRNA instability, high inherent immunogenicity, and ineffective in vivo transport. Instead, the field developed therapeutic strategies based on proteins and DNA [10, 23, 24].

mRNA vaccines can be created and produced quite quickly, which is one of their main benefits. This is because live bacteria or viruses are not necessary to create the mRNA sequence utilized in the vaccine. After all, it can be produced in the lab using the genetic sequence of the pathogen. Compared to conventional vaccine development techniques, this speeds up the creation and expansion of the production of mRNA vaccines. mRNA vaccines also have the benefit of not containing any live or inactivated viruses or bacteria, making them safer to administer to individuals with compromised immune systems or allergies to certain vaccine components. Furthermore, as mRNA vaccinations only carry a tiny amount of genetic material, they do not integrate into a person's DNA and are unlikely to have a long-lasting impact on the recipient's genetic makeup.

The most widely used method for producing mRNA in vitro is the use of linear DNA (either plasmid DNA that has been linearized or synthetic DNA created by PCR) with T3, T7, or SP6 RNA polymerase. The five-prime cap (5′ cap), five-prime untranslated region (5′ UTR), open reading frame (ORF) region, three-prime untranslated region (3′ UTR), and poly (A) tail structure are some fundamental structural components of mature mRNA in the eukaryote that are necessary to maintain mRNA functionality [11, 24]. Both mRNA stability and expression capacity benefit from maintaining the integrity of the mRNA structure. The effectiveness of an mRNA vaccination can be improved further by changing the mRNA sequence following its entire structure. Yet, a mixture of targeted mRNA, untargeted RNA, nucleotides, oligodeoxynucleotides, and proteins make up the initial product of mRNA in vitro transcription [25]. In this technology, common impurities are removed using precipitation and extraction procedures, and the

target mRNA is typically separated from other mRNA impurities using chromatographic techniques [26]. To continue functioning, mRNA must reach the host cytoplasm to express particular antigens; however, the mRNA molecule is too large to penetrate through the cell membrane via free diffusion [24]. Moreover, the negatively charged nature of both mRNA and the cell membrane makes mRNA distribution more challenging. Furthermore, extracellular ribonucleases found in the blood and skin can quickly breakdown mRNA [27]. Hence, one of the most challenging application difficulties of mRNA vaccines is getting mRNA into large numbers of cells with necessary high translation levels. This requires extremely targeted and effective mRNA delivery mechanisms [28, 29].

The global battle against COVID-19 has seen a considerable contribution from mRNA vaccines. Unprecedented attempts have been made to create vaccinations that can be quickly employed to stop the spread of the virus as a result of the COVID-19 pandemic brought on by the SARS-CoV-2 virus. One of the most promising vaccination platforms for the creation of efficient and secure COVID-19 vaccines has been mRNA vaccines. Both the Pfizer-BioNTech and Moderna COVID-19 vaccines are made of mRNA and have been approved for use in emergencies by regulatory bodies worldwide. These vaccines function by introducing mRNA, a little amount of genetic material, into the body's cells. The cells are given the go-ahead to make the spike protein, which is a protein that can be seen on the surface of the SARS-CoV-2 virus. The immune system produces the protein, detects it as alien, and mounts an attack to get rid of it. Also, by responding in this way, the immune system is set up to react rapidly and successfully the next time it comes across the virus.

Viral vector vaccines

The hepatitis-B surface antigen gene was put into a modified vaccinia virus approximately forty years ago, and this was the first time a recombinant viral vector was utilized as a vaccine delivery mechanism [30, 31]. Until 2020, only five of these vaccine vectors have advanced through clinical trials to licensure and use in humans. Since then, these vaccine vectors have been widely employed in veterinary medicine. To combat a wide range of infectious disease pathogens as well as noninfectious diseases, including cancer, several viral vector vaccines have been produced. Adenoviral vector vaccines have seen an increase in use as a result of the SARS-CoV-2 epidemic during the past two years, with doses administered to billions of individuals globally. This has provided a wealth of knowledge regarding the security, immunogenicity, and effectiveness of adenoviral vaccine technology, which will be outlined below together with a discussion of other viral vector vaccines currently in use.

