Research progress of recombinant novel coronavirus protein vaccine

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Abstract. The coronavirus situation is dire around the world, with more than 594 million confirmed infections and nearly 6.45 million deaths. It was found that SARS-CoV-2 and SARS-CoV have a high level of genomic similarity (peak glycoprotein serial similarity of 87.2%) , which provide a basis for vaccine development. In the context of the 2022 novel coronavirus pandemic, there is an urgent need for a vaccine that can effectively protect against the virus that must be relatively safe while being effective and predictable as well. We found that recombinant protein vaccines seem to be able to effectively solve most of the current problems after comparing several existing vaccines. This literature review mainly introduces its overall background and the development steps of this technology, including how to screen for pathogenic proteins, how to implant in CHO cells and culture after infusion, and how to isolate and purify mature spike proteins that have been cultured. And supplemented with animal clinical trials of vaccines and ACE2 receptors and prospects for the future.

Keywords: Coronavirus, Vaccine, Clinical.

1. Introduction

A unique coronavirus (CoV) was these days discovered in Wuhan, Hubei Province, China in December 2019. The novel coronavirus is spreading so rapidly that the WHO declared it a public health emergency of worldwide subject on January 30, 2020. The virus was renamed SARSCOV-2 because of its high serial similarity to the severe acute respiratory syndrome (SARS-CoV) coronavirus. Thus far, the COVID-19 pandemic has ended in greater than 594 million confirmed infections and almost 6.Forty five million deaths global, with a rapid increase inside the range of instances. Although the mortality rate of SARS-CoV-2 is lower than that recorded for SARS-CoV during the 2003 epidemic, SARS-CoV-2 is associated with severe respiratory dysfunction and high mortality rates in older adults and individuals with chronic health problems. A high level of genomic similarity between SARS-CoV-2 and SARS-CoV (peak glycoprotein serial similarity of 87.2%[1]) has been found to provide a basis for vaccine development. Various vaccine platforms are currently being used by research and development (R&D) organizations and institute around the world in an attempt to develop treatments for SARS-CoV-2 infection. Further to live vectors and inactivated viruses, novel recombinant technologies are getting used to increase COVID-19 -19 vaccine. The advantages of recombinant vaccines are their more predictable and effective responses and their relative safety. Especially in the context of the COVID-19 pandemic, their efficacy and efficacy and safety issues related to implementation are discussed.

Critically ill patients develop acute respiratory distress syndrome requiring admission to the ICU and oxygen therapy. The time between admission to acute respiratory misery syndrome became as brief as 2 days. At this degree, the mortality rate for 2019-nCoV became high, as 6 (15%) of the forty one sufferers on this cohort died. The death toll is rising rapidly [8]

In recent years, COVID-19 vaccines have accelerated at an unimaginable speed in the history of vaccines, and there are 199 candidate vaccines in pre-clinical development and 172 in clinical development. In China, inactivated vaccine, which is made by inactivating pathogenic microorganisms after culturing, is the current mainstream vaccine type. Although it is easy to be stored and transported, people need to be vaccinated multiple times in order to maintain serum

antibody levels, which sometimes causes severe local and systemic reactions to injection. Since the inactivated pathogen cannot enter the host cell to multiply, they are unable to the induce CTL generation by endogenous antigen presentation, so the immune effect has certain limitations.

The discovery that SARS-CoV-2 is transmitted from an infected person with no symptoms, and its ability to cause pandemic disease within weeks, suggests that without the prospect of a vaccine, the control of infection with this virus will be challenging [2]. The vaccine must be relatively safe while being effective and predictable. However, several new crown vaccines approved for use on the market have failed to achieve the effects we expected, both in terms of safety and efficacy. The development of vaccine platforms is also extremely important. After comparing several existing vaccines, we found that recombinant protein vaccines seem to be able to effectively solve most of the current problems.

This review focused on recombinant protein vaccines, which is relatively safe while being effective and predictable. Its ingredients are simple and clear, and the relative potential safety factor is high. Moreover, the environmental production requirements are relatively low, and it can be produced only under ordinary GMP production conditions, without the need for biosafety-grade factories. It can be transported at 2~8 degrees Celsius, no need for ultra-low temperature refrigerators. We decided to make a general integration of this technology to facilitate more people's research and will give a future outlook.

