

Coronavirus Pandemic

A vaccine is not too far for COVID-19

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Abstract

Over the last months and weeks of the pandemic of the Coronavirus Disease 2019 (COVID-19) (January-May 2020) caused by the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), there has been a significant hope for the development of vaccines against this emerging coronavirus. Dozens of vaccine candidates are currently under assessment in clinical trials already recruiting patients, then there is a real chance to have effective biologicals in relatively short-time, compared to other vaccines.

Key words: SARS-CoV-2; COVID-19; vaccines.

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The Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has brought the entire world at a halt [1,2]. Through the usage of the vaccine, several diseases have been eradicated or are on the verge of elimination. In the current situation of the Coronavirus Disease (COVID-19) menace, the vaccine appears to be the best and long-lasting solution for curbing this global public health emergency [3]. Multiple efforts made to develop an effective vaccine during earlier outbreaks of COVID were ended up without any productive results to subside the epidemic.

SARS-CoV-2 is a positive-sense single-stranded RNA virus (50–200 nanometres) having genome (~30 kb) enclosed in spike structured envelope laced with a spike (S), envelope (E), membrane (M), and nucleocapsid (N) structural proteins and also contains

non-structural proteins and enzymes including RNA-dependent RNA polymerases [4,5]. The N protein holds the RNA genome, whereas S protein helps in attachment, binding, fusion, and entry to host cells [5-7]. Every aspect of SARS-CoV-2, its structural and non-structural proteins, genetic material, or the disease pathogenesis, are being explored for devising effective vaccines. Identifying targets, locating effective epitopes, raising specific antibodies against these epitopes, and evaluating the antigenic potential for vaccine development are some of the areas currently being focused upon. Besides, biological mechanisms of viral pathogenesis and host immunity may have relevance in deciphering a few aspects of prophylactic strategies.

The SARS-CoV-2 is reported to utilize the angiotensin-converting enzyme 2 (ACE2) receptor-like SARS-CoV [8,9]. A thorough understanding of the antigenic structures of SARS-CoV-2 is necessary for the development of vaccine [10]. The structural proteins of SARS-CoV-2 include envelope (E), membrane (M), nucleocapsid (N), and spike (S) protein, which are being investigated as target antigens for vaccine development [10]. Epitopes present on the S and N structural proteins of SARS-CoV-2 showed dominant and robust T cell immune response for a long duration of time and hence can be well explored as a vaccine candidate against SARS-CoV2 as they are part of immunity in a large population.

Particular genotype and protein analysis of S, M, E, and N proteins of this virus suggested their suitability in determining dominant protective immune responses against SARS-CoV-2. In a population of Asia and Asia-Pacific regions, some immunodominant CD4 T-cell epitopes with a high binding affinity (HBA) to the S, E, M, and N proteins were investigated and can be explored to develop subunit vaccine of n-CoV [11]. Also, thorough knowledge of the structure, binding mechanisms, entry, and pathogenesis of the virus will prove crucial in the development of various prophylactic and therapeutic modalities [3]. The availability of furin-like proteases may influence the immunogenicity and pathogenicity of the virus, and hence such enzymes, proteases, and structural sites must be explored while looking for the vaccine candidate [12]. In this context, neutralizing antibodies were mainly reported to be directed against the S protein of the earlier zoonotic CoVs as it is the major structural protein hence can be targeted for the development of a vaccine against the SARS-CoV-2.

Many vaccine platforms like protein subunit vaccine, RNA vaccine, DNA vaccine, VLPs based vaccine, vector-based vaccine, live attenuated vaccine, an inactivated (killed) vaccine have been explored to date [7]. Nonetheless, still, further investigations exploiting genomic and structural organization of virus are utmost necessary to develop a harmless vaccine which can be used in different age groups with all possible physiological and pathological body conditions. In this context, the Chimpanzee adenovirus vaccine vector (ChAdOx1) developed by the researchers of Oxford's Jenner Institute was considered as the most suitable vaccine technology for the SARS-CoV-2. Additionally, it is a non-replicating virus and thought to initiate a robust immune response after administration of a single dose without causing an infection in the vaccinated person. Further, it is

considered safe for children, older adults, and individuals with comorbidities. Chimpanzee adenoviral vectors have been extensively studied and safely used in many subjects from 1 week to 90 years of age in more than ten different diseases (<https://covid19vaccinetrial.co.uk/about>).

