

# Genetic Variants of SARS-CoV-2: What Do We Know So Far?

September 15, 2021

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

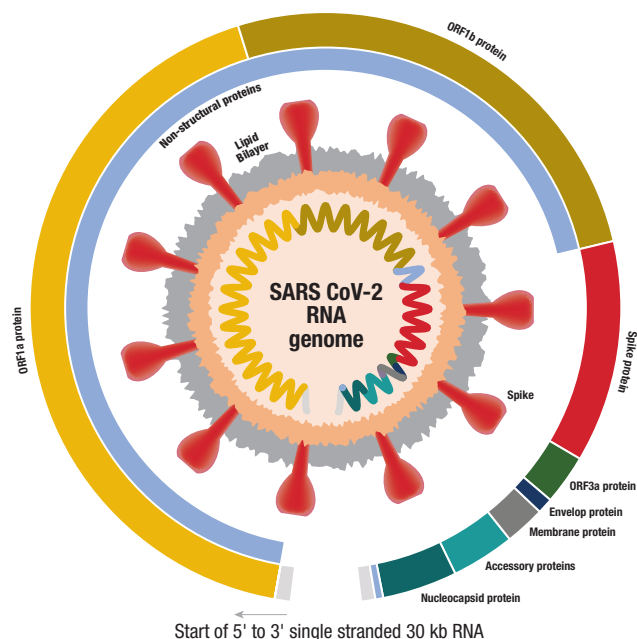
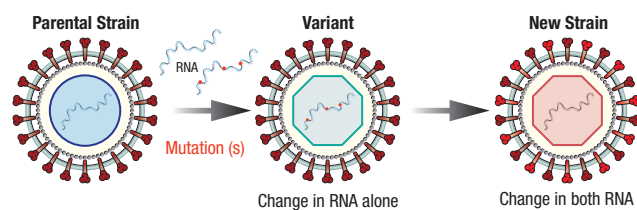


Fig.2: Demonstrates the difference between a new variant and a new strain



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: that appeared by the end of 2020, 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 suggesting that the named region somehow caused the virus, and to reinforce that everyone is at risk of infections. In May 2021, the WHO announced a new system for naming SARS-CoV-2 variants according to letters of the Greek alphabet. For example, the first variant identified in Britain (previously called B.1.1.7) will now be called Alpha. Other naming systems will still be used by scientists as well.

### 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

Transmissibility describes how easily a virus spreads from person to person.

Virulence refers to how likely the virus variant causes severe disease. Some variants like the Delta variant spread more easily. Some variants have been shown to cause more deaths, others may be both easier to spread and more virulent.

However all variants are high risk when many people are not vaccinated and can get easily infected.

### Implication of SARS-CoV-2 Variants for Vaccine Effectiveness

Current vaccines target 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 that do not contain a full virus so they cannot cause infection. The Janssen vaccine made by Johnson and Johnson uses a weakened adenovirus (a different virus) that has the same spike protein to produce immunity.

For more information about vaccines, please review [www.thoracic.org/patients](http://www.thoracic.org/patients)

As new variants develop, the current vaccines may not protect as well but to date all have some protection against known variants.

Even if the protection is not as complete, the risks of serious infection, hospitalization and death are much lower.

In the future, the vaccines can be adjusted to adapt to new variants just as other types of vaccines have been updated over the years. For example, there have been updates to vaccines for pneumonia and meningitis to cover more strains of bacteria or virus variants. The influenza vaccine is updated every year.

COVID-19 booster dose is currently recommended for some immunocompromised patients.

This should not keep you from choosing to get vaccinated now to protect yourself and others. There are great benefits and very small risks for the available vaccines.

### 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:

- Getting vaccinated as soon as you are able
- 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
- Quarantine when exposed if you are not fully vaccinated or if you are ill
- Provide information to contact tracers, if asked

**Authors:** Shazia Jamil, MD, Shirin Shafazand, MD, Susan Pasnick, MD, W. Graham Carlos, MD, Ryan Maves, MD, Charles Dela Cruz, MD, PhD

**Reviewer:** Marianna Sockrider MD, DrPH

### For More Information

#### American Thoracic Society

- [www.thoracic.org/patients](http://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>

#### World Health Organization

- <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>

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.