2. Features of protein vaccines

A recombinant protein vaccine, which uses the spike protein found on the surface of the new coronavirus. The spike protein in the vaccine is grown in cells in the lab. After vaccination, the immune system mounts an immune response against the spike protein. This is different from mRNA vaccines (Pfizer and Moderna): instead of using the spike protein directly to generate an immune response, mRNA vaccines communicate instructions to cells to make the spike protein. This allows the same effect to be achieved with a smaller dose. Amongst different benefit, because the recombinant protein vaccine is non-replicating and lacks any infective element of the virus particle, it is taken into consideration a safer technique in comparison to vaccines derived from live viruses.[5]

However, its antigenicity is affected by the selected expression system, so it is necessary to choose the expression system carefully when preparing the vaccine.

3. Vaccine Development Goals

SARS-CoV-2 shares a high level of genomic similarity with SARS-CoV, both of which belong to the genus Betacoronaviridae of the family Coronaviridae. First discovered in China (2001~2003). Studies have shown that both viruses are RNA single-stranded viruses. In the existing structural protein research, we found that no matter what kind of coronavirus they are, they lack the proofreading of recombinant genes, including the interaction of S1 subunit and ACE2 receptor when the new coronavirus enters the body, so the research direction of recombinant protein becomes A very important target for countermeasures against the new coronavirus, the importance of the S protein as a potential target for the development of vaccines against SARS-CoV-22 was also pointed out in previous protein studies on SARS-CoV and MERS-CoV. Similarly, more than one research has shown that anti-S antibodies can neutralize SARS-CoV and MERS-CoV and provide protection in animals and people. Furthermore, many S protein vaccines towards SARS-CoV and MERS-CoV were shown to elicit effective immune responses and defensive outcomes in preclinical fashions. [6]

4. A Brief History of Protein Drugs

In 1982, the sector's first recombinant protein drug, recombinant human insulin, was launched, establishing a glorious history of recombinant protein drug development. The Nineteen Nineties turned into a golden length for the improvement of recombinant protein drugs. Some of blockbuster

recombinant protein capsules were accepted for advertising for the duration of this period, presenting new means for sickness treatment, benefiting mankind and creating tremendous monetary benefits. Despite the fact that now not lengthy, this generation is pretty mature.

5. Principle of recombinant protein vaccine

The pathogenic protein or antigen part of the virus is recombined in vitro and then injected into the human body to stimulate the body to make an immune response.

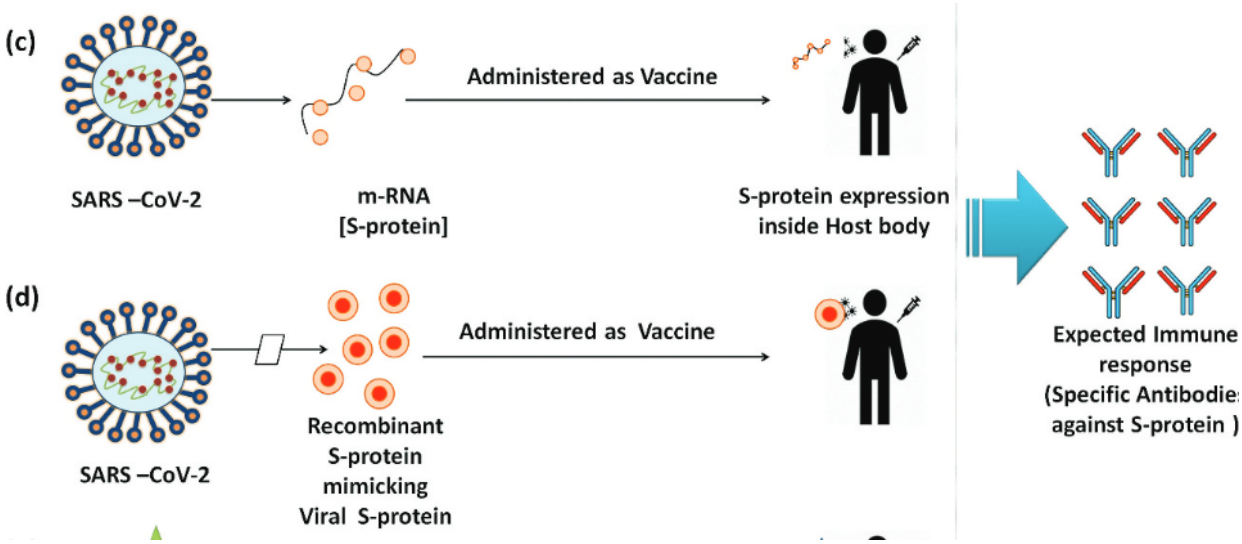

Figure 1. The mechanism of SARS-CoV-2 Vaccine

6. Coronavirus Vector

Viral vectors are one of the priority countermeasures against coronaviruses. Their efficiency is largely dependent on the ability to infect different types of cells. Due to its genetic specificity, its delivery after entry into the human body and the generation of a safe and healthy immune response are major advantages. At present, the main research vector types in the market include adenovirus, measles virus, influenza virus and animal adenovirus. They all demonstrated the observed surge in neutralizing antibodies and immune cells after vaccination (hypermutation).