Some SARS-CoV-2 vaccine candidates are under different phases of clinical trials over human beings. Candidates like mRNA-1273 SARS-CoV-2 Vaccine by Moderna, Inc., INO-4800 DNA coronavirus vaccine by INOVIO Pharmaceuticals, Inc. and Adenovirus type 5 vector vaccine candidate (Ad5-nCoV), altogether developed by CanSinoBIO and Beijing Institute of Biotechnology are under phase-I clinical trial. Besides this, some candidates like BNT162, Self-amplifying RNA vaccine, Plant-based COVID-19 vaccine, Ii-Key peptide COVID-19 vaccine, and oral recombinant COVID-19 vaccine are under the preclinical phase of the trial (<https://www.precisionvaccinations.com/vaccines/coronavirus-vaccines>).

World Health Organization (WHO) has mentioned in detail about various COVID-19 vaccine candidates who are under different steps of trials. Adenovirus type 5 vector vaccine candidate in non-replicating viral vector and LNP-encapsulated mRNA is under clinical evaluation. DNA plasmid vaccine, formaldehyde inactivated with alum, live attenuated virus vaccines, S protein, S-trimer, Ii-Key peptide as subunit protein vaccine are examples of vaccine candidates which are currently in pre-clinical phase (<https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf?ua=1>).

The use of convalescent sera, plasma therapy, and administration of immunoglobulin remains one of the earliest and easily possible preventive measures to conquer over COVID-19 while strategic planning to develop effective vaccine development continues. Convalescent sera obtained from the COVID-19 recovered individual may be effectively used as an immediate therapy [13]. Additionally, such sera can be obtained from genetically engineered animals like cows [14] and contain specific antibodies that can provide passive immunity by neutralizing the SARS-CoV-2.

Current situation is globally complex. There is now, up to May 29, 2020, more than 5.84 million cases of COVID-19 reported, with approximately 361,000 deaths. Then, vaccines against SARS-CoV-2 are desperately needed. Many efforts are being made to develop a vaccine that can minimize human suffering and counter this global emergency at the earliest [7]. More than 35 institutions and companies are leaving no

stone unturned to accomplish this motto prima-facie. The entire infrastructure, workforce, funds, and facilities are being invested in reiterating this supreme goal. However, in this race of vaccine development, various phases of trials need to be passed. Many a time's vaccine candidates having potential for the efficient vaccine may not make it to the final phase, while fewer other candidates reach the final phases of clinical trials. Some fail at the terminal trials, and only a few get official approvals after satisfactory trials by the designated regulatory authorities. There is always a chance of undesirability at any stage; hence adequate evaluation is a must for minimizing pros and cons. Although scientists are working hand-in-hand to develop a highly effective and desirable vaccine, the COVID-19 related sentiments may not affect the genuine testing and approval standards resulting in the release of a substandard vaccine detrimental to human health. In this context, a thorough evaluation of immune response must be done to avoid any damage caused, as in the case of the actual SARS-CoV-2 [15]. All due care must be taken before finalizing a vaccine to be commercialized even before running for the clinical trials [15]. An overview of designing and developing

