



Kermanshah
University of
Medical Sciences



دانشگاه علوم پزشکی و خدمات بهداشتی درمانی کرمانشاه

SARS-CoV-2 Mutations and new Variants

Jale Moradi, PhD

Department of Microbiology, School of Medicine,
Kermanshah University of Medical Sciences

COVID-19 situation at a glance

Numbers at a glance

183 934 913

Confirmed cases

Last update: 6 July 2021, 00:27 pm GMT-4

3 985 022

Confirmed deaths

Last update: 6 July 2021, 00:27 pm GMT-4

2 989 925

974
Vaccine doses
administered

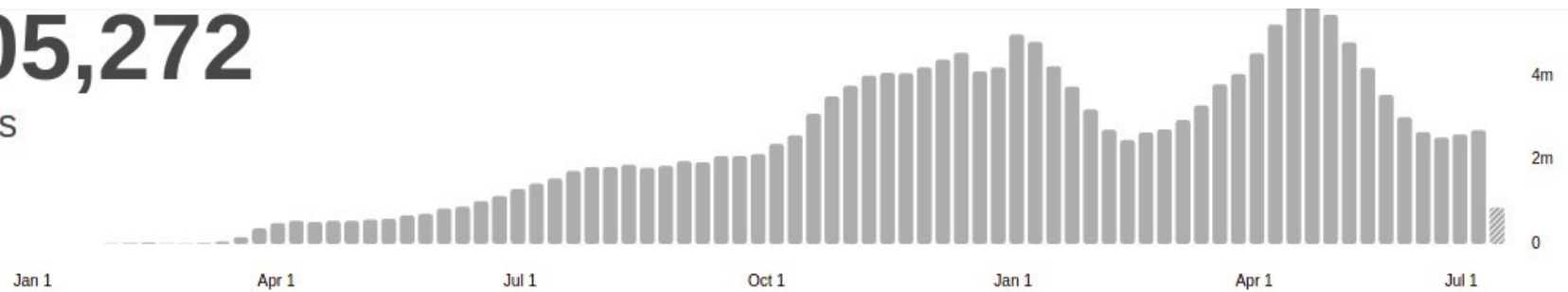
Last update: 5 July 2021

<https://www.who.int/>

COVID-19 situation

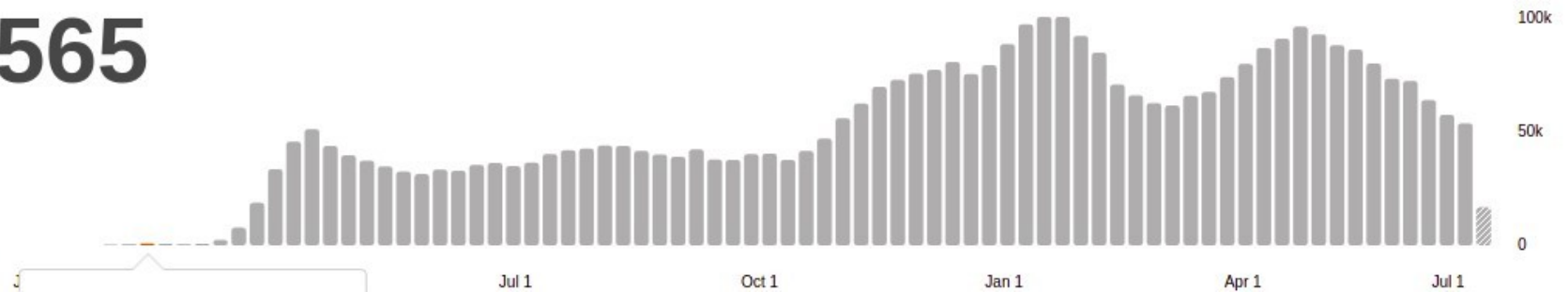
184,105,272

confirmed cases



3,988,565

deaths



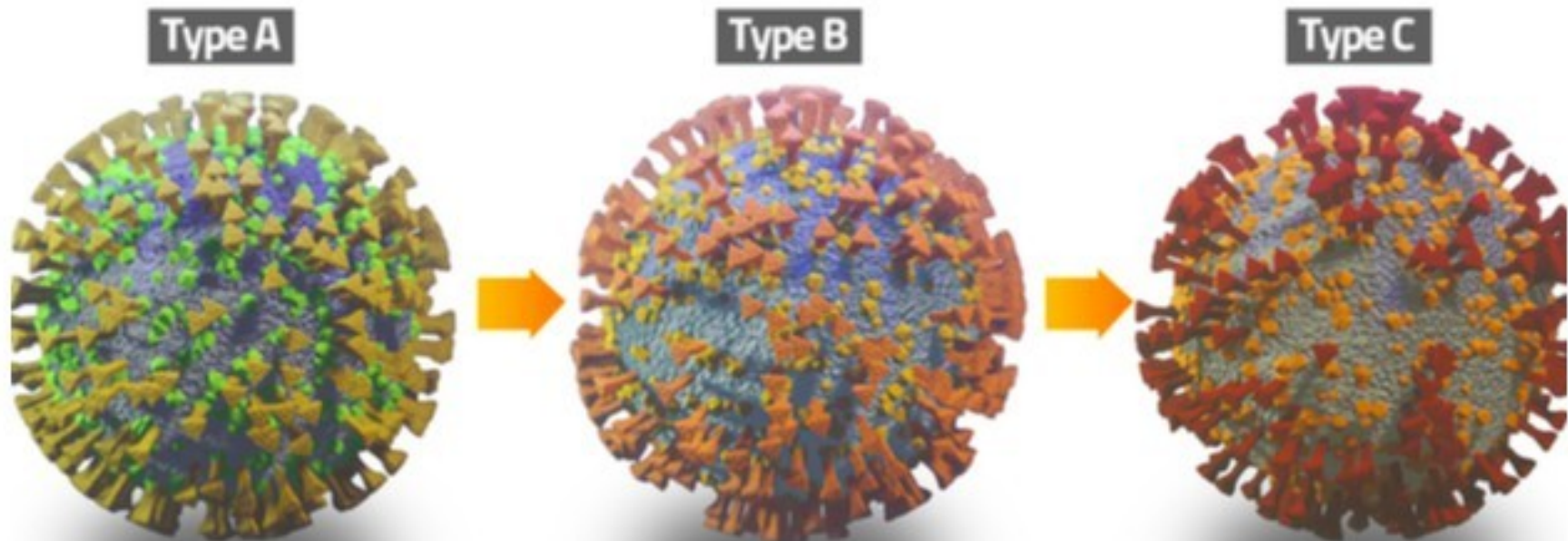
Source: World Health Organization

▨ Data may be incomplete for the

<https://www.who.int/>

Mutation

COVID-19 Will Mutate



<https://www.biospace.com/article/https-www-nature-com-articles-s41422-020-00430-4/>

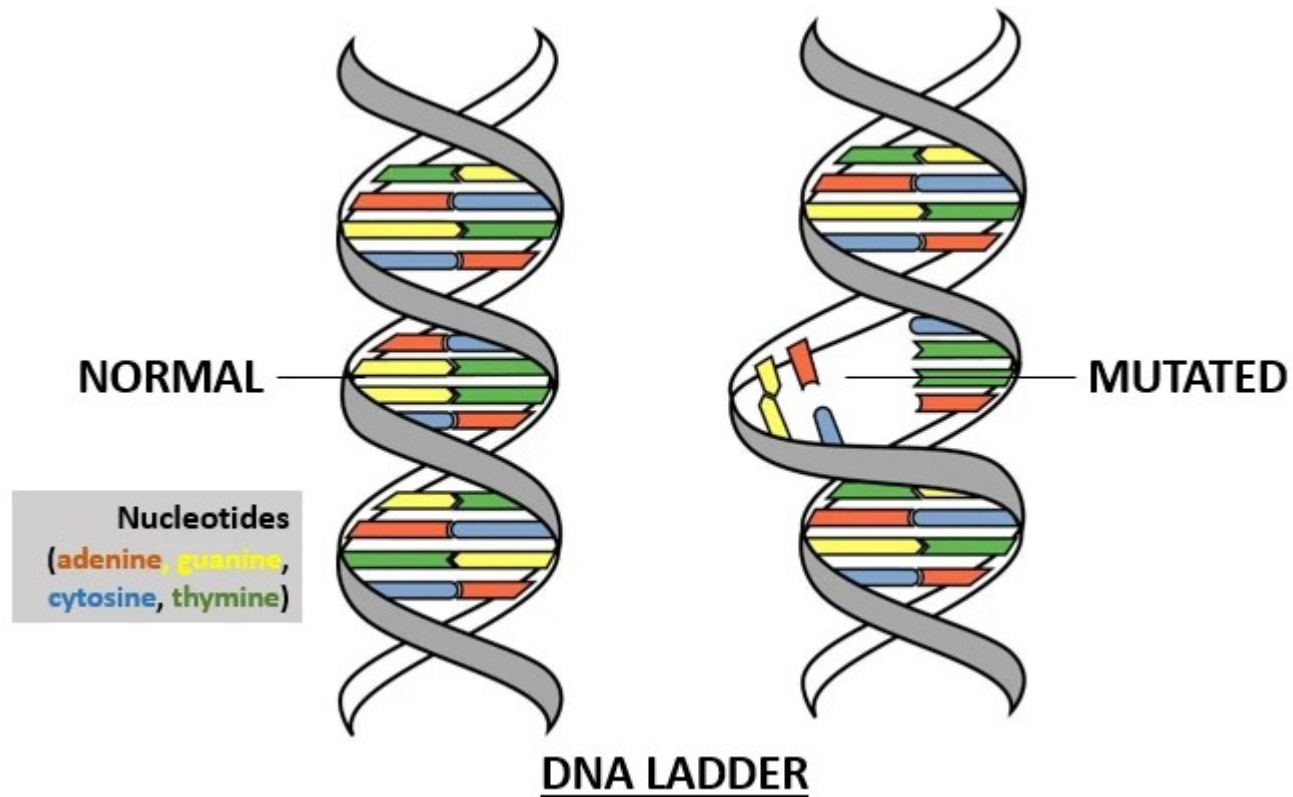


Mutation & Variant

All viruses evolve over time, When a virus replicates or copies itself, it occasionally changes slightly, which is normal for a virus. These modifications are referred to as "mutations."

