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Different types of vaccines in COVID-19 treatment

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Abstract. The pathogen in charge of the 2020 COVID-19 pandemic is the coronavirus SARS-CoV-2. Follo wing the outbreak, efforts to develop vaccines—biological products comprised of diverse pathogenic microorganisms and their metabolites—as a successful means of preventing infectious diseases have been stalled. This article concentrates on four distinct vaccine types that target SARS-CoV-2: attenuated vaccines, mRNA vaccines, VLP, and inactivated vaccines. The first vaccines to be developed are inactivated vaccines, which are basically dead pathogens. Although it's safety and convenient to prepare, the effectiveness is limited owing to the low pathogenicity. Compared to the inactivated vaccines, the attenuated vaccines are more effective, but the safety is controversial. mRNA vaccines can cause great immune response as a nucleoside pathogen, as well as a protein pathogen after translation. The side effect is significant. VLP, as a pseudo-virus particle, balancing the safety and effectiveness, is another category of vaccines. According to their advantages and disadvantages, a detailed analysis was carried out, which has a certain guiding role for people to know and choose vaccines. Based on this, it also points out the disadvantages of COVID-19 vaccine and provides a basic direction for the scientific research development, design and optimization of vaccine industry in the future.

Keywords: vaccine, COVID-19, immune.

1. Introduction

In December 2019, a novel coronavirus (CoV) was identified in Wuhan, Hubei Province, China. Because of the new coronavirus's rapid spread, the World Health Organization (WHO) declared it a public health emergency of global concern on January 30, 2020. The novel coronavirus was given the name SARS-CoV-2 due to its strong sequence similarity to the Severe Acute Respiratory Syndrome (SARS) coronavirus (SARS-CoV), which causes pandemic coronavirus illness (COVID-19). To date, the COVID-19 pandemic has been linked to over 25 million confirmed infections, nearly 1 million deaths, and the number of cases is still rapidly increasing. Despite the fact that SARS-CoV-2 has been linked to severe respiratory failure, its death rate is lower than that of SARS-CoV during the 2003 pandemic. Furthermore, the virus is particularly prevalent in the elderly and in those who have long-term medical issues like diabetes and high blood pressure. Since no intermediate host has been discovered, it is thought that wild bats served as SARS-CoV-2's original host [1]. An increasing number of people died from illnesses caused by SARS-CoV-2, the virus that caused COVID-19, as the epidemic spread in 2020. The SARS-CoV-2 virus, which makes up to the Betacoronavirus genus within the coronavirus family, is extremely comparable genetically to the SARS-CoV virus that was previously endemic and first appeared in 2002–2003. The approximately 30-kilobase single-stranded RNA viruses SARS-CoV-2 and SARS-CoV encode a diverse range of structural and non-structural proteins.

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Structural proteins encompass the glycoprotein spike (S), envelope (E), membrane (M), along with a nucleocapsid protein (N)[1]. Current study indicates that pangolins, bats, and Chinese horseshoe bats are among the wild animals that serve as the novel coronavirus's reservoir and source of transmission into human culture. Since this kind of virus is common in nature, humans are usually not directly infected by it until they consume certain wild animals that haven't been fully cooked or sterilized, in which case the virus enters the human body and stays there. Humans can contract the novel coronavirus by respiratory droplets, direct or indirect contact, fecal-oral contact, maternal contact, and other routes after contracting it.