ATS RAPID RESPONSE DOCUMENT | PUBLIC HEALTH SERIES

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 September 15, 2021.

SARS-CoV-2 Variant (new WHO Label) *	SARS-CoV-2 Variant (other terminology)	Variant of Interest (VOI) Vs Variant of Concern (VOC)	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	+	+	Increase ability to spread compared with original virus Rapid increased during early 2020 Accounted for most infections worldwide in 2020 All other variants descended from this
Alpha	B.1.1.7 VOC 202012/01 20I/501Y.V1	VOC	Sep., 2020 United Kingdom	Multiple mutations in S protein	+++	++	Now worldwide, including all 50 U.S. States Most new infections in the U.S. in April, 2021
Beta	B.1.351, B1.351.2, B 1.351.3 20H/501Y.V2	VOC	May, 2020 South Africa	Multiple mutations in S protein	+++	No evidence of change	Now worldwide, including many U.S. States Mutations may affect neutralization by some antibodies
Gamma	P.1, P.1.1, P.1.2, P.1.4, P.1.6, P.1.7 VOC 202101/02 20J/501Y.V3	VOC	Nov., 2020 Brazil	Multiple mutations in S protein	+++	+	Worldwide, including many US States Mutations may affect neutralization by some antibodies
Delta	B.1.617.2 AY.1 to AY.12 21A/S:478K	VOC	Oct., 2020 India	Multiple mutations in S protein, including mutations seen in California and UK variants	++++	+++	38% of samples from India in March 2021 83% of sequenced samples in the U.S. Mutations may affect neutralization by some antibodies Known to be twice as contagious as earlier variants and some study show variant might cause more severe illness Variant might reduce effectiveness of some monoclonal treatments and the antibodies generated by a COVID-19 vaccine
Kappa	B.1.617.1 21B 21A/S:154K	VOI	Oct., 2020 India	Multiple mutations in S protein	Unknown	Unknown	Identified in at least 41 countries including the U.S Mutations may affect neutralization by some antibodies
Epsilon	B.1.429 B.1.427 21C 20C/S:452R CAL.20C		Dec., 2020 California	Mutations in ORF1 Multiple mutations in S protein	++	Unknown	Dominant variant in Southern California, decreasing prevalence in the U.S. Worldwide Mutations may affect neutralization by some antibodies
Eta	B.1.525 21D 20A/S:484K	VOI	United Kingdom/ Nigeria Dec., 2020	Multiple mutations in S protein	Unknown	Unknown	Identified in at least 23 countries including the U Mutations may affect neutralization by some antibodies

Continued on next page.



SARS-CoV-2 Variant (new WHO Label) *	SARS-CoV-2 Variant (other terminology)	Variant of Interest (VOI) Vs Variant of Concern (VOC)	First Reported (Date Geographical Location)	Most Significant Mutation(s)	Transmissibility (compared with original D614)	Virulence (compared with original D614)	Public Health Impact
Iota	B.1.526 21F 20C/S:484K	VOI	2021 New York City	Multiple mutations in S protein	Unknown	Unknown	27% of NYC sequences in Feb 2021 So far reported in 53 countries Broader spread unknown Mutations may affect neutralization by some monoclonal antibody treatment
Lambda	C.37 21G GR/452Q.V1	VOI	Dec., 2020 Peru	Multiple mutations in N, ORF1 and S proteins	Unknown	Unknown	Identified in at least 30 countries including the U.S. Chile, Peru and U.S. have the highest reported cases Has not yet outcompeted any of the more dominant variants Mutations may affect neutralization by some antibodies
Mu	B.1.621, B.1621.1, GH, 21H	VOI	Jan., 2021 Colombia	Multiple mutations in S protein	Unknown	Unknown	Under investigation

\* The established nomenclature systems for track and naming SARS-CoV-2 genetic lineages such as GISAID, Nextstrain and Pango will remain in place to be used by scientists.