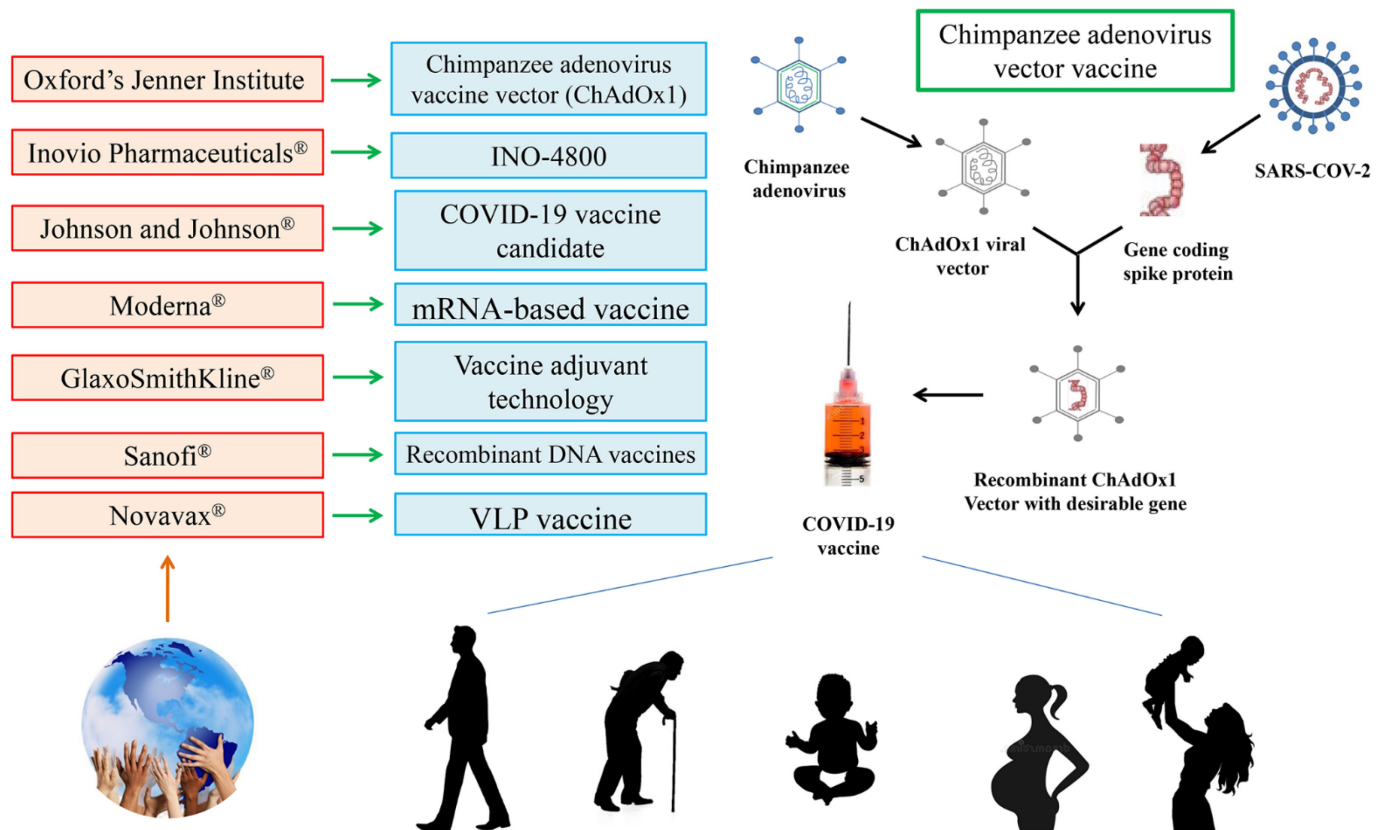
different kinds of vaccines and a few of the upcoming COVID-19 vaccines are depicted in Figure 1.

The development of the potent and effective vaccine has always been a challenging task, and we have conquered the same many times in the past and defeated many lethal pathogens. In the case of COVID-19, a vaccine still may take more than a year to be widely available, but efforts are ongoing in different countries to develop them. Additionally, we are not far from our goal to develop vaccines against this virus too. We must appreciate the efforts made worldwide by the researchers and hope for a potent and effective vaccine without any potential side effect shortly halting the ongoing pandemic timely. Cohesive, collaborative efforts made by all the participating agencies and companies of different countries must be duly acknowledged.

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Figure 1. An overview of designing and developing vaccines and few of the upcoming COVID-19 vaccines.



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