SARS-CoV-2 Novel Vaccine

Reza Jafari[1,2], Naime Majidi Zolbanin[3], Reza Farid Hosseini[4], Reza Nassiri[5*]

[*1]Solid Tumor Research Center, Cellular and Molecular Medicine Research Institute, Urmia University of Medical Sciences, Urmia, Iran.

[2]Department of Immunology and Genetics, School of Medicine, Urmia University of Medical Sciences, Urmia, Iran.

[3]Department of Pharmacology and Toxicology, Faculty of Pharmacy, Urmia University of Medical Sciences, Urmia, Iran.

[4]Allergy Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

[5]Departments of Pharmacology and Community Medicine, Michigan State University, East Lansing, Michigan, USA.

EDITORIAL

Please cite this paper as Nassiri R. SARS-CoV-2 novel vaccine. Archives of Healthcare [2020] 1(3):108-111.

***Corresponding Author:**

Prof. Dr. Reza Nassiri,

Departments of Pharmacology and Community Medicine, Michigan State University, B405 Life Sciences, 1355 Bogue Street, East Lansing, MI 48823, USA; Tel: (517) 884-1252;

E-mail: Reza.Nassiri@hc.msu.edu

Teams of scientists around the world are racing for development of safe and effective vaccines to halt the transmission of SARS-Cov-2 (COVID-19; the WHO nomenclature [Coronavirus disease 2019]). Currently, there are about 165 COVID-19 vaccine candidates, 26 clinical trials and 6 phase 3-4 trials (source: WHO). This global race is one of the most critical challenges of the 21st century in the healthcare delivery system raising ethical questions how to fairly inoculate the world's population, especially in resource-limited countries. Although SARS-Cov-2 vaccine delivery may not be a "silver bullet" due to complexity of not only the virus itself, but also peculiar immune response which is associated with this virus. For example, there are vaccine platforms being developed by novel technologies that they currently lack baseline information concerning their potential risk(s). In addition, limited vaccine manufacturing capacities can disrupt global distribution leading to imabalnced equity. An ideal vaccine profile must prove both its efficacy and safety when inoculated in the population. Other critical factors include immunogenicity data during phase trials, tolerability, and clinically acceptable antibody titers. Such critical mission poses a serious challenge for the world health community of vaccine researchers. It is 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). Thus, a vaccine for elderly people can turn out be less effective. It must be taken into account that current efficacy of the flu vaccine globally is about 40%. Such efficacy in individuals over 65 is about 20% (2). This observation indicates antibody-producing flu vaccine while helpful, it may not be preventive for the rest of the general population. It is evident 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 numerous 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 potential 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. On the other hand, novel technical platforms and cutting-edge biotechnological methods such as systems biology, protein and genetic engineering are synergistic tools in the acceleration of a novel vaccine distribution in the world's population (3). However, these novel tools had not previously been subject to intense evaluation of immunological outcomes, let alone to reach global immunity in the context of prevention via vaccine, it is widely agreed 70% of the world population must be vaccinated (4). Another expectation from a fragment of the general population is because development of current COVID-19 vaccines is proceeding in such a high and hasty pace, they may be reluctant to be inoculated against the first batches of vaccine. But, in an ideal world, granted the safety, efficacy and tolerability of a vaccine have undergone through the litmus tests, the first doses must optimally be distributed within the community of the healthcare workers (HCWs) throughout the world as well as vulnerable population.

The novel viral vaccines can primarily be classified into two major groups: gene and protein vaccines (5). The nucleic acid vaccines such as DNA or mRNA vaccines are new-generation gene vaccines (6). SARS-CoV-2 mRNA vaccine is packaged in lipid nanoparticle to the target cells, which then start producing viral protein, for example, the spike protein (7). Nucleic acid vaccines (e.g., mRNA) are unprecedented approaches which recently have been focused by the 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 considered in many research phases and lipid nanoparticles might be applicable carriers of mRNA vaccines (8).

The selection of a specific 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 (7). Among promising vaccine candidates is the spike protein of the virus. The precise mapping of spike protein is the critical step toward vaccine discovery because this receptor protein is one essential element of the virus that the immune system can potentially identify as non-self (9). 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. To further discuss the expectations of a novel vaccine, it is widely observed in asymptomatic and mild infections that the patients may not have detectable antibodies, but they develop virus-specific T cell response (10); T cells identify and kill infected cells and B cells produce new antibodies.