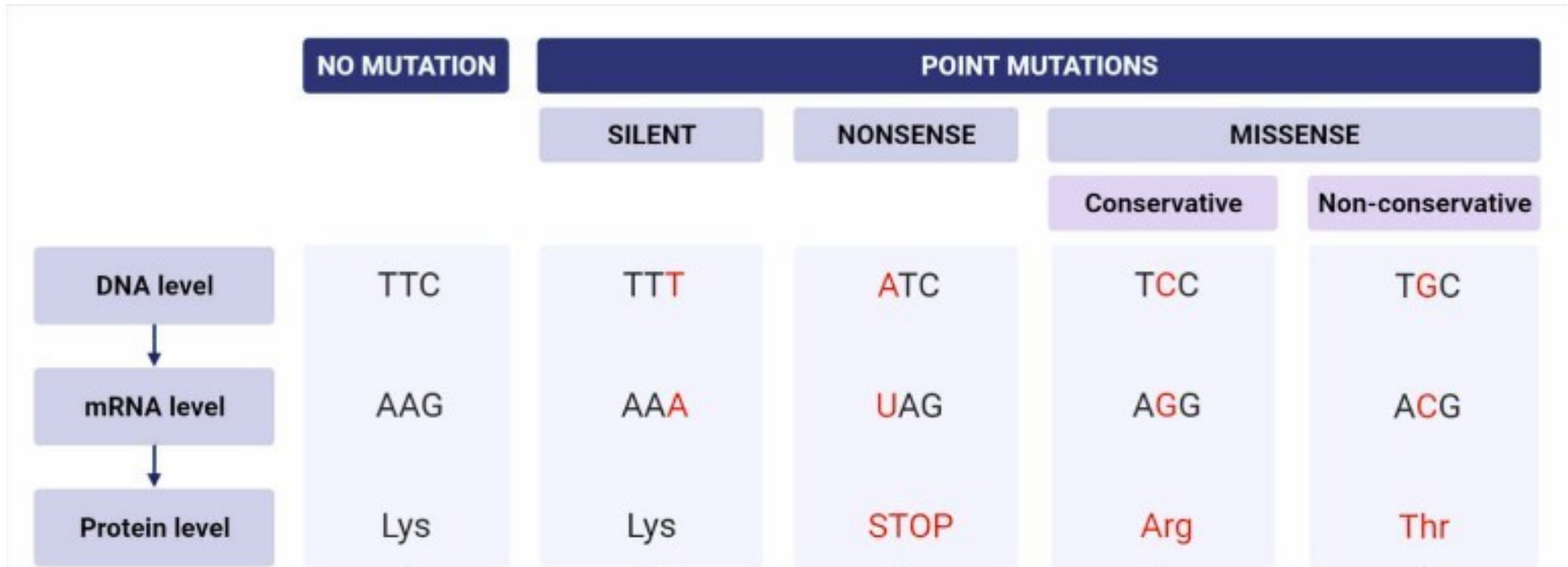
A virus that has one or more new mutations is known as a "variant" of the original virus.

Mutations



<https://www.melixgx.com/blogs>

Base substitution





What causes a virus to evolve into a new variant?

When a virus is widely circulating in a population and causing numerous infections, the virus's chances of mutating increase. The more chances a virus has to spread, the more it replicates – and the more chances it has to change.

<https://www.who.int/>

Impact of viral mutations!

- Most viral mutations have **little** to no impact on the virus's ability to cause infections and disease.
- Depending on where the changes are located in the virus's genetic material, they may affect a virus's properties, such as transmission or severity.

<https://www.who.int/>



WHO Virus Evolution Working Group (VEWG)

The group Monitors changes to SARS-CoV-2
to identify potential

variants of concern (VOC) and

variants of interest (VOI)

that pose a higher risk to global public
health.



Cont,

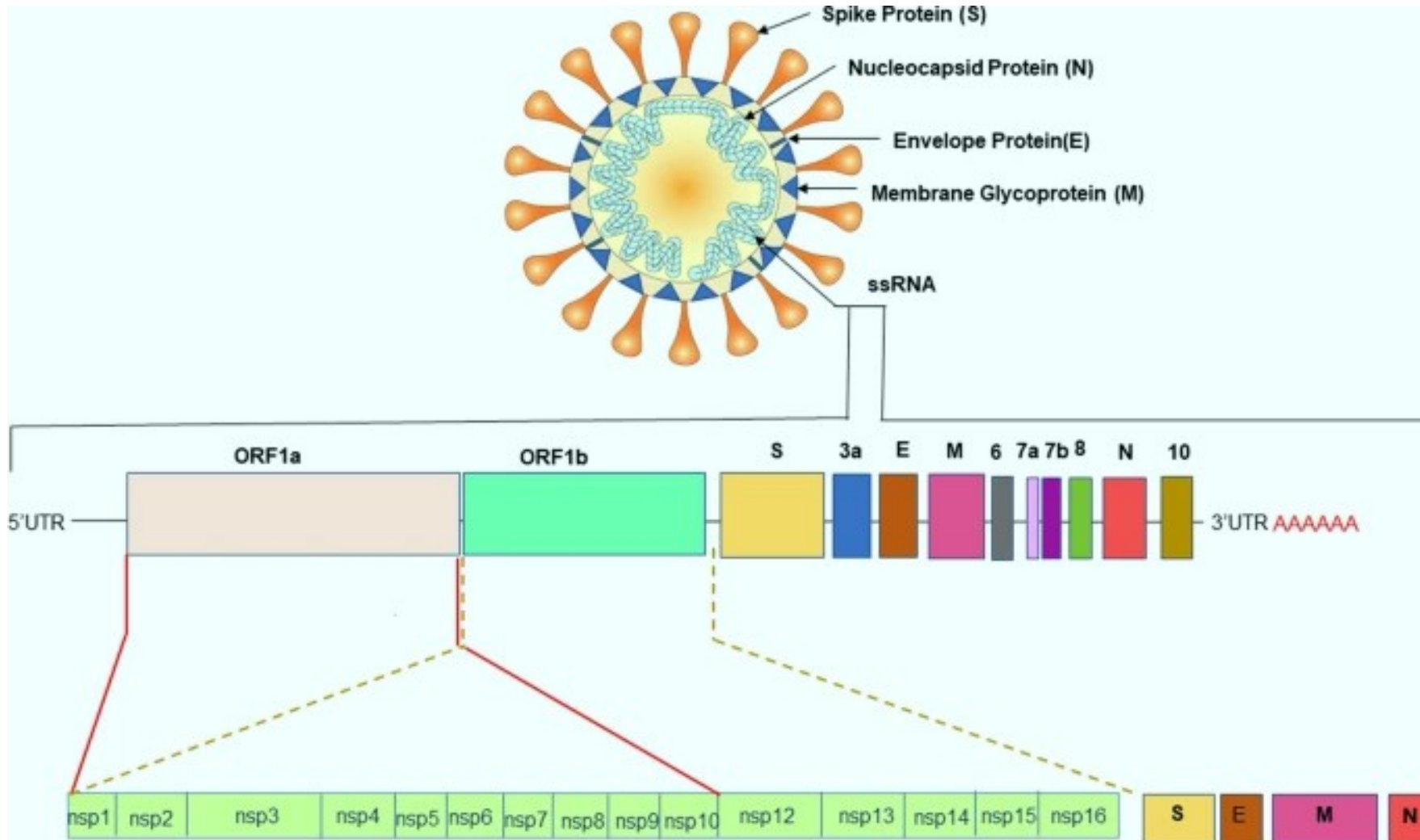
- The majority of virus changes are minor.
- If significant changes are discovered, the variants are given scientific names and the public is notified.

