EDITORIAL

AL-ANBAR MEDICAL JOURNAL
Anb. Med. J. 16(2): 25–27, 2020

Origin, Causative and New Approach of Vaccine Design of COVID-19

Mothana A. Khalil*
Department of Microbiology/Virology, College of Medicine, University of Anbar, Ramadi, Anbar, Iraq
(Received : 18 May 2020; Accepted : 1 June 2020; First published online: 4 June 2020)

DOI: 10.33091/amj.2020.170948

Coronavirus interactive disease 2019 (COVID-19) is a pandemic disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It begins suddenly in December 2019 in Wuhan City, Hubei Province, China, then spread in 213 countries with 4,818,296 confirmed cases, of the 316,925 dead with 6.68% case fatality rate (until the nineteenth of May 2020). It is characterized by a mild common cold-like illness, to severe viral pneumonia leading to the acute respiratory distress syndrome that is potentially fatal [1].

SARS-CoV-2 belongs to the family coronavaridae, its name is derived from the crown-like shape of the surface glycoprotein spike (Spike S glycoprotein) which appears under the electron microscope that projected on the lipid bilayer surrounding the virus particles. However, the Spike S glycoprotein or as known as S protein has a responsibility for the attachment of the virus on host cells specific receptors fusion, and it is a specific antigen for neutralizing antibodies and protection [2]. Gene carry code for Spike S glycoprotein is highly mutant or recombinant leading to enable the Spike S glycoprotein on the virus to change hosts and attach to the cells receptors of another host (human for example). At the same time, it can avoid the body's-immune defenses that have antibodies work against S protein of human coronaviruses, but it does not have antibodies against the S protein of the new mutant or recombinant virus [3].

Coronaviridae includes different genera (Alpha, Beta, and Gamma of coronaviruses) which is infect the animals. Four of the genera are infecting humans; Alpha coronavirus (229E and NL63) and Beta coronavirus (OC43 and HKU1) that cause common cold [3]. SARS-CoV (Beta coronavirus) causes severe acute respiratory syndrome (SARS) in the south of China in 2002 -2003. This outbreak was distributed in 26 countries with 8098 confirmed cases and killed 774 patients with a 9.6% case fatality rate [4]. MERS-CoV (Beta coronavirus) causes another syndrome called Middle East Respiratory Syndrome, this outbreak has begun suddenly in the Kingdom of Saudi Arabia in 2012. This outbreak was distributed in 27 countries with 2499 confirmed cases and killed 861 patients with a 34.4% case fatality rate [5].

Different studies have been shown the animal origin of SARS-CoV-2 that has responsibility for pandemic COVID-19, the first cases of COVID-19 have appeared in the seafood market worker in Wuhan, specifically in individuals who ate bate, fish, chicken, snake, frog, pig, civet cat soft meats and others living and nonliving animals. Another study has been sequenced SARS-CoV-2 RNA on 7 of January 2020 and demonstrated that homology of 95% SARS-CoV-2 RNA with bate coronavirus RNA and 75% with SARS-CoV RNA, therefore, this new virus has acquired with the name SARS-CoV-2 [4]. SARS-CoV-2 is a zoonotic like SARS-CoV and MERS-CoV. Bate coronaviruses are the ancestor and the bats are the reservoir of all zoonotic coronaviruses like SARS and MERS [4].

Many theories are explained the origin of SARS-CoV-2 including:

I. SARS-CoV-2 could result from the genetic recombination between bat coronavirus and another unknown Beta coronavirus following by a mutation and transferred to a pangolin due to the great SARS-CoV-2 coronavirus similarity between the pangolin and bat coronaviruses. The previous recombination leads to the change of the Spike S protein at the receptor-binding domain (RBD) region of the angiotensin-converting enzyme 2 (ACE2) receptor of SARS-CoV-2 and enhanced the transmission ability of the new virus to humans (cross-species). I.e. Scientist have shown two ways for human infection; viruses are transmitted from bate to intermediate (pangolin) to humans. Or it emerges in nature in persons with special conditions from the food market in Wuhan get adapted in him then passed

* Corresponding author: E-mail:med.mu.707070@uoanbar.edu.iq
Phone number: +96479026111165

to others [6].

II. Besides mutation in the spike S protein of bate, coronavirus was the second theory of the origin of the SARS-CoV-2, enabled it to change the original host (bate), and is infect new host (human). Humans might have a significantly enhanced binding, infectivity, and virulence of the mutated virus [7].

III. The third theory is depending on the new studies which have demonstrated that the pangolins like bates, both of them are considered as a reservoir or an intermediate host of SARS-CoV-2 (Zoonotic V). The similarity percentage between pangolin CoV and SARS-CoV-2 is about 90% and the closer relation to bate Rat Tg13 virus resulting to suggest that pangolin is passing the virus to humans [8]. A recent study has been shown that 19 amino acids of S protein in SARS-CoV-2 are different from bate coronavirus S protein whereas only 5 amino acids of S protein in SARS-CoV-2 different from pangolin coronavirus S protein. This means SARS-CoV-2 undergo 2 mutations while transmission from bate to pangolin and from pangolin to humans [8, 9].

