

COVID-19 Variants: What Does It All Mean?

USET COVID-19 ECHO Presentation

March 26, 2021

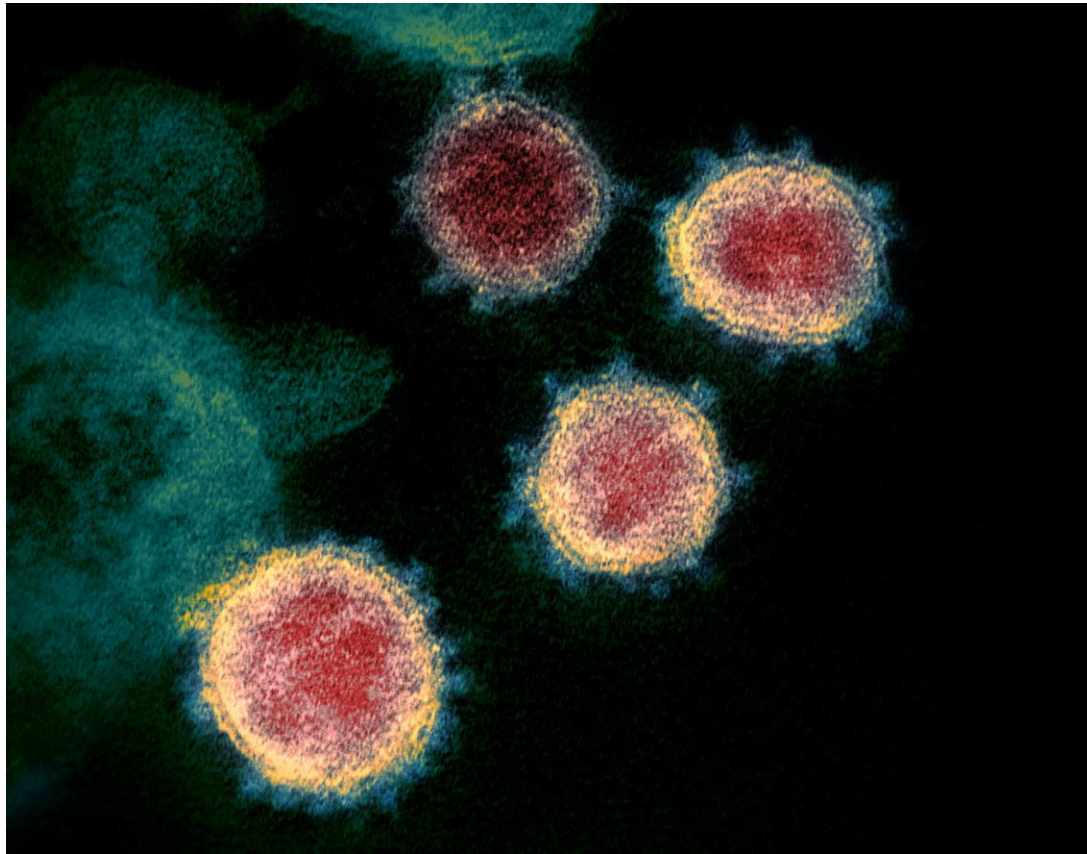
Harry J Brown, MD

USET Tribal Epidemiology Center

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Day 381 of the COVID-19 Pandemic

