Immune System Mechanism and Vaccination of SARS-Cov-2

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Abstract. The earliest coronaviruses were discovered in the 1960s and were named for the coronal spike-like protein located on the surface of the virus. SARS-CoV-2 disease rapidly had a profound impact worldwide, resulting in millions of infections and deaths. High transmission rates and high mortality rates have plunged many countries into crisis, mainly in medical and economic terms. Innate immunity also plays a central role in the fight against COVID-19 virus, which includes T lymphocytes, B lymphocytes and other types of immune cells. However, the SARS-CoV-2 virus appears to be new to the human immune system and often causes fatal complications and symptoms that are beyond the reach of natural human immunity. In the early stages, doctors tried treatment with antiviral drugs, as well as immunomodulators, using steroids and different kinds of cytokine blockers, which seemed promising, but it was still not effective in curing COVID-19 or curbing the infection rate. When a vaccine is established, the global pandemic will cease, which will greatly reduce mortality and prevent serious complications in patients. Various forms of vaccine development have strengthened the control of global COVID-19 infection, but challenges and barriers to containment of SARS-CoV-2 remain.

Keywords: SARS-CoV-2, Vaccinations, Immune Systems.

1. Introduction

It has been 3 years since the beginning of the Covid-19 epidemic. At the first, little was known about this virus, which was later named SARS-Covid-2. Ignorance about the coronavirus has caused tens of thousands of deaths around the world, and it has caused people to panic. In this case, hospitals, scientists and experts did their best to try to figure out how this virus works, the cause of the symptoms and the treatment. However, the most complicated thing was to research and invent a vaccine for people to fight this epidemic. In the experts' research, the Covid-19 virus is very similar to the SARS virus. They have a similar size and shape and both spread through the respiratory system, which is why they can spread from person to person with incredible speed. In addition, both viruses cause the same symptoms in humans, and they both work through protein regeneration and recombination. With these similarities, experts can refer to the previous cases against SARS. Once the working process of the virus was clearly discovered. Based on this discovery, scientists could more easily invent vaccines. Now, at least three types of vaccines have been designed. Although the virus has undergone many mutations, some of which still cause severe symptoms in humans, research and technology is much more advanced than in 2019. At least mortality rates have declined. With the development of the vaccine and the popularity of SARS-covid-2, people are more aware of how to protect themselves from infection, so they do not panic, instead they feel safer.

2. Passage of SARS-sars-CoV-covid-2 virus into animal cells

The SARS-covid-2 virus accesses the animal(human) body through the respiratory system. As a result, it causes a huge effect on the human respiratory tract. Respiratory system is divided into two parts, upper respiratory infection and lower respiration infection. The virus first accesses upper respiratory infection, which includes nose or mouth, pharynx and larynx in order [1]. Then arrive lower respiratory infections, which are trachea, bronchitis, bronchiolitis and lungs (alveoli). Once the

virus enters the alveoli, it starts to attack target cell (host cell) [1]. The offense starts from the cell surface receptors which is a protein called ACE2. This protein normally helps to regulate blood pressure. On the SARS-covid-2 virus membrane, a protein called Spikes protein (S protein), this protein binds the ACE2 and set off a chemical change that leads to the direct fusion of the virus and cells. As SARS-covid-2 is an envelope virus, the fusion begins with the fusion of the viral envelope and endosomal membrane. After the fusion process, the virus is able to release genetics materials-RNA materials which are the nucleoprotein packaged in viral capsid. It then traverses the cytoplasm and gets close to the protein-making "machinery" which is a nucleus. Once it reaches the cellular compartment, the viral capsid releases the viral genome into it for replication. In the protein-making machinery, the Genetic materials from viruses recombine and replicate with the DNA and RNA in the host cells [2]. Then the new viral particles are repackaged and released from the cell to infect more body cells. In this way, the cell is forced to produce tens of thousands of new virions. However, some of the RNA materials from the SARS-covid-2 still stay inside the cell for 3 main functions. The first is to stop the host cell send out the signals to the body immune system so that the virus can live for more time. The second one keeps stimulating the host cell to produce more and more virions. The third function is to resist innate immunity.