IV. The fourth theory is the weaker theory and has not been confirmed yet. It is concluded that SARS-CoV-2 is the result of genetic manipulation by humans in China. The official in the USA and Europe says that SARS-CoV-2 is leaked from the Chinese Central Laboratory in Wuhan City by an accident [10, 11].

Recent research in the USA was mentioned that the 14 mutations are happened to the SARS-Cov-2 in the USA especially in the S gene from March 2020 which lead to an increase in the virulence of this virus compared to the Wuhan original SARS-Cov-2. This is contributed to the increased severity and mortality rate of COVID-19 [12].

Regarding Phylogeny of SARS-CoV-2, recent studies were found three variants or subtypes distinguished by sequencing named A, B, and C (from 163 genomes). Variant A represents the ancestral type of bate coronavirus passed to humans in China, variants A and C are spread outside of East Asia to Europeans and America, and variant B is the common type in East Asia, it is spread outside of East Asia after mutated. Whoever mutated (A) has been observed in the USA cames from China, whereas the (C) variant is considered the major European type observed in the early patients from France, Italy, Sweden, and England [13].

Two types of common vaccines are currently available against different human viruses, killed inactivated viral vaccine, and live attenuated viral vaccine. Both of them have several disadvantages, for example, time-consuming through SARS-CoV-2 culturing and sub-culturing on tissue culture as well as other problems [14]. Genetic manipulation and molecular biology were the two methods used for the development of vaccines against SARS-CoV-2. Most of these methods for vaccine preparations do not need to grow the virus on tissue culture cells take into consideration the safety, sterilization, potential, and efficiency of these types of SARS-CoV-2 vaccines [14].

The vaccine development landscape has confirmed 78 vaccines against SARS-CoV-2, most of them are selected the molecular methods as following:

1. mRNA1273 encapsulated (Nanoparticle) S protein manufacture by Moderna under the supervision of the National Institute of Health (NIH) in the USA, Phase 1. Vaccine is encoding a piece of the genetic code for the S protein and fusing it with Fatty Nanoparticles that can be injected into the body to stimulate the production of antibodies against S protein of SARS-CoV-2 [15]. This vaccine has moved from the design straight in Phase 1 clinical trials of its mRNA vaccine tested on animals and 45 volunteers with three groups each with different low dose results showed safety, skipping tests in animal models and new persons are enrolled. The company is expected the first batch will be in July 2020 in the USA and it might be available at the beginning of 2021 in the USA [15]. The manufacture of this vaccine needs 42 days to recognize the sequence of nitrogen bases in the immune S protein gene of the virus, which is known since the diagnosis of the virus in China and is present in the gene bank, therefore, it does not urgent to have the virus or to multiply it [15].

2. Recently, the Pfizer company, (united with the American Company Biotech) the USA, Phase 1-11 was prepared BNT162 mRNA, making 4 types of vaccines according to the changes in S proteins. The first clinical trial has been done on 360 volunteers in the USA and Germany in May 2020, and the company will produce millions of doses at the end of the same year [16, 17].

3. The SARS-CoV-2 vaccine "CHAdOx1nCoV-vector" is developed under the supervision of Oxford University, UK via insertion or carries of Spike gene (S protein gene) of SARS-CoV-2 in a week adenovirus genome. Oxford University is aiming to produce approximately 100 million doses "CHAdOx1nCoV-vector" vaccine by the end of 2020. Tested in forest animals. In Phase 1-1. A similar vaccine to be prepared in China in December 2020 [18].

4. Inactivate SARS-CoV-2 virus vaccine: Phase I-II, China, in placebo control human trail Dec.2020. Similar vaccine by China in (VERO CELL) November 2021 [19].

5. INO-4800 DNA plasmid vaccine, Recombinant vaccine, USA, S Korea.Nov,2020 [20].

6. COVID-19/aAPC Lentaviral vectored vaccine, Phase I, China,2023 [21].

7. Bac TRL-Spike DNA,bacterial medium (oral) vaccine, phase I. Canada.Dec.2021 [22].

8. Protein subunit vaccine: Nanoparticles or lipid base delivery or micro-needle of S-subunit protein. The similar vaccine produces by the University of Queensland in Australia producing viral proteins in cell culture [14].

9. Novavaxs vaccine for SARS-CoV-2: is meant to create antibodies for S protein. This vaccine has been tested in animals, then the first clinical human trial in 130 Volunteers. The company is expected the first batch will be in mid-May 2020 and it might be available at the beginning of 2021 [23].

http://doi.org/10.33091/amj.2020.170948

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