<https://www.who.int/>

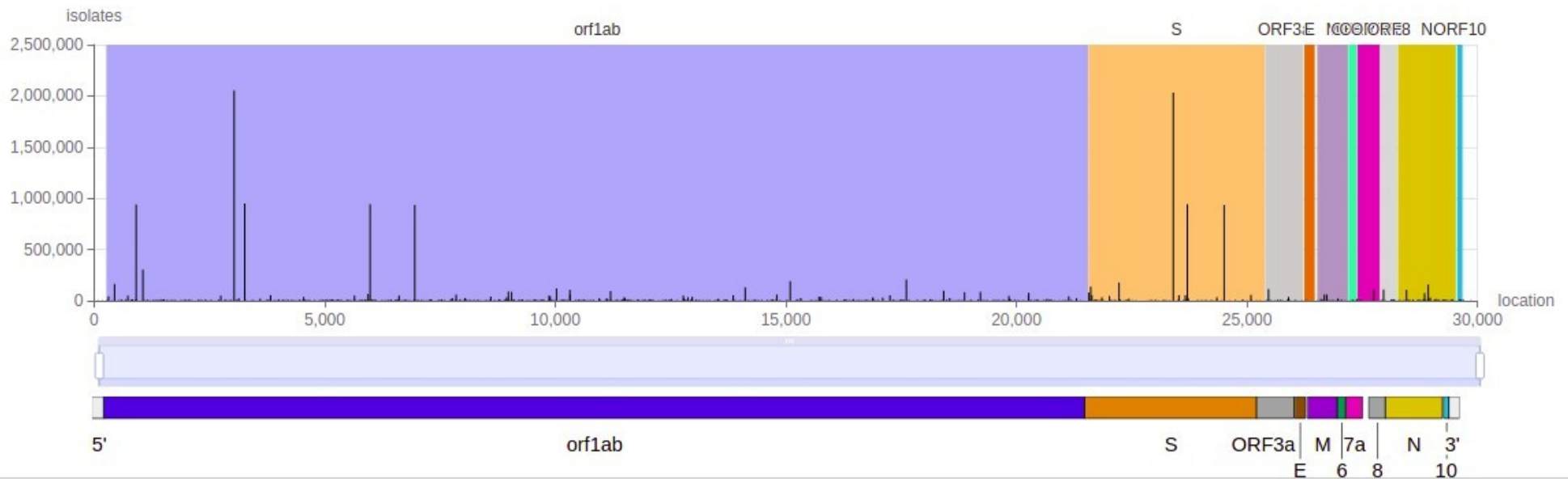


SARS-CoV-2 Genome

SARS-CoV-2 genome Structure



Mutations Frequency



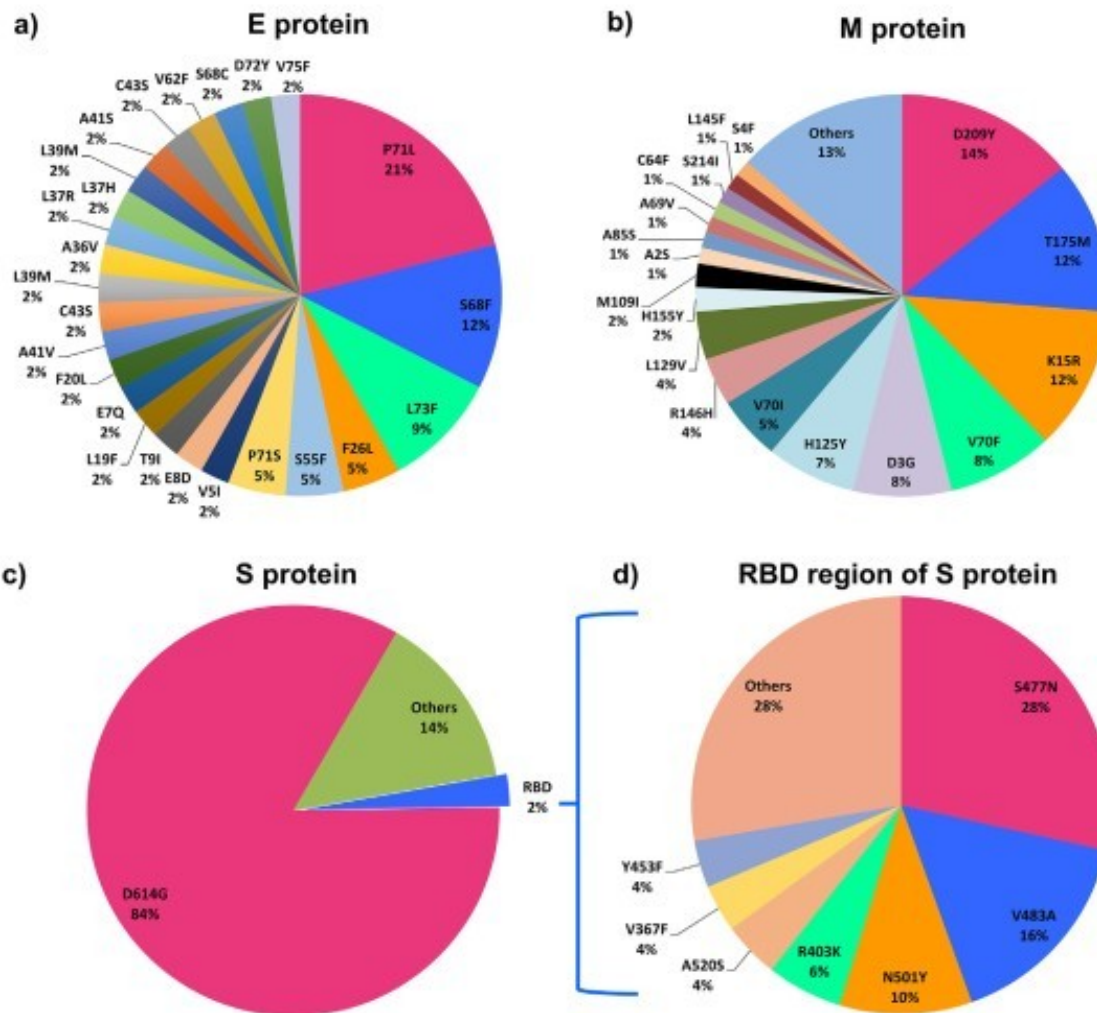
Computational Bioscience Research Center at the
King Abdullah University of Science and Technology
2020 Privacy policy Terms of Use
Alam I et.al., 2021, Lancet Infectious Diseases

This project is supported by King Abdulaziz City for
Science and Technology (KACST)

GISAID data provided on this website is subject to
GISAID's Terms and Conditions

<https://www.cbrc.kaust.edu.sa/covmt/index.php?p=vis-freqchart>

SARS-CoV-2 Structural proteins Mutations

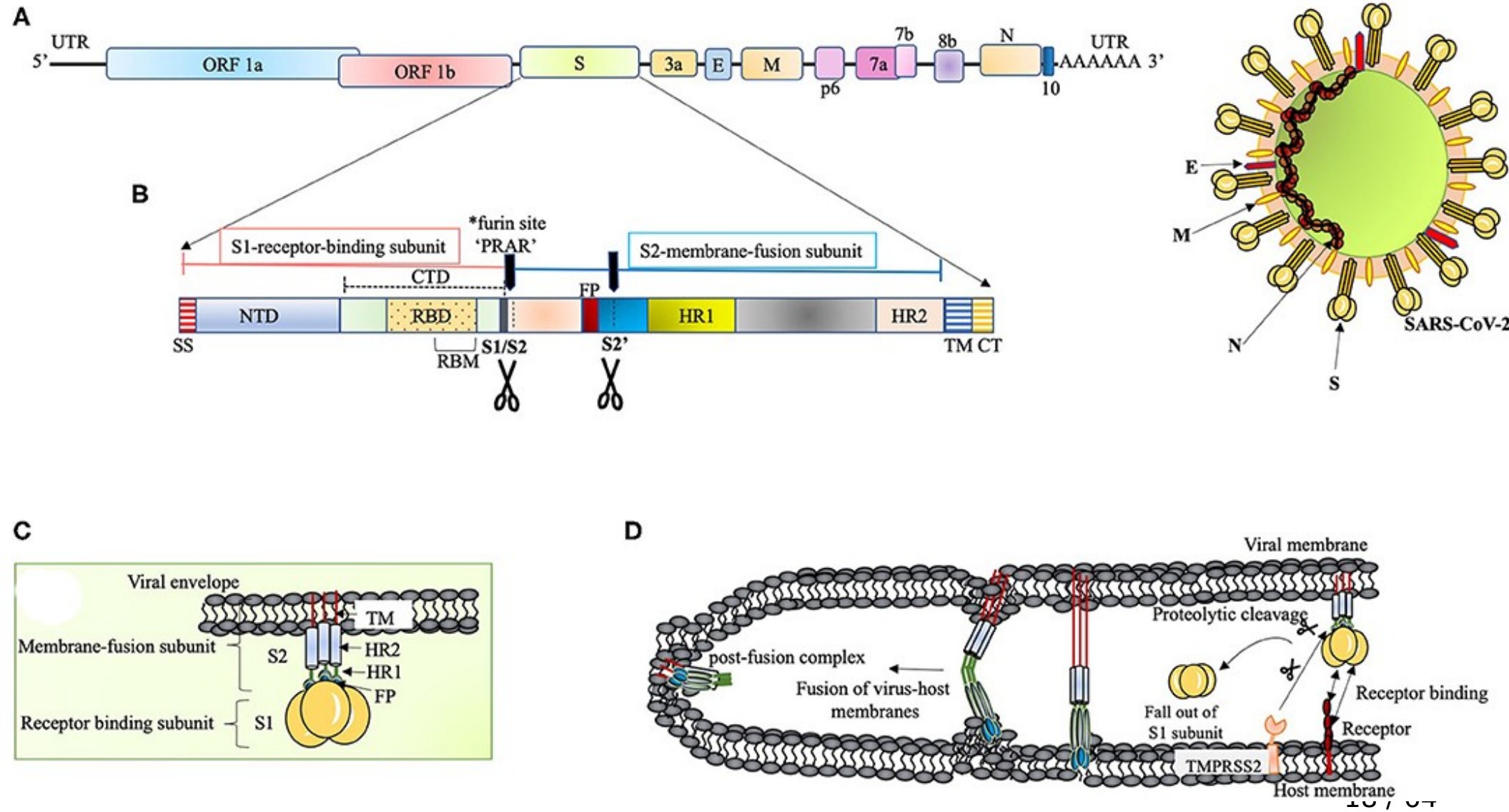




- **Spike (S) protein importance**

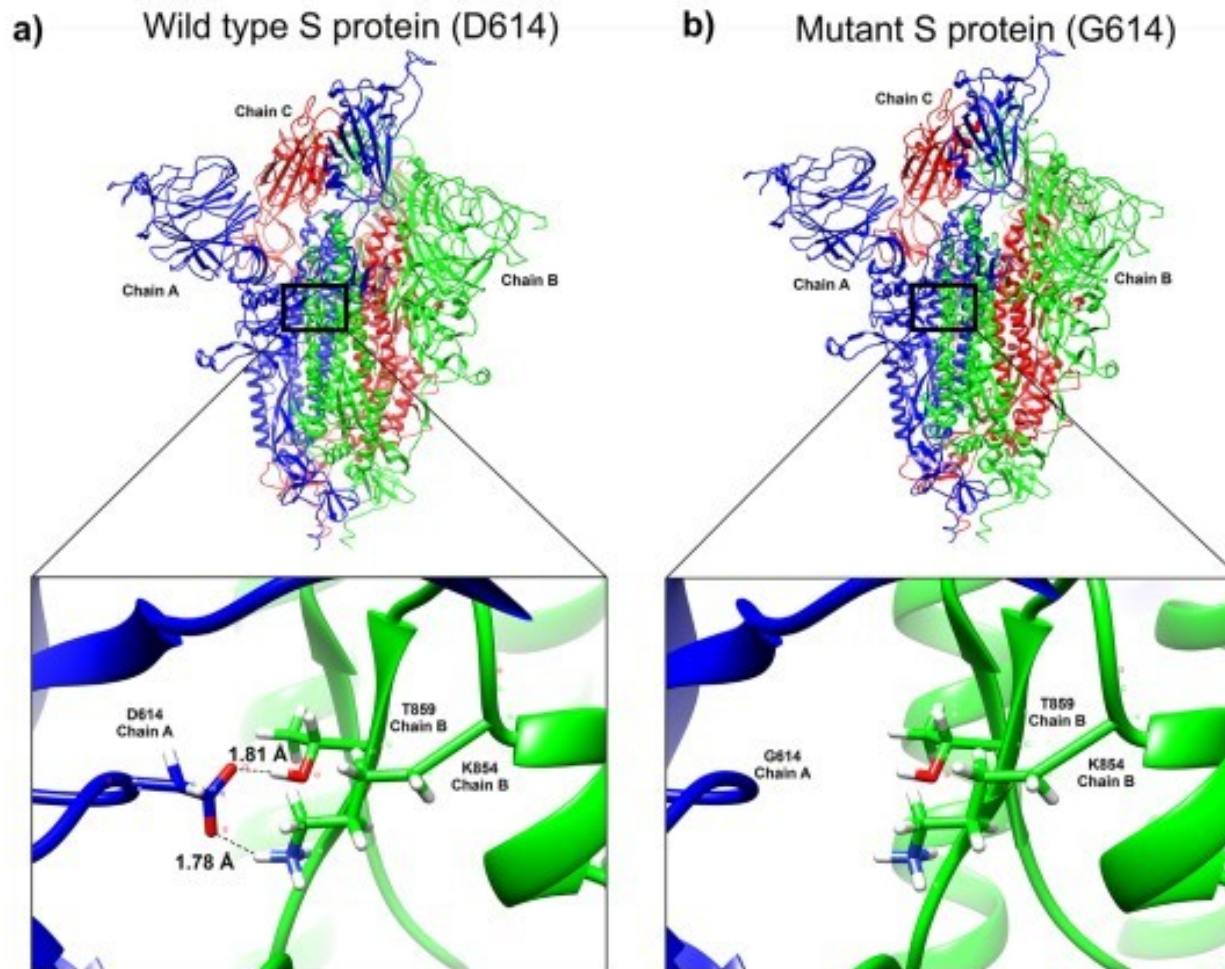
- It is a target for the development of antibodies, entry inhibitors, and vaccines because it plays the most important roles in viral attachment, fusion, and entry.
- Receptor-binding domain (RBD) in SARS-CoV-2 S protein bound strongly to human and bat angiotensin-converting enzyme 2 (ACE2) receptors.

