

Mutational Lines of Strains and Mutational Adaptive Selectivity of Coronaviruses

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ABSTRACT

The accumulated information about the waves of the pandemic is officially recorded in many countries of the world. These circumstances are associated with the formation and widespread spread of SARS-CoV-2 coronavirus strains that have undergone genetic mutations. A mutation is a molecular biological process where viral replication involves "knocking" during transcription and translation steps, i.e., during "overwriting" of the genetic code from the RNA of the virus onto the DNA of the host cell. Such errors in DNA lead to the formation of altered genes encoding proteins of the virus, as a result of which such new mutant viruses appear, with altered properties of their own proteins. The main mutations of the coronavirus occur in the glycoprotein S-protein gene. Thus, a mutation in the S protein leads to the replacement of the aspartic amino acid (abbreviated D) with the amino acid glycine (abbreviated G). American researchers have experimentally shown that the long-discussed D614G mutation in the S-protein gene of the SARS-CoV-2 coronavirus increases its infectiousness, so this variant of the virus spreads faster. A viral protein with such a mutation is also more stable. Mutations in the receptor-binding domain (RBD-receptor binding domain) have a higher affinity for the receptor of the angiotensin-converting enzyme type 2 (ASy2) of human epithelial cells, which allows coronaviruses to adaptively selectively penetrate into them.

Introduction

The presence of new mutated strains of the SARS-CoV-2 virus indicate possible pandemic waves in the world [1-8]. As of the end of April 2021, the total number of people infected with the SARS-CoV-2 virus in the world is more than 142 million, the death toll is more than 3 million. Thus, the number of cases of infection over the past 2 weeks - from 06.04.21 to 19.04.21 increased by 10 million people. In Russia, on the same date, the total number of cases is more than 4.5 million people, more than 105 thousand people died. The most leading in the number of deaths from COVID-19 (indicator per 100 thousand population): Great Britain - 201.8; Italy - 192.7; Brazil - 181.8; USA - 175.0; Spain - 165.8; France - 151.2; For Russia,

this indicator is 70.7 per 100 thousand people of the population (data from 18.04.21). An important coefficient of the degree of spread of the virus is the Rt indicator - as the ratio of the number of new detected cases of infection over the past 4 days to the number of new cases over the previous 4 days. The value of the indicator > 1 indicates a deterioration in the epidemiological situation and a greater spread of infection. In India, Brazil, Turkey, Italy, the RT indicator according to 18.04.21 exceeds 1. In Russia, this indicator is 1.07, in the United States - 0.92. According to Rospotrebnadzor, as of April 16, 2021, 192 samples of the British strain were identified in the Russian Federation, 21 of the South African strain.

Researchers in the UK reported that the risk of death in people infected with the “British” strain B.1.1.7 is higher than those infected with other strains, by an average of 64%. The absolute risk of death increases from 2.5 to 4.1 deaths per 1,000 infections. Scientists from Cape Town and Johannesburg (South Africa) examined antibodies in 89 people hospitalized with COVID-19 in early 2021. The authors showed that COVID-19, suffered during the first wave, does not provide protection against some new variants of the virus. However, people infected with the “South African” strain of SARS-CoV-2 have neutralizing antibodies against old variants of the virus, as well as against the “Brazilian” strain. Scientists from the United States examined a cohort of pregnant and breastfeeding mothers who received the Pfizer/BioNTech or Moderna vaccine. They showed that IgG, IgA and IgM levels to the S protein and Receptor-Binding Domain (RBD) increased in the blood of women from both groups. Antibodies, especially IgG, were transmitted to the baby through the placenta and mother’s milk. Japanese scientists, in particular Yoriyuki Konno et al., have shown in their work for 20 years that a protein expressed from the ORF3b gene of the new coronavirus SARS-CoV-2 strongly suppresses the synthesis of type I interferons in patients with COVID-19./ At the same time, the virus is sensitive to interferons, which indicates their potential effectiveness for the therapy of coronavirus infection [5].

In this regard, in clinical terms, it seems advisable, as measures of active antiviral protection, to provide patients with the prescription of recombinant interferon preparations - $\alpha 2b$ with antioxidants, both in the pre-vaccine period, when the process of formation of virus neutralizing antibodies is underway, and in the late post-vaccine period, when the antibody titer after vaccination begins to decline. According to Rospotrebnadzor, in the 15th week of 2022, the share of the omicron strain among detected cases of coronavirus in Russia increased to 97.5%. At the same time, the share of the delta strain decreased to 0.5%. On April 13, Kamil Khafizov, head of the scientific group for the development of new diagnostic methods based on sequencing technologies at TsNII Rospotrebnadzor, said that more than 90% of all detected cases of coronavirus infection occur in a subspecies of the omicron strain VA.2 or “stealth omicron.”