Due to the high contagiousness of this kind of respiratory infection, numerous researchers started looking into the best ways to treat pneumonia brought on by the novel coronavirus, which first causes blindness in vaccine recipients. In order to prevent infectious diseases, vaccines are autoimmune preparations that are created by genetically modifying, artificially attenuating, or rendering pathogenic microorganisms (like bacteria, viruses, rickettsia, etc.) and their byproducts inactive. Vaccines maintain the properties of pathogens that bolster an animal's immune system. Certain protective substances, such as immune hormones, active physiological substances, specific antibodies, etc., can be generated by an animal's immune system. in response to harmless pathogens. When these antigens re-infect the animal, the immune system will recall the previous infection and produce additional protective substances to keep the animal safe from the pathogen. There is a long history of vaccines. Since the smallpox vaccine was first developed in the 18th century, hundreds of years have passed, and three technological revolutions have occurred in the area of creating and investigating vaccines. The first started in the late 19th century when Pasteur successfully created the vaccines for rabies, sheep anthrax, and chicken cholera. He achieved this by treating pathogens using physical and chemical methods as well as biological propagation to produce attenuated and inactivated vaccines. The second happened during the 1980s when the hepatitis B vaccine was made using yeast. The third was the triumphant creation of nucleic acid vaccines in the 1990s; these had originally been invented in the United States by Wolff and associates. During this phase, vaccine research has been able to move from the level of the entire pathogen to the molecular level thanks to recent developments in molecular biology technology, exemplified by the development of recombinant DNA technology. Humans have been using vaccines to prevent disease for more than 200 years. Vaccines have been a powerful tool in the fight against disease, helping to eradicate or control a number of infectious diseases. Four vaccinations—inactivated, attenuated, mRNA, and virus-like particle—were suggested and tested by scientists for the COVID-19 pandemic. The purposes and effects of these vaccines vary [2]. This article compares the benefits and drawbacks of each vaccine, concentrating on the fundamental details and purposes of each.

2. Four vaccines: introduction, advantages and disadvantages

2.1. Inactivated vaccines

Inactivated vaccines are pathogens (here refers to the new coronavirus) that are cultured, proliferated, inactivated, and purified to make them lose their pathogenicity (because they have been inactivated and are dead viruses), but retain the antigenic activity of the S protein, which can stimulate the human body to produce antibodies and then play a protective role. The main components of inactivated vaccines are bacteria or virus particles, which are usually injected into the human body. The development of an inactivated vaccine requires the inactivation of the target virus, either chemically or through radiation. This can destroy the nucleic acid of the virus while maintaining the integrity of the viral antigen. Throughout the first SARS virus outbreak, investigations have been undertaken in animal models to examine the immunological properties and effectiveness of inactivated CoV vaccines. Upon its initial testing in rhesus monkeys, an inactivated SARS vaccine was found to elicit humoral and mucosal immunity, indicating that it could be utilized in clinical trials [3]. However, there are concerns that inactivation techniques have not completely eliminated potential risks that could trigger adverse immune or inflammatory responses in public health [4]. The Chinese authorities have given Sinovac permission to formally begin human clinical trials with an inactivated SARS-CoV-2 vaccine candidate. Furthermore,

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organizations including the Beijing Institute of Biological Products, the Osaka University Research Foundation for Microbial Diseases, the Wuhan Institute of Biological Products, the National Institute for Biomedical Innovation, Health and Nutrition, and numerous others are actively developing inactivated vaccines to address public health issues [5].

2.2. Attenuated vaccines

Spike proteins are proteins that protrude from the outer envelope of SARS-CoV-2 and can bind to cell receptors, thereby allowing the virus's genetic material to invade host cells. It is part of the COVID-19 virus that circulates around the body and binds to ACE2 in the body, and it is not known how long the spike protein can stay in the body. Spike protein is the protective antigen located in the surface of SARS-CoV-2, which is cleaved into S1 and S2 subunit while maturation. Under native state, it functions as a trimer. Within the S1 subunit, there is a domain called RBD (receptor binding domain), that is responsible for the binding of host receptor ACE2 (angiotensin receptor 2). Once the binding of antigen and its receptor, the S2 subunit is activated to perform a conformational change triggering the membrane fusion between the SARS-CoV-2 and the host, thus the release of virus into the host cell (Figure 1). The three monomers in the trimeric spike must coordinate well for SARS-CoV-2 to infect someone. One monomer's structure is altered in attenuated vaccines, but the binding monomer's activity is left unaltered, maintaining the vaccine's antigenicity. Meanwhile, in order to guarantee the safety of the vaccine, the genome of the virus is fixed using formaldehyde like that in inactivated vaccines. By means of these modifications, the vaccine can elicit an immune response from the body and stimulate the production of particular memory B cells and memory T cells, thereby offering the body with long-term protection with minimal incidence of disease. For attenuated COVID-19 vaccines, they are developed with live coronaviruses that have been attenuated under laboratory conditions to reduce their virulence. By using this method, the virus is able to multiply within the host and only cause minor sickness. Compared to inactive vaccine, the attenuated vaccine is more effective, however, one major safety concern is the potential transmission of coronavirus through fecal matter from people who have been exposed to live, attenuated vaccinations and their recombination with viral infections of the wild type. Another question arises regarding the suitability of these vaccines for elderly populations, who are more vulnerable to serious illnesses [6].

