

Review

Methods and Difficulties in the Creation of the 2019 Coronavirus Disease Vaccine

Pratibha Gupta, MSc, PhD*

Department of Biotechnology, Radha Govind University, Ramgarh 829122, Jharkhand, India

*Corresponding author

Pratibha Gupta, MSc, PhD

Assistant Professor, Department of Biotechnology, Radha Govind University, Ramgarh -829122, Jharkhand, India; Tel. +91 9304878508;

E-mail: pratibhagupta2007@gmail.com

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ABSTRACT

The novel coronavirus infection (coronavirus disease-2019 (COVID-19)) emerged from Wuhan in the Hubei Province of China in late 2019. Millions of people were infected with COVID-19 pandemic due to the long incubation period of the virus inside the human body and the dearth of available treatments or vaccines. High transmission rates created havoc, which highlighted the urgent need for effective interventions to stop the spread and clinical impact of the virus on patients and populations. Previous research on severe acute respiratory syndrome coronavirus (SARS-CoV) provides information on vaccination strategies that could inform how governments approach the elimination of this novel coronavirus. Numerous efforts have been made to develop vaccines against Middle East respiratory syndrome (MERS) and SARS. The spike glycoprotein or S protein is the critical target for most of the drugs and vaccines against coronavirus. The virus uses the spike (S) protein for entering the host cell, by interacting with the receptor called angiotensin converting enzyme-2 (ACE2). Various vaccine platforms are available such as nucleic acid vaccine, protein-based vaccines, virus-vectored vaccines and live or attenuated vaccines, with each having their advantages and disadvantages. This review focuses on the overview of different vaccine candidates used, those currently in development, and the challenges encountered while developing effective vaccines.

Keywords

SARS-CoV-2; Vaccine development; Clinical trials.

INTRODUCTION

The outbreak of coronavirus disease-2019 (COVID-19) was first reported in Wuhan, Hubei Province of China in late 2019. The disease was caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which spread to almost all parts of the globe. The symptoms include fever, cough, chest tightness, and fatigue upon exertion. Most patients experience mild symptoms whereas some are asymptomatic (have no clear or confirmed symptoms).^{1,2} Long incubation, high infection rates and mild to moderate symptoms make COVID-19 a troubling disease. The World Health Organization (WHO) declared this outbreak a pandemic on 30 January 2020. Physical distancing and other transmission mitigation strategies were implemented in most countries to prevent citizens from being infected. The SARS-CoV-1 outbreak in 2003 caused similar respiratory symptoms and amassed 774 deaths. Middle Eastern respiratory syndrome coronavirus (MERS-CoV) often involves similar symptomatology and infections in Saudi Arabia in

2012 were circulated between bats and camels before transmission to humans ("zoonotic" transmission).³

The coronavirus is an enveloped and positive sense single stranded ribonucleic acid (RNA) genome. It belongs to the *Beta-coronavirus* genus containing 30 kb genome with 14 open reading frames (ORF). The ORFs includes four viral structural proteins: Membrane (M), Spike (S), Nucleocapsid (N) and Envelope (E) protein.^{4,7} The S protein is functionally composed of two subunits, S1 (receptor binding) and S2 (cell membrane fusion).^{8,9} During infections, host cell proteases process the S protein at the S1/S2 cleavage site. Proteolytically processed S protein cleaves into two subunits, the N-terminal at the S1 subunit and the C-terminal of the S2 subunit. The S1 subunit consists of N-terminal, signal peptide, and receptor binding domains. The S2 subunit consists of a C-terminal domain, conserved peptide sequences, proteolytic sites, a transmembrane domain and a cytoplasmic domain.¹⁰⁻¹² As the virus enters the host cell, another cleavage occurs for the fusion of

membranes and the cleavage is mediated by endolysosomal proteases.⁸ Furin is highly expressed in lungs and the S protein contains the potential cleavage site for furin protease. Furin like cleavage appears to be the important for the activation of S protein which leads to the efficient entry of the virus into the host cell.¹³

Coronavirus (CoVs) can infect a range of host species such as animals, birds and humans. Different CoVs like SARS-CoV, MERS-CoV and SARS-CoV-2 have intricate host receptor recognition patterns, which indicate the structural diversity in the receptor binding domain of the S protein. The interaction between the S-protein and the angiotensin-converting enzyme 2 (ACE-2) receptor present on the host cell is the probable mechanism of the infection that is caused by SARS-CoV-2.¹⁴

