

Evolution of COVID-19 as well as its different variants

Yutong Sun*

Shanghai Southwest Weiyu Middle School, Shanghai, 200233, China

* Corresponding Author Email: 2021002390@poers.edu.pl

Abstract. COVID-19, first appeared in 2019, it has fulfilled every corner of our life, causing a lot of inconvenience to our daily life. People around the world all have the will to decrease the rate of infection. Some countries have used herd immunity, some use lockdown, other countries use social distancing and so on, but they cannot fully control the spread of COVID-19. Surveillance, vaccine development and its coverage are insufficient for a therapeutic and preventative approach. Besides, variants of COVID-19 further aggravate the tension due to their uncertainty. This research is based on a review of the literature with the goal of comparing different variations and their severity. Despite the fact that practically all countries have demonstrated active resistance to COVID-19 by unwavering efforts such as epidemic research and vaccine development, there are still many aspects that need to be investigated and researched.

Keywords: COVID-19, Evolution, Variants.

1. Introduction

The SARS-Cov-2 virus causes COVID-19, a contagious disease [1]. HCoV-229E and NL63 are all zoonotic. With a 96 percent identity, SARS-CoV-2 is most closely related to the bat SARS-like coronavirus strain RaTG13. SARS-CoV-2 is thought to have originated in bats, according to studies. The coronavirus genus and coronaviridae family contain an unsegmented positive-sense single-stranded RNA virus. Coronaviruses have genomes ranging from 26 to 32 kilobases, making them among the most complicated viruses. Because of its massive genome size, frequent recombination, and a high level of genomic flexibility this virus is prone to cross-species transmission. [2]. After that the WHO declared the COVID-19 outbreak a global health emergency [3]. For the first time, the WHO declared it a global pandemic on March 11, 2020 [4]. COVID-19 can spread quickly between people who are in tight proximity. In crowded and/or poorly ventilated interior conditions, the virus can potentially spread. This is due to the fact that aerosols can stay in the air or travel further than a conversational range [5].

COVID-19 is very contagious; more importantly, COVID-19 is continually changing. Alpha (B.1.1.7) was the first COVID-19 variation discovered in November 2020, followed by Beta, Delta, and Omicron [6]. Mutation is the cause of variants. Some versions pop up and then vanish, while others stick around. In the future, there will be more variations. Some variants spread more quickly and easily than others, potentially increasing the number of COVID-19 cases. For example, Omicron is less severe in general, but it is simpler to transmit than others, indicating that more people are likely to be exposed to Omicron, leading to an increase in cases and a huge increase in hospitalization and death [7]. Each variety has its own unique characteristics [8]. Scientists must investigate variants since some vaccinations will not work as well or at all if the virus evolves. As a result, individuals must be able to notice changes quickly, which necessitates confirmation of infection with a specific variant and identification of the variant. One option to confirm variation is to sequence the entire SARS-CoV-2 genome, or at least the complete or partial S-gene. It's also critical for scientists to figure out what COVID-19's side effects are and what harm they do. This is where researchers should concentrate their efforts. Recognizing COVID-19's adverse effects allows individuals to understand the virus's importance, arousing them, and possibly increasing their willingness to actively participate with the government's policy. It's also crucial to think at the adverse effects, which is something that is currently lacking.

Furthermore, COVID-19 mutation is a problem that humans must solve since different versions have varied characteristics and intensity. As a result, many of the therapies use to treat the existing virus may not work as well on the new variant, resulting in a new outbreak. As a result, stopping COVID-19's spread is crucial, as fewer mutations come from less spread.

2. Variants

Coronaviruses enter host cells through spike glycoproteins (S proteins). Spike glycoproteins protrude from the surface of the virus and have transmembrane functions. S protein consists of two major subunits, S1 and S2, as shown in Figure 1. S1 subunit consists of n-terminal domain (NTD) and receptor-binding domain (RBD), and its target is ACE2 receptor. On the other hand, S2 is mainly composed of fusion peptide, repeat sequence 1, transmembrane domain, etc., which contributes to the fusion between virus and host cell [10]. In all coronaviruses, the so-called S2 'site directly upstream of the fusion peptide is further disrupted by host proteases. This cleavage [11] is thought to prepare proteins for membrane fusion by inducing significant irreversible conformational changes. Sars-cov-2 becomes a functional receptor mediated by ACE2 and thus enters cells [12].