S Protein



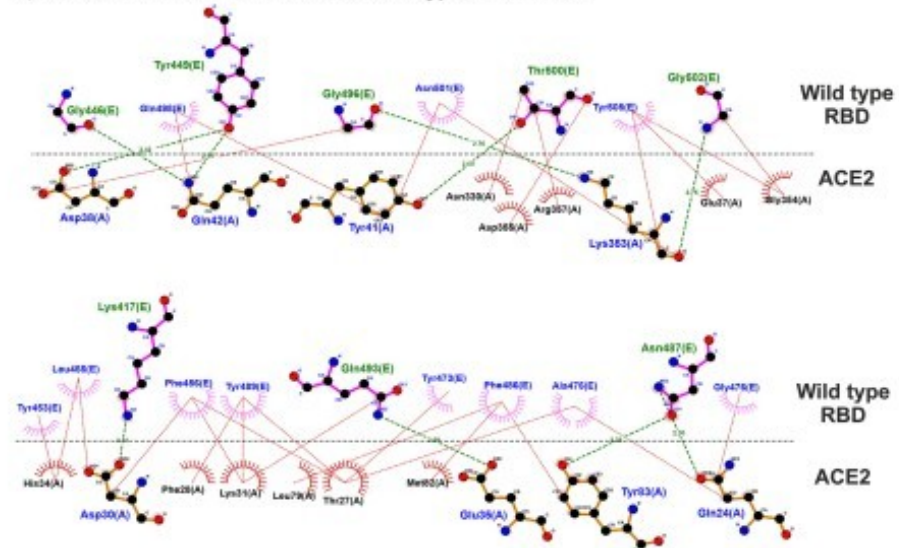
S Protein Mutation

QVRS0009.1 ISOLATE

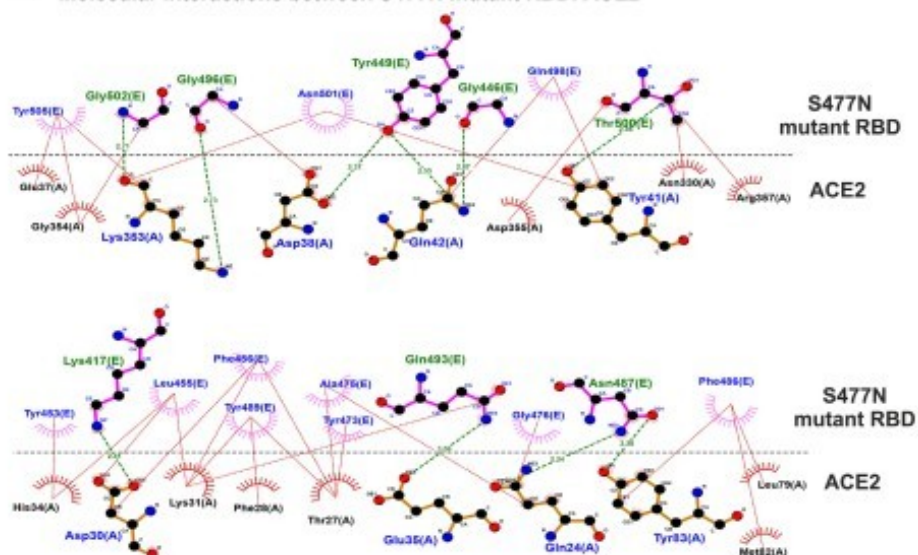


RBD Mutation

a) Molecular interactions between Wild type RBD: ACE2



b) Molecular interactions between S477N mutant RBD: ACE2





BRIEF REPORT

REVISED Interactive SARS-CoV-2 mutation timemaps [version 2;
peer review: 3 approved]

René L. Warren, Inanc Birol

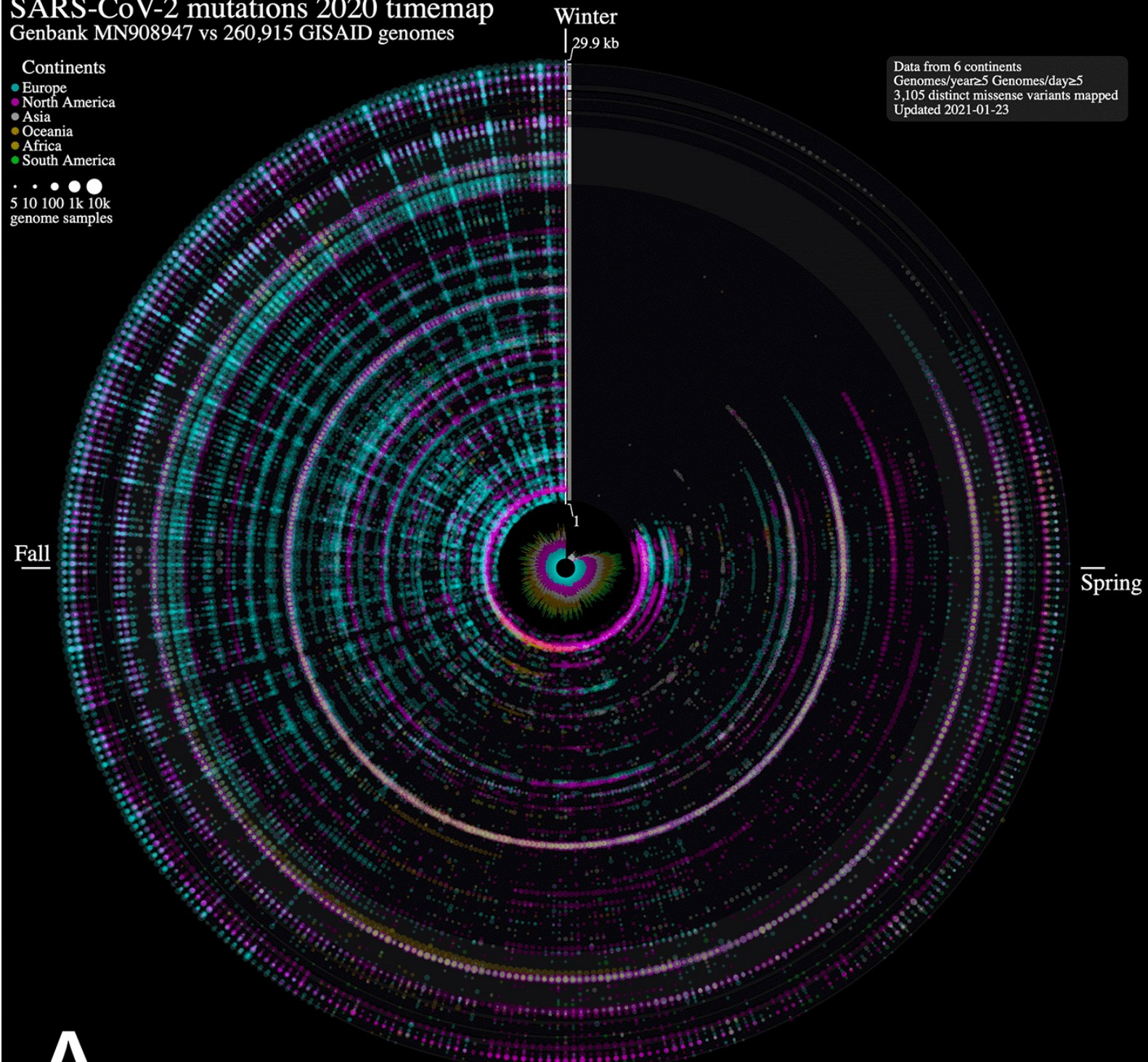
Genome Sciences Centre, BC Cancer Agency, Vancouver, British Columbia, V5Z 4S6, Canada

SARS-CoV-2 mutations 2020 timemap

Genbank MN908947 vs 260,915 GISAID genomes

- Continents
- Europe
 - North America
 - Asia
 - Oceania
 - Africa
 - South America
- • • • •
5 10 100 1k 10k
genome samples

Data from 6 continents
Genomes/year \geq 5 Genomes/day \geq 5
3,105 distinct missense variants mapped
Updated 2021-01-23



SARS-CoV-2 mutations 2020 timemap

Genbank MN908947 vs 165,514 GISAID genomes

- Top countries
- | | |
|---------------|--------------------|
| ● England | ● Germany |
| ● Denmark | ● Italy |
| ● Wales | ● Iceland |
| ● Scotland | ● Norway |
| ● Netherlands | ● Sweden |
| ● Switzerland | ● Portugal |
| ● France | ● Northern Ireland |
| ● Luxembourg | ● Finland |
| ● Spain | ● Ireland |
| ● Belgium | ● Russia |

● 1
● 10
● 100% daily sample fraction

Winter

25.5 kb

Data from 49 countries in Europe
Genomes/year ≥ 10 Genomes/day ≥ 2
690 distinct missense variants mapped
Updated 2021-01-23

Fall

Spring

21.5 kb

B

Summer



SARS-CoV-2 mutations nomenclature systems



Numerous nomenclature systems!!

GISAID, NEXTstrain, and Pango are well-established systems for naming and tracking virus variants to provide **scientists with a common language**.

WHO VEWG and other scientists developed simple-to-pronounce and non stigmatizing labels for SARS-CoV-2 variants to aid in **public discussions** of variants.

<https://www.who.int/>

Tracking of Variants

VOC Delta G/478K.V1 (B.1.617.2+AY.1+AY.2) first det...

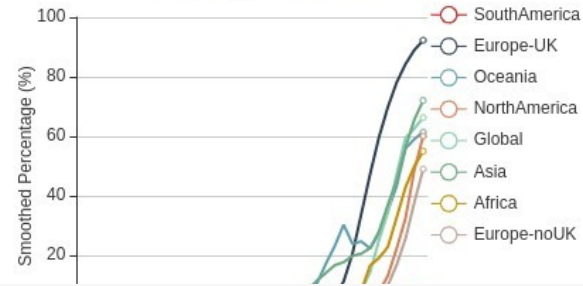
Map of tracked variant occurrence

Circle size proportional to number of variant genomes, zoom into region for more detail. Color by recency with red being most recent.



Relative Variant Genome Frequency per Region (exponentially smoothed alpha=0.3)

Click Legend to show/hide series



Tracking of Variants

VOC Delta G/478K.V1 (B.1.617.2+AY.1+AY.2) first det...

Supporting biases and do not represent exact prevalence. The frequency plot uses exponential smoothing.

