

Variant in COVID-19 Gene Mutation “The Past and the Future”

¹M. Santhiya, ²B.Senthamarai Kannan

¹PG Chemistry student, T.D.M.N.S. College, Tirunelveli, Tamil Nadu, India. ²Assistant Professor, PG Department of Chemistry, TDMNS College, Tirunelveli, Tamil Nadu. E- mail: santhiya15122001@gmail.com

Abstract: A new corona virus sparked the pandemic of the novel COVID-19 virus, which has spread around the world. SARS-CoV-2 (severe acute respiratory syndrome corona virus is a corona virus that causes severe acute respiratory syndrome. It is the sixth known corona virus to infect people; four of these coronaviruses are 229E, NL63, OC43, and HKU1 which spreads with mild symptoms. SARS-CoV, MERS-CoV, and SARS-CoV-2, on the other hand, elicit severe symptoms and have a 40% fatality rate. N501Y, D614G, K417N, and T478K are among the changes that may assist the virus resist neutralizing antibodies produced by vaccination or past infection. At this point, it's difficult to say how transmissible it is. In response to the continuous emergence of new SARS-CoV-2 variations, the FDA updated the EUAs of some authorized molecular, antigen, and serology tests on September 23, 2021, to establish additional Conditions of Authorization. These conditions necessitate, among other things, that test developers update their authorized labeling and assess the influence of SARS-CoV-2 viral changes on their test's performance. The Delta form then spread quickly until mid-December, accounting for nearly 99 percent of COVID-19 cases and causing a massive surge in hospitalizations. Sub Delta Variant (AY.4.2), which represents for 8% of corona virus cases sequenced, has two distinct mutations in the spike: Y145H and A222V. The Delta plus Variant (AY.1), on the other hand, has an extra mutation on the spike protein termed K417N. It's been suggested that this modification decreases the binding affinity of ACE2 by a little amount. On November 30, 2021, the United States identified the omicron version of SARS-CoV-2, B.1.1.529, as a Variant of Concern. The omicron variety has a lot more mutations than other SARS-CoV-2 variants, especially in the S-gene, which codes for the virus's spike protein. The FDA is collaborating with government partners and test producers to assess the effects of the omicron variant on SARS-CoV-2 diagnostic tests, as well as to create a vaccine and medication to combat the current mutant corona virus.

Keywords; SARS-CoV-2, FDA, MERS-CoV, Delta variant, ACE2 gene

Introduction: COVID-19's causal agent, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), was responsible for more than 143 million illnesses and three million fatalities globally as of April 2021 [1]. More than one million SARS-CoV-2 sequences are accessible via the Global Initiative on Sharing All Influenza Data (GISAID), allowing for near real-time surveillance of the epidemic [2]. The use of pathogen genomes on such a large scale to track viral distribution globally, investigate local outbreaks, and guide public health policy heralds a new era in virus genomic research [3]. Sequencing allows for the identification of new SARS-CoV-2 variations and sets of mutations that may be connected to changes in viral characteristics, in addition to epidemiology. Because extremely detrimental changes are

swiftly purged, most alterations found in circulating SARS-CoV-2 virions' genomes are likely to be neutral or modestly deleterious. Because high-effect mutations that contribute to viral adaptation and fitness are rare compared to tolerated low-effect or no-effect 'neutral' amino acid alterations, this is the case [4]. In terms of structural, SARS-CoV-2 is the most similar to SARS-CoV and MERS-CoV [5]. COVID-19 is the ninth member of the ortho coronavirinae subfamily of the Coronaviridae family [5]. The majority of this family's members are zoonotic viruses that spread to humans by contact with infected animals [5]. SARS-CoV-2, the virus that causes COVID-19, changes over time as do all viruses. The majority of the modifications have little to no effect on the virus's properties. Some modifications, however, may have an