According to WHO guidelines, the COVID-19 infected patients should receive supportive body system-focused therapies like fluid therapy, oxygen therapy and antibiotics. The major therapeutics drugs include lopinavir, ritonavir, remdesivir along with interferons, monoclonal antibodies and convalescent plasma for the treatment.¹⁵ Remdesivir was originally developed for the treatment of Ebola virus infection. It prevents the viral infection by premature termination of RNA transcription.¹⁶ Remdesivir is a nucleoside analogue drug which is in Phase III of clinical investigation against COVID-19 (NCT04292730, NCT04315948, NCT04257656). An open-label, randomized Phase II clinical trial found that triple antiviral therapy (lopinavir, ritonavir and interferon beta-1b) was safe in alleviating symptoms and shortening the duration of viral shedding. There is an unprecedented need to develop and distribute safe and effective vaccine to protect the entire global community from continued mortality from COVID-19 should be intact. The wide geographic diversity of the pandemic requires an effective vaccine approach, for this the collaboration between biotechnologist and pharmaceutical companies is needed which brings the convergence of a variety of vaccine development approaches. Over the past decade, the vaccine industry and scientific community responded urgently to several epidemics such as H1N1 influenza, Ebola, Nipah virus as well as against CoVs including MERS- and SARS-CoVs.¹⁷⁻¹⁹ Developing vaccine against H1N1 influenza is relatively rapid as influenza vaccine technology is well-established and key regulators were already decided. Many efforts have been directed to develop vaccine against CoVs infection but the limiting factor is most often the degree of cross-reactivity.²⁰ Immune response by the body against SARS-CoV-2 vaccine plays a vital role for preventing the pathogen's entry into human cells. However, an unregulated immune response may lead to immunopathogenesis.

There is a challenge in developing safe and effective vaccines, but manufacturing, distributing and administering it to the population within a short time frame is an extraordinary challenge. Approximately, 321 COVID-19 vaccine candidates are available, out of these 66 vaccines are in activeclinical trials (Table 1) and 176 are in the pre-clinical (animal) phase of testing.²¹

An ideal vaccine should be safe even to immunocompromised people, inexpensive, free from toxicity, have high thermal stability and should confer long-term protection.²² Various scien-

tific communities are using multiple approaches to shorten the development phase which include efficiency gains *via* over-laying on one other of the traditional, sequential clinical "phases" of progressive testing prior to approval. This, while accomplishing research objectives more quickly than is usual, must be carefully monitored for rigor and reliability of conclusions reached at such previously-unexpected speeds. In addition to the more usual scientifically cautious approach to study and conclusion-drawing, these diverse types of vaccine candidates face a variety of challenges that are related to development, manufacturing, storage, and distribution, to mass vaccination.