Date Range



Color By

Pangolin lineage

Tree Options

Layout

RECTANGULAR

RADIAL

CLOCK

Branch Length

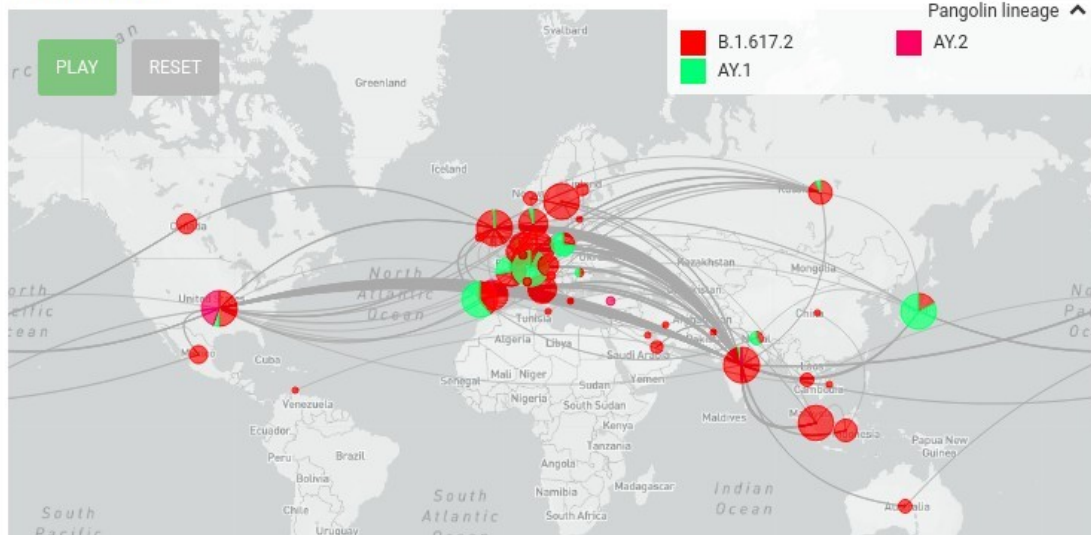
TIME DIVERGENCE

Show confidence intervals

G/478K.V1 (B.1.617.2) first detected in India

3,976 of 3,976 genomes collected between February 2021 and June 2021, last updated 2021-07-05

Transmissions



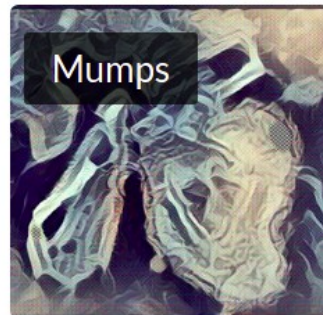
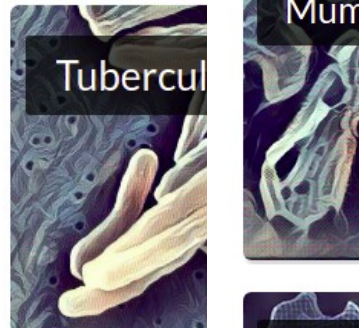
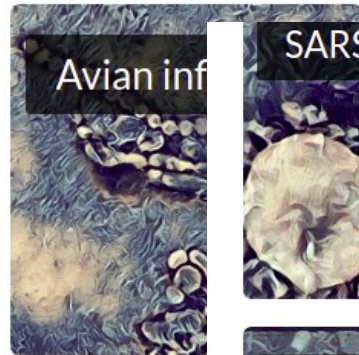
GISAID clade nomenclature

- S: C8782T,T28144C includes NS8-L84S
- L: C241,C3037,A23403,C8782,G11083,G26144,T28144 (early clade markers in WIV04-reference sequence)
- V: G11083T,G26144T NSP6-L37F + NS3-G251V
- G: C241T,C3037T,A23403G includes S-D614G
- GH: C241T,C3037T,A23403G,G25563T includes S-D614G + NS3-Q57H
- GR: C241T,C3037T,A23403G,G28882A includes S-D614G + N-G204R
- GV: C241T,C3037T,A23403G,C22227T includes S-D614G + S-A222V
- GRY: C241T,C3037T,21765-21770del,21991-21993del,A23063T,A23403G,G28882A includes S-H69del, S-V70del, S-Y144del, S-N501Y + S-D614G + N-G204R

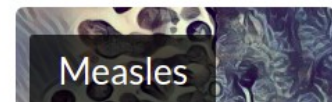
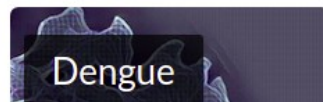
Nextstrain

Real-time tracking of pathogen evolution

Nextstrain is an open-source project to harness the scientific and public health potential of pathogen genome data. We provide a continually-updated view of publicly available data alongside powerful analytic and visualization tools for use by the community. Our goal is to aid epidemiological understanding and improve outbreak response. If you have any questions, or simply want to say hi, please give us a shout at hello@nextstrain.org.

[READ MORE](#)

tu/avian



Nextstrain SARS-CoV-2 clade naming strategy

Major (year-letter) clades are named when any of the following criteria are hit:

- A clade reaches >20% global frequency for 2 or more months
- A clade reaches >30% regional frequency for 2 or more months

Nextstrain SARS-CoV-2 clade naming strategy

At this moment, major clades from 2020 onwards are:

20A: basal pandemic lineage bearing S 614G that's globally distributed

20B: derived from 20A bearing N 203K, N204R and ORF14 50N, also globally distributed

20C: derived from 20A bearing ORF3a 57H and ORF1a 265I, also globally distributed

20D: derived from 20B bearing ORF1a 1246I and ORF1a 3278S, concentrated in South America, southern Europe and South Africa

20E: derived from 20A bearing N 220V, ORF10 30L, ORF14 67F and S 222V, concentrated in Europe

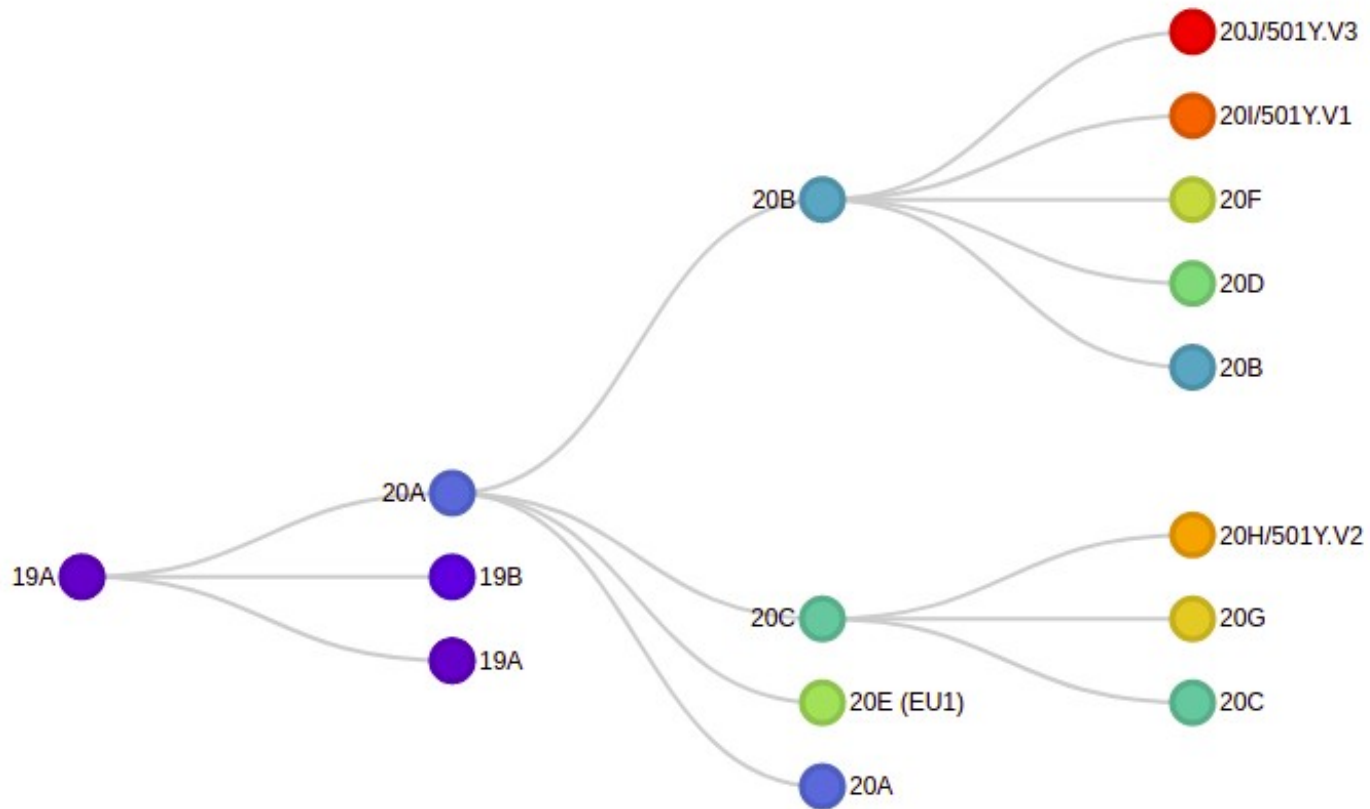
20F: derived from 20B bearing ORF1a 300F and S 477N, concentrated in Australia

20G: derived from 20C bearing ORF1b 1653D, ORF3a 172V, N 67S and N 199L, concentrated in the United States

20H/501Y.V2: derived from 20C bearing S 80A, S 215G, S 484K, S 501Y, S 701V, concentrated in South Africa

20I/501Y.V1: derived from 20B bearing S 501Y, S 570D, S 681H, ORF8 27*, concentrated in the United Kingdom