impact on the virus's features, such as how easily it spreads, the severity of the disease it causes, or the effectiveness of vaccines, therapeutic drugs, diagnostic instruments, and other public health and social measures. Viruses are constantly evolving, and this might result in the emergence of a new variant, or strain, of the virus. In most cases, a variation has little effect on how the virus functions. However, they can make it act in a variety of ways at times. Changes in the virus that causes COVID-19 are being tracked by scientists all over the world. For example, in April 2020, the spike protein amino acid mutation D614G was shown to be rising in frequency and to have appeared numerous times in the worldwide SARS-CoV-2 population, and the coding sequence had a high dN/dS ratio, indicating positive selection at codon position 614 [6,7]. D614G offers a considerable infectivity advantage, according to subsequent studies [8, 9]. The mutation rate of RNA viruses is substantially higher than that of their hosts, up to a million times higher, and this high rate is linked to virulence modulation and evolvability, both of which are regarded helpful for viral adaptability [10]. Their findings are assisting researchers in determining if some COVID-19 variants spread more quickly than others, how they influence your health, and how effective different vaccines are against them. Many of them can cause a wide range of ailments, from a simple cough to serious respiratory problems. COVID-19 is caused by a new (or "novel") corona virus, one of numerous known to infect humans. It's most likely been found in animals for a long time. Viruses that infect animals can occasionally infect humans. That's what scientists believe happened in this case. So, while this virus is not new to the rest of the planet, it is novel to humans. When scientists discovered it was causing illness in people in 2019, they dubbed it a new corona virus. SARS-CoV-2 is the name given to these strains by experts. Corona viruses have all their genetic material in something called RNA (ribonucleic acid) (ribonucleic acid). Although RNA and DNA have some similarities, they are not the same. When viruses infect you, they connect to your cells, enter them, and replicate their RNA, allowing them to spread. If a copying error occurs, the RNA is altered. Mutations are the term used by scientists to describe these alterations. COVID-19 is thought to be derived from a bat SARS-like corona virus with

mutations in the spike glycoprotein (protein S) and nucleocapsid N protein, according to structural studies. COVID-19's positive-sense RNA genomes are approximately 29.9 kb, 27.9 kb, and 30.1 kb, respectively, compared to SARS-CoV and MERS-CoV [11, 12]. These modifications occur at random and by chance. It's a natural component of the process of viruses multiplying and spreading. Because the changes are unpredictably occurring, they may have little or no impact on a person's health. They may also cause disease in some cases. One reason you need a flu vaccination every year, for example, is that influenza viruses evolve year to year. This year's flu virus isn't likely to be the same as the one that swept the country last year. When a virus undergoes a random mutation that makes it simpler to infect humans and spreads, that variety becomes more frequent. In the end, all viruses, including coronaviruses, can evolve over time.

2. Coronavirus Mutations and Variants: What Does It Mean?

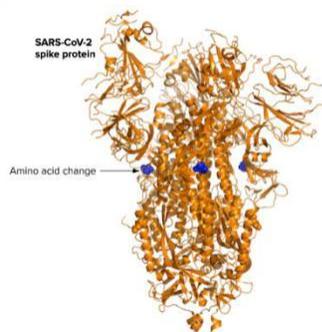
Genetic mutations occur in all organisms, including people, plants, insects, bacteria, and viruses, and can be useful or harmful. Viruses mutate and evolve as they infect a host's cell, duplicate, and move on to another cell or a new host, despite the fact that they are not technically alive. Transmission is the term used to describe how a virus spreads. The rates of mutation fluctuate amongst different types of viruses. The SARS-CoV-2 coronavirus, which causes the clinical entity known as COVID-19, for example, mutates every 11 to 15 days. This is around half of the influenza (flu) rate and a fifth of the HIV rate. Because viruses are not considered organisms per se, mutations create heterogeneity within a population, allowing natural selection to enhance qualities that are beneficial to the viral particle. The G strains are currently the most common strain in the planet. SARS-CoV-2 variants with D614G mutations in the spike (S) protein have become the most prevalent. It gets its name from the fact that one amino acid in the viral spike proteins is altered from D (aspartate) to G (glycine). The spike protein is responsible for attaching to receptors and fusing to the human cell membrane. The S protein protrudes from the viral membrane, giving the virus's surface a crown-like look for which it is called; corona is Latin for "crown." The majority of the problematic variants had