VACCINE DESIGN STRATEGIES

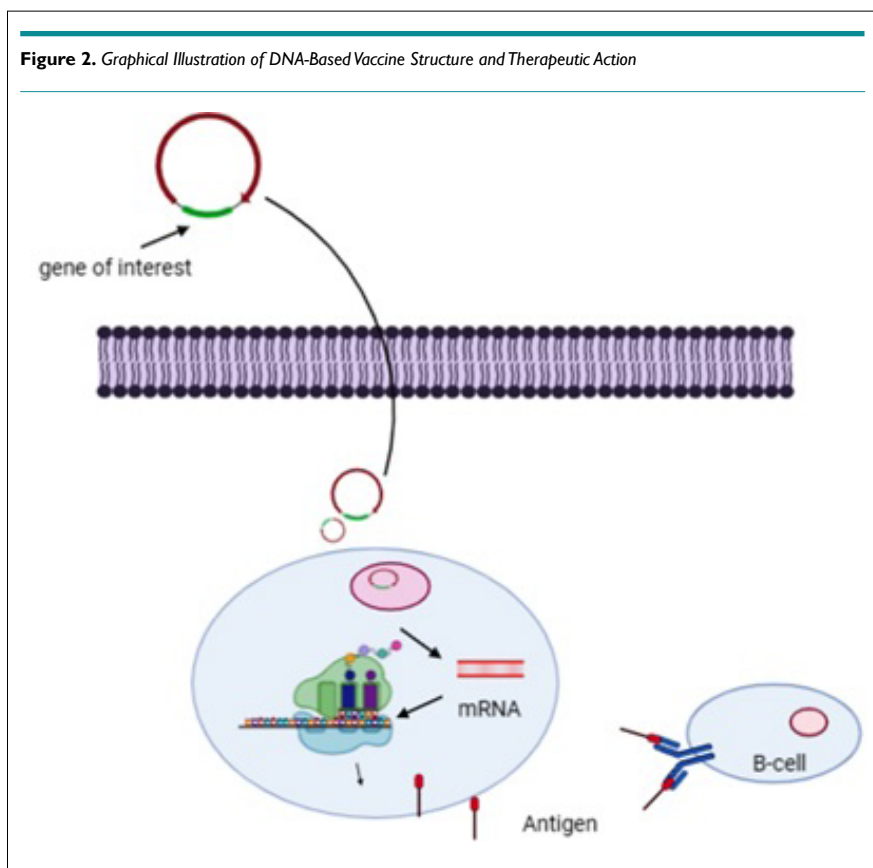
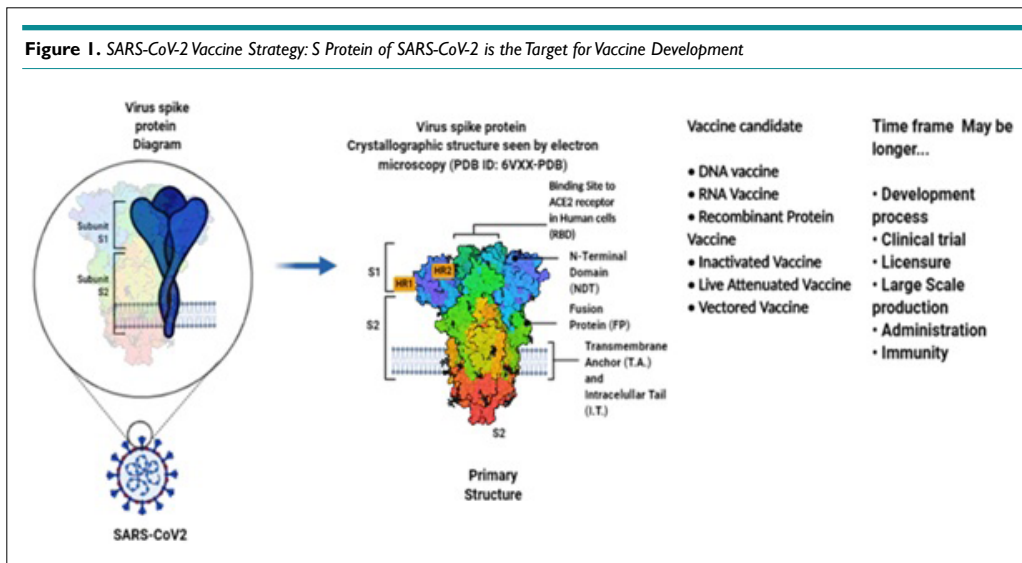
The SARS-CoV-2 pandemic created a devastating situation across the globe.¹⁴ Children and adults above 65-years of age are more vulnerable to COVID-19. Vaccination enable the natural viral infection defense system, which is the only way to control the COVID-19 outbreak. Vaccine design includes the selection of a target antigen key in the virus' infection process, a "vehicle" (viral, genetic/recombinant, chemical, etc.) for vaccine delivery into patients, and the intended or optimal vaccination administration route (oral, nasal, injection, etc.). The selection of a target antigen is based upon the structural and pathobiology information of SARS-CoV-2. The genome of SARS-CoV-2 is a single stranded positive sense RNA. The positive sense genome can act as messenger RNA that can be directly translated into viral protein by the host cell ribosome. The structural proteins present in the virus include Nucleocapsid (N) protein, spike (S) protein, membrane (M) protein and envelop (E) protein. N protein coats the positive stranded RNA genome which is enclosed in a lipid envelop into which S, M and E protein are inserted. The S protein located at the outer surface of virus binds with an ACE-2 receptor on the host cell surface, allowing receptor mediated endocytosis of the virus (Figure 1).²³ S protein plays an important role in the virus life cycle that enables it to enter human cells, so the spike protein is a rational priority prime target for most of the COVID-19 vaccines. Based on crystallography ACE2 binding patterns in SARS-CoV and SARS-CoV-2 are the same.²⁴ Previously, while developing vaccine against SARS-CoV, liver damage was observed when a full-length S protein was used as a vaccine antigen.²⁵ Thus, the fragment of S-protein, the receptor binding domain (RBD), was seen as a safer choice as a vaccine candidate for COVID-19. However, RBD-based vaccines face problems arising from low immunogenicity, identifying possible appropriate adjuvant(s), establishing an immunization schedule, and partial *versus* full fragment length approaches.²⁶ Vaccine candidates in development have several advantage and disadvantages. The most important features that should be considered to develop vaccine candidate are antigen-specific cellular immunity, long-term protection and the ability to induce a reliable and sufficient systemic immune system response.^{27,28} Vaccine candidates for COVID-19 were classified into vector-based vaccines, recombinant protein-based vaccines, deoxyribonucleic acid (DNA) vaccines, messenger RNA (mRNA) vaccines, recombinant protein vaccines, inactivated vaccines, live attenuated vaccines and viral vector-based vaccines.