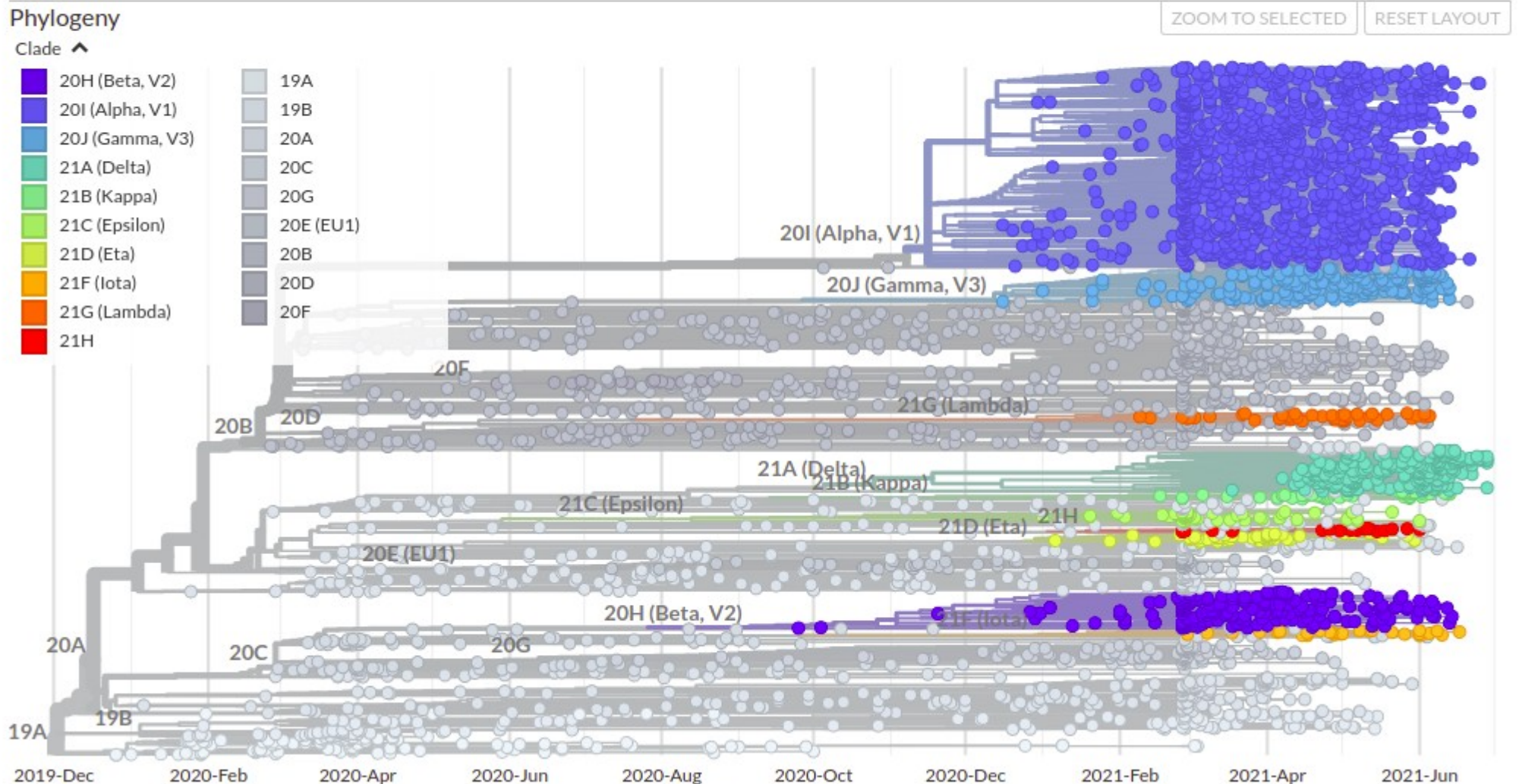
Cont,



Genomic epidemiology of Novel Coronaviruses_global

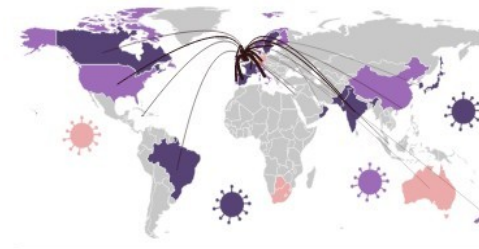
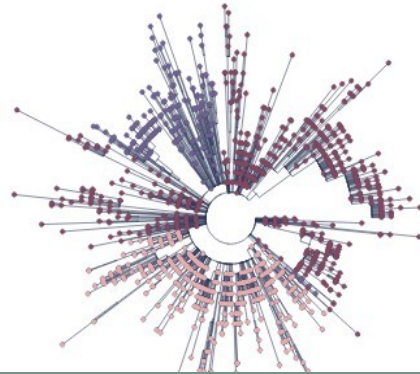
Built with [nextstrain/ncov](#). Maintained by the [Nextstrain team](#). Enabled by data from [GISAID](#).

Showing 3905 of 3905 genomes sampled between Dec 2019 and Jun 2021.





PANGO lineages



Rules for the Designation and Naming of Pango Lineages

In the vast majority of instances it is expected that Pango lineage names and designations will conform to the following rules. These rules also act as guidelines for the decisions made by the Lineage Designation Committee.

SECTION I. Criteria for designation of a new Pango lineage

1. A set of SARS-CoV-2 genome sequences may be considered for the designation of a new lineage name if it exhibits the following essential characteristics:

1a. At the time of designation, the set of sequences is expected to share a single common ancestor and represent a monophyletic or paraphyletic clade in the SARS-CoV-2 phylogeny (see I.1e).

1b. The clade should be distinguished by at least one unambiguous evolutionary event (single nucleotide change, insertion/deletion, or recombination event).

Pango lineages

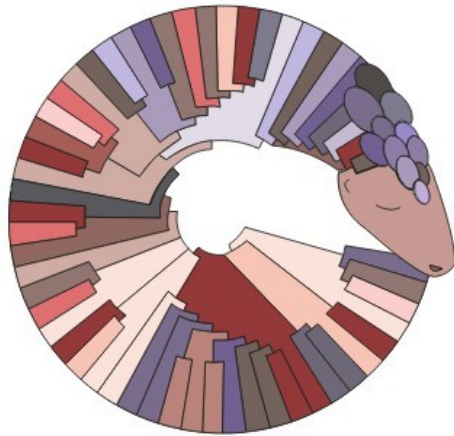
Lineage	Most common countries	Earliest date	Number designated	Number assigned	Description
<u>A</u>	United States of America 27.0%, United_Arab_Emirates 13.0%, China 9.0%, Germany 8.0%, Japan 5.0%	2019-12-30	1699	2124	Root of the pandemic lies within lineage A. Many sequences originating from China and many global exports; including to South East Asia Japan South Korea Australia the USA and Europe represented in this lineage
<u>A.1</u>	United States of America 82.0%, Australia 8.0%, Canada 6.0%, United Kingdom 1.0%, Iceland 1.0%	2020-02-22	2700	2891	USA lineage
<u>A.2</u>	Spain 71.0%, United Kingdom 6.0%, Panama 5.0%, United States of America 4.0%, Portugal 2.0%	2020-02-17	1107	1251	Mostly Spanish lineage now includes South and Central American sequences, other European countries and Kazakhstan.
<u>A.2.1</u>			0	0	Lineage reassigned. Withdrawn: Lineage with sequences predominantly from Panama

Pangolin

pangolin

PHYLOGENETIC ASSIGNMENT OF NAMED GLOBAL OUTBREAK LINEAGES

pangolin was developed to implement the dynamic nomenclature of SARS-CoV-2 lineages, known as the Pango nomenclature. It allows a user to assign a SARS-CoV-2 genome sequence the most likely lineage (Pango lineage) to SARS-CoV-2 query sequences.



Command-line tool

GNU General Public License v3.0



Web application

Developed by the [Centre for Genomic Pathogen Surveillance](#)



SARS-CoV-2 Variants definition by WHO

SARS-CoV-2 variant of concern (VOC)

SARS-CoV-2 variant of interest (VOI)



Variant of Interest

- Specific genetic markers that are predicted to affect transmission, diagnostics, therapeutics, or immune escape.
- Evidence that it is the cause of an increased proportion of cases or unique outbreak clusters.

SARS-CoV-2 variant of interest (VOI)

A SARS-CoV-2 isolate is a Variant of Interest (VOI) if, compared to a reference isolate, its genome has mutations with established or suspected phenotypic implications, and either:

- has been identified to cause community transmission/multiple COVID-19 cases/clusters, or has been detected in multiple countries; OR
- is otherwise assessed to be a VOI by WHO in consultation with the WHO SARS-CoV-2 Virus Evolution Working Group.

WHO label	Pango lineage	GISAID clade/lineage	Nextstrain clade	Earliest documented samples	Date of designation
Epsilon	B.1.427/B.1.429	GH/452R.V1	21C	United States of America, Mar-2020	5-Mar-2021
Zeta	P.2	GR/484K.V2	20B/S.484K	Brazil, Apr-2020	17-Mar-2021
Eta	B.1.525	G/484K.V3	21D	Multiple countries, Dec-2020	17-Mar-2021
Theta	P.3	GR/1092K.V1	21E	Philippines, Jan-2021	24-Mar-2021
Iota	B.1.526	GH/253G.V1	21F	United States of America, Nov-2020	24-Mar-2021
Kappa	B.1.617.1	G/452R.V3	21B	India, Oct-2020	4-Apr-2021
Lambda	C.37	GR/452Q.V1	20D	Peru, Dec-2020	14-Jun-2021

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

Variant of Concern

- Evidence of impact on diagnostics, treatments, or vaccines
- Widespread interference with diagnostic test targets
- Evidence of substantially decreased susceptibility to one or more class of therapies
- Evidence of significant decreased neutralization by antibodies generated during previous infection or vaccination
- Evidence of reduced vaccine-induced protection from severe disease
- Evidence of increased transmissibility
- Evidence of increased disease severity

SARS-CoV-2 variant of concern (VOC)

A SARS-CoV-2 variant that meets the definition of a VOI (see below) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:

- Increase in transmissibility or detrimental change in COVID-19 epidemiology; or
- Increase in virulence or change in clinical disease presentation; or
- Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics.

WHO label	Pango lineage	GISAID clade/lineage	Nextstrain clade	Additional amino acid changes monitored*	Earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY (formerly GR/501Y.V1)	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351 B.1.351.2 B.1.351.3	GH/501Y.V2	20H (V2)	-	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2	G/478K.V1	21A	-	India, Oct-2020	VOI: 4-Apr-2021 VOC: 11-May-2021

Overview of variants names

Nextstrain Clade	Pango Lineage	WHO Label ↗	Other Names	Old CoVariants Names
20I (Alpha, V1)	B.1.1.7 ↗	α Alpha	VOC 202012/01	20I/501Y.V1
20H (Beta, V2)	B.1.351 ↗	β Beta	501Y.V2	20H/501Y.V2
20J (Gamma, V3)	P.1 ↗	γ Gamma		20J/501Y.V3
21A (Delta)	B.1.617.2 ↗	δ Delta		21A/S:478K
21B (Kappa)	B.1.617.1 ↗	κ Kappa		21A/S:154K
21C (Epsilon)	B.1.427 , B.1.429	ε Epsilon	CAL.20C	20C/S:452R
21D (Eta)	B.1.525 ↗	η Eta		20A/S:484K
20E (EU1)	B.1.177		EU1	20A.EU1
21F (Iota)	B.1.526	ι Iota	(Part of Pango lineage)	20C/S:484K
20A .EU2	B.1.160			
20A/ S: 439 K	B.1.258			
20A/ S: 98 F	B.1.221			
20C/ S: 80 Y	B.1.367			
20B/ S: 626 S	B.1.1.277			
20B/ S: 1122 L	B.1.1.302			

<https://covariants.org/>

20I (Alpha, V1)


B.1.1.7 ([Pango lineage](#) )^a

Spike Protein Substitutions: 69del, 70del, 144del, (E484K*), (S494P*), N501Y, A570D, D614G, P681H, T716I, S982A, D1118H (K1191N*)