In one study, the mRNA-1273 vaccine encoded antigenic structure of the spike protein called S-2P. Forty five healthy adults revised an mRNA-1273 vaccine twice with 28 days' interval and different doses (25 μg, 100 μg, or 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 confirm the progression of the mRNA-1273 vaccine to further clinical trials (11).

Additionally, 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. Overall, 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 (12).

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 (13). 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 (14). 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 (15). To reach an ideal goal of a minimum requirement of 50% efficacy for COVID-19 vaccine, it is imperative vaccine researchers and manufactures keep this critical standard in their vaccine platform development (16).

Vaccine delivery remains an essential 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 evaluate the overall performance of a novel vaccine in general population throughout the world. Depending on preliminary clinical outcome, a booster shot may also be included. As for the fair global distribution of SARS-CoV-2 vaccine(s), GAVI (The Global Alliance for Vaccines and Immunizations) can play a pivotal role in implementation of vaccine delivery throughout the world. In the meantime, while preventive vaccine are not available, we encourage our clinical colleagues to consider the use of monoclonal antibodies for at risk groups such as frontline HCWs or individuals with comorbid conditions in whom there is an increased risk of viral transmission. We also believe parallel to vaccine platform efforts, discovery of novel targeted antivirals must be explored to stop the viral replication cycle during early phase of the infection.

REFERENCES

1. Aspinall R, Del Giudice G, Effros RB, Grubeck-Loebenstein B, Sambhara S. Challenges for vaccination in the elderly. Immunity & ageing: I & A. 2007; 4:9.
2. Weinberger B. Vaccines for the elderly: current use and future challenges. Immunity & ageing: I & A. 2018; 15:3.
3. Graham BS. Rapid COVID-19 vaccine development. Science (New York, NY). 2020; 368(6494):945-6.
4. Koff WC, Williams MA. Covid-19 and Immunity in Aging Populations - A New Research Agenda. The New England journal of medicine. 2020.
5. Afrough B, Dowall S, Hewson R. Emerging viruses and current strategies for vaccine intervention. 2019; 196(2): 157-66.
6. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines - a new era in vaccinology. Nature reviews Drug discovery. 2018; 17(4): 261-79.
7. Amanat F, Krammer F. SARS-CoV-2 Vaccines: Status Report. Immunity. 2020; 52(4): 583-9.
8. Hassett KJ, Benenato KE, Jacquinet E, Lee A, Woods A, Yuzhakov O, et al. Optimization of Lipid Nanoparticles

for Intramuscular Administration of mRNA Vaccines. Molecular therapy Nucleic acids. 2019; 15: 1-11.

9. Ou X, Liu Y, Lei X, Li P, Mi D, Ren L, et al. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. 2020; 11(1): 1620.
10. Grifoni A, Weiskopf D, Ramirez SI, Mateus J, Dan JM, Moderbacher CR, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. Cell. 2020; 181(7): 1489-501.e15.
11. Jackson LA, Anderson EJ, Rouphael NG, Roberts PC, Makhene M, Coler RN, et al. An mRNA Vaccine against SARS-CoV-2 - Preliminary Report. 2020.
12. Folegatti PM, Ewer KJ, Aley PK, Angus B, Becker S, Belij-Rammerstorfer S, et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. The Lancet.
13. Weinmayr LM, Steinhäuser J, Gehring SC, Goetz K. Vaccination management for elderly patients in primary care settings - documentation and responsibilities during a vaccination campaign. 2019; 13: 1295-302.
14. Abraham J. Passive antibody therapy in COVID-19. Nature reviews Immunology. 2020; 20(7): 401-3.
15. Vankadari N, Wilce JA. Emerging WuHan (COVID-19) coronavirus: glycan shield and structure prediction of spike glycoprotein and its interaction with human CD26. 2020; 9(1): 601-4.
16. Philip Krause, Thomas R. Fleming, Ira Longini, Ana Maria Henao-Restrepo, Richard Peto. COVID-19 vaccine trials should seek worthwhile efficacy. The Lancet, August 27, 2020.

PEER REVIEW

Not commissioned. Externally peer reviewed.