A REVIEW OF SOME CORONAVIRUS VACCINES

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ABSTRACT:

Intelligence immune responses to the coronavirus that induces extreme acute respiratory syndrome is important for understanding disease pathogenesis and the efficacy of link treatments including hyperimmune globulin and recovery human plasma, as well as improving monoclonal antibody, antiviral and vaccines. SARS-CoV-2, a modern coronavirus (CoV), is quickly spreading across the world, posing a significant public health threat. In response to this public health crisis, numerous prevention initiatives have been undertaken; among them, vaccine production is at the frontline. A vaccine against SARS-CoV-2 or (COVID-19) has been produced using many sophisticated designs, and more than 300 candidates have already entered clinical trials and some of them have already been tried in some countries.

Keywords: Covid-19, Humoral immunity, Cellular immunith, Trial phases

I. INTRODUCTION:

SARS-CoV-2 is a single-stranded RNA virus with a positive sense genome, SARS-coronavirus and MERS-coronavirus are genetically associated to other coronavirus species. All three of these viruses provide a natural reservoir in bats [⁴]. In the case of SARS-CoV-2, infection of humans most likely occurred by intermediate hosts including pangolins. Since CoVs are RNA viruses, they can quickly develop by homologous, non-homologous recombination and mutation, allowing them to propagate through a wider variety of hosts. CoVs have a club-like appendix with spherical shape on the top that are called "spikes." [⁴,37]. The spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins are the 4 structural composition of the virus membrane. In SARS-CoV-2, The surface protein helps in the binding of angiotensin converting enzyme (ACE) 2 to the trans membrane host receptor. Protein is the main factor of host transmissibility and pathogenicity, as well as the primary source for neutralizing antibodies, so it is a primary target for vaccine production [⁴].

Figure 1: The structure of SARS-CoV2 is depicted in this diagram [⁴].
Immune Responses of the Host to SARS-CoV-2

Antibodies, especially those that “neutralize” viruses, are essential components of immunity. A successful vaccine will aim to imitate this form of natural defense. It is important to test the ((cellular and humoral immunity)) to SARS-2 . in order to create a vaccine. Some experiments In 70% to 100% of COVID-19 patients, SARS-CoV-2-specific CD8+ and CD4+ T cells were circulating all the time, respectively. The intensity of anti-SARS-CoV-2 IgG and IgA titers was associated with the strong CD4+ T cells immune responce to the surface antigen. Non-exposed individuals T cell reactivity to SARS-CoV-2 clustered epitopes was observed, suggesting potential cross-reactivity with other coronaviruses circulated in the population [5].

Infected patients with the extreme acute respiratory syndrome (SARS-CoV-1) or the Middle East respiratory syndrome coronavirus had humoral immunity markers. These markers were detectable for 2-3 years, but when patients were re-tested 5-6 years later, they were no longer detectable. Understanding the processes of short-term immunity after a live pandemic is essential because these pathways have significant consequences for vaccine-stimulated immunity protection and survival [6,38].

Identifying, testing, and recognizing the immune response to SARS-CoV-2 infection is becoming When the number of people suffering from virus infected, so does the cost of treatment increased , this is becoming more necessary. SARS-CoV-2 after -infection immunity is unknown, and genetic and biological mechanisms causes wide range of this diseases are unknown [7].

SARS-CoV-2 humoral immunity

Antibodies directed at The spike glycoprotein and the nucleocapsid protein are viral surface glycoproteins. immediate Humoral inflammatory responses to SARS-CoV-2. Antibodies to angiotensin-converting enzyme 2 (ACE2) Infection in human cells and tissues with a virus may be neutralized the receptor (ACE2)

The glycoprotein spike with (180 kDa) has 2 subunits ( N (S1) and C (S2) terminal domain ) and its believed to be a antigenic determining factor with the ability to stimulate a defensive immune response. A binding domain for is found in the S1 subunit, SARS-corona virus 2 neutralizing antibodies and viral binding to functional angiotensin converting enzyme receptors on susceptible cells are also focused is mediated by this protein [8]. The primary functions of neutralizing antibodies are interaction with cells that contain Fc-receptors, which monitor immune responses in the future. SARS-CoV-2 proteins elicited large IgG responses (open reading frame (9b), nucleocapsid protein, surface antigen, nsp5, etc) have been discovered used SARS-CoV-2 gene - expression microarray technologies in convalescent serum samples from patients that have recovered from coronavirus-19 infection [9].