Name ([Nextstrain](#) )^b: 20I/501Y.V1

WHO Label: Alpha

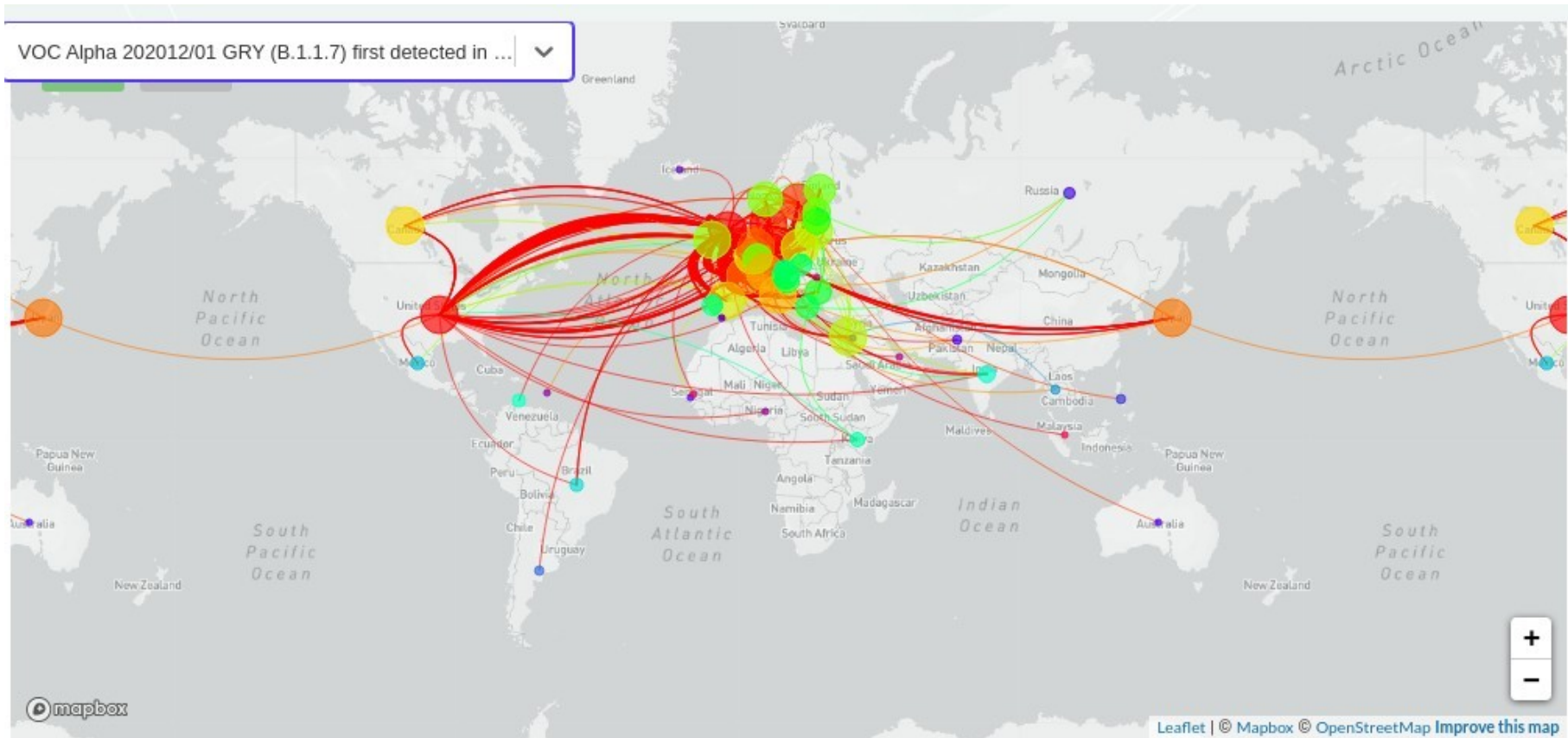
First Identified: United Kingdom

BEI Reference Isolate^c: [NR-54000](#) 

Attributes:

- ~50% increased transmission ⁵
- Potential increased severity based on hospitalizations and case fatality rates ⁶
- No impact on susceptibility to EUA monoclonal antibody treatments ^{7,14}
- Minimal impact on neutralization by convalescent and post-vaccination sera ^{8,9,10,11,12,13,19}

Alpha variant distribution

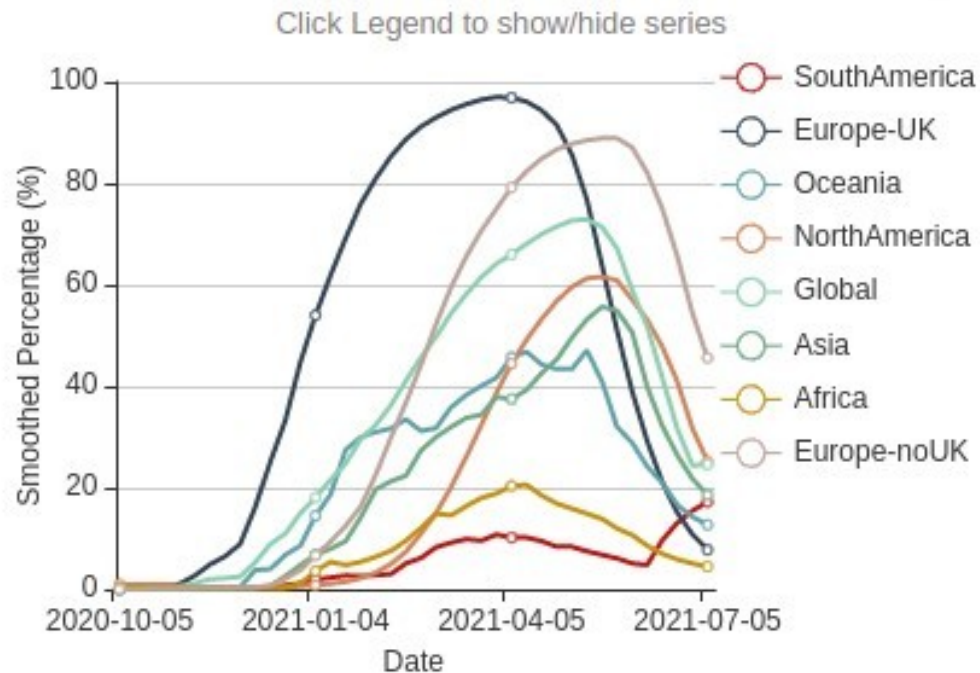


Country Submission Count

Country	Total #Alpha 202012/01 GRY (B.1.1.7)	#Alpha 202012/01 GRY (B.1.1.7) in past 4 weeks	%Alpha 202012/01 GRY (B.1.1.7) in past 4 weeks
United Kingdom	265,686	1,081	2.3
USA	193,624	2,057	36.5
Germany	101,250	1,639	61.1
Denmark	59,652	1,233	64.5
Sweden	53,906	972	59.3
France	31,475	261	39.4
Netherlands	27,111	834	75.7
Italy	22,657	651	46.2
Japan	21,839	68	46.6
Switzerland	21,501	398	67.0

Alpha variant frequency per region

Relative Variant Genome Frequency per Region (exponentially smoothed alpha=0.3)



20H (Beta, V2)

B.1.351 ([Pango lineage](#) )^a

Spike Protein Substitutions: D80A, D215G, 241del, 242del, 243del, K417N, E484K, N501Y, D614G, A701V

Name ([Nextstrain](#) )^b: 20H/501.V2

WHO Label: Beta

First Identified: South Africa

BEI Reference Isolate^c: [NR-55282](#) 

Attributes:

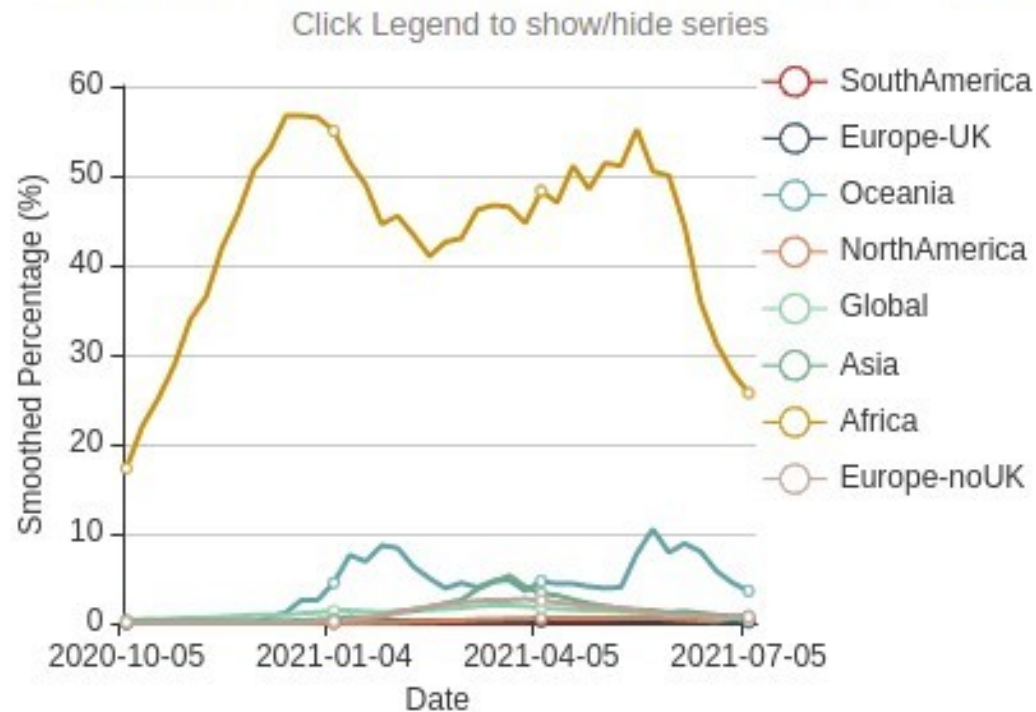
- ~50% increased transmission ¹⁶
- Significantly reduced susceptibility to the combination of bamlanivimab and etesevimab monoclonal antibody treatment,⁷ but other EUA monoclonal antibody treatments are available ¹⁴
- Reduced neutralization by convalescent and post-vaccination sera ^{8,12,18,19,20}

Country Submission Count


Country	Total #Beta GH/501Y.V2 (B.1.351)	#Beta GH/501Y.V2 (B.1.351) in past 4 weeks	%Beta GH/501Y.V2 (B.1.351) in past 4 weeks
South Africa	6,095	69	18.9
USA	2,283	8	0.1
Sweden	2,280	8	0.5
Germany	2,186	13	0.5
France	2,053	36	5.4
Finland	1,096	0	0.0
Belgium	1,033	6	0.6
Canada	822	0	0.0
United Kingdom	809	10	0.0
Luxembourg	745	0	0.0

Beta variant frequency per region

Relative Variant Genome Frequency per Region (exponentially smoothed alpha=0.3)



20J (Gamma, V3)

B.1.617.2 ([Pango lineage](#) )^a

Spike Protein Substitutions: T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, D950N

Name ([Nextstrain](#) )^b: 20A/S:478K

WHO Label: Delta

First Identified: India

Attributes:

- Increased transmissibility ²⁹
- Potential reduction in neutralization by some EUA monoclonal antibody treatments ^{7, 14}
- Potential reduction in neutralization by post-vaccination sera ²¹

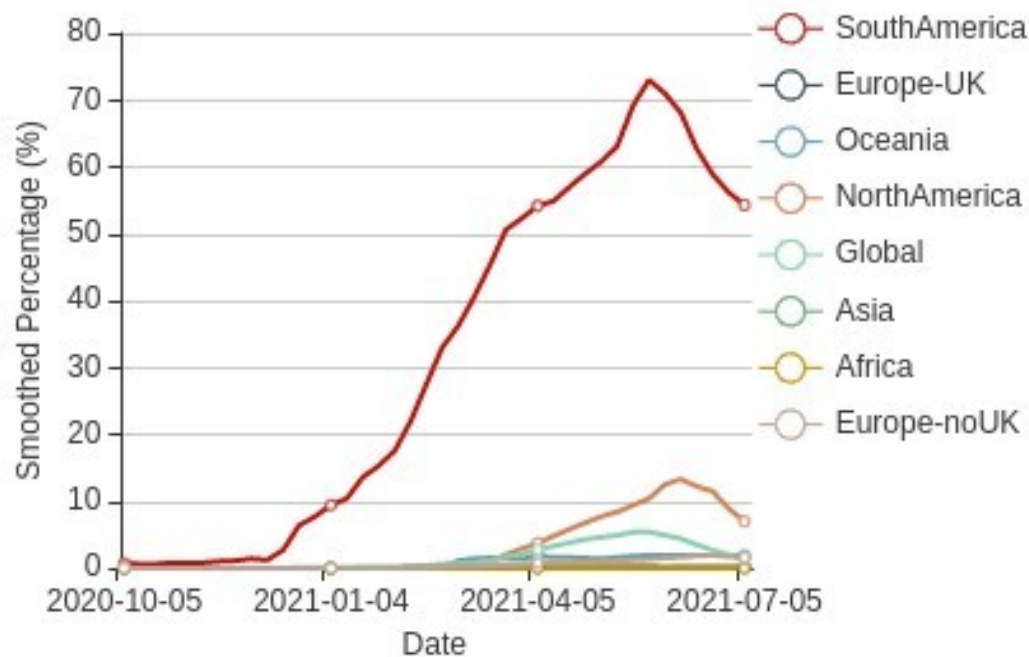
Country Submission Count

Country	Total #Gamma GR/501Y.V3 (P.1)	#Gamma GR/501Y.V3 (P.1) in past 4 weeks	%Gamma GR/501Y.V3 (P.1) in past 4 weeks
USA	18,373	576	10.2
Brazil	12,511	10	76.9
Canada	7,459	0	0.0
Belgium	1,607	59	6.0
Mexico	1,285	101	16.3
Chile	1,185	63	75.0
Spain	826	79	6.2
Italy	554	60	4.3
Netherlands	518	16	1.5
Colombia	322	5	25.0