3. The response of an immune system

So how does the immune system respond and against the virus from infecting more cells? The first line response is the innate response. When the virus goes inside a cell and replicates, the infected cell produces and releases interferous, this is a type of cytokine, which is a signaling protein. The interferons play a role of warning the neighboring cells by binding to the interferon receptors on the uninfected cells. Then those uninfected cells generate an antiviral protein that can avoid the replication from virus and being infected. Apart from that, interferons also give the other function. It makes other cells to rise the expression of the major histocompatibility class (MHC). MHC has 2 essential functions on sending the signal- present antigens to adaptive immune system cells and innate immune cells. The next step is to kill the infected cells. Those infected cells are removed by specific lymphocytes called NK cells, which can recognize the antigen on MHC. Normally, T cell can bind to the antigen and check whether the cells are infected. However, the covid-19 virus can prevent those infected cells from synthesizing the MHC molecules. In this situation, The NK cells can recognize the loss of MHC and produce toxic substances that can kill the infected cells. In addition, the macrophages can also remove those infected cells by phagocytosis. The macrophage first surrounds and engulfs the virus. Then mixes the virus with its digestive enzymes, which break down the virus totally. Macrophage is an antigen-presenting cells, because it is able to capture, process and present antigen from pathogens. There is also another types of antigen-presenting cell that is dendritic cells. These cells connect the innate and adaptive immune responses [3]. When the innate system is not able to fight the virus, the adaptive system will be involved to give help in fighting the virus. The adaptive immune system includes lymphocytes (T cell and B cell) and antibodies. The T cell and B cell do cooperation to destroy the pathogen and prepare for the next fight. The T cell can kill the infected cell directly which will explain later. The B cell fight virus via producing specific antibodies, this will also explain more detail below. After several process, the virus is killed and memory cells is produced and memorize the virus.

3.1. Function of T-cell

T cells in the immune system plays an essential role, especially for against the SARS-covid-2 virus. There are two types of T cell, CD3+CD4+ T cell and CD3+CD8+ T cell. CD4+ T cell assist the generating of neutralizing antibody by B cell through cell-to-cell interaction (CD40L-CD40) and release of cytokines. The neutralizing antibodies act as sterilizing immunity. Apart from that, CD4+ T cell access B cell follicles in order to providing assist called TFH cells [4]. These cells help to develop the B cell memory and make the antibody-making plasma cell to live longer. There are some

CD4+ T cells' co-stimulatory ligand, which assist the improvement of B cell activation and antibody production ability. CD4+ T cell also give supplementary to CD8+ T cell [4]. CD8+ T cell is enhanced to give stronger and quicker response, and the functional pathogen-specific memory is also improved through the aid from CD4+ T cell. In addition, CD4+ T cell is able to regulate the inflammatory response. The other type, which is CD8+ T cell plays a dominant position on destroying the virus. The circulation of CD8+ T cell rely on the secondary lymphoid [5]. During the circulation, the signs of the exteral intruders are able to be access by CD8+ T cell. CD8+ T cell receive the message through the dectection of the appearing of the dendritic cells, which have to be matured [5]. This is because the mature dendritic cells express MHC-peptide and some co-stimulatory molecules. Once the CD8+ T cell is stimulated or activated, it will experience a dramatically expansion period (from 0.001% to around 3-50%). These CD8+ T cells start to kill the virus directly. On the CD8+ T cell, there are many different receptors which is able to bind with the virus antigen. When the receptor from CD8+ T cell completely fits with virus antigen, the CD8+ T cell release 2 substance-perforin and cytoxins. The perforin response for generate a pore on the infected cell surface membrane, and the cytotoxin go into the infected host cell directly then destroy the virus. The responsibility of cleaning the remaining fragment of virus and infected host cell is given to the macrophages.

3.2. B cell response to SARS-CoV-2

B lymphocytes generally use as regulate humoral immune response and secrete antibodies during SARS-CoV-2 infections [6, 8]. B cells act as an irreplaceable character in adaptive immune system which response in humoral for killing invaders such as bacteria and viruses. The role for particular virus infection is virus identification, cytokine production, antibody secretion, and antigen presentation [6].

When the SARS-CoV-2 virus enter the body humoral, the virus will bind to the B cell which have the exact matching key and specific antibody, then the B cell will be activated. B lymphocytes activation response will show B cell in 6 different forms. Pre-B cell is the first form after stem cell (counted as 1 form), developing cytoplasmic μ heavy chain and pre-B receptor. Membrane lgM will appear in immature B cell stage just before mature B cell which add membrane lgD. After B cell be activated, lg secretion will be at low rate, switching to heavy chain isotope and affinity become mature. Antibody secreting cell will secrete lg at high rate for COVID-19 immune response at last. Proliferation will cause B lymphocytes divide into different kinds of memory B cells (MBCs) and effector cells. MBCs contribute more in dividing the severity and occurrence in the recrudescence of SARS-CoV-2 and COVID-19 vaccine development [6]. Worth mentioning the CD11c+ T-bet+ memory B cells which developed from GCs, keeping low-level chronic antigen stimulation and under conditions of inflammation and being a role as preventing COVID-19 re-infections [6-7].

To be more specific, the mature B cell can also be subdivided to different subpopulations like B-1, B-2 and regulatory B cell [6]. B-2 cells exist after birth, growing in the bone marrow. B-1 cells are CD-5+B cells that first appear in the fetal period, maintaining resting immunoglobulin levels in the body without any stimulus or immunization [9], therefore, B-1 cells are innate immune cells and play a role in the early stage of COVID-19 immune response.

