

THE MANY FACES OF SARS-COV-2 AND COVID-19

In January 2020, the first cases of COVID-19 were reported in the United States. Since that time, SARS-CoV-2, the viral agent that causes COVID-19, has spread throughout the country, afflicting over 33 million people and resulting in over 600,000 deaths. Nevertheless, the spread of the virus has begun to diminish thanks to a combination of mitigating strategies, immunity and vaccination. While the fight against COVID-19 has taken a turn for the better, the virus's emerging variants may continue to pose a significant risk to our nation's public health. One of them is the Delta variant which arose in India and has spread rapidly to every continent. This viral variant is characterized by a promiscuous rate of transmission among non-immunized individuals and rapid dominance as the most frequently occurring virus. Full immunization with the RNA vaccines or the one-shot adenovirus-based Johnson and Johnson vaccine has been reported to protect against the Delta variant; however, states with a low incidence of vaccination in the U.S. have shown a high prevalence of this virus.

SARS-CoV-2 is a member of the coronavirus family of viruses. Coronaviruses can infect a multitude of animal species and cause illness in multiple organ systems, particularly the respiratory system. Once an infection occurs within a host, the virus replicates and generates numerous copies of itself to infect other potential hosts. During this replication phase, the virus acquires changes in its genome due to random mutations. When enough mutations occur in the right places, a new variant of the virus emerges.

The emergence of new viral variants during an outbreak is not uncommon; no outbreak remains static over time. As a virus propagates from person to person, some variants become better at infecting hosts, while others remain inconsequential. Many factors determine whether or not a mutated virus becomes more virulent. For example, the altered virus could better infect cells or avoid the host's immune system, or disable the innate response,

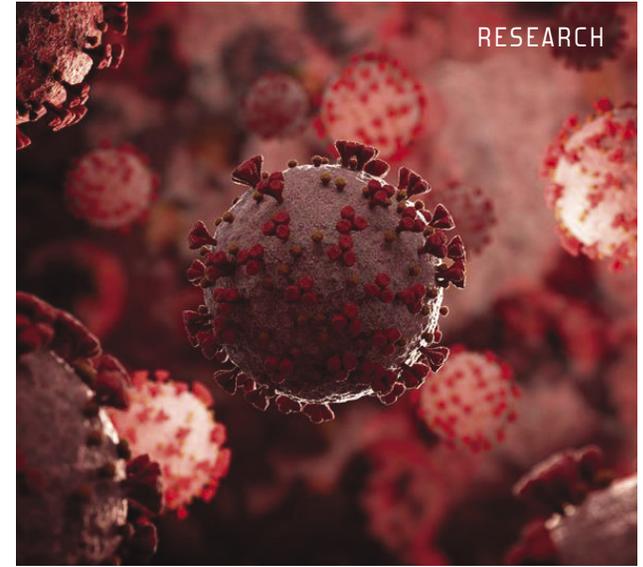
the first response against pathogens. Regardless of the mechanism, the mutations that offer an advantage in replicative efficiency become dominant. More virulent viral variants have shown up in every U.S. state, even as others have originated in other countries. Once a new variant emerges in a particular geographical location, it becomes the dominant strain in that area and may spread to other areas.

There are several variants of SARS-CoV-2 that scientists and clinicians are tracking in the U.S. These variants include:

- Brazil (P.1). First reported in four individuals in Japan who had returned from a trip to Brazil.
- California (B.1.427).
- South Africa (B.1.351).
- U.K. (B.1.1.7). First identified in the United Kingdom.



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Each of these four variants shares a common trait: they all contain mutations in a unique part of the SARS-CoV-2 virus known as the spike protein. The spike (S) protein is a glycosylated protein that projects from the surface of coronaviruses. The S protein allows the virus to bind to the angiotensin-converting enzyme 2 (ACE2) receptor on host cells and mediate viral entry. The four variants have different mutations associated with the S protein. Some help the virus better avoid the body's immune response, while others may help it bind to ACE2. Additional research could determine how the mutations help the virus spread more efficiently.

The S protein is critical for the proper function of the virus. The protein helps define the host species, the receptor on host cells and the specific binding sites on the host cell receptor; therefore, it represents a primary target for COVID-19 therapeutics and immune responses. Consequently, the available U.S. Food and Drug Administration (FDA) emergency use authorized

COVID-19 vaccines from Pfizer-BioNTech, Moderna and Johnson & Johnson all target the S protein sequence from the original viral line first isolated in China. A big question facing scientists and clinicians is whether the vaccines are effective against emerging mutations that contain slight alterations in their S protein. Some preliminary data suggest that the vaccines offer some protection against the variants; however, more studies are needed before any definitive conclusions can be made. Regardless of the degree of their current effectiveness against the variants, the fact that the Pfizer-BioNTech and Moderna vaccines are based on messenger RNA technology means that those vaccines will be easier to adapt to genetic changes within the virus.

SARS-CoV-2 spread throughout the world in less than a year and infected millions before mutating into a more transmissible disease. Viruses have no conscience, no malevolent conspiracy other than to survive the next cycle of replication. This is the essence of the cycle of a pandemic.

Viruses mutate as they move from host to host, and mutations occur due to the error-borne nature of RNA replication. The world was bound to encounter new variants of the virus in time. Now that we have, we must continue to remain vigilant in tracking mutations of the virus and steadfast in implementing our safety protocols. Vaccine manufacturers have already begun testing booster shot safety to help combat the SARS-CoV-2 variants, and modified versions of the vaccines can be quickly generated if needed. This could be the light at the end of the dark pandemic tunnel or the next round in our battle with this formidable virus.

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