SARS-CoV-2 and cellular immunity

Case studies of limited numbers of patients also shown that within the amount of CD38+, HLA-DR+ T cells in both CD4+ and CD8+ in the first 7-10 days of corona virus -19 symptoms increases and then returns to baseline about 20 days [10].

After in vitro re-stimulation with viral antigens, SARS-CoV-2-specific T cells release granzymes and perforin 1 . The proportion of SARS-CoV-2-specific T cells tended to be related to the severity of the disease. incidence in some reports but not in others. This observation raises a significant unresolved issue that may have consequences for vaccine production. Severe disease has also been related to a lower number of CD4+ and CD8+ T cells in the peripheral blood relative to non-danger disease, suggesting a relationship between the severity of the disease however, the strength of the cellular immune response, further research is needed to confirm this connection, figure:2 [11].
Figure 2: Adaptive immune responses attack SARS-CoV-2 proteins

The red boxes depict the four basic proteins. The blue boxes depict non-structural proteins and accessory causes. Antibodies are linked to the viral proteins they attack, and arrows point to viral proteins that comprise epitopes recognized by CD4+ or CD8+ T cells. SARS-CoV-2 is the coronavirus that causes extreme acute respiratory syndrome [12].

Vaccines against Coronavirus 2 (SARS-CoV-2)
Coronavirus 2 (SARS-CoV-2) vaccines that produce immune responses that are protective and important for preventing in addition its decrease the SARS-CoV-2 infection-related death rates. A strong humoral and cellular immune response directed at Th1, according to current knowledge, may be critical for defense against coronavirus 19 and the avoidance of illness caused by vaccines [13]. Virus-vectored, nucleic acid, killed, live attenuated, antigen or peptide subunit vaccines are among the candidate vaccines being produced and tested (table 1). Each strategy has benefits and drawbacks that have been discussed elsewhere [14].

II. DEVELOPMENT OF COVID-19 VACCINES

1-Inactivated vaccines and live-attenuated vaccines
Live-attenuated and killed (Inactivated) immunization Various SARS-CoV-2 vaccine types, nucleic acid, killed or inactivated, recombinant subunit, adenovirus-based vector vaccines are among the vaccines currently being produced to control on coronavirus 19 (Figure: 3). Non-infectious viruses are inactive viruses that have been rendered via physical or chemical processes, it is non-infectious. They appeal to researchers because they show many identification of viral proteins by the immune system, have stable expression of conformation-dependent antigenic epitopes, which could be mass-produced [15].

Historically, modified Vaccines made from inactivated viruses have been found to be beneficial in preventing infectious diseases such as influenza. In animal models, BBIBP-CorV, an inactivated SARS-CoV-2 vaccine candidate, has shown potency and safety, and clinical trials are expected [16].

PiCoVacc, is a pure Candidate vaccine for SARS-CoV-2 virus that has been inactivated, found to cause SARS-CoV-2 antibodies in rhesus macaques, mice, rodents, and, with no significant Changes in cytokine levels or pathology in rhesus [17].
2- Vaccines based on nucleic acids

The Plasmid RNA and DNA encoding antigens, replicon or messenger RNA (mRNA) of virus are used in the development of nucleic acid vaccines. Similar to normal infection, when a cell picks up a nucleic acid, it causes protein synthesis, which triggers and cell-mediated and humoral immune response. For veterinary infectious diseases, vaccines for the treatment mouth and foot infection, deer powassan virus, and rabies virus, for example, have been tested and shown to be immunogenic [18].

The Ebola, measles, and Zika virus nucleic acid vaccinations are still being researched in humans in phase I trials. The advantage of a simplicity of the nucleic acid network with which antigens can be manipulated and the rabidly with which they can be generated, as processing It is possible for it to be endogenous and cell-free, eliminating the need for BSL2 laboratories. Nucleic acid, specifically mRNA, has a number of drawbacks [19].

III. CORONAVIRUS VACCINE TYPES

AstraZeneca

AstraZeneca and Oxford University have developed an adenovirus-vectored experimental vaccine for chimps against SARS-CoV-2 glycoprotein spikes. A prime-boost vaccine protocol was given to nonhuman primates (viral particles in each dose in concentration \(2 \times 5 \times 10^{10}\) ), the vaccine demonstrated both immunogenicity and defensive efficacy [18].