7. Cell expression

Cellular Expression Technology We have so far succeeded in creating the first recombinant expression system using Escherichia coli that provides a large number of defined proteins. Insect cell expression is a novel expression system that uses insect ovarian cells from Drosophila sporozoites to infect the baculovirus vector California nuclear polyhedron virus. Can effectively control the expression of polyhedral proteins [3]. Mammalian cell expression, this type of system expression is more inclined to natural selection rather than complete artificial intervention. The new coronavirus vaccine also uses a large number of mammalian cell expression such as CHO engineered cells, as well as the real processed protein of the subunit vaccine, which may be the expression level is slightly lower [3].

8. Isolation and Purification

Obtaining Excessive yield, purity and activity of recombinant proteins is essential for different applications. And a couple of downstream utility techniques. Affinity protein purification the usage

of antibody-primarily based separations or matrices with specific ligands for affinity tag binding are common methods.

CBMs, Previously known as carbohydrate-binding domains, are protein domain names derived from carbohydrate-related enzymes that show off precise binding affinity for certain carbohydrate polymers [4]. CBM has long been used as an affinity tag for protein purification/recombinant protein immobilization, and at the same time as a fusion accomplice for recombinant manufacturing of antimicrobial peptides [4]. Furthermore, CBMs had been fused with different peptides/proteins and carried out in completely distinctive contexts along with cosmetics, biosensors or biomedical packages [4].

9. Animal Clinical Results of Covid-19 Recombinant Protein Vaccine

Advanced and examined in 35 rhesus monkeys inside the America. Vaccinated macaques exhibited particular humoral and cellular immune responses. Immunized animals exhibit specific T-cell responses [1]. The experiments in this document use cryo-electron microscopy (cryo-EM) to reveal the complex structure of the SARS-CoV S glycoprotein and its host cell receptor ACE2 , the complex structure shows that only the receptor-binding domain within the S1 subunit of the trimeric S-glycoprotein binds ACE2 with a prominent "up" conformation [9]. This has proved that ACE2 exists as a receptor in the human body, and as long as the spike protein and ACE2 can be cut off from each other, the preventive effect can be achieved. Looking at the experimental results, the antibodies not only neutralize SARS-CoV-2 and block the S protein-ACE2 interaction, but also circulate in the lungs [1], but some individuals have less antibody retention, which still needs to be overcome.

10. Prospects for recombinant protein vaccines

Recombinant protein vaccines may be the most immunogenic and safe vaccines to date. With multiple recombinant protein vaccines showing extraordinary efficacy and unique advantages in research and trials, recombinant protein vaccines have the potential to become the new crown epidemic containment vaccine. long-term strategy.

At present, 2 recombinant protein vaccines have been approved for use in the world, 8 have entered Phase III clinical trials, and recombinant protein vaccines in Phase II and Phase I clinical stages also account for a relatively high proportion of all vaccine species. Generally, the development of latest vaccines takes 10 to 20 years, with a achievement rate of less than 10%, even for vaccines that input scientific trials [7]. Inside the beyond 30 years, the us FDA has approved nearly 3,000 vaccine clinical trials, and much less than 20 vaccines had been authorised for advertising[7]. Even though the research and improvement, manufacturing and sales of vaccines are strictly regulated, for the sake of human health, we have to lay a solid basis and conduct studies in accordance with these scientific legal guidelines [7].

11. Conclusion

In the dire coronavirus situation around the world, recombinant protein vaccine is one of the best vaccines that are used for prevention of novel coronavirus, with advantages of the simple, clear ingredients, and the relative safety hazard is high. Moreover, the production requirements for the environment are relatively low, and it only needs to be produced under ordinary GMP production conditions, without the need for biosafety-level factories, and it is easy to be transported as well. In the animal clinical results of covid-19 recombinant protein vaccines, the vaccine got impressive data that this kind of vaccines is effective against viruses. Recombinant protein vaccines may be the most immunogenic and safe vaccines to date with those advantages that is mentioned above. The vaccines in clinical stages account for a relatively high proportion of all vaccine varieties show that it has good prospects as well.

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