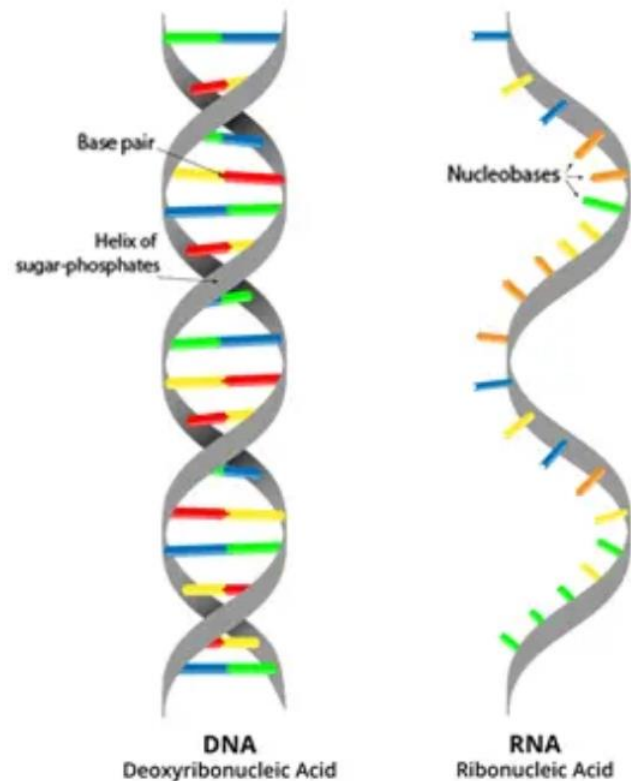


- Viral Variants
- Genomic Surveillance
- CDC Classification
- Individual Variants and Their Clinical Implications
- Resources

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What's the difference between RNA and DNA?



- DNA is composed of 2 strands of nucleotide base pairs
- RNA is a single strand of single unpaired nucleotide bases
- RNA is inherently less stable
- A mutation occurs when one nucleotide is substituted for another in the chain

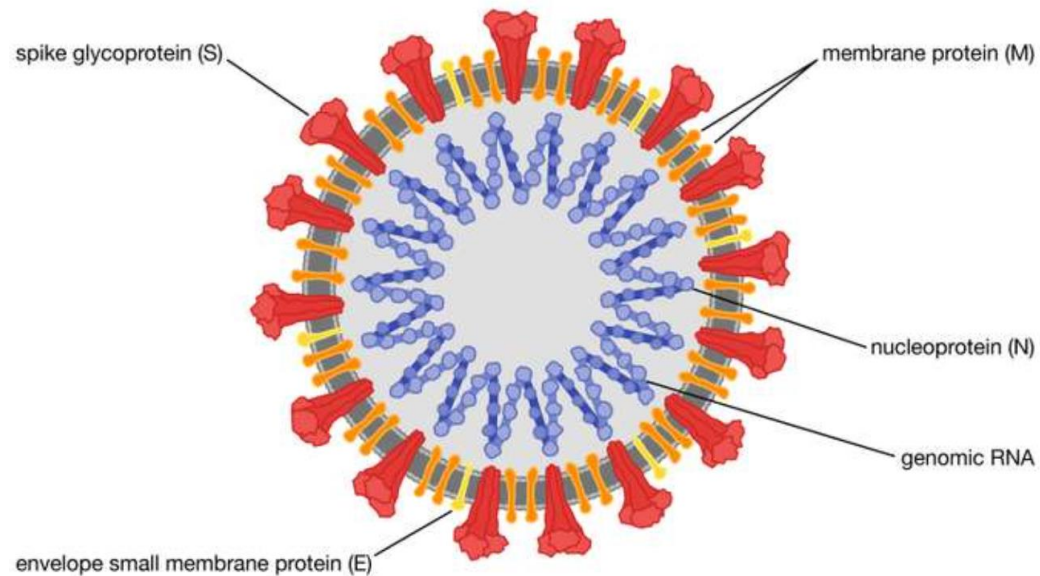
<https://www.technologynetworks.com/genomics/lists/>

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SARS-CoV-2

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)



© Encyclopædia Britannica, Inc.