2.3. mRNA vaccine

mRNA vaccine, here mRNA refers to the mRNA encoding the new coronavirus S protein (which can be roughly understood as the blueprint for making S protein). After entering human cells, the mRNA vaccine can use the raw materials in the human body to synthesize the new coronavirus S protein, and then stimulate the body to produce antibodies and play a protective role . mRNA vaccines are safer compared to DNA vaccines because they are not integrated into the human host DNA sequence [7]. Moreover, mRNA vaccines are manufactured in plants very quickly. With affordable production of over 1 billion doses, simple amplification technology can quickly fulfill a substantial demand for supply [8]. The mRNA vaccine is one of the key components in the COVID-19 pandemic because of these advantages [9].The production of mRNA vaccines offers a number of noteworthy benefits. First, reduction of adverse reactions: Since mRNA vaccines do not directly inject viral proteins, they reduce adverse reactions that can be caused by direct exposure to viral proteins. Second, rapid preparation: mRNA vaccines can be quickly prepared by transportation technology.. Third, in vivo induced antigens: mRNA vaccines induce cells to produce spike antigens in vivo without the need to manufacture and purify these antigens in vitro. This not only simplifies the production process, but also reduces production costs and time. Because of its unique advantages, mRNA vaccines have important application prospects in vaccine development and response to infectious diseases [10]. The human body may mount a strong immune response in response to the mRNA novel coronavirus vaccine, resulting in inflammation and other discomfort as well as the possibility of local irritation or allergy. The novel coronavirus vaccine has strict storage requirements, including low temperature and light protection. As a result, many materials will be used during the vaccine's clinical transportation and storage.

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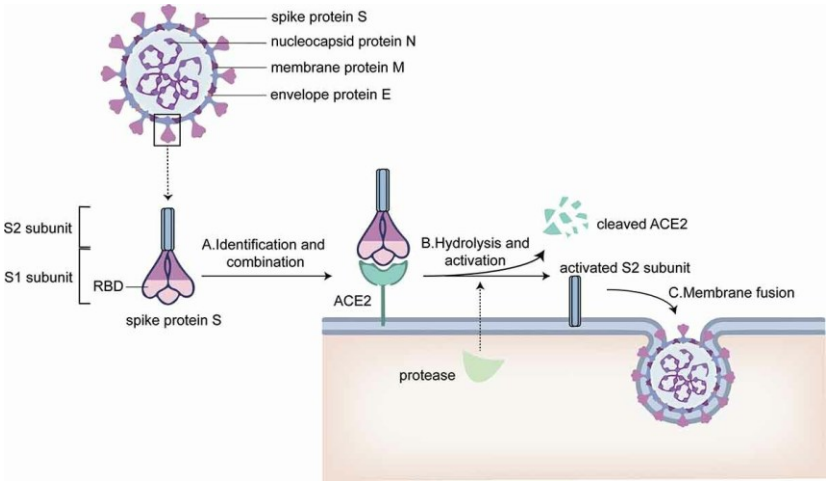

Figure 1. SARS membrane surface protein and the way the virus invades cells [11].

2.4. Virus-like particles(VLP) vaccine

Virus-like particles vaccine is injected with a recombinant virus, and the nucleus of this recombinant virus is usually changed or modified to eliminate the expression of its own surface protein, and an additional plasmid is employed to express the substitute surface protein, which has a single replication cycle within susceptible host cells. Because the surface protein must be present for the virus to enter the cell that it is attacking, its conformational structure is remarkably comparable to that of the instinctual transmissible protein; But the pseudovirus's virulence is reduced in comparison to the wild-type (WT) virus, making it safe to handle in P2 labs and on people. Virus-like particles (VLP) are highly malleable and scalable and has been utilized in the creation of influenza vaccinations against several subtypes including the subtypes H5, H6, H7, and H9, which can be produced through multiple expression systems, which include plant cells alongside mammalian cells, and insect cells-baculoviruses [12]. Through a variety of delivery methods, influenza VLP vaccinations can elicit a thorough immune response, offering cross-protection against influenza virus infections that are both homologous and heterologous. Consequently, one of the most promising substitutes for conventional inactivated vaccines is the influenza VLP vaccine [13]. The risks of vaccinating virus-like particles are also simultaneous. The main reason is that the vaccine is essentially a virus, so there is still a risk of virus, the injection of virus may also produce fever, fatigue, muscle and joint pain and other side effects. However, there are many diseases in society that have been vaccinated against virus-like particles, such as the papillomavirus (HPV) (Figure 2), hepatitis E virus (HEV), and hepatitis B virus (HBV) (Figure 3). With the development of technology, the research on VLP as a therapeutic vaccine for inflammation, pain, allergy, tumor, etc., and as a drug delivery carrier has also made great progress [14].

