

Genetic Variants of SARS-CoV-2: What do we know so far?

Viruses are not living cells. They are made up of a coat of protein wrapped around a genetic code (RNA or DNA). A virus needs to get into a living cell (host) to make more virus copies (replicate). Viruses constantly change parts of their genetic code as they replicate, which can lead to variations in how the virus behaves. Some variations in the genetic code weaken the virus while others make the virus more transmissible (make it spread more easily), more virulent (make it cause more severe disease and death), or help the virus better escape the body's defense system. SARS CoV-2 is the virus causing the COVID-19 pandemic. This fact sheet describes what we currently know about variants of SARS CoV-2, why they are important, and what you can do to stay safe.

SARS-CoV-2 Genome

A genome is the complete set of genetic information in a virus (or other living thing). The name SARS-CoV-2 refers to a specific virus and its genetic code. SARS-CoV-2 virus genome is made of about 30,000 letters of RNA. The RNA produces 4 structural proteins, known as S (spike), E (envelop), M (membrane) and N (nucleocapsid) proteins (Figure 1). The N protein holds the RNA genome, while the S, E, and M proteins together create viral envelop. The Spike protein is used by virus to attach to human cells and hence gain cell entry.

When scientists talk about changes in viruses over time, several terms may be used that are important to understand.

Mutation: Refers to changes in the genetic composition that occur naturally over time. Some mutations can change a virus's ability to cause infection and disease.

Variant: When viruses of the same class develop different genomic sequences due to mutation, they are termed variants. For example, there are thousands of variants of SARS-CoV-2 that differ from each other by at least one mutation. Most of these variants are not more dangerous. Variants may weaken or strengthen the virus. (Figure 2)

Strain: When a variant has very different features from the original virus, such as differences in its ability to spread or to cause severe disease, then it is termed a strain. All strains are variants, but not all variants are strains. (Figure 2)

Lineage: A distinct branch of viral classification is termed as part of a lineage. e.g., lineage A.1 was the primary outbreak in Washington State, U.S.A., while the current circulating SARS-CoV-2 belongs to lineage called B.

Clade: Clade refers to the various ways a virus species relate to each other and is used to track how virus bounces around various geographical regions.

Fig.1: SARS-CoV-2 Genome and proteins it produces

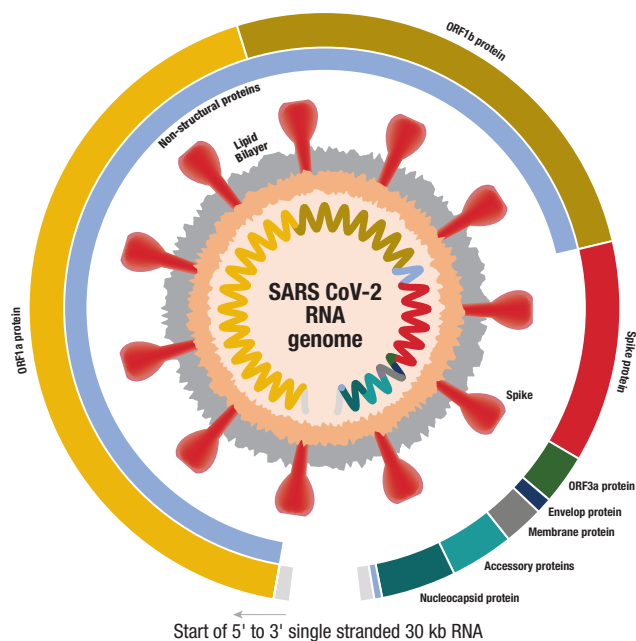
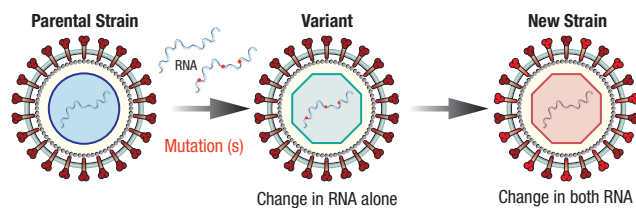


Fig.2: Demonstrates the difference between a new variant and a new strain



Source: <https://theconversation.com/whats-the-difference-between-mutations-variants-and-strains-a-guide-to-covid-terminology-154825>

Mutations in Spike Protein

SARS-CoV-2 virus contains spike proteins that bind to specific places such as angiotensin converting enzyme 2 receptors (ACE2) that are present in many human cells. Mutations in the spike protein genetic code have been found that change how the virus is able to work. Each variant mutation is named with letters and numbers such as:

- D614G: the earliest mutation which appeared in early 2020, which is presently >98% of all SARS-CoV-2 isolated in the world
- N501Y: helps virus bind more tightly to human cells by binding to ACE2 receptor

Naming SARS-CoV-2 Variants

The World Health Organization (WHO) has introduced guidelines to end the practice of associating viral diseases with geographical locations (such as Middle East respiratory virus or Zika virus). This was done in order to avoid suggestion that the named region somehow caused the virus, and to reinforce that everyone is at risk of infections. Unfortunately, there is no agreed upon system for naming viral variants. Currently, coronavirus variants are being named either according to geographical locations where the first cases are identified, or one of the following: date of detection, position of mutations, lineage classification system. For example, 501Y.V2 (substitution of 501st amino acid site in Spike protein), which is also called South Africa variant and VOC 202012/01 (variant of concern, 2020 Dec.), also called U.K. variant or B.1.1.7 (based on lineage).