SARS-CoV-2

The coronavirus SARS-CoV-2, the cause of the COVID-19 pandemic.
Encyclopædia Britannica, Inc./Patrick O'Neill Riley

- SARS-CoV-2 is an RNA virus
- Genetic code is contained in RNA inside the viral envelope
- Mutations tend to occur frequently in RNA viruses
- SARS-CoV-2 is less prone to mutation than the average RNA virus, but mutations still happen all the time

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Viral Variants


- Mutation – change in the genetic sequence (or code)
- Variant – viral genome that varies in sequence from the original
- Strain – viral variant that has demonstrably different characteristics
- Different characteristics could be differences in:
 - Ability to replicate
 - Transmission – ability to infect human or animal host
 - Ability to escape from immunity

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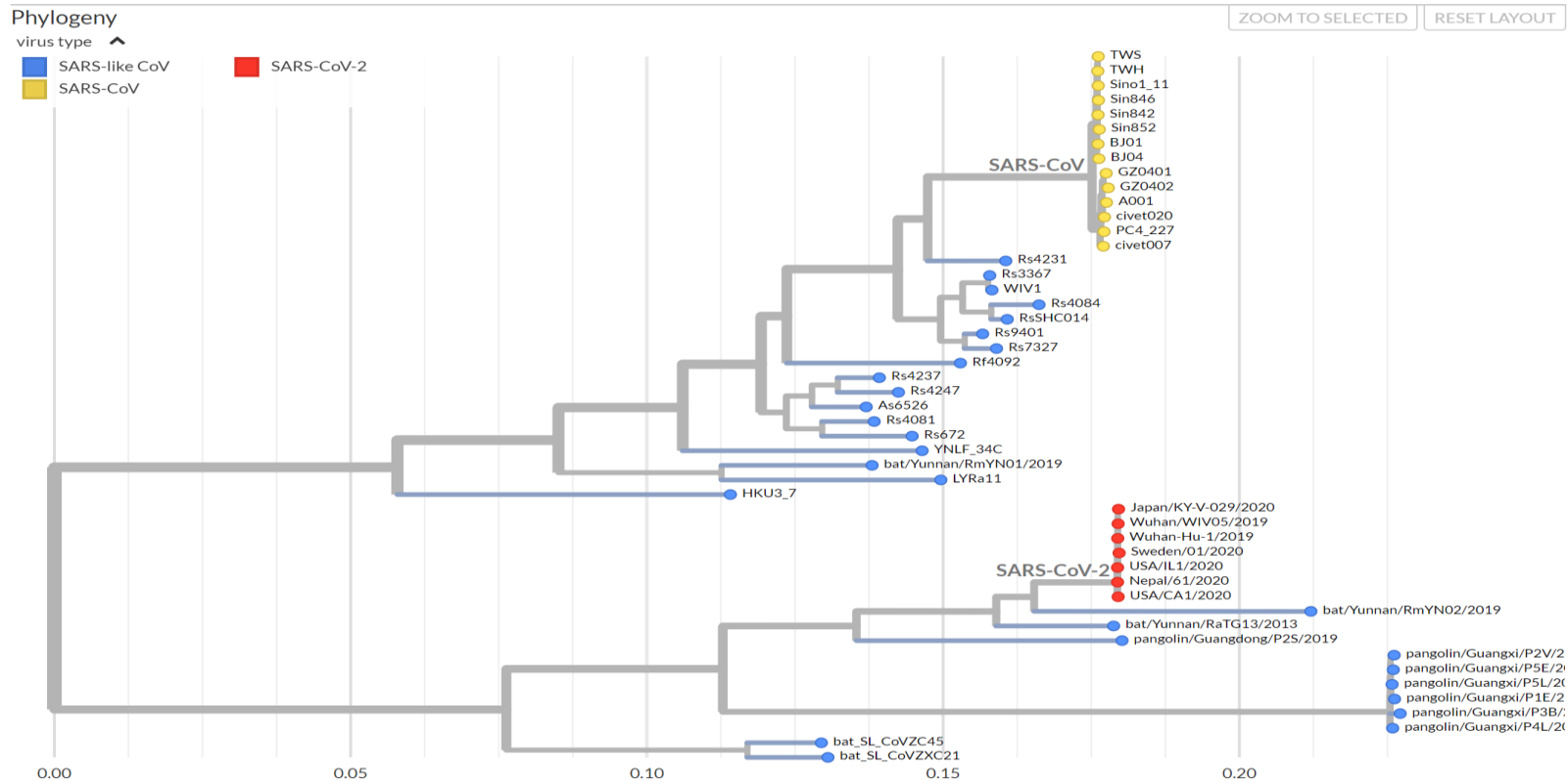


SARS-like Betacoronavirus

Phylogeny of SARS-like betacoronaviruses including novel coronavirus SARS-CoV-2

 Built with [blab/sars-like-cov](#). Maintained by [Trevor Bedford](#) and [Emma Hodcroft](#).