4. Vaccine basic principles

Although the body natural immunity usually plays the principal role during infections, some naturally-acquired infections can lead to complications, causing severe physical disorders. The vaccine has the ability to protect patients from infecting this disease and its fatal symptoms. In the 20th century, the most vaccine needs decades to apply to clinical for human use. However, the COVID-19 vaccine cleared the threshold for emergency use in less than 11 months. Patients usually get once vaccination or regular vaccination for different kinds of disease. After the injection, the killed or weakened virus particles will teach human immune cells to defend or kill these invade virus and produce antigens, letting the memory cells memorize the virus in order to response much quicker

next time. This will not let human body really infect with the disease, but activate a series of immune response and memorization. DNA-based vaccines, RNA-based vaccines, recombinant subunit vaccines, adenovirus-based vectors, and inactivated viruses are 4 types of SARS-CoV-2 vaccines that have been developed for clinical use [10].

4.1. Different kinds of vaccine

4.1.1 mRNA vaccine

mRNA vaccine uses our body's existing cellular machinery to trigger immune response, basing on the principle of mRNA is an intermediate messenger to be translated to an antigen after the delivery into host cell [11]. As mRNA enters the host cell, ribosome will translate mRNA for encoded protein, therefore, mRNA vaccine usually uses for diseases or cancer which need protein replacement [11]. Researchers usually use trillions mRNA segments for specific viral protein, injecting into nanoparticles which made of lipids. Nanoparticles containing nanoparticles will fuse the hose cell membrane and enter the host cell, which because the similar fatty acid membrane structures. Using mRNA vaccine as COVID-19 vaccine has several merits. The main advantage should be quick development, as using mRNA-LNPs platform technology [12]. Compare to other kinds of vaccines, mRNA vaccine may be more valid for COVID-19 prevention. The quick speed in manufacture brings benefits especially in emergency use such as COVID-19 pandemic [12]. There are approximately 7 mRNA vaccine for preventing SARS-CoV-2 which are mRNA-1273, BNT162b2, CVnCoV, ARCoV, ARCT-021, LNP-nCoVsaRNA, ChulaCoV19 mRNA vaccine. First two COVID-19 mRNA vaccines have been approved for market use, and others are still in clinical trials [13]. One of the disadvantage of using mRNA vaccine is the storage or transport condition should be at lower -70℃, however, mRNA vaccine can only live about 5 days in standard refer-Temperature required.

4.1.2 Live attenuated vaccine

Live attenuated vaccine uses a weaken form of virus which can still grow and replicate. Although the virus has been weakened, it is still dangerous for specially group of people such as HIV patient and pregnant woman. COVI-VAC Vaccine is a COVID-19 live attenuated vaccine which produced by the United Kingdom's Codagenix and Serum Institute of India. Since lived attenuated vaccine use the whole COVID-19 virus protein rather than a part of spike protein like RBD, COVI-VAC live attenuated vaccine usually cause a robust immune response, resulting in long-lasting cellular immunity.

4.1.3 Inactivated vaccine

Inactivated virus usually known as killed virus. Heat, radiation and chemicals such as formaldehyde, glutaraldehyde, ultraviolet, and gamma rays are ways for killing a virus, causing protein shell and viral genetic material break down [11]. The remaining parts are inactive and can no longer causing the disease, but they can still activate the immune response. Unlike live attenuated vaccine, inactivated vaccine is much more stable because its genetic code has been destroyed. The high speed of development and the storage environment is not strict as mRNA vaccine lower the difficulty for emergency use. However, there are some drawbacks that we should concern about. There are possibilities that virus antigen and epitopes can be destroyed or damaged during the inactivated process, causing the low-level immune response [14]. More noteworthy is because the natural selection, there are more SARS-CoV-2 variation appear, resulting in the genetic change in COVID-19 genome [15-16]. Research has accentuated that the Omicron variant declines the neutralization ability of vaccines by evading neutralizing antibodies, which reduces immune responses and might lead to re-infection [16]. Boosts are then required for this situation, which might need several additional doses.

5. Conclusion

The COVID-19 pandemic caused by the novel virus SARS-CoV-2 threaten the humane society in many aspects like public health, social order and especially people's mental health. Like other pandemic infectious virus, SARS-CoV-2 infect human without discrimination like region, nationality and color, however, it's speed of transmission is rare with 213 countries reported confirmed cases just. This global pandemic does not only remind human to be aware of control and management of unknown infectious disease but also stimulate the human potential in medical development. Even though autoimmunity plays a decisive role in fighting against invaders, it's still confused when facing unfamiliar aggressor. Vaccine being as a lecturer teach innate immune cells the way to defend these invaders. Vaccines made from different material and platform usually creat by considering the effectiveness, cost, specificity, feasibility and practicability. Various new types of vaccines have been investigated and use in clinical practice, monitoring clinical safety is still needed and even plays the uppermost role in the vaccine development. Although the COVID-19 vaccine is developed, there is still chances for vaccinated humans to infect SARS-CoV-2 and we cannot ignore the adverse reaction and the effective time period after vaccinated.

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