In 1/2 phases experiment, 543 people were given the vaccine and were given protocol for primates (viral particles in concentration \(5 \times 10^{5}\) and a prime-boost schedule (\(2 \times 5 \times 10^{10}\) or \(5 \times 10^{5}\) viral particles). Following the first vaccination dosage, several recipients developed antibody responses, which included neutralizing antibodies and anti-spike glycoprotein IgG, as well as IFN T-cell response and the second dose of vaccine, there was also an improvement in humoral immune outcomes [20].

COVID-19 Vaccine by Moderna Company

Vaccine by Moderna is also called (mRNA-1273), this vaccine is a novel nucleoside-modified, messenger RNA vaccine that encodes a membrane-anchored, full-length SARS-CoV-2 spike (S) protein with two-point mutation proline substitutions to preferentially lock the protein in an antigenic prefusion conformation. This mRNA is encapsulated in a lipid nanoparticle formulation that allows the RNA to be taken up by host cells and translated into the viral S protein. This S protein then incorporates into the cell membrane to induce an adaptive immune response.

Figure 3: An description of the different types of vaccines available, as well as their possible benefits and drawbacks [17].
response, including both B-cell mediated neutralizing antibodies as well as antigen specific T-cell mediated immunity [21].

The vaccine is administered as a two-shot series of 100-g doses given as intramuscular (IM) injections at a 28-day interval. The manufacturing process, which has been in use for 10 years in the development of mRNA vaccines, is cell-free and does not use any vectors, animal products, adjuvants or preservatives [22].

**Pfizer and BioNtech**

COVID-19 vaccines based on mRNA have also been produced by Pfizer and BioNtech. According to preliminary findings from phase 1/2 in (sixty six trials) Pfizer is lipid nanoparticle-formulated, nucleoside-modified mRNA vaccine, induce RBD-binding IgG and neutralizing antibodies with mainly mild side effects in 45 volunteers in a study comparing two types of vaccines (BNT162b1 and BNT162b2). For example, tension at the injection site, nausea, headaches, Chills, body pain, and joint pain are all symptoms of this vaccine. The 18–55 year old participants were given two intramuscular doses of 10 g, 30 g, or 100 g of BNT162b1 (given as 0•5 mL doses and held at –80°C) at random. separated by 21 days due to enhanced reactogenicity. The vaccine was not given a second dose of 100 g. At day 21 after the first vaccine injection, geometric mean titres of RBD-specific IgG were measurable, ranging from 534 U/mL to 1778 U/mL, and were equal to, or higher than, those present in a human convalescent serum panel [23].

**Johnson and Johnson vaccine**

Johnson Pharmaceutical Companies have begun with the Ad26- SARS coronavirus vaccine, which expresses glycoprotein spikes form (replication-defective vaccine) and was tested in a phase 3 randomized, double-blind, placebo-controlled trial with 60000 participants aged 18 and over.

In rhesus macaques aged 6–12 years, a single immunization with serotypes adenovirus type 26 vectored vaccine (1•0 10¹¹ viral particles through the intramuscular route without adjuvant) produces strong neutralizing antibody responses and protects against SARS-CoV-2 challenge [24]. This candidate vaccine, which must be stored between 2 and 8 degrees Celsius, currently about 1045 individuals distribution (18–55 and 65 years old) took part of this vaccine in 1/2 experiment in the United States and Belgium. The safety profile of this vaccine and effectiveness have yet to be made public by the firm. On September 23, 2020, the vaccine's phase 3 trial will begin [25].

**Gamaleya**

Gamaleya is the National Center Research for microbiology and epidemiology in (Russian Federation) has released the effects of clinical trials two phase (1/2) of covid-19 vaccine, which contains of adenovirus serotype vector recombinant ((types 5, 26)) , all of which include the gene for the SARS-CoV-2 spike glycoprotein. About 76 healthy individuals aged between 18–60 years, these candidate vaccines (1•0 10¹¹ viral particles per vaccine dose) were tested (in each trial 38 participants) [26].