Showing 49 of 49 genomes.



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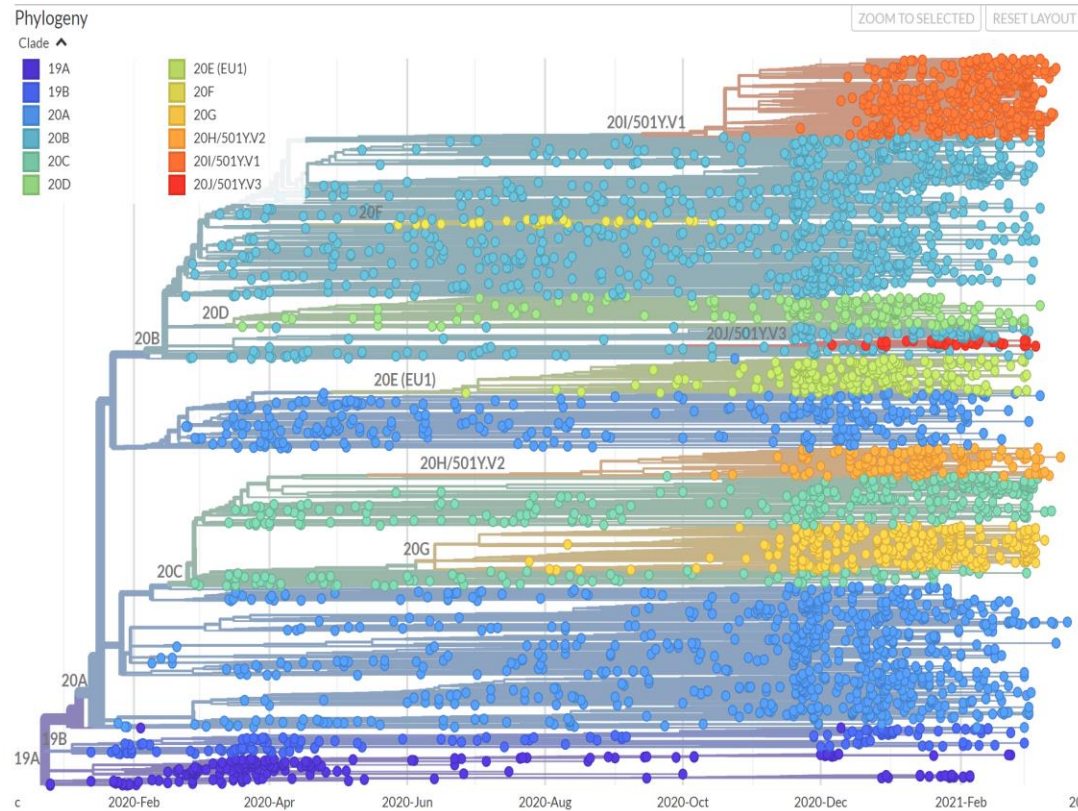


Many, Many Variants of SARS-CoV-2

Genomic epidemiology of novel coronavirus - Global subsampling

Maintained by the Nextstrain team. Enabled by data from GISAID

Showing 4003 of 4003 genomes sampled between Dec 2019 and Mar 2021.