Deoxyribonucleic Acid Based Vaccine

Deoxyribonucleic acid vaccines are encoded with an antigen-pre-

Table 1. Vaccine Candidates against COVID-19 in Development with Stage

Candidate	Vaccine Characteristic	Sponsor/Lead Partner	Clinical Stage	Registration Number
DNA-Based Approach				
ZyCoV-D	DNA vaccine	ZyduScadila	Phase I/II	CTR/2020/07/026352
INO-4800	DNA plasmid that encodes S protein delivered by electroporation	Inovio Pharmaceuticals	Phase I/II	NCT04336410
AG0301-COVID19	DNA vaccine that encodes S protein	Osaka University/ AnGes	Phase I/II	NCT04463472
GX-19	DNA vaccine that encodes S protein delivered by electroporation or needle free	Genexine Consortium	Phase I/II	NCT04445389
RNA-Based Approach				
mRNA-BNT162	LNP-encapsulated mRNA that encodes stabilised S antigen	Pfizer/BioNTech	Phase II/III	NCT04368728
mRNA	mRNA encoding the RBD	Walvax Biotechnology	Phase I	ChiCTR2000034112
mRNA-1273	LNP-encapsulated mRNA that encodes S protein	Moderna Therapeutics/NIAID	Phase III	NCT04470427
ARCT-021	LNP-encapsulated self-replicating mRNA that encodes the prefusion S protein	Arcturus Therapeutics	Phase I/II	NCT04480957
LNP-nCoVsaRNA	LNP-encapsulated self-amplifying RNA that encodes the S protein	Imperial College London	Phase I/II	ISRCTN17072692
CVnCoV	LNP-encapsulated mRNA that encodes the S protein	CureVac	Phase I	NCT04449276
Protein-Based Approach				
Covax-19	Recombinant SARS-CoV-2 spike protein with Advax-SM adjuvant	Vaxine Pty/Medytox	Phase I	NCT04453852
SCB-2019	Recombinant SARS-CoV-2 trimeric S protein subunit vaccine	Clover Biopharmaceuticals	Phase I	NCT04405908
UQ-I-SARS-CoV2-Sclamp	Recombinant SARS-CoV-2 spike protein 'molecular clamp' plus MF59 adjuvant	University of Queensland/CSL	Phase I	ACTRN12620000674932p
NVXCoV2373	Stable, prefusion protein, includes MatrixM™ adjuvant	Novavax	Phase II	NCT04368988
Adjuvanted recombinant protein-based vaccine	Recombinant protein-based S protein vaccine together with ASO3	Sanofi / GSK	Phase I/II	NCT04537208
EpiVacCorona	Synthesized peptide antigens of SARS-CoV-2 proteins	FBRI SRC VB VECTOR	Phase I/II	NCT04527575
Coronavirus-like particle COVID-19 vaccine	Plant-derived virus-like particle with/without ASO3 or CPG1018 adjuvant	Medicago	Phase I	NCT04450004
Recombinant new coronavirus vaccine (CHO cell)	Recombinant SARS-CoV-2 RBD protein subunit vaccine	Anhui ZhifeiLongcom Biopharmaceutical/ IMCAS	Phase II	NCT04466085
Recombinant SARS-CoV-2 vaccine	Recombinant SARS-CoV-2 vaccine (Sf9 cell)	Sichuan University	Phase I	ChiCTR2000037518
Inactivated Virus Approach				
BBV 152	Whole-virion inactivated	Bharat Biotech, Indian Council of Medical Research, National Institute of Virology	Phase I/II	CTR/2020/07/026300
Inactivated SARS-CoV-2 vaccine	Inactivated novel coronavirus (2019-CoV) vaccine	Beijing Institute of Biotechnology/ Sinopharm	Phase I/II	ChiCTR2000032459
Inactivated SARS-CoV-2 vaccine	Inactivated novel coronavirus Pneumonia vaccine (Vero cells)	Wuhan Institute of Biological Products/ Sinopharm	Phase III	ChiCTR2000034780
Inactivated SARS-CoV-2 vaccine	SARS-CoV-2 inactivated vaccine	Institute of Medical Biology, Chinese Academy of Medical Sciences	Phase I/II	NCT04470609
Adsorbed COVID-19 (inactivated) vaccine	SARS-CoV-2 inactivated vaccine	Sinovac Biotech	Phase III	NCT04456595
Viralvector-Based Approach				
V591	Measles virus vector	Merck Sharp &Dohme	Phase I	NCT04497298
Ad5-nCoV	Adenovirus type 5 vector that expresses S protein	CanSino Biological/ Beijing Institute of Biotechnology	Phase II	ChiCTR2000031781
Gam-COVID-Vac	Recombinant adenovirus vector based on the human adenovirus type 5, 26, containing S protein	Gamaleya Research Institute	Phase III	NCT04530396
GRAd-COV2	Gorilla adenovirus vector that expresses S protein	ReiTheraSrl	Phase I	NCT04528641
AZD1222	ChAdOx1 vector that expresses S protein	AstraZeneca/Oxford University	Phase III	NCT04516746
Ad26.COV2-S	Adenovirus type 26 vector that expresses S protein	J&J-Janssen	Phase I/II	NCT04436276
LV-SMENP-DC	DCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins	Shenzhen GIMI	Phase I/II	NCT04276896
Pathogen-specific aAPC	aAPCs modified with lentiviral vector expressing synthetic minigene based on domains of selected viral proteins	Shenzhen GIMI	Phase I	NCT04299724