mutations in the receptor-binding domain (RBD). Increased viral infectivity, pathogen city, and immune evasion potency appear to be caused by these changes. Because the RBD is known to have a role in viral recognition as well as cell receptor binding and interaction, any structural alterations appear to be linked to viral transmissibility and virulence. Antibodies produced against the RBD have also been demonstrated to have the greatest effectiveness against the SARS-CoV-2 in multiple investigations [13-17]. Knowing the mutations is the first step in comprehending the variations and their influence on infection, reinjection, and probable implications on vaccinations and therapies. Although there are hundreds of mutations, seven of them are the most important to understand thus far.

The Types of COVID – 19 spike Mutations:

3.1. Corona virus Variants from the Past. You may have heard that there were many strains of the new corona virus earlier in 2020, when the pandemic was still emerging. Is this correct? Yes, it looked that the answer was yes. A research in China led to the idea of multiple versions of the novel corona virus. Researchers were looking at how corona virus RNA changed over time in order to find out how different corona viruses are connected to one another. They used image analysis to examine 103 samples of the novel corona virus gathered from people, as well as corona viruses from animals [18-25]. The corona viruses identified in people were not all the same, it turned out. There were two varieties, dubbed "L" and "S" by the researchers. They're nearly identical, with two minor variances. The S type appears to have come first. The L type, however, was more frequent early in the outbreak, according to the research.

A small change to the spike protein may have made SARS-CoV-2 more infectious



3.2. Spike Mutation D614G. Early in the epidemic, the D614G Spike mutation was detected as the first mutation of concern in China. This mutation soon propagated throughout the world, allowing mutated viruses to quickly replace non-mutated ones. Despite the fact that it appeared to enhance infectiousness, it was not linked to more severe illness or decreased vaccination efficacy. 3.3. Spike Mutation N501Y. The following five mutations found are more concerning. The N501Y Spike mutation, which has been found in at least three variations of concern, is the first. This mutation, which is found near the protein's tip, appears to create a tighter and hence more efficient fit to human cell receptors. 3.4. Spike Mutation E484K. The E484K Spike mutation is of particular significance since it has been found not only in three worldwide variations, but also in three newly characterized American forms. This mutation changes the structure of the proteins in the viral spike in vitro, which might potentially disguise the antigenic part from antibodies. There's been a lot of debate about whether this mutation may affect the efficacy of monoclonal antibody therapy and lead to reinjection in some people. 3.5. Variant B.1.1.7. The Centers for Disease Control and Prevention have classified variations into three degrees of hazard. These are variations of high consequence (B.1.526, B.1.525, and P.2), variants of interest (B.1.526, B.1.525, and P.2), and variants of concern (B.1.1.7, P.1, B.1.351, B.1.427, and B.1.429). Only the first two types have been recognized in the United States. There is evidence of higher transmissibility, more severe illness, and lower treatment efficacy for the variations of concern. At this time, globally-identified variations have been discovered in a number of states. The variety known as B.1.1.7 was first discovered in the United Kingdom and is currently found in at least 90 nations and 51 states, including Washington. A large number of mutations were found in this variation, including six in the spike protein. The N501Y mutation, which has been discovered to assist the virus make a firmer connection to the ACE2 receptors, is the most remarkable of the 17 detected. This variation is roughly 50% more infectious than the wild form of virus, and it is projected to double every 10 days in the United States. 3.6 Variant B.1.351. In South Africa, another variety with the same sort of N501Y mutation was

discovered at the same time as the B.1.1.7 variant. The B.1.351 variation comprises additional mutations such as the K417N and, more importantly, the E484K mutation. The latter has been discovered in 48 nations and 30 states, including the United States of America. In vitro investigations have revealed that there is a chance of a slowed immune response and a little reduction in vaccination efficiency.

