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Current Application of Different Kinds of COVID-19 Vaccines

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Abstract. Nowadays, the mortality and morbidity of malignant neoplasms in people is rising, which pose serious risk to human beings. Therefore, finding suitable methods to treat these diseases effectively is arousing more and more attention. Among them, phototherapy, such as PDT and PTT is a good strategy due to the advantage of antibiotic-free. This review focused on the near-infrared light-induced materials involving in conjugated polymer, organic small molecule, quantum dots, metal organic frameworks, covalent organic frameworks and inorganic semiconductor, and discussed their applications in NIR-guided PDT/PTT synergistic therapy. The review further provides a critical analysis of the future development of PDT and PTT. It is believed that NIR-guided PDT/PTT synergistic therapy will promote the therapeutic development of cancer.

Keywords: near-infrared light, PTT, PDT

1. Introduction

At the end of 2019, a sudden infectious disease swept the world, and everyone was caught off guard. At the begin-ning of 2020, scientists named this infectious disease covid-19. In the first six months, the number of infected people worldwide reached hundreds of millions. At first, many people thought it was very similar to SARS broke out in 2003 because it was a pneumonia-like disease, but over time, scientists found that the new crown is not equivalent to SARS. When covid-19 infected most countries, various countries also began to develop vaccines against covid-19.

Before the development of the new coronary pneumonia vaccine, vaccines in the world against COVID-19 has been roughly divided into three types: subunit vaccine, mRNA vaccine and attenuated live vaccine. Subunit vaccines has been mainly applied in two aspects, one for the treatment of viral diseases , another for the treatment of bacterial diseases. There are also hormonal subunit vaccines. mRNA vaccine is an emerging third-generation vaccine, which is subdivided into the non-replicating mRNA vaccine and self-amplifying mRNA\SAM mRNA vaccine. The attenuated live vaccine is one of the most common vaccines, such as the BCG vaccine which must be vaccinated by newborns. Of course, the new crown vaccine also belongs to these three categories. But due to the different directions of scientists' research, different countries have different new crown vaccines. Recently, in China, vaccines which against covid-19 are inactivated vaccines and recombinant subunit vaccines.

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Because of the coronavirus outbreak, almost all countries are scrambling to produce vaccines against the virus. Because these vaccines are not produced depending on the normal process, people remain doubtful about the safety and efficacy of these new crown vaccines. In addition, various countries produce various types of new crown vaccines, people resist to vaccination. In this regard, we will analyze these three vaccines in this paper. We will introduce the mechanism of action of each vaccine, the activities of these three vaccines after entering the body, the choosing of these three types of vaccines by comparing the effects and advantages in different infectious and current clinical tri-als. Of course, no vaccine is perfect. There are specific side effects behind their effectiveness. So, in the end, we will summarize the side effects and transportation and storage difficulties of these three vaccines. This side effect is not only a side effect of the new crown vaccine but also a side effect of other ordinary vaccines.

2. Subunit vaccine, mrna vaccine and attenuated vaccine

Here we are going to discuss two mainstream recombined vaccines, subunit vaccine and mRNA vaccine and a tra-ditional vaccine, attenuated vaccine. In order to have a clear difference between these vaccines, we will introduce the mechanisms of these vaccines.

