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**

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 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.

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

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. It would not be a surprise if we need to update COVID-19 vaccines in the future and/or offer booster doses.

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

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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)

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

<table>
<thead>
<tr>
<th>SARS-CoV-2 Variant (new WHO terminology)</th>
<th>SARS-CoV-2 Variant (old terminology)</th>
<th>First Reported (Date/Geographical Location)</th>
<th>Most Significant Mutation(s)</th>
<th>Transmissibility (compared with original D614)</th>
<th>Virulence (compared with original D614)</th>
<th>Public Health Impact</th>
</tr>
</thead>
</table>
| Epsilon                                  | 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 | Rapid increase during early 2020  
Accounts for most infections worldwide  
All other variants descended from this |
| Alpha                                    | B.1.1.7  
VOC 202012/01  
20I/501YV1 | 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 |
| Beta                                     | B.1.351  
501.V2  
20H/501YV2 | 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 |
| Gamma                                    | P.1  
VOC 202101/02  
20I/501YV3 | Dec., 2020  
Brazil | Multiple mutations in S protein | +++ | + | Now worldwide, including 29 US States |
| Delta                                    | B.1.617 | Oct., 2020  
India | Multiple mutations in S protein, including mutations seen in California and UK variants | +++ | +++ | 38% of samples from India in March 2021  
Also found in Britain, US, Israel |
| Lota                                     | 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 |

References:


Other references included in the table and additional resources.