- SARS-CoV-2 mutates all the time
- Genetic sequencing is a valuable tool
- Most mutations have little clinical significance

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Potential Consequences of Viral Mutation

- 1) Ability to spread more quickly in people
- 2) Ability to cause either milder or more severe disease in people
- 3) Ability to evade detection by specific diagnostic tests
- 4) Decreased susceptibility to therapeutic agents, such as monoclonal antibodies
- 5) Ability to evade natural or vaccine-induced immunity

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SARS-CoV-2 Variants and Nomenclature

- D614G - China
- Y453F – Denmark – mink farms
- N501Y – UK (aka B.1.1.7, aka 20I/501Y.V1)
- N501Y – South Africa (aka B.1.351, aka 20H/501Y.V2)

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Genomic Surveillance

- Relatively new field of genomic epidemiology
- Genome – the complete set of genes or genetic material of an organism
- Genetic sequencing – determining the genetic “code”
- CDC has greatly increased genetic sequencing of SARS-CoV-2 samples
- NS3 system – National SARS-CoV-2 Strain Surveillance system
- SPHERES consortium – **SARS-CoV-2 Sequencing for Public Health Emergency Response, Epidemiology, and Surveillance**

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CDC SARS-CoV-2 Variant Classifications

- **Variant of Interest** – a variant with specific genetic markers that may cause problems
- **Variant of Concern** – a variant for which there is evidence of clinical significance
- **Variant of High Consequence** – a variant that has clear evidence that prevention measures or medical countermeasures have significantly reduced effectiveness

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Variant of Interest

- B.1.526 – New York, Nov 2020
- B.1.525 – New York, Dec 2020
- P.2 – Brazil, Apr 2020

- All have *potential* for reduced effectiveness of some monoclonal antibodies or reduced effectiveness of neutralizing immunity from infection or vaccination

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Variants of Concern

Current as of March 23, 2021:

Variant	Reported Cases in US
B.1.1.7	7501
B.1.351	219
P.1	61

- Currently sequencing >10,000 samples each week
- Still, less than 5% of samples get sequenced
- Some States do very little sequencing

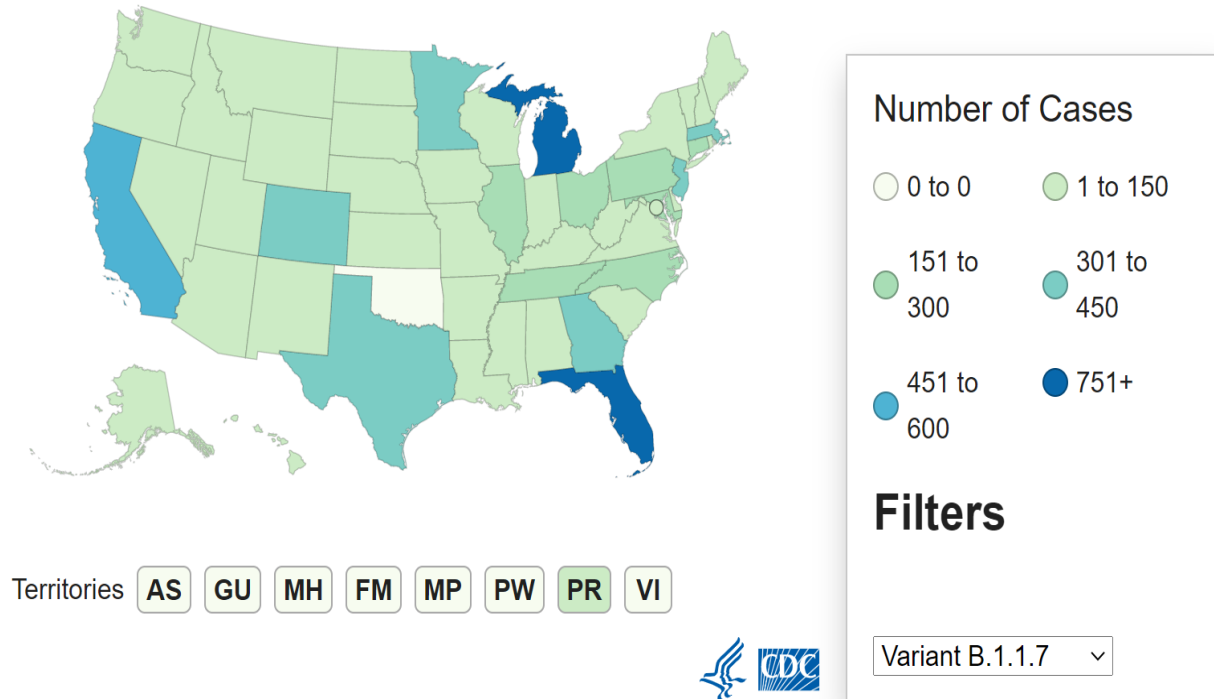
<https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html>