A type of vaccine known as a viral vector vaccine uses an unharmful virus to introduce a small portion of the target pathogen's genetic material into the body. The body's cells are subsequently instructed by this genetic information to generate a protein that is present on the pathogen's surface, which sets off an immune response. When the actual infection is encountered in the future, the immune response aids in defending the body against it. These vaccines often use a modified strain of an infection-free virus called an adenovirus as their viral vector. Although the adenovirus family of viruses can cause colds and other minor respiratory ailments, the strains used in viral vector vaccinations have been altered so that they are unable to multiply and spread disease. They are utilized to convey the genetic material required to elicit an immunological response instead [32]. Viral vectors can be used as platforms for vaccines because they enable the generation of an innate immune response without the need for adjuvants. This reaction is essential for triggering later processing and adaptive immune responses. Viral vectors' capacity to infect host cells and produce heterologous antigens enables antigen presentation and activation of host MHC pathways through direct and cross-presentation, resulting in a potent cellular response. Antigen expression levels and duration are correlated with CD8+ T-cell-protective immunity. As responses to viral vector vaccines against intracellular infections, such as HIV and malaria, have been correlated with protection, earlier targeting of these vaccines has been made possible by this powerful T-cell activation. The ability to utilize viral vector vaccines to combat a variety of infections is one of its benefits. This is so that genetic material from various pathogens can be carried by the viral vector, which can be altered to do so. The same viral vector technology, for instance, can be utilized to make vaccines against COVID-19, Ebola, and Zika. The ability to produce lifelong immunity is another benefit of the viral vector vaccine. These vaccines can produce an immune response that lasts for years, offering long-term defense against the target disease. This is so that a potent and robust immune response can be produced. The viral vector employed in the vaccination can penetrate cells and deliver the genetic material directly. Viral vector vaccines, however, could have significant disadvantages. They include the potential for innate immunity to the viral vector, which can lower the vaccine's efficacy. The viral vector used in the vaccine may have already been exposed to some people, which can result in the development of antibodies that prevent the vaccine from working as intended. Viral vector vaccines are potentially a possible source of safety issues. Even though the viral vector used in the vaccine is normally changed to limit the risk of spreading disease,

there is still a very small possibility of negative side effects from their use. Viral vector vaccines are a subset of vaccinations that transfer genetic material and elicit an immune response via a modified virus. They can be used to target a variety of diseases and have the potential to offer long-lasting immunity. Yet, there may also be negative effects and security issues that need to be properly considered. In general, vaccines against viral vectors are a crucial weapon in the struggle against infectious disorders like COVID-19.

DNA vaccines

A DNA vaccine is a form of vaccination that works by inducing an immune response against a particular pathogen using a small piece of DNA, typically a plasmid. DNA vaccines use genetic material to guide cells to generate a protein that prompts an immunological response, in contrast to conventional vaccines that use pathogens that have been weakened or rendered inactive to stimulate the immune system. DNA vaccines offer a fresh method of expressing antigens in living organisms to trigger cellular and humoral immune reactions. They have also induced a protective immune response in several disease-related preclinical models. Instead of employing the pathogen's or tumor's actual proteins, a live-replicating vector, or an attenuated version of the pathogen, DNA vaccines use genes that code for those proteins. DNA vaccines are made up of the target gene, a polyadenylation/transcriptional termination sequence, and a bacterial plasmid with a potent viral promoter. The plasmid is simply injected into the host after being generated in bacteria (E. coli), purified, and dispersed in a saline solution. By taking in the DNA plasmid, host cells produce the encoded protein. The plasmid is created without a replication origin that can work in eukaryotic cells; as a result, it cannot replicate in mammals or integrate with their chromosomal DNA. For intramuscular (I.M.) immunization, where muscle cells are the main protein-expressing cell type, the role of antigen-presenting cells (APC) in the immune responses that follow upon expression of the encoded foreign protein has been studied (see the section on Mechanisms of Immune Responses), but not for other immunization methods, such as those that use a "gene gun" to fire gold beads coated with DNA into the epidermis [14].

DNA vaccines have been used to examine the effects of various vaccination conditions, such as the use of different antigen forms (secreted vs. membrane-bound), the effect of different intracellular targeting signals for a protein, and the effects of co-expressed cytokines, due to the ease of altering constructs or mixing different plasmids. The immune responses resulting from DNA vaccines may be influenced by the DNA itself, even though DNA vaccines do not experience the immunologic complications of a vector delivery system, where the viral vector itself or the proteins normally expressed by the vector engender or alter immune responses. Long recognized as cytokine-inducing polynucleotides, bacterial DNA motifs with specific sequences can also operate as mitogens [33]. When the plasmids are administered intradermally, including such a motif in the plasmid seems to boost both antibody and cytolytic T lymphocyte (CTL) responses to a protein encoded by the same or a different plasmid. Plasmid DNA injected intramuscularly has been shown to enhance or modify immune responses to a co-injected recombinant protein or a protein encoded by a co-injected plasmid [34].

Conclusion

The pharmaceutical industry nowadays offers various kinds of vaccines, and vaccines are essential for preventing infectious diseases and improving public health around the world. It can be mentioned that each vaccination type that is now on the market has its benefits and drawbacks, which may even change from sickness to disease. While inactivated or dead vaccinations are safer and can be administered to persons with compromised immune systems, live attenuated vaccines offer robust and long-lasting immunity. In addition to viral vector vaccines and DNA vaccines, which are both promising vaccine technologies, mRNA vaccines present a novel strategy that has demonstrated excellent efficiency in preventing COVID-19.

There are still issues to resolve, such as the introduction of new and constantly changing diseases, despite such incredible innovation. Research and development continue to take place toward resolving these issues. Finally, it can be said that vaccination has been crucial in the fight against infectious diseases, has helped to save millions of lives, and will likely continue to do so in the future.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: As we have just reviewed the research work carried out in the filed of vaccines. We are not involved in carrying out any human or animal trials of this study and hence no ethical clearance required for completion of this manuscript.

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