The Main Mutation Lines of the Virus SARS-CoV-2

1. “British” strain of coronavirus. Name: B.1.1.7. The most important mutations it contains are: - N501Y (this mutation makes the virus more infectious). WHO reported that the “British” strain of coronavirus has been identified in at least 60 countries.
2. “South African” strain of coronavirus. Titles: B.1.351 and 501Y.V2. The latter mutation is considered the most dangerous - viruses with the mutation are able to more effectively evade antibodies obtained from the blood plasma of patients who

have recovered from COVID-19. Scientists have warned that the strain found in South Africa is transmitted about 50% faster and overcomes some antibodies produced in response to other variants of the virus.

3. “Brazilian” strain of coronavirus. Title: B.1.1.248. The “Brazilian” strain is the most contagious to date. It has resistance to immunity acquired after the first wave of coronavirus. So, the main mutation of the coronavirus is contained in the gene encoding the synthesis of S-protein (“Spike,” Spike). This mutation is also characteristic of two other strains - “South African” and “Brazilian.” This mutation changes the shape of the “spike” (S-protein), with which it attaches more effectively to the ACE2 receptor. According to the authors, the “British” strain with this mutation is 50-70% more infectious than the classic SARS-CoV-2 virus.
4. It should be noted that the most dominant in Europe was the so-called “Spanish strain” of the coronavirus - the 20A.EU1 line, the main mutation in the S-protein. Immunoglobulins are less effective at neutralizing the “Spanish” strain of coronavirus.
5. “Californian” strain. Opened in the USA - the name of the CAL.20C.
6. The “Romanian” strain - a type of “British” - is resistant to vaccines.
7. Siberian and Northwestern coronavirus strain. These are newly formed new mutations in Russia. So far, there is little data on these strains, but mutations are also known to occur in the zone of the gene responsible for the S-protein.

Adaptive Mutation Selectivity of Coronavirus Strains

Studies on the detected mutations and their effect on the variability of coronaviruses, on the isolated genotypes in SARS-CoV-2 are important for assessing the biological properties of coronaviruses, determining the epidemiological routes for the introduction and spread of the virus. If you look at the relative number of nucleotide substitutions of different types in the early evolutionary history of SARS-CoV-2 before the infection of people, it is difficult to notice something special. The frequencies of such substitutions are similar to those of SARS-CoV and HKU1. This aligns well with work indicating the natural origin of the virus. How the nature of SARS-CoV-2 mutagenesis changed after it jumped to people. About a thousand fully read SARS-CoV-2 genomes indicate that the relative frequencies of unique single mutations when one nucleotide A, U, G or C changes to another. All mutations occurred during the spread of the virus among humans. After switching to humans, SARS-CoV-2 increases the proportion of G mutations in U by about ten times. Moreover, such an effect is not observed for

SARS-CoV or HKU1. The result is replicated regardless of whether we use genomes from the US or China. Not a kind of symmetric increase in the number of complementary C mutations in A. The SARS-CoV-2 genome is represented by a positive strand of the RNA molecule. When a virus infects a cell, a positive strand is used to synthesize negative strands, which in turn are used to synthesize new positive strands that are packed into shells and passed on to the next cells. Nucleotides A, U, G, C on the positive chain correspond to nucleotides U, A, C, G on the negative. If an excess of G mutations in U arose due to RNA copying errors, then such errors would probably occur when copying both positive and negative chains. The G mutations in U on the negative strand are C in A on the positive. But the excess of such mutations is not visible. That is, one of the chains performs the mutation selectively [9]. Which indicates an adaptive mutation process [10]. Coronavirus diseases in 2022 become asymptomatic. Shanghai authorities reported 19,831 cases of asymptomatic disease on Sunday April 10, 2022.

Conclusion

Coronavirus mutations do not end on any strain. The mutation of coronavirus strains will continue if coronaviruses are not separated from humans. Enhanced strict sanitation and hygiene measures, self-isolation and protective equipment and activities can help wean coronaviruses from humans and stop the pandemic [11]. For example, in China, since March 28, the city authorities have limited public transport in the city due to an increase in the number of asymptomatic patients with COVID-19. 25 million Shanghai residents are sitting at home due to the largest outbreak of coronavirus since the beginning of the pandemic - 20,000 cases were detected there on April 10, 2022. Most of them carry Omicron asymptomatic. China still has a "zero COVID-19" strategy. And even with isolated cases of the disease, the entire population is sent to the most severe lockdowns bordering on a total sanitary blockade.

Stealth omicron the invisible coronavirus subvariant takes over the world. As of April 5, 2022, it was found already in 109 countries of the world.

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