Gamma variant frequency per region

Relative Variant Genome Frequency per Region (exponentially smoothed alpha=0.3)

Click Legend to show/hide series



21A (Delta)


P.1 ([Pango lineage](#) )^a

Spike Protein Substitutions: L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I

Name ([Nextstrain](#) )^b: 20J/501Y.V3

WHO Label: Gamma

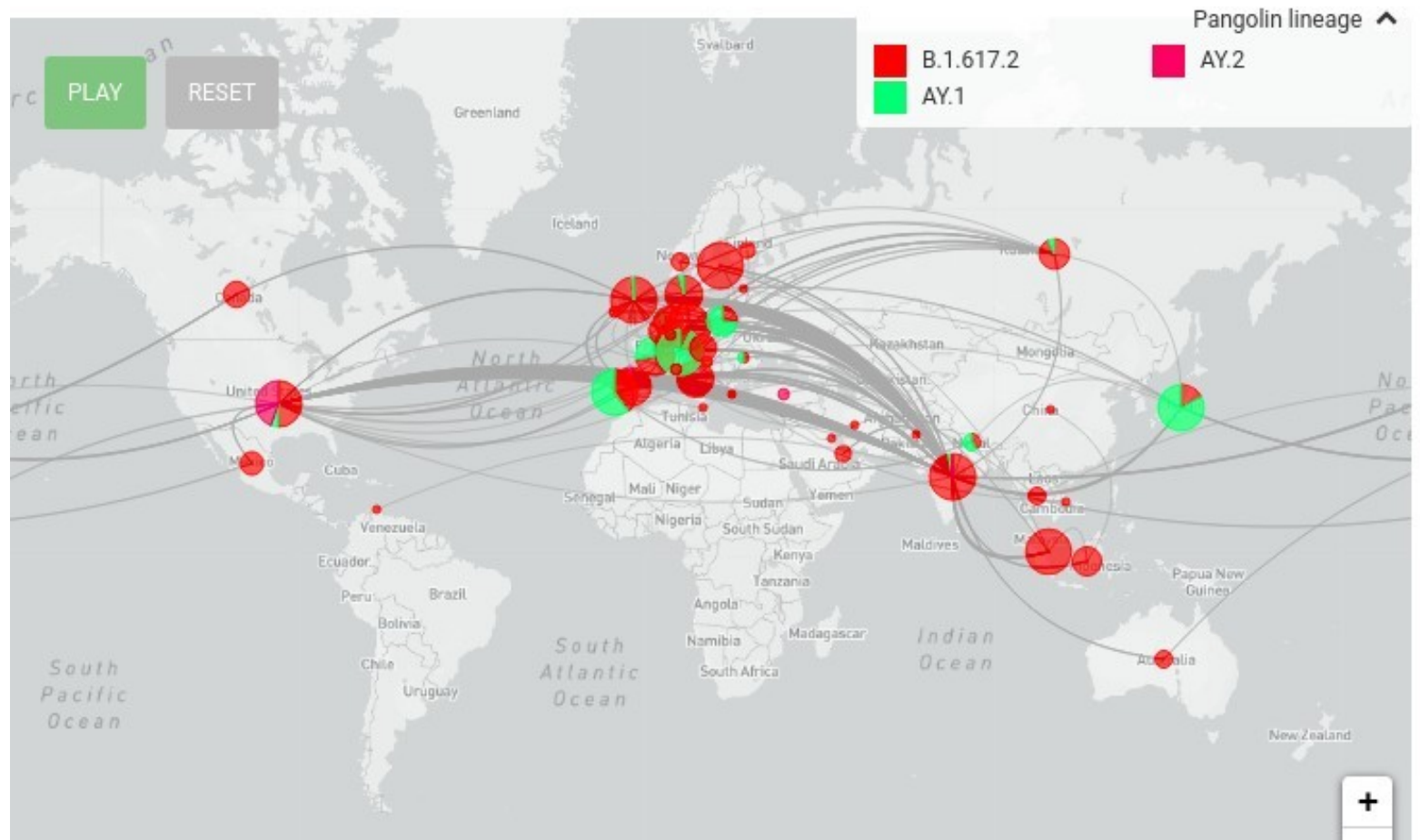
First Identified: Japan/Brazil

BEI Reference Isolate^c: [NR-54982](#) 

Attributes:

- Significantly reduced susceptibility to the combination of bamlanivimab and etesevimab monoclonal antibody treatment,⁷ but other EUA monoclonal antibody treatments are available¹⁴
- Reduced neutralization by convalescent and post-vaccination sera¹⁵

Delta variant distribution



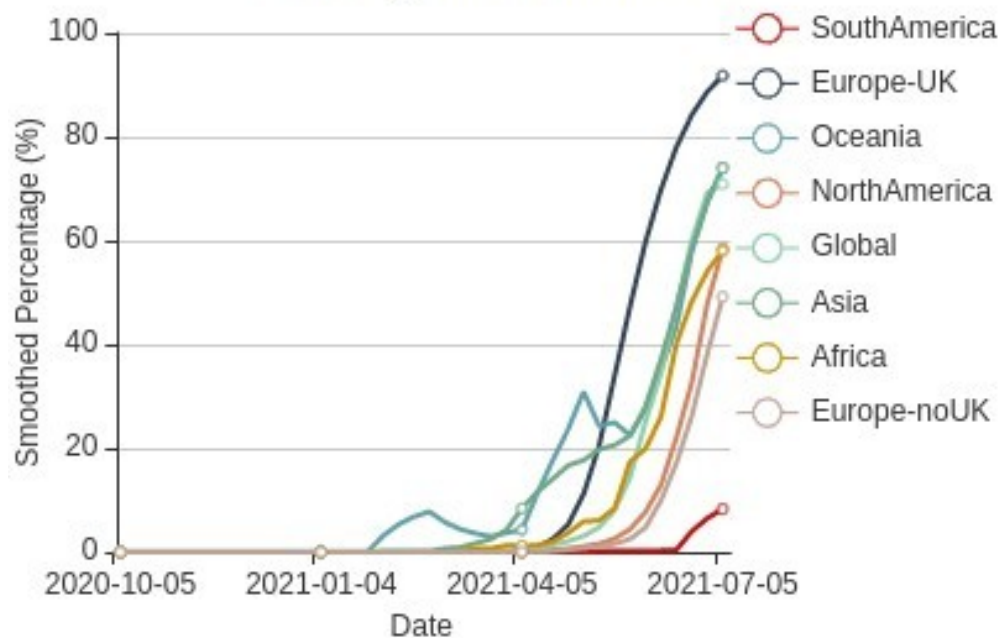
Country Submission Count

Country	Total #Delta G/478K.V1 (B.1.617.2+AY.1+AY.2)	#Delta G/478K.V1 (B.1.617.2+AY.1+AY.2) in past 4 weeks
United Kingdom	101,041	46,627
India	9,192	213
USA	6,872	2,411
Germany	2,077	808
Canada	1,710	0
Portugal	1,505	981
Sweden	1,105	644
Spain	1,095	555
Singapore	1,012	246
Denmark	859	658

Delta variant frequency per region

Relative Variant Genome Frequency per Region (exponentially smoothed alpha=0.3)

Click Legend to show/hide series



Global Variants Report



COVID Data Tracker

United States
At a Glance

Cases Total **33,545,316**
Last 30 Days

Deaths Total **603,181**
Last 30 Days

67.1% of Adults with At Least
One Vaccination

Community
Transmission **Moderate**

Data Tracker Home

COVID Data Tracker Weekly
Review

Your Community

Health Equity Data

Global Variants Report

Countries that have reported variants of SARS-CoV-2.

A new SARS-CoV-2 variant has one or more mutations that differentiate it from predominant virus variants already circulating among the general population. Variants are expected to occur as viruses are constantly changing. Surveillance can help investigate how some variants may impact COVID-19 disease transmission or severity and the effectiveness of vaccines and therapeutics.

CDC works with partners around the world to respond to the pandemic. As part of these efforts, CDC is working to expand the capacity to detect and respond to newly identified variants of the virus that causes COVID-19.

To assist with public discussions of variants, the [World Health Organization \(WHO\)](#) recently proposed

Impact of SARS-CoV-2 new variants on vaccines!

- COVID-19 vaccines elicit a **broad immune response** involving a variety of antibodies and cells, and are thus expected to provide some protection against new virus variants.
- Mutations in the virus should not make vaccines **completely** ineffective.
- This is an area where the evidence remains preliminary and is developing quickly by WHO.
- Manufacturers may need to adapt to the COVID-19 virus's evolution: vaccines may need to incorporate **more than one variants** when developing, booster shots may be required, and other vaccine changes may be required.

How can the impact of virus variants on the efficacy of COVID-19 vaccines be monitored and understood?

- Sequencing of the virus and shared these sequences on public databases, including **GISAID**, allowing scientists to better track how the virus evolves.
- WHO recommends that all countries increase virus sequencing where possible and share data to help each other monitor and respond to the evolving pandemic.
- A SARS-CoV-2 Risk Monitoring and Evaluation Framework has also been established by WHO to identify, monitor, and assess **variants of concern**.

Prevent future new variants of SARS-CoV-2

Stopping the spread at the source is still critical

- Reduce transmission by washing hands frequently, wearing a mask, keeping a safe distance, using good ventilation, and avoiding crowded or enclosed areas.

continue to work against new variants by reducing the amount of viral transmission and therefore also reducing opportunities for the virus to mutate

Vaccination and emergence of new variants

- Vaccines are **an important tool** in the fight against COVID-19, and there are clear public health and lifesaving benefits to using what we already have.
- We must not postpone vaccination due to concerns about new variants, and we must proceed with vaccination even if the vaccines are slightly **less effective against** some of the virus variants.



Question



Thank you for your consideration