Testing for SARS-CoV-2 Variants

At this point in time most diagnostic tests currently in use will detect the variant strains. Importantly, vaccination does not interfere with the testing process. As new variants emerge genetic sequencing is used to identify new testing targets. (<https://www.jhsph.edu/covid-19/articles/variants-vaccines-and-what-they-mean-for-covid19-testing.html>)

Transmissibility and Virulence of New Variants

New variants can change the transmissibility of the virus (ability to spread) and the virulence (ability to cause severe disease). Some appear to spread more easily than the initial SARS-CoV-2 virus, while others may also be more virulent. Viruses that spread more easily (even if they are not more virulent) are still a risk because they may cause more deaths in a population just because many more people become infected.

Implication of SARS-CoV-2 Variants for Vaccine Effectiveness

Current vaccines are all designed to expose the body to several parts of the spike proteins so that the body can recognize it and attack it if infected with the real virus.

The Pfizer/BioNtech and Moderna are mRNA vaccines, which use the machinery of our own cells to produce the coronavirus's spike protein, leading to immunity without the possibility of infection. The Janssen vaccine made by Johnson and Johnson uses a weakened adenovirus (a different virus) that also includes that same spike protein to produce immunity.

These vaccines should still provide some protection against these new variants, although possibly not as much as they do against the original type. Studies show that patients who

received the mRNA vaccines still made protective antibodies against the B.1.351 /South African variant, although not at quite as high a level as they did against the original strain and against the strain seen in the B.1.1.7 / UK variant. Studies of the Johnson and Johnson/Janssen vaccine have also shown protection against the B.1.351/South African variant.

These new vaccines can be changed more easily to adapt to new virus strains than older vaccine technologies. In the last ten years, common vaccines for pneumonia, meningitis, and human papilloma virus (HPV) have all been updated to prevent new strains, while the influenza vaccine has to be updated every single year. It would not be a surprise if we need to update COVID-19 vaccines in the future.

Impact of SARS-CoV-2 Variants on Healthcare Systems

The COVID-19 pandemic is straining healthcare systems all around the world. With the ongoing spread of new variants, there is serious concern that the already stretched resources will not be capable of taking care of those who need help. This is why both research and public actions to control this pandemic are so vital.

Protecting Yourself and Others From SARS-CoV-2 Variants

Now, more than ever, it is crucial for everyone (vaccinated and not vaccinated) to continue to follow basic public health measures, including:

- Mask covering includes your mouth, nose, and chin
- Hand washing for at least 20 seconds with soap and water or using hand sanitizer with at least 60% alcohol content
- Physical distancing 6 feet or more
- Avoiding of large gatherings and poorly ventilated spaces
- Clean and disinfect frequently touched surfaces
- Monitor for symptoms
- Getting vaccinated as soon as you are able
- Quarantine when exposed if you are not fully vaccinated or if you are ill
- Provide information to contact tracers, if asked

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For More Information

American Thoracic Society

- www.thoracic.org/patients
 - COVID-19: How Do We Stay Safe?
 - COVID-19 Vaccines
 - Vaccines—How They Work

Centers for Disease Control (CDC)

- <https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html>
- <https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html>

This information is a public service of the American Thoracic Society. The content is for educational purposes only. It should not be used as a substitute for the medical advice of one's healthcare provider.



Table 1 summarizes what we know about the most common circulating SARS-CoV-2 variants. The more + signs, the stronger the feature. Evidence regarding transmissibility and virulence of variants is rapidly evolving. This table reflects the most current available information as of May 1st, 2021.

SARS-CoV-2 Variant	First Reported (Date/Geographical Location)	Most Significant Mutation(s)	Transmissibility (compared with original D614)	Virulence (compared with original D614)	Public Health Impact
D614G	Jan./Feb., 2020 China	1 mutation in S protein	+	+	Rapid increase during early 2020 Accounts for most infections worldwide All other variants descended from this
B.1.429 B.1.427 20C/S:452R CAL.20C CA VUI1	Dec., 2020 California	Mutations in ORF1 Multiple mutations in S protein	++	Unknown	Dominant variant in Southern California Now worldwide Mutations may affect neutralization by some antibodies
B.1.1.7 VOC 202012/01 20I/501Y.V1	Sep., 2020 United Kingdom	Multiple mutations in S protein	+++	++	Now worldwide, including all 50 US States Now source of most new infections in the US
B.1.351 501.Y.V2 20H/501Y.V2	Dec., 2020 South Africa	Multiple mutations in S protein	++	No evidence of change	Now worldwide, including 35 US States Mutations may affect neutralization by some antibodies
P.1 VOC 202101/02 20J/501Y.V3	Dec., 2020 Brazil	Multiple mutations in S protein	+++	+	Now worldwide, including 29 US States
B.1.617	Oct., 2020 India	Multiple mutations in S protein, including mutations seen in California and UK variants	++	Unknown	38% of samples from India in March 2021 Also found in Britain, US, Israel
B.1.526 B.1.525	2021 New York City	Multiple mutations in S protein	Unknown	Unknown	27% of NYC sequences in Feb 2021 Broader spread unknown

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