senting cell which is intended to elicit humoral immune response that is like that of an atural infection.²⁹ The antigen-encoding DNA is enclosed with lipid nanoparticles can be delivered into the cytoplasm of the host cell and further it is processed into antigen peptide that elicits CD8⁺ T-cell response.³⁰ DNA plasmids cross the plasma and nuclear membrane, enter the target cell, reach the nucleus and achieve transcription and thus propagates the desired and validated immune response (Figure 2). DNA vaccines have various advantages such as eliminating the use of live viruses, ease of production scaling, lower production costs when compared to protein vaccine production, more stability for storage and trans-

portation and they may even be administered to immuno-compromised patients. Manufacturing DNA based vaccines is relatively straight forward and is more stable than viral protein and RNA vaccines. The only pro-inhibitory factor is the low immunogenicity that sometimes requires multiple booster doses.^{31,32} Overcoming the immunogenic issues of DNA vaccines, immunostimulants and adjuvants maybe required. Combined use of granulocyte-macrophage colony-stimulating factor (GM-CSF) and a cytokine-based therapy directed against interleukin-4 (IL-4) have proven useful in enhancing immune response in some medical settings.³³ DNA vaccines show promising effects against several emerging viral dis-

eases such as Dengue, MERS, and Chikungunya.³⁴⁻³⁶ Yet, no DNA vaccine has been licensed for use in human. DNA-based vaccines encoding S protein from SARS-CoV-2 appears to be in clinical Phase I/II testing on the pathway to approval.³⁷

Ribonucleic Acid Based Vaccines

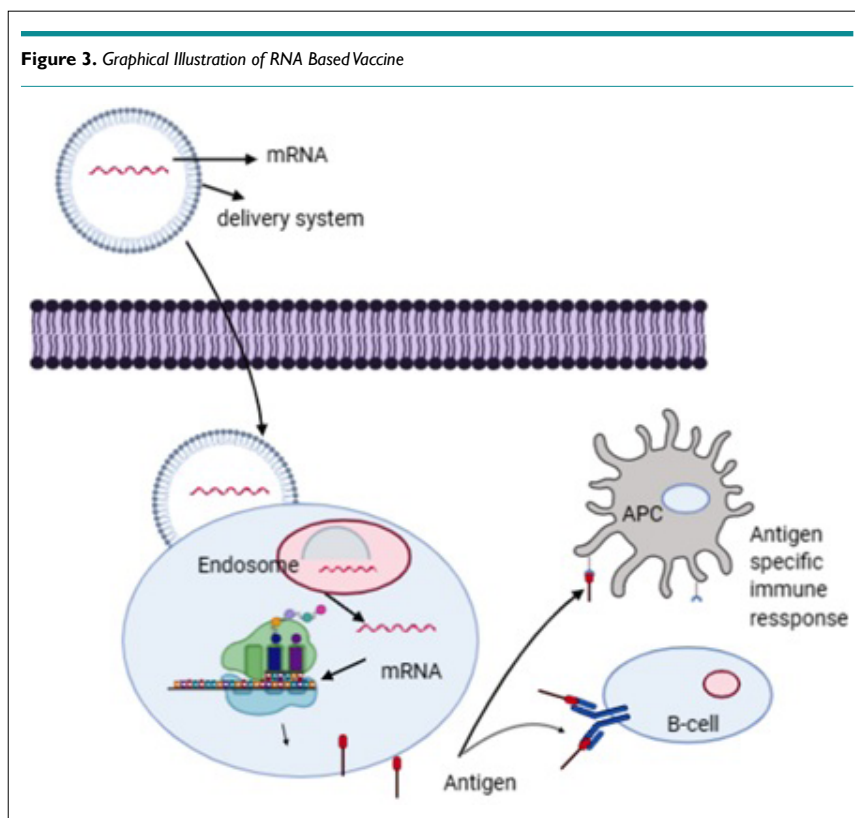
Messenger RNA (mRNA) sequences that code for disease specific antigens enclosed with lipid nanoparticles (LNPs) are the current, most widely pursued mechanism of action for approved COVID-19 vaccines.³⁸ Once the LNP is phagocytosed (eaten/incorporated) by the human cell, the RNA condensing lipid nanoparticle punctures the endosome and allows the mRNA molecule to release into the cytosol inside the human cell (Figure 3). Messenger RNA vaccines are synthesized by *in vitro* transcription and are non-infectious. This feature of mRNA vaccines does provide advantages that differentiate it from recombinant viral vector vaccines, live attenuated viral vaccines and inactivated viral vaccines that enable inexpensive and rapid production of vaccine doses.³⁹ The mRNA vaccine does not integrate permanently into the human host genome and does not produce any live infectious particles that elicit immune responses and this further reduces safety concerns.