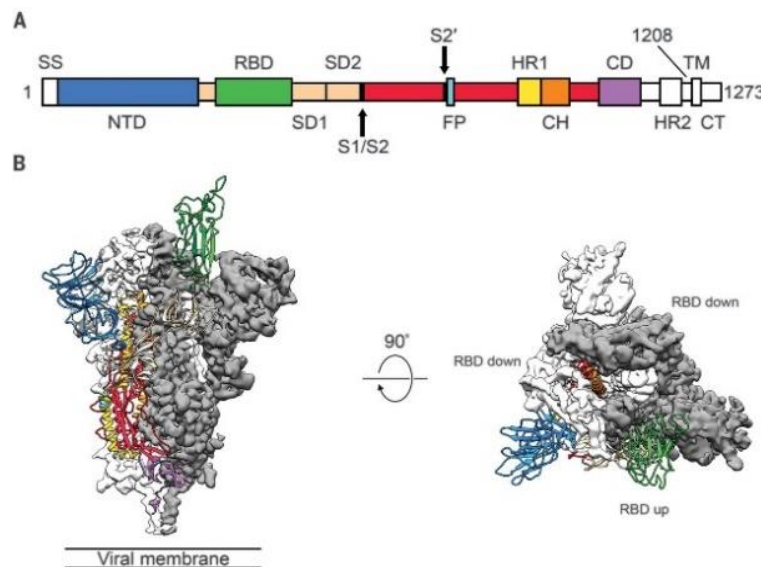


Figure 1. Structure of S protein [13].

COVID-19 is an RNA virus with an unstable genomic sequence and the potential for mutation. RNA viruses are considerably more prone than DNA viruses and bacteria to produce errors when duplicating RNA strands, resulting in novel coronavirus varieties. Furthermore, the unique coronavirus subtype can thrive in a variety of conditions. The immune system's ability to recognize spike proteins and bind antibodies to them becomes increasingly difficult as the virus evolves [15]. The three novel coronavirus strains, Alpha, Delta, and Omicron, will be the subject of the next paragraphs. The distinctions between them will be clearly shown.

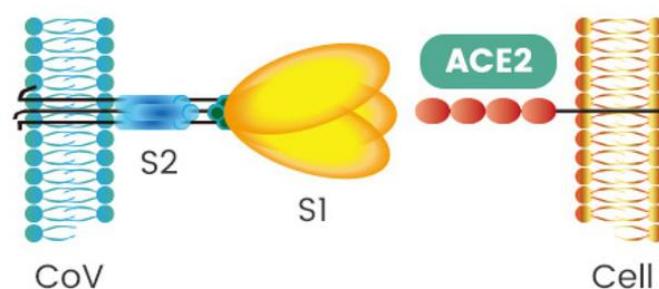


Figure 2. Function of S1 and S2 [14].

2.1. Alpha

First, alpha was the first species found in the UK. Because the S protein in the Alpha of SARS-COV-2 strain has a higher affinity for binding to receptors than the original strain, its infectivity is 50% higher than that of the original strain [16]. The strain, known as B.1.1.7, is composed of mutations in spike proteins and three missing residues. Compared with the original SARS-COV-2 strain, the B.1.1.7 SARS-COV-2 variant strain showed 7 missense mutations and 3 large fragment deletions. One of the most significant mutations in the B.1.1.7 variant is the P681H mutation, which swaps proline (P) at the furin cleavage site of S protein "PRRAR" with Histidine (H), resulting in changes in the structure of S protein, thus improving the infectivity of the novel SARS-COV-2 variant [17].

2.2. Delta

Delta spikes bind to cell membranes, but only if the cell receptor ACE2 is kept low. Its pseudotype virus infects target cells much faster than all the other tested variants, which may account for its greater transmissibility. There are six Delta gene mutations and the most notable spike protein mutations are L452R and P681R. The L452R mutation substitutes a leucine with an arginine at position 452. This property, according to the study, allows the spike protein to attach to the ACE2 receptor with increased affinity. The SARS-CoV-2 spike protein can connect to the ACE2 receptor, which is found in numerous cells throughout the human body. Because the ACE2 receptor has a higher affinity for the spike protein, it may be able to prevent vaccine-stimulated antibodies from attaching to it [18].

2.3. Omicron

The Omicron spike structure had a very closely packed RBD organization with long-term ramifications that the Delta spike did not have [19]. Because modifications at the ACE2-RBD interface promote tight binding by enhancing hydrogen bonding interaction and enlarging hidden solvent accessible surface area, RBD of Omicron binds to the human ACE2 protein more firmly. [20]. Several changes in the spike protein's receptor-binding region suggest that the Omicron variation may be immune to antibody-mediated protection. Omicron may frequently evade existing immunity long enough to cause an infection, symptoms, and transmission to the next person. Furthermore, Omicron's DNA contains 72 mutations [21].

