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

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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.

Mutations in Spike Protein

SARS-CoV-2 virus contains spike proteins that bind to specific places such as angiotensin converting enzyme 2 receptors (ACE2)

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

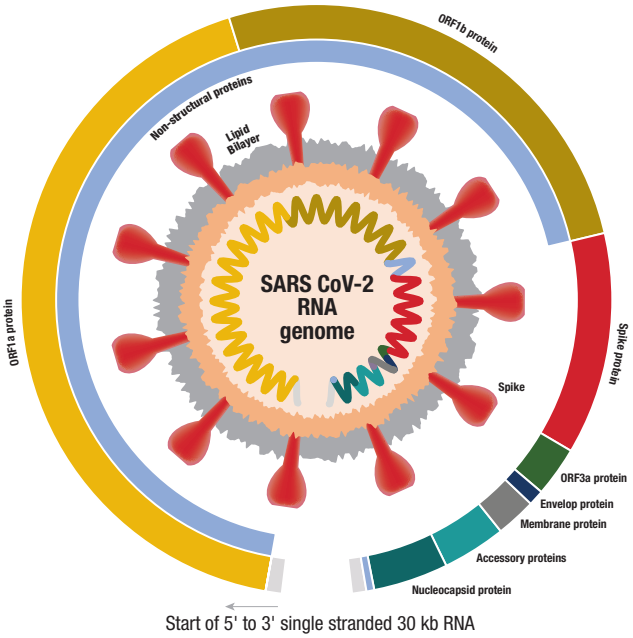
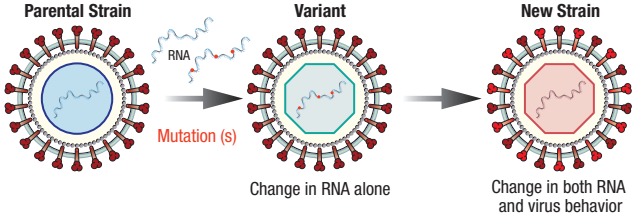


Fig.2: Demonstrates the difference between a new variant and a new strain



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

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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

Mutations have also been identified in M, E and N proteins and Non-structured proteins, however to a much less extent. Mutation in N gene has been reported in Omicron variant and has been reported to impact diagnostics of a few commercially approved kits.

Classifying SARS Co-V2 Variants

Due to continuous evolution of SARS Co-V2, variants are further re-classified based on their attributes and prevalence in the U.S. as follows:

- Variants being monitored (VBM)
- Variants of Concern (VOC)
- Variant of Interest (VOI)
- Variant of high consequence (VOHC).

As of January, 2023, no SARS Co-V2 variants are designated either VOI or VOHC.

The U.S. Department of Health and Human Services (HHS) established a SARS-CoV-2 Interagency Group (SIG) to enhance coordination among CDC, National Institutes of Health (NIH), Food and Drug Administration (FDA), Biomedical Advanced Research and Development Authority (BARDA), and Department of Defense (DoD). This interagency group is focused on the rapid characterization of emerging variants and actively monitors their potential impact on critical SARS-CoV-2 countermeasures, including vaccines, therapeutics, and diagnostics.

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.cdc.gov/coronavirus/2019-ncov/variants/genomic-surveillance.html (updated on Dec., 2022 so current and easy to follow)

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 Omicron and some of the Omicron variants 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

Four COVID-19 vaccines are approved in the U.S. They have been shown to be highly effective in protecting people from getting seriously ill, hospitalized, and dying. The best protection occurs when people stay up to date with recommended vaccinations and boosters which are adjusted to adapt to new variants. 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. Novavax vaccine contain protein pieces of spike protein which helps immune system recognize and respond to virus spike protein on exposure.

For more information about vaccines, please review www.thoracic.org/patients

Even if the protection is not 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 is currently recommended for ages 6 months and older after initial vaccination. The updated boosters are called bivalent as they protect against both the original virus that causes COVID-19 as well as the Omicron variant.

Protecting Yourself and Others From SARS-CoV-2 Variants

It continues to be important for everyone to continue to follow basic public health measures, including:

- Getting vaccinated as soon as you are able. There are great benefits and very small risks for the available vaccines.
- Hand washing for at least 20 seconds with soap and water or using hand sanitizer with at least 60% alcohol content.
- Monitor for symptoms.
- Quarantine when exposed if you are not fully vaccinated or if you are ill.
- Take extra actions (masking, distancing, avoiding large crowds/poorly ventilated spaces) to protect yourself and others particularly if there is an increase in COVID activity in your community.

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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 and https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/masks.html

World Health Organization

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

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 January, 2023.

SARS-CoV-2 Variant (new WHO Label) *	SARS-CoV-2 Variant (other terminology)	Variant being monitored (VBM) Vs Variant of Concern (VOC)	First Reported (Date Geographical Location)	Most Significant Mutation(s)
	D614G		Jan./Feb., 2020 China	1 mutation in S protein
Alpha	B.1.1.7 VOC 202012/01 20I/501Y.V1	VBM	Sep., 2020 United Kingdom	Multiple mutations in S protein
Beta	B.1.351, B1.351.2, B 1.351.3 20H/501Y.V2	VBM	May, 2020 South Africa	Multiple mutations in S protein
Gamma	P.1, P.1.1, P.1.2, P.1.4, P.1.6, P.1.7 VOC 202101/02 20J/501Y.V3	VBM	Nov.., 2020 Brazil	Multiple mutations in S protein
Delta	B.1.617.2 AY.1 to AY.12 21A/S:478K	VBM	Oct., 2020 India	Multiple mutations in S protein, including mutations seen in California and UK variants
Kappa	B.1.617.1 21B 21A/S:154K	VBM	Oct., 2020 India	Multiple mutations in S protein
Epsilon	B.1.429 B.1.427 21C 20C/S:452R CAL.20C	VBM	Dec., 2020 California	Mutations in ORF1 Multiple mutations in S protein
Eta	B.1.525 21D 20A/S:484K	VBM	United Kingdom/Nigeria Dec., 2020	Multiple mutations in S protein
Iota	B.1.526 21F 20C/S:484K	VBM	2021 New York City	Multiple mutations in S protein
Lambda	C.37 21G GR/452Q.V1	VBM	Dec., 2020 Peru	Multiple mutations in N, ORF1 and S proteins
Mu	B.1.621, B.1621.1, GH, 21H	VBM	Jan., 2021 Colombia	Multiple mutations in S protein
Zeta	P.2/ 20J	VBM	April, 2020 Brazil	Multiple mutations in S protein
Omicron	B.1.1.529, BA.1, BA.1.1, BA.2, BA.3, BA.4, BA.5/ 21K	VOC	Nov., 2021 South Africa	Multiple mutations in S protein

* 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.

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