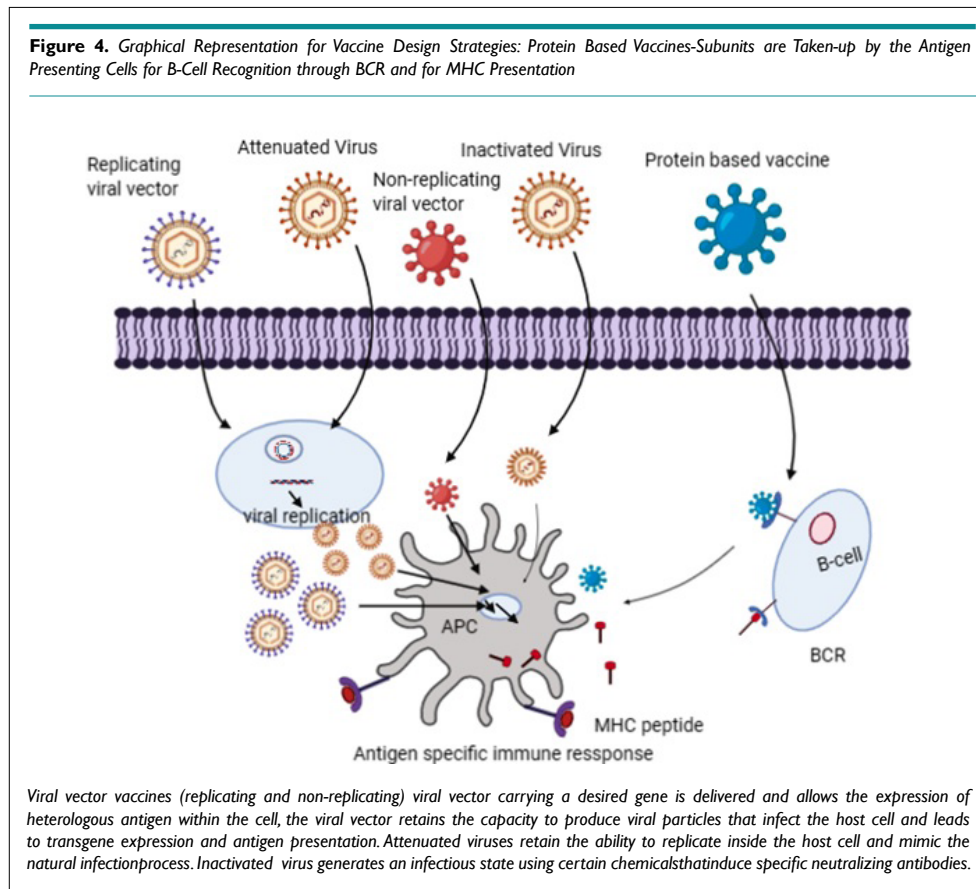
Moderna's COVID-19 vaccine candidate mRNA-1273, encodes SARS-CoV-2 S protein encapsulated in lipid nanoparticles, and is in Phase III clinical trials.