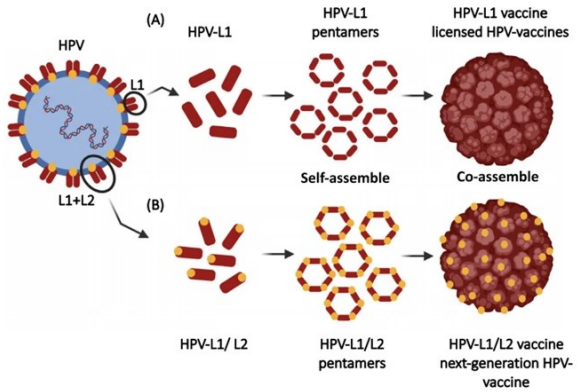

Figure 2. Schematic diagram of HPV and HPV-VLP vaccine structure [14].

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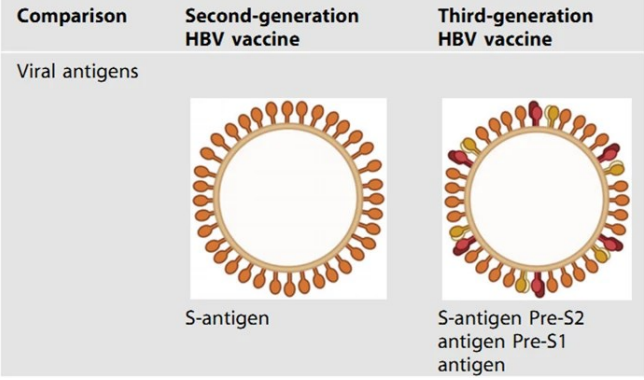

Figure 3. Structure diagram of HBV-VLP vaccine [14].

3. Conclusion

In conclusion, people from all walks of life have been interested in the new coronavirus since it first surfaced in 2020. At the same time, as an effective means of disease prevention and treatment, more and more people began to try to study different vaccines with shortcomings. In this article, four different types of vaccines are introduced against the background of the novel coronavirus. As a vaccine that can completely kill the virus, inactivated vaccine has the greatest safety effect, but it has great limitations in the selection of viruses and treatment effects. Although the attenuated vaccine strain has a natural advantage in the use effect, the virus itself still has a certain activity, so it is still a potential risk. Based on this, we have carried out research on mRNA vaccine. Being a nucleic acid vaccine, mRNA vaccines can induce the host's mutation response in addition to causing innate immunity by translating mRNA into protein and acting as an antigen. Therefore, the mRNA vaccine is more effective than the first two vaccines. However, because the effect is relatively strong, it is easy to cause a strong immune response of the host, and it is also accompanied by greater side effects. The VLP vaccine is an innovative sort of assembled vaccine the fact that has been used in the course of creating the COVID-19 vaccine as well as for the prevention of HIV, influenza, and other maladies. Nanovaccines are superior to conventional vaccines in that they enhance lymph node access, antigen presentation and packaging, and the induction of a sustainable immune response. In the future vaccine research, although there are many different kinds of vaccines with efficacy on the market, they all have their own advantages and disadvantages. No vaccine can perfectly meet the needs of all diseases, for example, the effectiveness of a vaccine is defective or the treatment is relatively inefficient. Vaccines have weak cross-protection against viruses that mutate easily. Therefore, the development direction of future vaccines will mainly focus on these aspects, improving the specificity, effectiveness, and cross-protection of vaccines.

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