#### References:

- Rambaut, A., Holmes, E.C., O'Toole, Á. et al. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. *Nat Microbiol* 5, 1403–1407 (2020). <https://doi.org/10.1038/s41564-020-0770-5>
- Tang JW, Tambyah PA, Hui DS. Emergence of a new SARS-CoV-2 variant in the UK. *J Infect*. 2020 Dec 28;50163-4453(20)30786-6. doi: 10.1016/j.jinf.2020.12.024. Epub ahead of print. PMID: 33383088; PMCID: PMC7834693.
- Schachar RA, Schachar IH. A SARS-CoV-2 mRNA Vaccine - Preliminary Report. *N Engl J Med*. 2020 Sep 17;383(12):1190-1191. doi: 10.1056/NEJMc2026616. Epub 2020 Aug 19. PMID: 32813940.
- Zhang W, Davis BD, Chen SS, Sincuir Martinez JM, Plummer JT, Vail E. Emergence of a Novel SARS-CoV-2 Variant in Southern California. *JAMA*. 2021 Feb 11:e211612. doi: 10.1001/jama.2021.1612. Epub ahead of print. PMID: 33571356; PMCID: PMC7879386.
- Mascola JR, Graham BS, Fauci AS. SARS-CoV-2 Viral Variants-Tackling a Moving Target. *JAMA*. 2021 Feb 11. doi: 10.1001/jama.2021.2088. Epub ahead of print. PMID: 33571363.
- Lauring AS, Hodcroft EB. Genetic Variants of SARS-CoV-2-What Do They Mean? *JAMA*. 2021 Feb 9;325(6):529-531. doi: 10.1001/jama.2020.27124. PMID: 33404586.
- Burki T. Understanding variants of SARS-CoV-2. *Lancet*. 2021 Feb 6;397(10273):462. doi: 10.1016/S0140-6736(21)00298-1. PMID: 33549181; PMCID: PMC7906644.
- Walensky RP, Walke HT, Fauci AS. SARS-CoV-2 Variants of Concern in the United States—Challenges and Opportunities. *JAMA*. 2021;325(11):1037–1038. doi:10.1001/jama.2021.2294
- Mahase E. Covid-19: Where are we on vaccines and variants? *BMJ*. 2021 Mar 2;372:n597. doi: 10.1136/bmj.n597. PMID: 33653708.
- Moore JP, Offit PA. SARS-CoV-2 Vaccines and the Growing Threat of Viral Variants. *JAMA*. 2021 Mar 2;325(9):821–822. doi: 10.1001/jama.2021.1114. PMID: 33507218.
- Callaway E. Multitude of coronavirus variants found in the US - but the threat is unclear. *Nature*. 2021 Mar 5. doi: 10.1038/d41586-021-00564-4. Epub ahead of print. PMID: 33674807.
- Mahase E. Covid-19: Where are we on vaccines and variants? *BMJ*. 2021 Mar 2;372:n597. doi: 10.1136/bmj.n597. PMID: 33653708.
- Moore JP, Offit PA. SARS-CoV-2 Vaccines and the Growing Threat of Viral Variants. *JAMA*. 2021 Mar 2;325(9):821–822. doi: 10.1001/jama.2021.1114. PMID: 33507218.
- Flemming A. SARS-CoV-2 variant evades antibodies whilst maintaining fitness. *Nat Rev Immunol*. 2021 Mar;21(3):136. doi: 10.1038/s41577-021-00510-5. PMID: 33542501; PMCID: PMC7860165.
- McNally A. What makes new variants of SARS-CoV-2 concerning is not where they come from, but the mutations they contain. *BMJ*. 2021 Feb 22;372:n504. doi: 10.1136/bmj.n504. PMID: 33619064.
- Walensky RP, Walke HT, Fauci AS. SARS-CoV-2 Variants of Concern in the United States—Challenges and Opportunities. *JAMA*. 2021 Mar 16;325(11):1037–1038. doi: 10.1001/jama.2021.2294. PMID: 33595644.
- <https://theconversation.com/whats-the-difference-between-mutations-variants-and-strains-a-guide-to-covid-terminology-154825>
- <https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html>, accessed March, 9th, 2021