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Variant of Concern – B.1.1.7

Cases of Variants of Concern in the United States*†



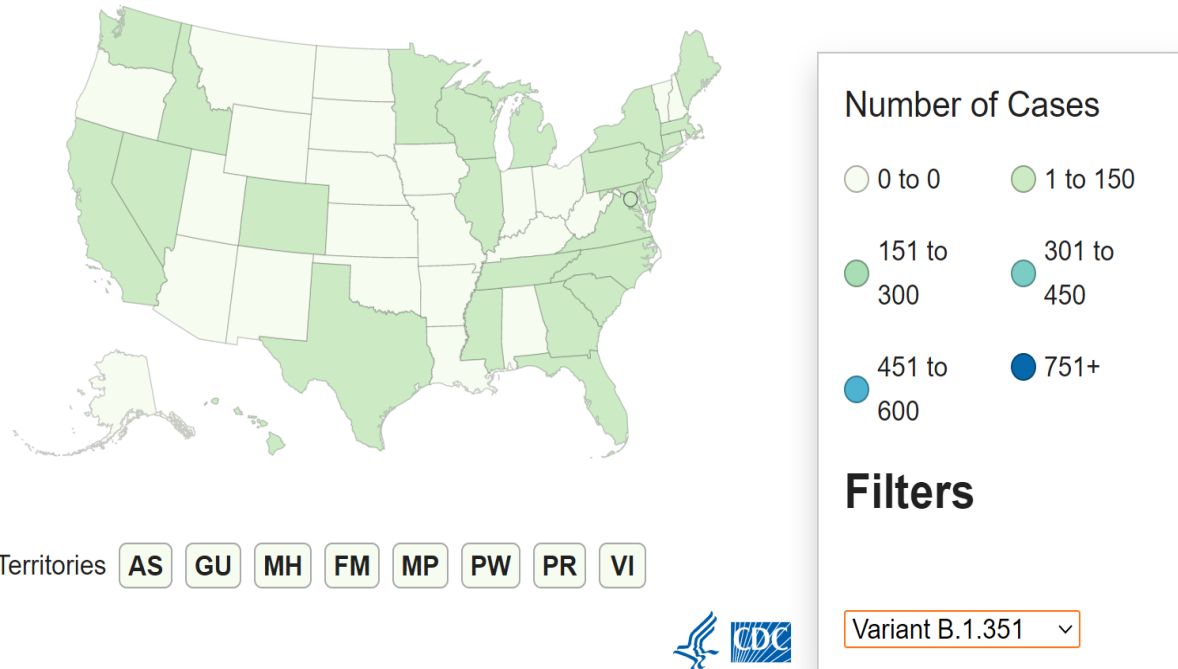
- UK in fall of 2020, first in US in late December 2020
- ~50% increase in transmission
- Maybe increase in severity
- Minimal impact on monoclonal antibody and natural/vaccine immunity

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Variant of Concern – B.1.351