2.4. Comparison

When compared to the Alpha variation, the Delta variant was associated with more breakthrough infections in thoroughly vaccinated persons who were mostly symptomatic [22]. Delta has a high level of transmissibility and travels more quickly. It spreads at a rate that is 50 percent quicker than Alpha. In comparison to the Alpha type, it was estimated to be 80 to 90% transmissible according to Connecticut data [23]. Furthermore, Delta produced more severe infections in those who were not inoculated than other variants [24]. Cold symptoms such runny nose, headache, sore throat, and fever seem to be more severe in the Delta type than in the Alpha type [25]. Furthermore, it is 50% more infectious than Alpha, and vaccines' protective effect against symptomatic disease may be diminished, meaning that even if people are vaccinated, the vaccine's activity against the virus may be less effective than Alpha's [21].

In comparison to the original SARS-CoV-2 strain, Omicron has 72 mutations throughout its genome. 1 mutation, 3 mutations, and 2 mutations, respectively. Half of the changes have occurred in the spike protein, a critical surface protein that helps the virus to latch on and infect cells [22]. The Omicron variant has multiple genetic modifications compared to the original strain, including mutations in the spike (S) glycoprotein, more than three times the number of mutations found in the first four VOCs. The receptor binding domain (RBD) mutations of Omicron spikes are much larger than those of Alpha, Beta, Delta, etc., with 1, 3, 3 and 2 mutations, respectively [23]. Furthermore, 6.5 2.2 hydrogen bonds are generated on average between ACE2 and RBDO, which is nearly 10%

Recently, a team first established a technical platform for the efficient preparation of high-purity circRNAs in vitro [27]. For novel Coronavirus and its variant strains, a circRNA vaccine encoding the Novel Coronavirus Spike protein RBD was designed. The circRNA vaccine (CircRNA^{RBD-Delta}) prepared in this study against novel Coronavirus Delta variants has broad spectrum protection against multiple Coronavirus variants. The circRNA^{RBD-Omicron} vaccine (CircRNA^{RBD-Omicron}) has a narrow protective range and induces antibodies that only neutralize the Omicron strain. The CircRNA^{RBD-Delta} vaccine, designed for the Delta variant, can induce the production of a broad spectrum of neutralizing antibodies in mice, effectively neutralizing a variety of COVID-19 variants, including omicron.

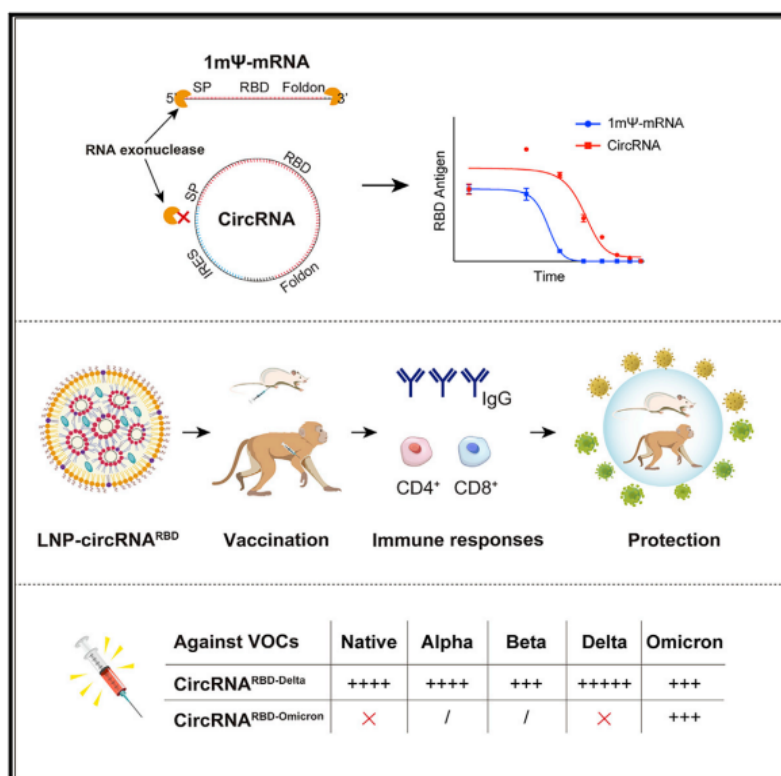


Figure 4. The mechanism of Circular RNA vaccines [27].

3. Conclusion

The introduction of consistent new variants of COVID-19, increases the difficulty of eradicating COVID-19 because distinct variants have their own characteristics, and previously established immunizations and surveillance may not have a significant impact on reducing disease transmission and severity. To minimize the occurrence of COVID-19 mutation, it is necessary to stop the spread of COVID-19 because if the likelihood of spreading it is reduced, there are not so many chances for COVID-19 to spread if their pathways are no longer exist. Furthermore, experts have not yet determined the differences in symptoms among the many types. More emphasis should be placed on identifying the nuance between variants and determining the most appropriate treatment for each variant.

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