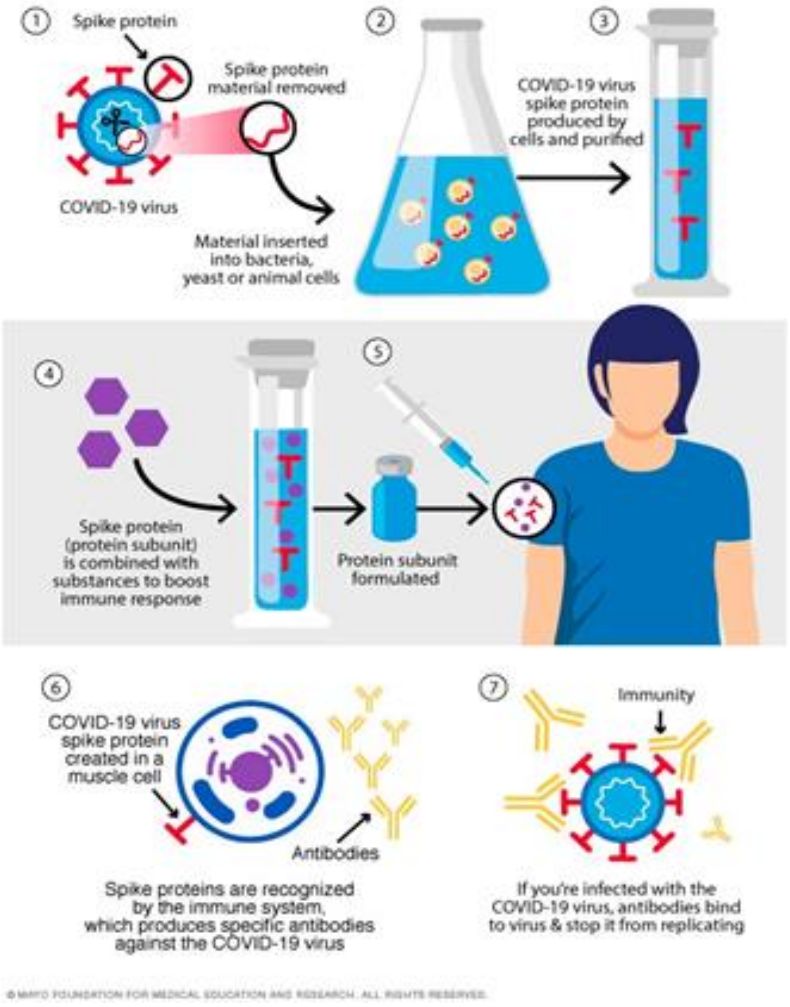

Figure 1. The process of production of a subunit vaccine, ① to ④, with an example of COVID-19. The effects, ⑤ to ⑦.

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Subunit vaccine is based on spike protein (S protein) which is present on the surface of the virus that is able to trigger immune response. The spike protein is a part of the virus.

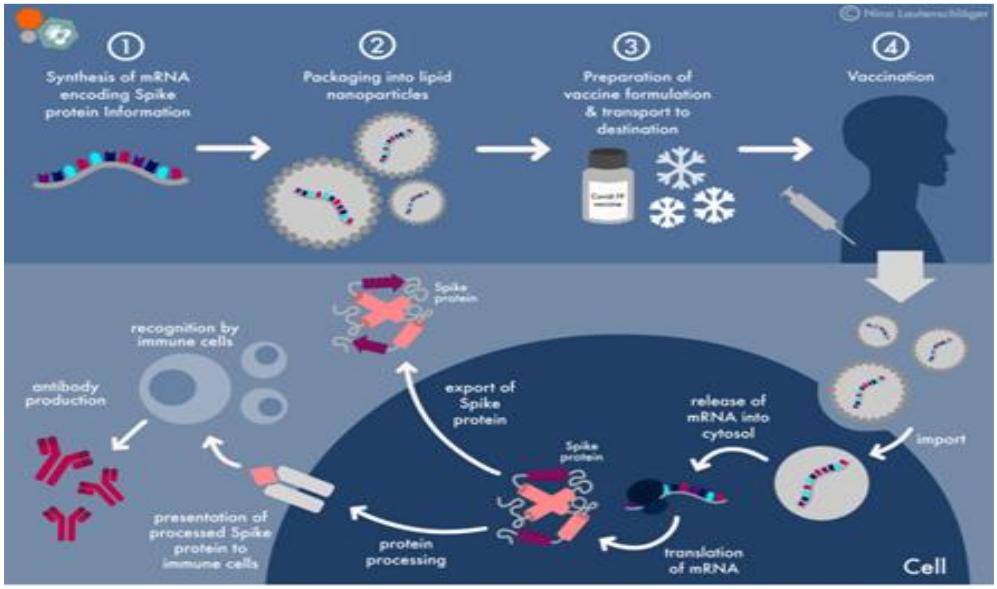

Figure 2. The synthesis of mRNA vaccine, ① to ③.The effects, after ④.