Cases of Variants of Concern in the United States*†



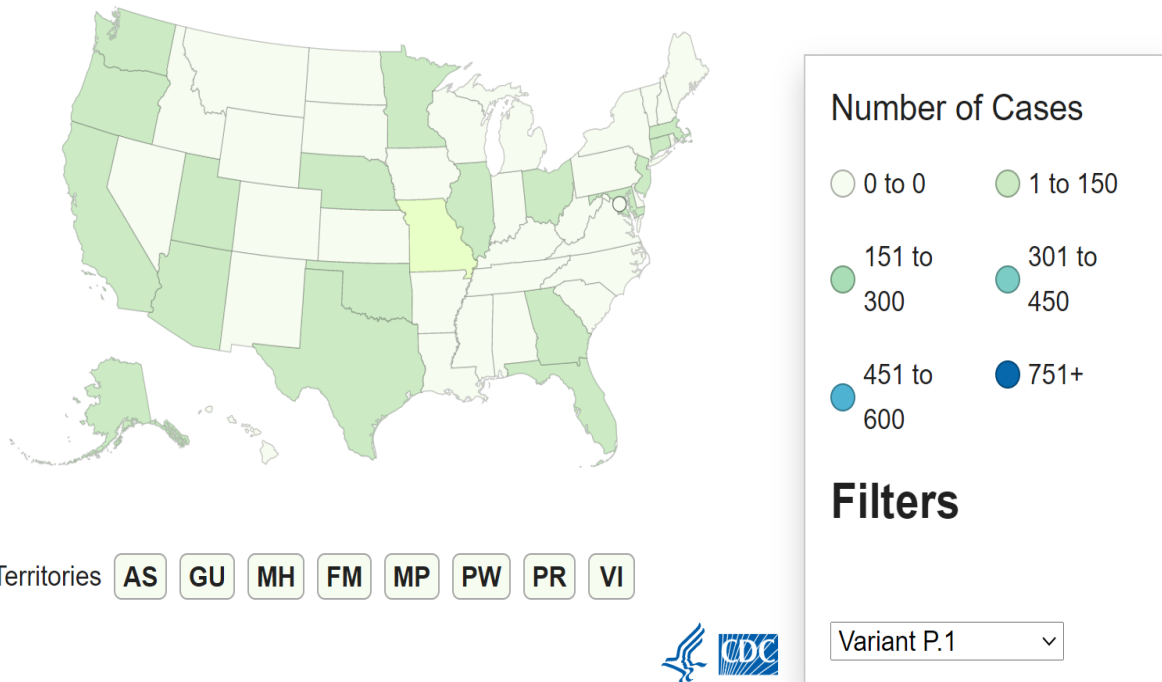
- First detected in South Africa in early October 2020, first in the US end of January 2021
- ~50% increase in transmission
- Moderate impact on monoclonal antibody and natural/vaccine immunity
- Current vaccines still protective

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Variant of Concern – P.1

Cases of Variants of Concern in the United States*†



- First detected in Japan in early January 2021 in travelers from Brazil; first detected in the US at the end of January
- Moderate impact on monoclonal antibody and natural/vaccine immunity
- Current vaccines still protective

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Variants of Concern – B.1.427 and B.1.429

- Aka 20C/S:452R (L452R)
- Both emerged in California
- ~20% increased transmissibility
- Significant impact on some, but not all monoclonals
- Moderate impact on neutralizing titers from natural and vaccine induced immunity

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Key Points

- Genetic variation happens all the time
- Most variants are clinically insignificant
- Variants can cause increased transmissibility, increased disease severity, false negative tests, and failure of immunity
- So far none of the variants have caused complete vaccine failure (vaccines induce “polyclonal” antibody responses)

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Resources

- IHS website:
<https://www.ihs.gov/coronavirus/vaccine/>
- CDC website:
<https://www.cdc.gov/coronavirus/2019-nCoV/index.html>
- <https://www.cdc.gov/coronavirus/2019-ncov/variants/index.html>
- USET website:
<https://usetinc.org/covid19>

NextStrain

<https://nextstrain.org>

JAMA article: *Genetic Variants of SARS-CoV-2 – What Do They Mean?*

<https://jamanetwork.com/journals/jama/fullarticle/2775006>

(doi: 10.1001/jama.2020.27124)

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Thank You for Your Time and Attention!

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Have a great weekend!

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