**CanSino Biologics**

The Chinese company "CanSino" has produce anew COVID-19 vaccine created adenovirus recombinant serotype 5 vectored vaccine that expresses the whole spike glycoprotein for SARS-CoV-2 that also called Wuhan-Hu-1 virus strain. This vaccine candidate received an examination about 108 volunteer adults in age stratum between 18 to 60 years old. In a phase 1 clinical trial ((38)). Participants were given a single vaccine containing 5•0 10¹⁰ viral particles. viral particles in concentration (1•0 × 10⁹ and 1•5 × 10⁹) neutralizing antibody titers increased from (31% to 50%) at day 14 and 18 and in day 28 , then elevated -dose group at (75%) at day 28 had improved from baseline. The majority of adverse effects were moderate, intermittent, and occurring within one week of vaccination, including discomfort, fever, fatigue, muscle or joint pain, as well as redness and swelling at the injection site are also possible side effects [27].
Biotech Sinovac

Biotech Sinovac is vaccine for coronavirus and was chemically inactivated, entire virus administration that is given in 2 doses (0-28 days) and received an essential use authorization from In July 2020, Chinese authorities will be in control, prior to the start of phase 3 studies. According to reports, almost 90% of company staff were immunised as a result of this authorization. Healthy Participants in age stratum between 18–59 years old in clinical trials 1/2, which were completed [20].

A total of 143 people took part in the phase one experiment. On day 0 and day 14, or day 0 and day 28, 600 patients were randomly allocated to receive either 3 µg /0•5 mL or 6 µg /0•5 mL of the trial vaccine, or placebo, in two intramuscular injections [29].

Sinopharm

Sinopharm has developed and is evaluating two alum-adjuvanted inactivated whole-virus vaccines. Wuhan Institution of Biological Products is a Wuhan-based research institute, China created the candidate for the first vaccine (COVID-19- New Crown). The results of The results of both the phase 1 and phase 2 experiments have been made available to the public. The stage 1 trial "number of volunteer 96" focused on a three-dose chain, while the stage 2 trial "number of volunteer 224" focused on a 5-µg dose of vaccination in 2 groups included days 0 and 14 with number of volunteer (n=84) & (n=28) respectively, and second dose of vaccination included on days 0 and 21 within number of volunteer (n=84) (n=28) respectively. Adults between the ages of 18 and 59 were enrolled in this trial experiment [30].

The Beijing Institute of Biological Products created the second vaccine candidate Sinopharm is testing. In the UAE a phase 3 experiment (number of volunteer is 5000) is ongoing [28].

IV. CONCLUSION

In a rapidly spreading pandemic, the possibility of anti-SARS-coronavirus 2 vaccine has a lot of appeal. The sheer diversity of the novel forms of vaccines under investigation, as well as the methods They make use of it in whatever shape it can take, may help us prepare for potential emergence of infectious illness. At this time, It's uncertain how efficient coronavirus-19 vaccine would be or whether it'll be a one-time injection, such as the polio vaccine, or a monthly shot, such as the influenzae vaccine. And if a vaccine is developed by the year 2021, that would be even better, the research will continue [31].

Furthermore, various vaccine types would almost certainly be needed for various demographics (e.g., immune-impaired babies, teenagers, Immunocompromised individuals, pregnant mothers, and immunosenescent people over 65). Some evidence indicates that, in addition to the adaptive immune response, qualified innate immunity will play a role in COVID-19 defense [32].

Unrelated vaccinations, for example Measles, mumps, and rubella vaccines, as well as the Bacillus Calmette–Guérin vaccine, are being tested in several clinical trials to see whether the molecular causes of infection must be understood, as well as vaccine stimulation the cellular immunity and humoral to SARS-Corona virus 2 disease induce competent innate immunity and provide protection against COVID-19, is important, trying to determine the long-term resistance and maintenance of protective immunity after infection or vaccination, determining the long-term durability and maintenance of protective immunity after infection or vaccination, determining the long-term viability and preservation of protective immunity following infection or vaccination, characterizing the B-cell receptor and T-cell receptor repertoire elicited by infection or vaccination, and identifying detailed targets of cellular and humoral immune responses at the epitope level [33].

Even if continuous immunity is achieved after infection with SARSCoV2, it is estimated To establish SARS-CoV2 herd immunity, 60–70% of a population would need to be immune [34].

The simplest and best regulated method for efficient and long-term In order to have effective and effective COVID-19 protection in a population, the majority of the population must be effectively vaccinated. In order to have global effectiveness, the vaccine could also be conveniently mass-produced at a low cost and transportable with minimum cold chain requirements. In primate models, immunity following the primary infection with COVID-19 helps in protecting against re-infection., as is likely to happen in humans [35].
It's also unclear whether or not this can be replicated in vaccines, and for how long immunity lasts can survive. IgG and neutralizing antibody were observable for 1–3 years after SARS-CoV exposure, implying that vaccine-induced immunity is unlikely to be long-lasting, and that re-immunization might be needed [36].

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