In order to produce subunit vaccine, we need to identify the specific S protein which can cause immune response most. After that, the gene which code for the S protein is removed from the virus, inserting to a vector which can be bacteria or yeast. The product, S protein (protein subunit) is purified and then dose an infected person. The produced S protein is also injected with adjuvants, a kind of material which increase the sufficient to produce high immuno-genicity. After the injection, the immune system can recognize the S protein, creating antibodies and defensive white blood cells. Finally, the body can get resistance. In 1997, Doctor Takeshi Arekawa and his team use potato as a vector to produce the subunit of nontoxic cholera toxin B, which have an effect on against cholera [1].

The first step is synthesis of mRNA that encoding S protein, then pack it into lipid nanoparticles. These particles ensure the transportation of mRNA into the cell, defense it from digest enzymes in the body. The combination of mRNA and nanoparticles is the mRNA vaccine. When it is injected to the body, mRNA will be released into the cell, usually muscle cells, translate into S proteins which will trigger immune response in the body. The cell is like a S protein 'factory' that can produce it

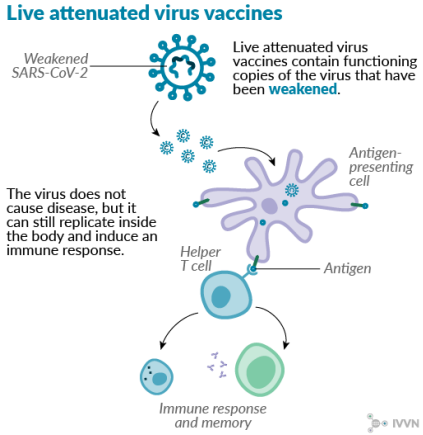

Figure 3. The mechanism of attenuated vaccine.

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continuously.

In this case, few mRNA doses can also create a strong immunogenicity. After the immune response, the body gain the resistance.

Attenuated vaccine is a kind of traditional vaccine which means it is used in early centuries. It has the simplest mechanism and produces method in these three vaccines. However, it still has a high efficiency. The crucial process of developing attenuated vaccine is to produce non-functional virus or bacteria which do not cause infection. Some-times we use methanal to reduce the toxicity for example, different reagent is used in different virus or bacteria. Then the non-functional antigen is injected to the body to cause an immune response. The antigen is similar to the func-tional one, so the immune response is strong, have a high probability to gain the resistance.

3. Current application

3.1 Subunit Vaccine

At present, many subunit vaccines have been developed at home and abroad. There are viral and bacterial diseases, as well as hormonal subunit vaccines [2]. There are foot-and-mouth disease subunit vaccines that can prevent foot-and-mouth disease virus infection, influenza antigenic epitope subunit vaccines, chicken infectious bursal disease genetically engineered subunit vaccines, Newcastle disease virus subunit genetically engineered vaccines, and trans-genic plants to express immunogenicity Vaccines, etc.

At the same time, there are also some clinical trials using the vaccine to treat tuberculosis. Subunit vaccines are made of antigens combined with adjuvants, which overcome the safety problems associated with live attenuated vac-cines or inactivated vaccines and have more controllable components and higher efficiency [3]. At the same time, it can also be used to treat Escherichia coli. The oral-formalin inactivated enterotoxigenic Escherichia coli (ETEC) vac-cine is well tolerated and can also elicit an immune system response.

3.2 mRNA Vaccine

Compared with the other two vaccines, the mRNA vaccine is a new vaccine and belongs to the third-generation vaccine. It is divided into non-replicating mRNA vaccine and self-amplifying mRNA\SAM mRNA vaccine.

Due to mRNA vaccines have the flexibility of genetic vaccines that has not yet been achieved, an excellent safety profile, and favorable immunological properties [4]. Many nations are presently researching it for the treatment of genetic disorders, protein replacement therapy, tumor immunotherapy, and infectious disease. Of course, preventing new coronary pneumonia is currently the vaccine's most popular use [5].

4. Side effects

4.1 Subunit Vaccine

For research and development, it is difficult to find a suitable expression system. And it requires a high scientific research and technical content, and the research and development take a long time. For subunit vaccines, its side ef-fects are local redness, swelling, pain, and generalized fever [7].