Protein Vaccines

Protein vaccines contain partial or full-length SARS-CoV-2 S pro-

tein that induces a CD4⁺ TH-cell and antibody response. Unlike nucleic acid-based vaccine, protein subunit vaccines could have improper epitope conformation, until they are produced by mammalian cells.⁴⁰ Protein vaccines are designed to provoke the immune response towards neutralizing epitopes, thus preventing the production of non-neutralizing antibodies that may promote antibody-dependent enhancement (ADE) of disease.⁴¹ Protein subunits (when used alone) are poorly immunogenic and thus serve as poor activators of the CD8⁺ T-cell response, which requires adjuvant and repeated administrations. Recombinant proteins are enclosed in a virus like particles (VLPs) devoid of viral genome. The VLPs generate high numbers of antigenic epitope copies, thereby preserving viral immunogenicity, enabling the ability to crosslink to B-cell receptors on the B-cell surface and facilitate uptake by the antigen presenting cells (APCs) (Figure 4).^{42,43} In protein-based vaccines, subunits are taken up by the antigen presenting cells for B-cell recognition through B cell receptor (BCR) and for major histocompatibility complex (MHC) presentation. In viral-vector vaccines, (replicating and non-replicating) viral vectors or cellular vehicles, carrying a desired gene, are delivered and facilitate the expression of heterologous antigen within the cell. The viral vector retains the capacity to produce viral particles that infect the host cell and that lead to transgene expression and antigen presentation. Live virus vaccines retain the ability to replicate inside the host cell and mimic the natural infection process. The inactivated virus vaccines deploy virus cells that were once alive and have been completely attenuated, yet still generate an infectious state. They do so by using certain chemicals that induce specific neutralizing antibodies in response to what the viral vaccine presents to the human body.





Attenuated and Inactivated Virus Vaccine

The attenuated vaccines are obtained by mutating a virus, which infects the human cell until a substantial number of cells adopt the mutation that generates the desired immune response (Figure 4). Their most important advantage is that they offer more than one antigenic component to host, thus inducing or mobilizing various immunological effectors against the virus.⁴⁴ The drawback associated with attenuated vaccines are potential safety concerns. They often have high reactogenicity compared to protein-based vaccines.⁴⁵ Several successful vaccines such as bacillus-calmette-guerin (BCG) and measles vaccines are based on attenuated strains of the viruses.⁴⁶ The coronavirus genome has various genes that are not required for replication and can be deleted. Deletion of various genes that code for non-structural proteins and structural E proteins may also be used as a strategy to design new vaccines.^{45,47,48} Therefore, deletion of the virulence factor and the induced codon deoptimization (where nucleic acid sequence is modified that encodes the wild type of amino acid sequence, and slows the translation of viral protein) may be a suitable mechanism of attenuation. A codon deoptimization approach yields vaccine-ready virus that is highly attenuated *in vivo* and *in vitro* and can replicate if the correct viral protein(s) is/are selected for de-optimization.^{49,50}

In inactivated vaccines, the whole pathogen is killed either by exposure to chemical (formaldehyde) or heat induced inactivation.⁵¹ Inactivated viruses have been used traditionally for vaccine development and were found to be safe and effective for prevention of diseases caused by the hepatitis influenza, and polioviruses.

They are generally less immunogenic and require multiple doses or an additional adjuvant (Figure 4).^{52,53} Currently there are five vaccine candidates for SARS-CoV-2 (Table 1) apart from that there are nine inactivated vaccine that is in preclinical stage (WHO). Inactivated vaccine candidate (NCT04456595) developed by Sinovac Biotech Ltd in China, is currently in phase III clinical trials.⁵⁴

Viral Vector Based Vaccines

Viral vector-based vaccines use either replicating or non-replicating viruses (Figure 4) to induce the human immune response. It represents the biotechnological evolution of inactivated and attenuated vaccines, which are viral backbones devoid of replication machinery and used as a vehicle to deliver *in vivo* and express antigens derived from target pathogens. The viral-based vaccine has ability to induce strong T-cell responses without the need for any adjuvants.^{55,56} One of the drawbacks of viral vector vaccines is that it requires multiple immunizations to achieve the level of immunogenicity and thus protection against the virus but may also lead to a host response against the structural viral protein, thus limiting the efficacy of immunization (called a neutralizing antibody).⁵⁵ This limitation is overcome by using a heterologous prime boost regimen that is introduced in several clinical trials.⁵⁷

Heterologous prime-boost vaccine regimens means to deliver the same or similar antigens through different vaccine types, the first to prime and the second to boost the immune system.

Currently there are eight viral-based vaccine candidates

is in clinical trials (Table 1). Ad5-nCoV (NCT04341389) is a viral vector-based vaccine candidate that has been in Phase III of clinical trials. The replicating viral vaccine candidates are based on a vaccine strain derived from the human pathogen. It is important to consider this very specifically, if the potential recipient of the vaccine has pre-existing exposure and presumed subsequent immunity against the virus. Pre-existing antibodies can impair the ability of vaccine to elicit the immune response required for protection. Non-replication viral vector vaccine candidates are mostly based on adenovirus (Ad5) and express the S protein or receptor binding domain (RBD) of SARS-CoV-2.

