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Editorial

The Urgent Priority of Global Health Research is to Prevent Transmission of Covid-19 through Vaccine Development

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Editorial

There are currently unprecedented challenges of SARS-CoV-2 (COVID-19; the WHO nomenclature) on key fronts such as vaccine development and delivery, discovery of selective and targeted antiviral agents, and most importantly, application of public health sciences to overcome the transmission of COVID-19 worldwide consistent with evidenced-based policy and disease management. Given the urgency of pandemic, in this editorial, we offer an academic perspective on vaccine development approaches. Researchers are intensely working toward a common global health goal to develop a safe and effective vaccine(s) protecting the global population from the spread COVID-19. While vaccine research and development is a central effort with uncertainties of reaching the goal of a scientifically sound and ideal product, a key question is how long will the protection last? An ideal vaccine profile must prove both its efficacy and safety when inoculated in the population. This is a critical mission and poses a serious challenge for the world health community of vaccine researchers. It is scientifically and widely agreed that in older ages the function of the immune system is altered and enters the phase of immunosenescence. Accordingly, altered innate and adaptive immunity such as reduction of phagocytosis, chemotaxis, naïve T and B lymphocytes, and impaired antibody production increase the dysfunctionalilty of memory which leads to susceptibility to infectious agents and diminished response to vaccination [1]. Therefore, the possibility exists a vaccine for elderly people can turn out be less effective. For example, the 2017-2018 flu vaccine (USA) turned out 40% effective in the general population; however, about 20% effective in individuals over 65 [2]. This observation indicates antibody-producing flu vaccine while helpful, it may not be preventive for the rest of the general population. It is scientifically ironic that the population should be exposed to fragments of the virus before the live virus begins its race with the immune system. Currently, there are more than 100 biotech/pharmaceutical companies working alongside with the world-class university research centers for the development of a novel vaccine against COVID-19. To date, there are few vaccine candidates that show optimistic grounds for clinical trials, and thus, the promise of a vaccine is on the horizon (https://clinicaltrials.gov). Efforts have increasingly accelerated worldwide to deliver such a promise, a global marathon to also gain the market share of vaccine delivery. Nevertheless, the development of a vaccine is a time-consuming process and needs clinical trial studies for final approval. On the other hand, novel technical platforms and cutting-edge biotechnological methods such as systems biology, protein and genetic engineering are synergic tools in the acceleration of a novel vaccine distribution in the world's population [3].

Novel viral vaccines can be classified into two major groups: gene and protein vaccines [4]. The nucleic acid vaccines such as DNA or mRNA vaccines are new-generation gene vaccines [5]. The selection of a selective target as an antigenic determinant in the molecular structure of SARS-CoV-2 is the most important step in vaccine design. It can be packaged as a recombinant protein eliciting neutralizing antibody production. Accordingly, the precise conformation of the protein is consequential in humoral immune responses [6]. Among promising vaccine candidates is the spike protein of the virus. This pivotal viral receptor binds to the host cells at least 10 times as tightly as has been reported for COVID-19. Precise mapping of this protein is the critical step toward vaccine discovery because the spike protein is one essential element of the virus that the immune system can potentially identify as non-self [7]. Once the delivery of this initial step is established to the immune cells, such cells are likely to trigger an immune response and subsequent production of antibodies. Right now, the focus of vaccine research is primarily in the domain of spike protein. Thus, such a concept eventually needs a clinical trial challenge. Gene vaccines such as the mRNA vaccine are an unprecedented approach which recently has been focused by pharmaceutical companies. The mRNA sequence can encode the immunogenic domain of spike protein, and in addition to the neutralizing antibodies response, it induces strong T cytotoxic lymphocytes. Choosing a proper carrier for mRNA delivery has been

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considered in many research phases and lipid nanoparticles might be applicable carriers of mRNA vaccines [8].

Recently, the introductory results of the phase 1 trial of an mRNA vaccine have been reported. The mRNA-1273 vaccine encodes antigenic structure of the spike protein called S-2P and the lipid nanocarrier formulated for mRNA delivery. Fourty five healthy adult's revised an mRNA-1273 vaccine twice with 28 days interval and different doses (25 μg, 100 μg and 250 μg). Following the initial vaccination, the highest antibody titers were observed in volunteers who received the higher dose (250 μg). After the secondary administration, the activity of neutralizing antibodies was detected in all participants and this phenomenon was increased with the increasing doses of the vaccine. The cellular immune responses were also assessed and the induction of both T helper 1 (Th1) and T helper 2 (Th2) responses was significant. From the safety point of view, the mRNA-1273 vaccine was overall tolerable without severe adverse reactions in the first phase of vaccination. These findings were confirms the progression of the mRNA-1273 vaccine to further clinical trials [9].

Additionally, phase 1/2 clinical trials of Chimpanzee Adenovirus-Vectored vaccine (ChAdOx1 nCoV-19) expressing the SARS-CoV-2 spike protein have been completed in the multicenter sites in the UK. The results showed local and systemic reactions were frequent and could be prevented by the administration of paracetamol (acetaminophen) prior to vaccination. On day 14 after vaccination, the highest spike-specific T-cell responses were reached and anti-spike IgG responses were increased on day 28 as well as these humoral responses were also boosted following a second dose. Finally, neutralizing antibody responses against SARS-CoV-2 were detected in 91% of participants after a single dose. Overally, ChAdOx1 nCoV-19 indicates satisfactory safety which induced humoral and cellular immune responses, but more comprehensive clinical studies are warranted to assess the efficacy and efficacy of the vaccine [10].

There are also other questions whether we are capable of finding age-specific vaccine for COVID-19. This particular concept is infrequently discussed in the world scientific community. For example, shingles and pneumonia vaccines are now routinely administered to the elderly population [11]. It sounds reasonable to develop a COVID-19 vaccine for the elderly population that performs in slower or less efficient ways. The key immune cells in fighting a virus are T and B lymphocytes. As such, antibody therapy can potentially neutralize the spike protein and prevent viral entry into the host cells [12]. In individuals who are already infected with COVID-19, this unique approach could help reduce symptoms and the length of viral infection. Finally, with the most recent discovery of that SARS-Cov-2 can present with a camouflage; the enzyme nsp16, to the point such a viral enzyme can fool the host cells recognizing it as "self". This in turn would pose further challenge for vaccine research and development [13].

The optimism that principles of basic science supports the clinical outcome, which in this case the preventive approach, it will eventually enables the global health community to overcome the existing challenge of COVID-19 vaccine and other zoonotic infections that may threaten our global health stability in the future. We believe vaccine delivery remains the best option and strategy in controlling the transmission of COVID-19. The first batch of COVID-19 vaccine may not specifically address the immune responses in elderly population, but such an effort is a first step to better understand and evaluation of the overall performance of a novel vaccine in general population throughout the world.

Keywords

COVID-19; SARS-CoV-2; Vaccine; Clinical trials, Antibodies

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