4.2 mRNA Vaccine

mRNA vaccines have strict requirements for storage and transportation, and as a new technology, there is a lack of experimental accumulation. Localized swelling at the injection site, dizziness, itching, rash, reduced appetite, gener-alized weakness, headache, myalgia, chills, fever, nausea, joint aches, sweating, and localized discomfort, muscle spasms, poor sleep, and brain fog were the symptoms of vaccine adverse reactions that were reported the most fre-quently (due to decreasing frequency) [8].

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4.3 Attenuated Vaccine

This vaccine is a microbial preparation and still contains some toxicity. Although the toxicity is small, it can also cause some diseases for some people with low immunity. At the same time, it will also cause environmental pollution. Therefore, there are certain requirements for transportation and storage. At the same time, to ensure that the vaccines people get are as virulent as possible, scientists need to breed many generations of the virus, so it takes a long time to screen for the right virus [9].

5. Comparison

5.1 Subunit Vaccine

As a result, clinical trials with two types of HSV subunit vaccinations on volunteer of 18 that doesn't carry a his-tory of herpes simplex type 1 or type 2 infection were conducted on 15 people out of the 18 volunteers with HSV1 recurrences and 44 patients with severe recurrent genital type 2 HSV infections. The vaccine dramatically raised on antibody titers in virtually all of the patients carrying type 1 or type 2, and it produced humoral and CMI in 97% of participants without past HSV infections. The immunization specifically induced the formation of antibodies for this specific use in 96% of those with recurrent HSV 2 infections. This could, at least in part, account for the clinical suc-cess of the vaccination [10].

5.2 mRNA Vaccine

30,420 volunteers were enlisted in the trial for the particular mRNA vaccine, and they were randomly randomized to receive either the vaccine or a placebo in a 1:1 ratio (15,210 participants in each group).

The outcome of this clinical study demonstrates the importance of including assessments 14 days after the first dosage, analysis in participants 65 years of age or older, and analyses in persons who had SARS-CoV-2 infection at baseline. All 30 people with severe Covid-19—including one fatality—were in the placebo group. The mRNA-1273 group experienced moderate, transitory reactogenicity more frequently after vaccination. As a result, the Covid-19 illness, including severe disease, was prevented by the mRNA-1273 vaccination with an efficacy of 94.1%. Other than brief local and systemic reactions, there were no safety issues found.

5.3 Attenuated Vaccine

A total of 1600 volunteers were included in this influenza vaccination trial, and the patient inclusion rate was 89%. 28% of youngsters tested positive for influenza; 317 had influenza A(H3N2) and 110 had influenza B. The majority of influenza isolates were identified as drifted strains of influenza A(H3N2) or B/Yamagata. The adjusted VE for all influenza was 50% (95% confidence interval, for influenza A(H3N2) it was 30% (95% CI, -6% to 54%), and for type B it was 87%.

6. Conclusion

We have presented the mechanism, the current application, side effect and the comparison of three kind of vac-cines. We found that research on mRNA vaccines is the scarcest one, but the attenuated vaccine makes the most re-search in these vaccines. The mechanism of mRNA vaccine is the most complex one, but the mechanism of attenuat-ed vaccine is the simplest one. The data from Subunit Vaccine are somewhere in between of them. By contrast, atten-uated vaccine has the most current applications due to earlier inventions and applications. However, mRNA vaccines were invented later and have the least current application based on difficult and complex manufacturing processes and theories. According to these founding, our comparison shows the different vaccine behavior in different experi-ment, and all of them shows high efficiency in their experiments individually, which indicate that all of these vaccines are available in the treatment or prevention of some kinds of diseases, such as HSV and COVID-19. The ability of distinguish of different mechanism and curative effect is important in the aspect of choosing the most effective vaccine in the therapy of a specific disease. It provides a general idea of the vaccine invention for investigators, help-ing them to assume which vaccine might be the most effective

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one. In the future, these kinds of vaccines play an es-sential role in the prevention of infectious disease. Attenuated vaccine can be fastest one to give immunity when the outbreak of pandemic due to its mature production process. The subunit vaccine can give immunity more efficiency than attenuated one, which can produce a more stable and effective vaccine base on the mechanism of it. Although there are several research on mRNA vaccine, it has the greatest potential to give the strongest immune response and more durable immunogenicity. Not only that, but mRNA vaccine also (or therapy) has a more effective therapeutic effect in the field of tumor treatment, which was a study that attracted worldwide attention.

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