3.7. Variant P.1.A Brazilian version was discovered on four persons screened at an airport outside of Tokyo, and it was the first time it was reported in Japan. The passengers are thought to have acquired the P.1 strain while in Brazil, where the lineage may be traced back to Manaus, and the main city in the Amazon area. This variation includes 17 distinct mutations in the spike protein, including the previously mentioned N501Y, E484K, and K417N. It has been found in at least 25 nations and 22 states, including the United States of America. Anecdotal accounts of reinjection in patients who had recovered from sickness are particularly concerning.

3.8. The Omicron Variant: The new variation (B.1.1.529) was discovered for the first time in Botswana on November 11, 2021. On Nov. 24, 2021, experts in South Africa reported the Omicron variant to the World Health Organization (WHO, Fig.1). They detected the variation following an increase in COVID-19 infections. In+S:R346K, further amino acid alterations were examined. Omicron is classified as a "Variant of Concern" by the World Health Organization. This classification indicates that the variation may be more transmissible, produce more severe illness, and be less likely to react to immunizations or therapies. However, additional data is needed to substantiate these factors. Early data shows that the Omicron variation, when compared to other variants, increases the likelihood of reinjection. Current COVID-19 PCR assays are capable of detecting Omicron instances.

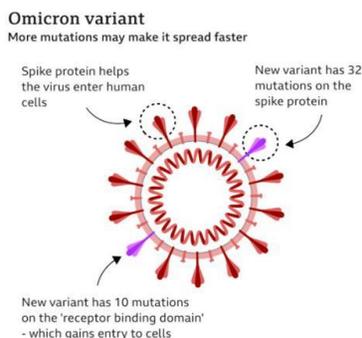


Fig.1. Omicron variant a change in the spike proteins of COVID-19

Experts discovered that one of the three target genes (dubbed the S gene dropout) in persons infected with Omicron is missed by a specialized PCR test. As a result, these tests can distinguish between positive Omicron instances and, as a result, can discover this variety sooner than prior surges. Even if you're completely vaccinated, breakthrough infections with the Omicron strain are conceivable, according to studies. A viral variation is a slightly modified (mutated) form of the virus. Thousands of Covid variations exist over the world, which is to be anticipated given that viruses constantly change. The extensive array of genetic alterations that Omicron has undergone distinguishes it from many other kinds. There are hundreds of mutations to the spike protein, which is the portion of the virus targeted by the vaccine.

Other Corona virus Variants:

4.1. Delta (B.1.617.2). In December 2020, this variation was discovered in India. In mid-April 2021, it resulted of a massive increase in instances. This extremely contagious form has now been discovered in 178 countries, including the United States, the United Kingdom, Australia, and the entirety of Europe. It is the most common strain in the United States and the United Kingdom. Two doses of the Pfizer-BioNTech vaccine were 88 percent effective two weeks after the second dosage, according to a study assessing the COVID-19 vaccine's efficacy against this variation. Two doses of the AstraZeneca vaccine, which is available in the United Kingdom, were shown to be 60% effective. Three weeks following the first dosage, both vaccinations are only 33% effective. Because the dosages provide different levels of protection, physicians recommend having the second injection as soon as you're eligible. Changes to the spike protein may render the Delta version up to 50% more transmissible than other COVID-19 variants, according to research. The Delta variant of the corona virus may cause more severe disease in persons who have not received the corona virus vaccination than the original strain of the virus. People who have been vaccinated may have a "breakthrough infection," but they are less likely to become extremely ill or die. The Delta strain has been able to spread so quickly and shows no signs of slowing

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