Safety Measures for Coronavirus Disease-2019 Vaccines

COVID-19 cases do not seem to be declining and the ebb and flow of cases are mostly driven by human attitude towards physical distancing and protective measures. All eyes remain on pharmaceutical companies and research institute involved in vaccine development. Traditionally new vaccine development and approval requires 10-12-years, and there are enormous pressures and challenges to minimize that time frame. The safety of a vaccine is generally determined by the choice of adjuvant, nature of vaccine platform, mode and route of vaccine administration, status of pre-existing vaccine immunity and age of vaccines. In the particular case of SARS-CoV-2, the individual is either symptomatic or asymptomatic, and COVID-19 vaccines are developed with a goal of mass immunization or protection and not addressing symptomatology. Any loophole in the lack of safety considerations may support the mobilization of anti-vaccination movements or messaging, which would jeopardize the effect of achieving mass immunization.

As other respiratory viral infections, vaccine strategies for COVID-19 require additional safety vigilance. There is a possibility of antibody-dependent enhancement (ADE) of disease if an insufficient immune response is mounted in a situation of the unresolving, active, and serious disease. Over production of pro-inflammatory cytokines in lung immunopathology that cause additional damage when vaccines cannot stop SARS-CoV-2 pathology early in the process. In this regard, COVID-19 vaccine trials were initially conducted in healthy adults with age of 55-years or younger and later stage trial includes seniors.^{58,59}

DISCUSSION

The COVID-19 pandemic emerged as wide spread SARS-CoV-2 infection in December 2019, according to most estimates. Several challenges exist in the development of vaccines against COVID-19 as the novel SARS-CoV-2 is undergoing several genomic changes, even as of the time of this writing. Developed vaccine candidates include approaches with inactivated viruses, live attenuated viruses, virus nucleic acid-based vaccine, and protein subunit vaccines. All are in different clinical phases. Moderna's vaccine; the inactivated virus vaccine being developed by Sinopharm, the Wuhan institute of Biological products; and Sinovac Biotech are on the market as of this writing. According to WHO Global Advisory Committee, AstraZeneca (adenovirus vector vaccine) is that, it is safe and effective for protecting people from the serious risk of COVID-19. The ideal vaccine candidate for COVID-19 should be safe, effective

and have a good immunogenicity profile among all age groups and be safe for including pregnant women and immuno compromised individuals. For ease of success, the effective vaccine should generate humoral and cellular immunity with a single dose of vaccination. Generating effective vaccines has required initiating a large number of official projects by the WHO, various companies, universities and laboratories. Approval of the first COVID-19 vaccine increased the enthusiasm and possibilities for developing second and third generation vaccine approaches and candidates for approval.^{60,61} COVID-19 eradication programme is time taking after vaccination, as the various mutant strains are available now e.g. South Africa variant (501Y.V2), which show different symptoms in infected humans than previous strains.

CONCLUSION AND FUTURE GUIDANCE

Various companies and institutes are in the position to offer several treatment strategies against the COVID-19 pandemic. Tireless and ongoing scientific efforts have led to the development of 242 COVID-19 vaccines candidates. We are in the early stage of SARS-CoV-2 identification and adequate vaccine preparation, manufacturing, and distribution to populations. Based on previous studies, it may be inferred that the COVID-19 vaccines approved thus far provide acceptable (if not higher than previously experienced) immunity and protection via a durable neutralizing antibody and a lasting T-cell response.

Various vaccine strategies are being pursued now with attendant advantages and disadvantages. According to the WHO, the vaccine must be of high efficacy and producing only mild or transient adverse effects an acceptable and benefit-risk contour. Various vaccine platforms depend upon adjuvants for inducing the T-cell response. Live attenuated vaccines are not recommended, as a delivery vector increases the risk of pathogen conversion to actual viral infection. Viral vectored vaccines are effective in inducing T-cell response but sometimes their efficiency is affected by cross-reactive immunity (antibodies that neutralize the antibodies mobilized by the vaccine). Nucleic acid based vaccines are also a successful candidate but they need specific delivery vehicles or adjuvants. In many countries, emergence of new cases and transmission of COVID-19 diseases is significantly declining whereas in some countries the number of new cases increase day-by-day. Approved vaccines must be suitable for persons of all ages, pregnant mother, lactating mother as well as immunocompromised person. To meet the need or demand of less wealthy countries, the funding committed through the COVAX program (COVID-19 Vaccine Global Access) and coalition for epidemic preparedness innovation (CEPI) unite rich and low-income countries to achieve rapid and fair access to the most effective COVID-19 vaccines. Since vaccines alone cannot combat the pandemic and assure its elimination, prevention strategies and social strategies will remain needed and such strategies will also help us to face future pandemics.

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